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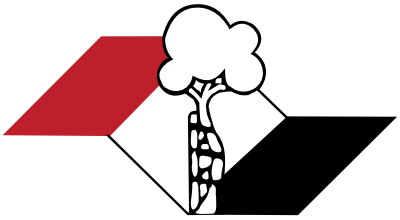

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CHEGOU

FOXIS
CELECOXIBE

Eficácia, segurança e preço acessível
no tratamento anti-inflamatório.[1-4]

- **Melhora significante** dos sinais e sintomas de osteoartrite.[6]
- **Eficaz** no tratamento de dor aguda.*[7]
- Inibidor da COX-2 **mais utilizado no mundo.**[5]

* Devido a entorse de tornozelo em 24 horas após o início do tratamento.

Referências bibliográficas: 1. SIMON, L.S. et al. Anti-inflammatory and upper gastrointestinal effects of celecoxib in rheumatoid arthritis: A randomized controlled trial. JAMA, v. 282, n. 20, 1999. **2.** ESSEX, M.N; BHADRA, P; SANDS, G.H. Efficacy and tolerability of celecoxib versus naproxen in patients with osteoarthritis of the knee: a randomized, double-blind, double-dummy trial. The journal of international medical research, v. 40, p. 1357-1370, 2012. **3.** LÉRIAS, J.R. Celecoxibe e rofecoxibe: eficácia e segurança dos inibidores selectivos da Cox-2 comparativamente aos AINEs não selectivos. Rev Port Clin Geral, v. 20, p. 47-64, 2004. **4.** Kairos Web Brasil. Disponível em: <http://brasil.kairosweb.com>. Acesso em: Abr/2017. **5.** SOLOMON, S.D. et al. Cardiovascular risk of celecoxib in 6 randomized placebo-controlled trials: The cross trial safety analysis. Circulation, v. 117, p. 2104-2113, 2008.2008. **6.** BENSEN, W.G. et al. Treatment of osteoarthritis with celecoxib, a cyclooxygenase-2 inhibitor: A randomized controlled trial. Mayo ClinProc, v. 74, p. 1095-1105, 1999. **7.** CARDENAS-ESTRADA, E. et al. Efficacy and Safety of Celecoxib in the Treatment of Acute Pain due to Ankle Sprain in a Latin American and Middle Eastern Population. The Journal of International MedicalResearch, v. 37, p. 1937-1951, 2009. **8.** Internal report. **9.** Bula do produto FOXIS: cápsulas. Farmacêutica Responsável: Gabriela Mallmann. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A.

FOXIS - celecoxibe. Cápsulas. 200 mg. USO ORAL. USO ADULTO. Indicações: Tratamento dos sinais e sintomas da osteoartrite e da artrite reumatoide; alívio dos sinais e sintomas da espondilite anquilosante; alívio da dor aguda (principalmente no pós-operatório de cirurgia ortopédica ou dental e em afecções musculoesqueléticas), alívio dos sintomas da dismenorreia primária e da lombalgia. **Contraindicações: Não deve ser usado por pacientes: que tenham tido crise de asma, urticária ou reações alérgicas após uso de ácido acetilsalicílico ou outros anti-inflamatórios; com doença hepática e/ou com insuficiência renal grave; que tenham dor relacionada à cirurgia de revascularização do miocárdio; com hipersensibilidade ao celecoxibe ou a qualquer componente da fórmula. Cuidados e advertências:** O uso de AINEs pode retardar ou inibir a ovulação, o que pode estar associado com a infertilidade reversível em algumas mulheres. Não deve ser usado por grávidas sem orientação e seguimento médico; especialmente durante o primeiro e segundo trimestres. O uso de celecoxibe durante a gravidez requer que se pesem os potenciais benefícios para a mãe e riscos para a criança. **Celecoxibe é um medicamento classificado na categoria C de risco de gravidez.** Embora reduza o risco de desenvolvimento de complicações gastrintestinais associadas ao uso de anti-inflamatórios, esse risco não está eliminado pelo uso de celecoxibe, sendo maior em maiores de 65 anos, consumo de bebidas alcoólicas ou com história anterior de perfuração, úlcera ou sangramento gastrintestinal. Celecoxibe deve ser usado com cautela em pacientes com: hipertensão, pois pode piorá-la; portadores de insuficiência renal, alterações da função hepática em idosos; portadores das alterações das enzimas metabolizadoras CYP2C9. Celecoxibe deve ser descontinuado ao aparecimento de rash cutâneo, lesões nas mucosas ou outros sinais de alergias.**Interação medicamentosa: anticoagulantes; anti-hipertensivos das classes dos inibidores da enzima conversora de angiotensina (ECA) e/ou antagonistas da angiotensina II diuréticos e betabloqueadores podem ter seu efeito reduzido; em pacientes idosos, com desidratação (incluindo aqueles em tratamento com diuréticos) ou com função renal comprometida, a coadministração de antiinflamatórios, incluindo os inibidores específicos da COX-2, com inibidores da ECA, pode resultar no comprometimento da função renal, incluindo possível insuficiência renal aguda; fluconazol pode aumentar os níveis sanguíneos de celecoxibe; lítio pode ter seu nível sanguíneo aumentado; medicamentos anti-inflamatórios podem aumentar o risco de toxicidade no rim associada à ciclosporina; a administração concomitante de dextrometorfano ou metoprolol com celecoxibe 200 mg duas vezes ao dia resultou em aumento de 2,6 vezes e 1,5 vezes das concentrações no sangue de dextrometorfano e metoprolol, respectivamente; lisinopril administrado concomitante com celecoxibe pode não controlar a pressão alta. Foxis 200 mg: Este produto contém o corante amarelo de TARTRAZINA que pode causar reações de natureza alérgica, entre as quais asma brônquica, especialmente em pessoas alérgicas ao ácido acetilsalicílico. Atenção: Este medicamento contém Açúcar, portanto, deve ser usado com cautela em portadores de Diabetes. Reações adversas: Comuns** (ocorre entre 1% e 10% dos pacientes) inflamação dos brônquios e seios da face, infecção do trato respiratório superior, infecção urinária, insônia, tontura, hipertensão e piora da hipertensão, tosse, vômito, dor abdominal, dispepsia, flatulência, prurido, rash, edema periférico. Incomuns (ocorre entre 0,1% e 1% dos pacientes): faringite; rinite, anemia, hipersensibilidade, ansiedade, hipertonia, sonolência, visão borrada, zumbido; palpitação, úlceras no estômago; doenças dentárias; aumento da quantidade de enzimas hepáticas, urticária, equimose, edema facial, doença semelhante à gripe, lesão. Infecção pela bactéria Helicobacter, pelo vírus Herpes zoster, infecções na pele, em feridas e gengiva, labirintite, infecção por bactéria, lipoma, distúrbio do sono, infarto cerebral, hemorragia conjuntival, depósitos no humor vítreo, hipoacusia, angina instável, insuficiência da valva aórtica; aterosclerose da artéria coronária; bradicardia sinusal, hipertrofia ventricular; trombose venosa profunda; hematoma; disfonia, sangramento da hemorroida; evacuações frequentes; ulceração da boca; estomatite; dermatite alérgica; cisto sinovial, noctúria, cisto ovariano, sintomas da menopausa; sensibilidade nas mamas; dismenorreia; aumento da quantidade de potássio e sódio no sangue, redução da testosterona no sangue; redução do hematócrito, aumento nos níveis de hemoglobina, fraturas, epicondilite, ruptura do tendão. Posologia: Celecoxibe deve ser engolido com ou sem alimentos. Para o tratamento de dor aguda e dismenorreia primária: 400 mg na primeira dose, seguidos de uma dose de 200 mg por via oral após 12 horas, seguido de 200 mg a cada 12 horas nos dias seguintes conforme necessário. Uso para o tratamento de dor crônica: menor dose diária eficaz durante o menor período possível. As doses sugeridas de celecoxibe para essas doenças são as seguintes: Osteoartrite e Espondilite anquilosante: 200 mg em dose única ou 100 mg duas vezes; Artrite reumatoide: 100 ou 200 mg duas vezes ao dia; Lombalgia: 200 mg ou 400 mg em dose única ou dividida em duas vezes de 100 mg ou 200 mg. SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO. **VENDA SOB PRESCRIÇÃO MÉDICA. SÓ PODE SER VENDIDO COM RETENÇÃO DA RECEITA. MS - 1.0573.0491. MB 02 VP_SAP 4591400_SAP 4585100. *Material técnico científico de distribuição exclusiva a profissionais de saúde habilitados à prescrição e/ou dispensação de medicamentos.**

CONTRAINDICAÇÕES: Não deve ser usado por pacientes: que tenham tido crise de asma, urticária ou reações alérgicas após uso de ácido acetilsalicílico ou outros anti-inflamatórios; com doença hepática e/ou com insuficiência renal grave; que tenham dor relacionada à cirurgia de revascularização do miocárdio; com hipersensibilidade ao celecoxibe ou a qualquer componente da fórmula. **INTERAÇÕES MEDICAMENTOSAS:** Anticoagulantes; anti-hipertensivos das classes dos inibidores da enzima conversora de angiotensina (ECA) e/ou antagonistas da angiotensina II diuréticos e betabloqueadores podem ter seu efeito reduzido; em pacientes idosos,) ou com função renal comprometida, a coadministração de anti-inflamatórios, incluindo os inibidores específicos da COX-2, com inibidores da ECA, pode resultar no comprometimento da função renal, incluindo possível insuficiência renal aguda; fluconazol pode aumentar os níveis sanguíneos de celecoxibe; medicamentos anti-inflamatórios podem aumentar o risco de toxicidade no rim associada à ciclosporina.

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ACTA ORTOPÉDICA BRASILEIRA

INSTRUCTIONS TO AUTHORS

(Reviewed January 2016)

The journal *Acta Ortopédica Brasileira*, official organ of the Department of Orthopedics and Traumatology, Faculdade de Medicina da Universidade de São Paulo (DOT/FMUSP), is published bimonthly in six issues per year (Jan/Feb, Mar/Apr, May/Jun, Jul/ Aug, Sep/Oct and Nov/Dec) with Portuguese and English printed and online versions. *Acta* is distributed to orthopedists and leading educational and research institutions in Brazil. The publication follows entirely the international standard of the International Committee of Medical Journal Editors (ICMJE) – Vancouver Convention – and its uniform requirements [http://www.icmje.org/]. Submitted papers are sent for double-blind peer review evaluation to decide whether they should be published or not, suggesting improvements, asking the authors for clarification and making recommendations to the Editor-in Chief. The concepts and statements contained in the papers are the sole responsibility of the authors.

We ask authors to observe the following instructions for publication.

ARTICLES FORMAT

NUMBER OF WORDS RECOMMENDED ACCORDING TO THE PUBLICATION TYPE: The criteria specified below should be observed for each type of publication. The electronic counting of words should start at the Introduction and end at the Conclusion.

Recommendations for articles submitted to Acta Ortopédica Brasileira

Type of Article	Abstract	Number of words	References	Figures	Tables	Maximum number of authors allowed
Original	Structured, up to 200 words	2.500 Excluding abstract, references, tables and figures	20	10	6	6
Update / Review*	Non-structured, up to 200 words	4.000 Excluding abstract, references, tables and figures	60	3	2	2
Editorial*	No abstract	500	0	0	0	1

*These contributions shall be published at the Editors' criteria, with due replica, when applicable.

MANUSCRIPT PREPARATION: The journal *Acta Ortopédica Brasileira* receives the following types of contributions: Original Article, Update Article and Review Article. The Update and Review articles are only considered by invitation from the Editorial Board.

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It is recommended that authors do not use abbreviations in the title and limit their use in the abstract and in the text.

The generic names should be used for all drugs. The drugs can be referred to by their trade name, however, the manufacturer's name, city and country or electronic address should be stated in brackets in the Materials and Methods section.

ABBREVIATIONS: The use of abbreviations should be minimized. Abbreviations should be defined at the time of its first appearance in the abstract and also in the text. Non-standard abbreviations shall not be used, unless they appear at least three times in the text.

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ACKNOWLEDGEMENTS: Authors can acknowledge financial support to the work in the form of research grants, scholarships and other, as well as professionals who do not qualify as co-authors of the article, but somehow contributed to its development.

CORRECTION OF GALLEY PROOFS: As soon as they are ready, the galley proofs in electronic form will be sent by e-mail to the corresponding author. Authors should return proofs, also by e-mail, with the necessary corrections within 48 hours maximum after its receipt. This aims to expedite the review process and publication of the article.

ORGANIZING THE ELECTRONIC FILE: All parts of the manuscript should be included in a single file. It should be formed by the cover page, then the text, references, figures (with their captions) and finally, tables and charts (with their respective captions).

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a) The article category (original article, review article or update article);
b) The full title in Portuguese and English with up to 80 characters. The title should be concise, but informative;
c) The full name of each author (no abbreviations) and their affiliation (hierarchical units should be presented in descending order, for example, university, college/institute and department. The names of institutions and programs should be submitted preferably in full and in the original language of the institution or in the English version when writing is not Latin (e.g. Arabic, Mandarin, Greek);
d) The place where the work was performed;
e) Name, address, telephone number and e-mail of the corresponding author.

ABSTRACT: The abstract in Portuguese and in English should be structured in cases of original articles and shall present the study's objectives clearly, methods, results and main conclusions and should not exceed 200 words (do not include any reference citations). Moreover, the abstract should include the level of evidence and the type of study, according to the classification table attached at the end of this text.

KEYWORDS: The article should include at least three and at most six descriptors in Portuguese and in English, based on the Descriptors of Health Sciences (DeCS) http://decs.bvs.br/ or Medical Subject Headings (MeSH) of the National Library of Medicine, available at http://www.nlm.nih.gov/mesh/meshhome.html

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Authors should precisely identify all drugs and chemicals used, including generic names, dosages and administration. Patients' names, initials, or hospital records should not be included. References regarding statistical procedures should be included.

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Link the conclusions with the goals of the study, but avoid statements and conclusions that are not supported by the data, in particular the distinction between clinical and statistical relevance. Avoid making statements on economic benefits and costs, unless the manuscript includes data and appropriate economic analysis. Avoid priority claim ("this is the first study of ...") or refer to work that has not yet been completed.

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ACKNOWLEDGEMENTS

When applicable, briefly acknowledge the people who have contributed intellectually or technically to the study, but whose contribution does not justify co-authorship. The author must ensure that people agree to have their names and institutions disclosed. Financial support for the research and fellowships should be acknowledged in this section (funding agency and project number).

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STATEMENT OF AUTHORS' CONTRIBUTION: The declaration of authors' contribution should be included at the end of the article, using minimum criteria for authorship, including:

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- Writing the article or critically reviewing its intellectual content;
- Approval of the final version of the manuscript to be submitted for publication;
- Agree to be responsible for all aspects of the work, to ensure that any matters regarding the completeness or accuracy of any of its parts are properly investigated and resolved;

All articles should include a description of the authors' contribution, as follows:

"Each individual author contributed individually and significantly to the development of this work. MJ (0000-0000-0000-0000)*: wrote and reviewed the and performed the surgeries; CPV (0000-0002-3904-2836)*: performed the surgeries, analyzed the data analysis and wrote the articles; JVC (0000-0003-3910-714x (0000-0000-0000-0000)*: performed statistical analysis, participated at the surgeries and reviewed the article; OMA (0000-0000-0000-0000)*: analyzed the slides and reviewed the article; MASP (0000-0000-0000-0000)*: drafted and reviewed the article and contributed to the intellectual concept of the study; ACA (0000-0001-6891-5935)*: performed the surgeries, wrote the article, performed statistical analysis and contributed to the intellectual concept of the study and the entire research project. *ORCID (Open Researcher and Contributor ID)."

REFERENCES: Original articles may include up to about 20 references, restricted to the essential bibliography to the article's content. Number the references consecutively in the order in which they are first mentioned in the text, using superscript Arabic numerals in the following format: (e.g., Reduction of terminal plate functions.[1]).

Authors should make sure that all references are cited in the text. Several citations within a single set of parentheses should be separated by commas without space ([1,5,7]). Where there are 3 or more sequential citations, use a numeric range ([4-9]). Include the first six authors followed by et al.

The titles of journals should be abbreviated according to *Index Medicus*.

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Ex.: Campbell CJ. The healing of cartilage defects. Clin Orthop Relat Res. 1969;64:45-63.

b) Book: Author(s) or editor (s). Book title. Edition, if it is not the first. Translator (s), if it applies. Publication place: publisher; year.

Ex.: Diener HC, Wilkinson M, editors. Drug-induced headache. 2nd ed. New York: Spriger-Verlag; 1996.

c) Book chapter: Chapter author (s). Chapter title. Book Editor (s) and supplementary data, likewise the previous item.

Ex.: Chapman MW, Olson SA. Open fractures. In: Rockwood CA, Green DP. Fractures in adults. 4th ed. Philadelphia: Lippincott-Raven; 1996. p.305-52.

d) Abstract: Author(s). Title, followed by [abstract]. Journal. Year; volume (supplement and its number, if it applies): page (s).

Ex.: Enzensberger W, Fisher PA. Metronome in Parkinson's disease [abstract]. Lancet. 1996;34:1337.

e) Personal communications: should only be mentioned in the text, between parentheses.

f) Thesis: Author, title, level (Master, PhD, etc.), city: institution; year.

Ex.: Kaplan SJ. Post-hospital home health care: the elderly's access and utilization [dissertation]. St. Louis: Washington Univ.; 1995.

g) Electronic material: Author (s). Article title. Abbreviated Journal title [medium]. Publication date [access date followed by the expression "accessed on"]; volume (number):initial page-final page or [approximate number of pages]. URL followed by the expression "Available from:"

Ex.: Pavezi N, Flores D, Perez CB. Proposição de um conjunto de metadados para descrição de arquivos fotográficos considerando a Nobrade e a Sepiades. Transinf. [Internet]. 2009 [acesso em 2010 nov 8];21(3):197-205. Available from: http://periodicos.puc-campinas.edu.br/seer/index.php/transinfo/article/view/501

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Levels of Evidence for Primary Research Question[a]

(This chart was adapted from material published by the Centre for Evidence-Based Medicine, Oxford, UK. For more information, please visit www.cebm.net.)

	Types of study			
Level	**Therapeutic Studies Investigating the Results of Treatment**	**Prognostic Studies – Investigating the Effect of a Patient Characteristic on the Outcome of Disease**	**Diagnostic Studies – Investigating a Diagnostic Test**	**Economic and Decision Analyses – Developing an Economic or Decision Model**
I	High quality randomized trial with statistically significant difference or no statistically significant difference but narrow confidence intervals	High quality prospective study[d] (all patients were enrolled at the same point in their disease with ≥80% of enrolled patients)	Testing of previously developed diagnostic criteria on consecutive patients (with universally applied reference ''gold'' standard)	Sensible costs and alternatives; values obtained from many studies; with multiway sensitivity analyses
	Systematic review[b] of Level RCTs (and study results were homogenous[c])	Systematic review[b] of Level I studies	Systematic review[b] of Level I studies	Systematic review[b] of Level I studies
II	Lesser quality RCT (eg, < 80% followup, no blinding, or improper randomization)	Retrospective[f] study	Development of diagnostic criteria on consecutive patients (with universally applied reference ''gold'' standard)	Sensible costs and alternatives; values obtained from limited studies; with multiway sensitivity analyses
	Prospective[d] comparative study[e]	Untreated controls from an RCT	Systematic review[b] of Level II studies	Systematic review[b] of Level II studies
	Systematic review[b] of Level II studies or Level I studies with inconsis tent results	Lesser quality prospective study (eg, patients enrolled at different points in their disease or <80% followup)		
		Systematic review[b] of Level II studies		
III	Case control study[g]	Case control study[g]	Study of non consecutive patients; without consistently applied reference ''gold'' standard	Analyses based on limited alternatives and costs; and poor estimates
	Retrospective[f] comparative study[e]		Systematic review[b] of Level III studies	Systematic review[b] of Level III studies
	Systematic review[b] of Level III studies		Case-control study	
			Poor reference standard	
IV	Case series[h]	Case series		Analyses with no sensitivity analyses
V	Expert opinion	Expert opinion	Expert opinion	Expert opinion

[a] A complete assessment of quality of individual studies requires critical appraisal of all aspects of the study design.

[b] A combination of results from two or more prior studies.

[c] Studies provided consistent results.

[d] Study was started before the first patient enrolled.

[e] Patients treated one way (eg, cemented hip arthroplasty) compared with a group of patients treated in another way (eg, uncemented hip arthroplasty) at the same institution.

[f] The study was started after the first patient enrolled.

[g] Patients identified for the study based on their outcome, called "cases" eg, failed total arthroplasty, are compared with patients who did not have outcome, called ''controls'' eg, successful total hip arthroplasty.

[h] Patients treated one way with no comparison group of patients treated in another way.

SUMMARY

VOLUME 25–Nº 3–2017

Original Articles

Case Report

OSTEOBAN
ibandronato de sódio

Segurança na prevenção e tratamento da Osteoporose.[1,2]

Detalhes
que fazem a diferença
no combate
à Osteoporose[1,5,6,7]

Prevenção:
- **34% de redução de risco** de fraturas não vertebrais.*[3]
- **Redução de risco** de fraturas vertebrais.*[4]

Eficácia:
Melhora da **densidade mineral óssea** em mulheres com osteopenia e osteoporose.[5]

Comodidade:
Posologia cômoda: **1x ao mês.[1]**

* Refere-se ao ibandronato de tratamento diário

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Referências Bibliográficas:1) Bula do produto OSTEOBAN: comprimido revestido. Farmacêutica Responsável: Gabriela Mallmann. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A. 2) BUMBASIREVIC, M. et al. Prospective clinical study of monthly ibandronate in the treatmetn of osteoporosis and prevention of fractures in postmenopausal women: ORPHEUM study. Srp Arh Celok Lek, v. 139, n. 11-12, p. 790-7694, 2011. 3) MILLER, P. D. et al Efficacy of monthly oral ibandronate is sustained over 5 years: the MOBILE long-term extension study. Osteoporos Int, v. 23, n. 6, 2012. 4) HARRIS, S. T. et al. Ibandronate and the risk of nonvertebral and clinical fractures in women with postmenopausal osteoporosis: results of a metaanalysis of phase III studies. Curr Med Res Opin, v. 24, n. 1, p. 237-245, 2008. 5) BOCK, O. et al. Impact of oral ibandronate 150 mg once monthly on bone structure and density in post-menopausal osteoporosis or osteopenia derived from in vivo ?CT. Bone, v. 50, p. 317-324, 2012. 6) Kairos Web Brasil. Disponível em: < http:// brasil.kairosweb.com>. Acesso em: Jul/ 2016. 7) Programa Cuidados pela Vida (O Programa Cuidados pela Vida pode alterar ou interromper esta campanha sem aviso prévio. Desconto calculado sobre o Preço Máximo ao Consumidor).

Interação Medicamentosa: Os pacientes devem esperar 60 minutos após ingerir OSTEOBAN, antes de tomarem outros medicamentos orais. Contraindicação: OSTEOBAN é contraindicado a pacientes que não conseguem ficar em pé ou sentados durante, pelo menos, 60 minutos.

Osteoban. ibandronato de sódio 150mg comprimido revestido. USO ORAL USO ADULTO. Indicações: OSTEOBAN é indicado para o tratamento da osteoporose pós-menopausa, com a finalidade de reduzir o risco de fraturas vertebrais. Em um subgrupo de pacientes de risco, com escore T < -3,0 DP no colo do fêmur, ibandronato de sódio também demonstrou reduzir o risco de fraturas não vertebrais. **Contraindicações**: **OSTEOBAN é contraindicado a pacientes com hipersensibilidade ao ibandronato de sódio ou aos demais componentes da fórmula e a pacientes com hipocalcemia não corrigida; pacientes com anormalidades do esôfago, como demora no esvaziamento esofágico, estenose ou acalasia; pacientes que não conseguem ficar em pé ou sentados durante, pelo menos, 60 minutos. Precauções e advertências: OSTEOBAN é contraindicado a pacientes com hipocalcemia não corrigida. Bisfosfonatos administrados por via oral podem causar irritação local da mucosa gastrintestinal superior. O risco de experiências adversas esofágicas graves parece ser maior para pacientes que não seguem as instruções de uso e/ou que continuaram a tomar bisfosfonatos por via oral após desenvolver sintomas sugestivos de irritação esofágica. Os pacientes devem prestar especial atenção e serem capazes de cumprir as instruções de administração. Considerando-se que anti-inflamatórios não esteróides e bisfosfonatos associam-se, ambos, à irritação gastrintestinal, recomenda-se cautela durante a administração concomitante de anti-inflamatórios não esteroides e ibandronato de sódio. Osteonecrose de mandíbula foi relatada em pacientes tratados com bisfosfonatos. A maioria dos casos em pacientes oncológicos submetidos a procedimentos dentários, mas alguns casos ocorreram em pacientes em tratamento para osteoporose pós-menopausa e outros diagnósticos. Fatores de risco conhecidos para osteonecrose de mandíbula: câncer, terapias concomitantes (ex: quimioterapia, radioterapia e corticosteroides) e distúrbios concomitantes (ex: anemia, coagulopatia, infecção e doença dentária pré-existente). A maioria dos casos foi relatada em pacientes tratados com bisfosfonatos de administração intravenosa, mas também em alguns pacientes tratados com bisfosfonatos orais.Relatos na literatura médica indicam que os bisfosfonatos podem estar associados à inflamação ocular, como uveíte e esclerite. Não foram realizados estudos sobre os efeitos de ibandronato de sódio sobre a capacidade de dirigir veículos e operar máquinas. Gestação e lactação: Categoria de risco na gravidez: B. Este medicamento não deve ser utilizado por mulheres grávidas sem orientação médica ou do cirurgião-dentista.** Não há experiência sobre o uso clínico de ibandronato de sódio em mulheres durante a gestação. OSTEOBAN não deve ser utilizado por mulheres que estejam amamentando sem orientação médica ou do cirurgião dentista. **Atenção diabéticos: contém açúcar (lactose). Interações medicamentosas:** é provável que suplementos à base de cálcio, antiácidos e alguns medicamentos orais que contenham cátions multivalentes (tais como alumínio, magnésio e ferro) interfiram na absorção de ibandronato de sódio. Os pacientes devem esperar 60 min após ingerir OSTEOBAN, antes de tomarem outros medicamentos orais. Foi demonstrada, em estudo de interação farmacocinética em mulheres na pós-menopausa, a ausência de qualquer interação potencial com tamoxifeno ou tratamentos de reposição hormonal (estrogênio). Não se observou interferência quando ibandronato de sódio foi administrado concomitantemente com melfalano / prednisolona em pacientes com mieloma múltiplo. **Interações com alimentos:** a ingestão de alimentos deve ser postergada em 60 min após a administração oral de ibandronato de sódio. **Reações adversas: reações adversas comuns (> 1/100 e ≤ 1/10): doença do refluxo gastroesofágico, diarreia, dor abdominal, dispepsia, náusea, flatulência, cefaleia, síndrome influenza-like, fadiga, artralgia, mialgia, exantema. Reação incomum (>1/1.000 e <1/100):** distúrbios gastrintestinais (gastrite, esofagite, incluindo ulcerações esofágicas ou estenose, vômitos e disfagia), distúrbios do sistema nervoso (tonturas), distúrbios musculoesqueléticos e do tecido conjuntivo (dor nas costas). **Reação rara (>1/10.000 e <1/1.000):** distúrbios gastrintestinais (duodenite), distúrbios do sistema imunológico (reações de hipersensibilidade), distúrbios da pele e do tecido subcutâneo (angioedema, edema facial e urticária). **Posologia** deve ser administrado em jejum, 60 min antes da ingestão do primeiro alimento ou bebida do dia (exceto água) e antes da administração de qualquer outro medicamento ou suplemento, inclusive cálcio. Os comprimidos devem ser deglutidos inteiros, com um copo cheio de água filtrada (180 a 240 mL). O paciente não deverá deitar-se nos 60 min seguintes após tomar o medicamento; A dose recomendada de OSTEOBAN é um comprimido de 150 mg, **uma vez por mês. Pacientes idosos:** não é necessário ajuste de dose. **Pacientes com insuficiência renal:** não é necessário ajuste de dose para pacientes com insuficiência renal leve a moderada e com depuração de creatinina ≥ 30 mL/min. Em pacientes com depuração de creatinina < 30 mL/min, a decisão de administrar OSTEOBAN deve ser baseada na avaliação individual da relação risco / benefício. **Pacientes com insuficiência hepática:** não há necessidade de ajuste de dose para pacientes com insuficiência hepática. "SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO." **VENDA SOB PRESCRIÇÃO MÉDICA.** MS - 1.0573.0422. **"Material técnico científico de distribuição exclusiva a profissionais de saúde habilitados à precrição e/ou dispensação de medicamentos"**. Para informações completas, consultar a bula na íntegra através da Central de Atendimento ao Cliente. MB 02-SAP. 4408302.

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MOTORE
Curcuma longa 250 mg

O ANTI-INFLAMATÓRIO **COMPROVADAMENTE**[3] **EFICAZ E SEGURO** A LONGO PRAZO[1]

EXTRATO DE CURCUMINA COMPLEXADO
TECNOLOGIA **EXCLUSIVA**[3,4]

posologia

CURCUMINA[1]

CÁPSULA GELATINOSA[1]

Exclusivo complexo curcumina-fosfatidilcolina (fitossomo): **18X mais biodisponível** em comparação à curcumina não complexada.[3]

Cientificamente comprovado
Curcumina principal fração (curcuminoide) com ação anti-inflamatória amplamente estudada.[3]

Referências Bibliográficas: 1) BELCARO, G et al: Efficacy and Safety of Meriva®, a Curcumin-phosphatidylcholine Complex,during Extended Administration in Osteoarthritis Patients. Alternative Medicine Review 15(4):337-344,2010. 2) BOSI,PL: saúde baseada em evidências. disponível em: http://disciplinas.nucleoead.com.br/pdf/Livro_SaudeBaseadaemEvidencias.pdf. Acesso em 11/2015. 3) JURENKA, S. J. Anti-inflammatory properties of Curcumin, a major constituent of Curcuma longa: a review of preclinical and clinical research. Alternative Medicine Review, v.14, n.2, p. 141-153, 2009. 4) CUOMO, J. et al. Comparative absorption of a standardized curcuminoid mixture and its lecithin formulation. J Nat Prod, v.74, p.664-669, 2011. 5) Bula do produto MOTORE: cápsulas. Responsável Técnico: Gabriela Mallmann. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A.

Contraindicações: contraindicado em caso de alergia à curcumina, açafrão *(Curcuma longa)* ou a qualquer outro componente da fórmula. É contraindicado em pacientes que estejam em tratamento com medicações que alterem as características de coagulação como antiagregantes plaquetários, anticoagulantes, heparina de baixo peso molecular e agentes trombolíticos. É também contraindicado em casos onde haja risco de obstrução de vias biliares ou casos de cálculos biliares, úlceras estomacais e hiperacidez do estômago.

MOTORE curcuma longa Extrato seco. **Cápsulas 250 mg. USO ORAL. USO ADULTO. Indicações**: medicamento fitoterápico destinado ao tratamento da osteoartrite e artrite reumatóide, e tem ação antiinflamatória e antioxidante. **Cuidados e advertências: a curcumina é muito bem tolerada em seu uso por via oral pela grande maioria dos pacientes, sendo raros os relatos de efeitos prejudiciais. Raramente podem ocorrer queixas como desconforto gástrico leve e movimentos intestinais mais frequentes. Precauções e advertências: o uso da curcumina por via oral mostrou ser bem tolerada pela maioria dos pacientes. Em casos esporádicos foram relatados episódios de menor gravidade como desconforto gastrointestinal. Não há relatos de overdose ou efeito tóxico grave. Em caso de ocorrência de reação de hipersensibilidade, a medicação deve ser imediatamente descontinuada e os sintomas avaliados pelo médico. Motore deve ser tomado apenas por via oral. Os riscos do uso por via de administração não recomendada são a não obtenção do efeito desejado e a ocorrência de reações adversas indesejadas. Não há dados de segurança relativo ao uso da curcumina em portadores de insuficiência hepática e/ou renal, não sendo recomendável o uso da medicação em pacientes nessas condições. As doses de tratamento recomendadas não devem ser excedidas. Informe ao seu médico ou cirurgião-dentista se você está fazendo uso de algum outro medicamento. Não use medicamento sem o conhecimento do seu médico. Pode ser perigoso para a sua saúde. Gravidez e lactação:** apesar de não haver estudos conclusivos em humanos que mostrem efeito negativo na fertilidade humana, alguns estudos realizados em animais sinalizaram efeito negativo na implantação de embriões após uso injetável de altas doses de extrato etanol da curcuma. Desta maneira sugere-se evitar o uso da curcumina em pacientes com intenção de engravidar ou em gestantes. Mulheres em fase de lactação também devem evitar o uso desta medicação. Categoria de risco na gravidez C: Este medicamento não deve ser utilizado por mulheres grávidas sem orientação médica ou do cirurgião-dentista. **Interações medicamentosas: é contraindicado para uso em pacientes que estejam fazendo uso de medicações que alterem as características de coagulação como antiagregantes plaquetários, anticoagulantes, heparina de baixo peso molecular e agentes trombolíticos, pois, pode haver aumento no risco de casos de sangramento. Reações adversas: o uso da curcumina por via oral mostrou ser bem tolerada pela maioria dos pacientes. Em casos esporádicos foram relatados episódios de menor gravidade como desconforto gastrointestinal. Não há relatos de overdose ou efeito tóxico grave.** Em caso de ocorrência de reação de hipersensibilidade, a medicação deve ser imediatamente descontinuada e os sintomas avaliados pelo médico. Motore deve ser tomado apenas por via oral. Os riscos do uso por via de administração não recomendada são a não obtenção do efeito desejado e a ocorrência de reações adversas indesejadas. Não há dados de segurança relativo ao uso da curcumina em portadores de insuficiência hepática e/ou renal, não sendo recomendável o uso da medicação em pacientes nessas condições. As doses de tratamento recomendadas não devem ser excedidas. **Posologia:** Motore deve ser ingerido por via oral, com um pouco de água. A dose habitual para adultos é de 2 cápsulas a cada 12 (doze) horas, ou seja, duas tomadas diárias, totalizando 500mg de medicação a cada tomada. "SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO." **VENDA SOB PRESCRIÇÃO MÉDICA.** MS - 1.0573.0442. **MB 03 SAP 4437701.**

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REFERÊNCIAS BIBLIOGRÁFICAS: 1) IOLASCON, G. et al. Risendronate's efficacy: from randomized clinical trials to real clinical practice. Clinical Cases in Mineral and Bone Metabolism, v. 7, n. 1, p. 19-22, 2010. 2) Kairos Web Brasil. Disponível em: http://brasil.kairosweb.com. Acesso em: Março/2016. 3) Programa cuidados pela Vida (O Programa Cuidados pela Vida pode alterar ou interromper esta campanha sem aviso prévio. Desconto calculado sobre o Preço Máximo ao Consumidor). 4) BRASIL. ANVISA. Agência Nacional de Vigilância Sanitária. Resolução – RE nº1.101, de 9 de abril de 2015. Concede Certificação de Boas Práticas de Fabricação ao Aché. Diário Oficial da União, Brasília, DF, P. 133, 9 abril 2015.

CONTRAINDICAÇÕES: OSTEOTRAT está contraindicado em pacientes com hipersensibilidade a qualquer componente da fórmula, com hipocalcemia, durante a gravidez, lactação e para pacientes com insuficiência renal severa ("clearance" de creatinina < 30 mL/min). INTERAÇÕES MEDICAMENTOSAS: Não foram realizados estudos formais de interação medicamentosa, entretanto, durante os estudos clínicos não foi observada qualquer interação clinicamente relevante com outros medicamentos.

OSTEOTRAT. risedronato sódico 35 mg. comprimidos revestidos. USO ORAL. USO ADULTO. Indicações: tratamento e prevenção da osteoporose em mulheres no período pós-menopausa para reduzir o risco de fraturas vertebrais e não vertebrais. Tratamento da osteoporose em homens com alto risco de fraturas. C**ontraindicações: hipersensibilidade a qualquer componente da fórmula, hipocalcemia, gravidez e lactação e para pacientes com insuficiência renal severa ("clearance" de creatinina <30 mL/min), Precauções e advertências: Alimentos, bebidas (exceto água) e drogas contendo cátions polivalentes (tais como: cálcio, magnésio, ferro e alumínio) podem interferir na absorção dos bisfosfonatos e não devem ser administrados concomitantemente. Em mulheres mais idosas (> 80 anos), a evidência de manutenção da eficácia de risedronato sódico, é limitada. Alguns bisfosfonatos foram relacionados a esofagites e ulcerações esofágicas. Em pacientes que apresentam antecedentes de alteração esofágica que retardam o trânsito ou o esvaziamento esofágico (ex. estenosose ou acalasia), ou que são incapazes de permanecerem em posição ereta por pelo menos 30 minutos após a ingestão do comprimido, o risedronato deve ser utilizado com especial cautela. Os prescritores devem enfatizar a importância das instruções posológicas para pacientes que apresentam antecedentes de alterações esofágicas. A hipocalcemia deve ser tratada antes do início do tratamento com OSTEOTRAT. Outras alterações ósseas e do metabolismo devem ser tratadas quando iniciada a terapia com OSTEOTRAT.** Osteonecrose de mandíbula, geralmente associada com extração dentária e/ou infecção local foi relatada em pacientes com câncer em regimes de tratamento com bisfosfonatos, principalmente, na administração intravenosa. Osteonecrose de mandíbula também foi relatada em pacientes com osteoporose recebendo bisfosfonatos orais. Este medicamento contém lactose. Pacientes com problemas hereditários raros de intolerância à galactose, a deficiência da Lapp lactaseou má absorção da glucose-galactose, não devem tomar esse medicamento. Gravidez e lactação: O risco potencial para humanos é desconhecido. Risedronato sódico só deve ser utilizado durante a gravidez, se o risco benefício justificar o potencial risco para a mãe e o feto. A decisão de descontinuar a amamentação ou o produto deve considerar a importância do medicamento para mãe. Interações medicamentosas: Se considerado apropriado, OSTEOTRAT pode ser utilizado concomitantemente com a terapia de reposição hormonal. A ingestão concomitante de medicamentos contendo cátions polivalentes (ex. cálcio, magnésio, ferro e alumínio) irá interferir na absorção de OSTEOTRAT. O uso concomitante de antiácidos pode reduzir a absorção de risedronato. OSTEOTRAT não é metabolizado sistemicamente, não induz as enzimas do citocromo P450 e apresenta baixa ligação protéica. **Reações adversas: Estão listadas a seguir de acordo com a seguinte convenção: muito comum (>1/10); comum (>1/100; <1/10); incomum (>1/1000; <1/100); raro (>1/10000; <1/1000); muito raro (<1/10000). Comuns: dor de cabeça, constipação, dispepsia, náusea, dor abdominal, diarréia, dor musculoesquelética. Incomuns: gastrite, esofagite, disfagia, duodenite, úlcera esofágica Raros: glossite, estenose esofágica. Muito raramente foram observadas reações como: uveite, irite, osteonecrose de mandíbula, hipersensibilidade e reações cutâneas, incluindo angioedema, rachaduras generalizadas e reações bolhosas de pele, algumas severas. Raramente observaram-se anormalidades nos testes de função hepática. Relatos laboratoriais: foram observados em alguns pacientes discreta diminuição nos níveis de cálcio sérico e fosfato, as quais foram precoces, transitórias e assintomáticas. Posologia**: A dose recomendada nos adultos é de 1 comprimido de 35 mg uma vez por semana, por via oral. Deve ser administrado no mínimo 30 minutos antes da primeira refeição, outra medicação ou bebida (exceto água) do dia. Os comprimidos devem ser engolidos inteiros, sem deixá-los dissolvendo na boca ou mastigá-los. Os pacientes devem utilizar OSTEOTRAT enquanto estiverem na posição vertical, com um copo de água (120 mL) para auxiliar a chegada ao estômago. Os pacientes não devem deitar por 30 minutos após ingestão de OSTEOTRAT. O comprimido de Osteotrat deve ser tomado no mesmo dia de cada semana, não devem ingeridos dois comprimidos no mesmo dia. Nenhum ajuste de dose é necessário para pacientes com insuficiência renal leve a moderada. O uso do risedronato sódico é contraindicado em pacientes com insuficiência renal severa ("clearance" de creatinina menor que 30 mL/min.) "SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO." VENDA SOB PRESCRIÇÃO MÉDICA. MS - 1.0573.0418. 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DILUÍDO EM ÁGUA
ou deglutido inteiro*

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Suíça[9]

A eficácia da nimesulida. [1,2,3]

- Reduz a dor em 15 minutos[1]
- Medicamento referência[5]
- Reduz significativamente sinais e sintomas inflamatórios em doenças ORL[2,3]
- Boa tolerabilidade gástrica[6,7]
- Eficaz no controle dos sintomas da dismenorreia[8]

Referências Bibliográficas: 1) BIANCHI, M; BROGGINI, M. A randomised, Double-blind, clinical Trial comparing the efficacy of nimesulide, celecoxib and rofecoxib in osteoarthritis of the knee. Drugs, v.63,suppl.1,p.37-46,2003. 2) CITTARANI, A.; MANTOVANI, M.; SCARCABAROZZI, I. A multicentre clinical study of nimesulide in inflammatory diseases of the ear, nose and throat. Drugs 45, s. 1, p. 96-99, 1993. 3) MOURI, M.E. Nimesulide for treatment of acute inflammation of the upper respiratory tract. Clinical therapeutics, v.6, n.2, p. 142-150, 1984. 4) Bula do Produto NISULID comprimidos dispersíveis. Responsável Técnico: Dr. Wilson R. Farias. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A. 5) BRASIL. ANVISA. Agência Nacional de Vigilância Sanitária. Lista "A" de Medicamentos de Referência. Disponível em: http://portal.anvisa.gov.br Acesso em: maio 2012. 6) MARIN, U. et al. Double Blind Endoscopic Study Comparing the Effect of Nimesulide and Placebo on Gastric Mucosa of Dyspeptic Subjects. Drug Invest, v.2, n.3, p.162-166, 1990.7) BJARNASON, I.; TAKOLEFSSON, B. Gastrointestinal toxicity of non-steroidal anti-inflammatory drugs: theeffect of nimesulide compared with naproxen on the human gastrointestinal tract. Rheumatology, v.36, s.1, p.24-32, 1999. 8) MUGGIAN, G. et al. Un nuovo trattamento farmacologico nella dismenorrea essenziale. Clin Ter, v.117, p. 481-492, 1986. 9) Internal Report.

Contraindicação: crianças menores de 12 anos. Interação medicamentosa: Não se aconselha usar medicamentos que provoquem irritação no estômago durante o tratamento com NISULID® (nimesulida).

NISULID, nimesulida. 100 mg comprimidos. 100 mg comprimidos dispersíveis. 100 mg / envelope granulado. 50 mg/ml gotas. 10 mg/ml suspensão oral. uso oral. 100 mg supositórios. uso retal. uso adulto e pediátrico. MS – 1.0573.0301. INDICAÇÕES: Indicado em condições clínicas que requeiram atividade anti-inflamatória, analgésica e antipirética. CONTRAINDICAÇÕES: **Hipersensibilidade à nimesulida ou a qualquer outro componente do medicamento; história de hipersensibilidade ao ácido acetilsalicílico ou a outros AINES. Pacientes com úlcera péptica em fase ativa, ulcerações recorrentes ou com hemorragia gastrintestinal; paciente com distúrbios de coagulação grave; pacientes com insuficiência cardíaca grave; pacientes com disfunção renal grave; pacientes com disfunção hepática; crianças menores de 12 anos. A nimesulida não deve ser administrada durante a gravidez ou em mulheres que estejam amamentando.** CUIDADOS E ADVERTÊNCIAS: Raramente nimesulida foi relatada estar associada com reações hepáticas sérias, incluindo casos fatais. Pacientes que apresentaram sintomas compatíveis com dano hepático durante o tratamento com nimesulida (por exemplo, anorexia, náusea, vômitos, dor abdominal, fadiga, urina escura ou ictericia) devem ser cuidadosamente monitorados. A administração concomitante com drogas hepatotóxicas conhecidas e abuso de álcool, devem ser evitados durante o tratamento com nimesulida. Pacientes que apresentaram testes de função hepática anormais devem descontinuar o tratamento e não devem reiniciar o tratamento com a nimesulida. Em raras situações, onde ulcerações ou sangramentos gastrintestinais ocorrem em pacientes tratados com nimesulida, o medicamento deve ser suspenso. Em pacientes com insuficiência renal ou cardíaca, cuidado é requerido, pois o uso de AINES pode resultar em deterioração da função renal. Pacientes idosos são particularmente sensíveis as reações adversas dos AINES, incluindo hemorragia e perfuração gastrintestinal, dano das funções renal, cardíaca e hepática. O uso prolongado de AINES em idosos não é recomendado. A nimesulida deve ser usada com atenção em pacientes com história de ulceração péptica ou inflamações intestinais. Como os AINES podem interferir na função plaquetária, eles devem ser usados com cuidado em pacientes com hemorragia intracraniana e alterações da coagulação, como por exemplo, hemofilia e predisposição a sangramento. As drogas antiinflamatórias não-esteroidais podem mascarar a febre relacionada a uma infecção bacteriana subjacente. Com relação ao uso da nimesulida em crianças, foram relatadas algumas reações graves, incluindo raros casos compatíveis com síndrome de Reye. O uso concomitante de outros anti-inflamatórios não-esteroidais durante a terapia com nimesulida não é recomendado. Como os outros anti-inflamatórios não-esteroidais, a nimesulida deve ser usada com cuidado em pacientes com insuficiência cardíaca congestiva, hipertensão, prejuízo da função renal ou depleção do volume extracelular, que são altamente suscetíveis a uma redução no fluxo sanguíneo renal. Por ser a eliminação do fármaco predominantemente renal, o produto deve ser administrado com cuidado a pacientes com prejuízo da função hepática ou renal. Em pacientes com clearance de creatinina de 30-80 ml/min, não há necessidade de ajuste de dose. Em caso de disfunção renal grave o medicamento é contra-indicado. Em pacientes com história de perturbações oculares devido a outros AINES, o tratamento deve ser suspenso e realizado exames oftalmológicos caso ocorram distúrbios visuais durante o uso da nimesulida. Pacientes com asma toleram bem a nimesulida, mas a possibilidade de precipitação de broncoespasmo não pode ser inteiramente excluída. Os riscos de uso por via de administração não-recomendada são: a não-obtenção do efeito desejado e ocorrência de reações adversas. Atenção diabéticos: contém açúcar (nas apresentações da suspensão oral (300 mg/ml), granulado (1,774 g por envelope) e gotas (300 mg/ml)). GRAVIDEZ E LACTAÇÃO: Categoria de risco de gravidez C: este medicamento não deve ser utilizado por mulheres grávidas sem orientação médica ou do cirurgião-dentista. INTERAÇÕES MEDICAMENTOSAS: A potencial interação com glibenclamida, teofilina, varfarina, digoxina, cimetidina e uma preparação antiácida (ou seja, uma combinação de hidróxido de magnésio e alumínio) foram estudadas in vivo. Nenhuma interação clínica significante foi observada. A nimesulida pode antagonizar os efeitos dos diuréticos e em particular bloquear o aumento da atividade da renina plasmática induzida pela furosemida. O uso concomitante de furosemida e nimesulida requer cautela em pacientes renais ou cardíacos suscetíveis. A administração concomitante de nimesulida com anticoagulantes (varfarina) ou ácido acetilsalicílico pode causar efeitos aditivos (aumento do risco de complicações de sangramento). Portanto, esta combinação não é recomendada e é contra-indicada em pacientes com distúrbios de coagulação graves. Se a combinação não puder ser evitada, a atividade antitrombótica deve ser cuidadosamente monitorada. Se nimesulida for prescrita para um paciente sob terapia com lítio, os níveis de lítio devem ser monitorados cuidadosamente. Deve-se ter cuidado com pacientes que apresentem anormalidades hepáticas, particularmente se houver intenção de administrar nimesulida em combinação com outras drogas potencialmente hepatotóxicas. Não há evidência de que a nimesulida afete a glicemia em jejum ou a tolerância à glicose em pacientes diabéticos tratados com sulfoniluréias. Pode haver potencialização da ação da fenitoína. Embora não tenham sido relatados especificamente com a nimesulida, foram documentadas interações entre antiinflamatórios não-esteroidais e lítio, metotrexato, probenecida e nimesulida. Portanto, recomenda-se cuidado na administração concomitante de nimesulida com qualquer uma destas drogas, devido ao aumento do risco de hemorragias gastrintestinais. Devido ao seu efeito sobre as prostaglandinas renais, os inibidores da prostaglandina-sintetase como a nimesulida podem aumentar a nefrotoxicidade das ciclosporinas. Recomenda-se tomar NISULID após as refeições. Não se aconselha a ingestão de bebidas alcoólicas durante o tratamento. REAÇÕES ADVERSAS: **Pele e tecidos subcutâneos: prurido, rash e sudorese aumentada. Gastrintestinais: diarréia, náusea e vômito. Hepatobiliar: alterações dos parâmetros hepáticos (transaminases), geralmente transitórias e reversíveis. Casos isolados de hepatite aguda, falência hepática fulminante (algumas fatalidades foram relatadas), icterícia e colestase. Sistema nervoso: tonturas e vertigens. Sistemas visual e auditivo: raramente visão borrada. Sistema cardiovascular: hipertensão. Renais: raramente: disúria, hematúria e retenção urinária. Sistema sanguíneo e linfático: raramente: anemia e eosinofilia. Sistema imunológico: raramente hipersensibilidade. Sistema endócrino: raramente hiperglicemia. Respiratórios: casos isolados de reações anafiláticas como dispnéia, asma e broncoespasmo, principalmente em pacientes com histórico de alergia ao ácido acetilsalicílico e a outros AINES. Distúrbios gerais: edema.** POSOLOGIA: USO PARA ADULTOS E CRIANÇAS ACIMA DE 12 ANOS. Comprimidos: 50 - 100mg (1/2 a 1 comprimido tomado com 1/2 copo de água) duas vezes ao dia, podendo alcançar até 200 mg duas vezes ao dia. A administração é por via oral. Comprimidos dispersíveis: 100mg (1 comprimido) duas vezes ao dia, podendo alcançar até 200 mg duas vezes ao dia. Dissolver o comprimido em 1/2 copo de água (100 mL) ou, se preferir, o comprimido poderá ser deglutido inteiro, sem a necessidade de dissolução prévia. A administração é por via oral. Granulado: 50 a 100mg (1/2 a 1 envelope dissolvido em um pouco de água ou suco) duas vezes ao dia, podendo alcançar até 200mg duas vezes ao dia. A administração é por via oral. Supositórios: 1 supositório de 100mg duas vezes ao dia, podendo alcançar até 200mg (2 supositórios de 100mg) duas vezes ao dia. Aplicar o supositório por via retal. Gotas: administrar 1 gota (2,5mg) por kg de peso, duas vezes ao dia, diretamente na boca da criança ou se preferir dilua em um pouco de água açucarada. Lembramos que cada gota contém 2,5mg de nimesulida e cada mL de NISULID contém 50mg de nimesulida. Cada mL do produto contém 20 gotas. Suspensão: a posologia recomendada é de 5mg/kg/dia - fracionada a critério médico em duas administrações. Agitar antes de usar. Colocar a dose recomendada no copo-medida que acompanha o produto e pedir para a criança tomar pela boca (1mL da suspensão contém 10mg de nimesulida). Pacientes com insuficiência da função renal: não há necessidade de ajuste de dose em pacientes com insuficiência renal moderada. Em casos de insuficiência renal grave o medicamento é contra-indicado. Pacientes com insuficiência hepática: contra-indicado em pacientes com insuficiência hepática. VENDA SOB PRESCRIÇÃO MÉDICA. SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVE PA SER CONSULTADO. Material técnico científico de distribuição exclusiva à classe médica - Documentação Científica e informações adicionais estão à disposição da classe médica, mediante solicitação. MB_ 05 SAP4094207(A,09/09.

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WEBER C ANKLE FRACTURES WITH TIBIOFIBULAR DIASTASIS: SYNDESMOSIS-ONLY FIXATION

FRATURAS NO TORNOZELO WEBER C COM DIÁSTASE TIBIOFIBULAR: FIXAÇÃO APENAS DA SINDESMOSE

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ABSTRACT

Objectives: To evaluate syndesmosis-only fixation in Weber C ankle fractures with tibiofibular diastasis and to assess the need for additional fibular fixation. Methods: Twenty-one patients with Weber C ankle fractures and tibiofibular diastasis were followed for at least 24 months after treatment. In treatment of the Weber C fractures, only a syndesmosis screw was used through a mini open lateral incision if the syndesmosis could be anatomically reduced and fibular length and rotation could be restored. At follow-up, anteroposterior tibiofibular distance, lateral fibular distance, medial mortise distance and fracture healing were compared and patients were clinically evaluated using the Olerud and Molander ankle scale scoring system. Results: The average duration of follow-up was 49 months and the decreases in anteroposterior tibiofibular distance and lateral fibular distance were statistically significant. At the last follow-up the average clinical score was 86. Ankle mortise was reduced at follow-up in all cases except one, which resulted in a late diastasis. Conclusions: Syndesmosis-only fixation can be an effective method of treating Weber type-C lateral malleolar fractures with syndesmosis disruption in cases where intraoperative fibular length can be restored and anatomical syndesmosis reduction can be achieved. ***Level of Evidence IV, Case Series.***

Keywords: Ankle injuries. Fracture fixation, internal. Fractures, bone. Follow-up studies.

RESUMO

Objetivos: Avaliar a fixação apenas da sindesmose em fraturas do tornozelo de Weber tipo C com diástase tibiofibular e a necessidade de fixação adicional. Métodos: Vinte e um pacientes com fraturas de tornozelo Weber C e diástase tibiofibular foram seguidos por pelo menos 24 meses após o tratamento. No tratamento dessas fraturas, apenas um parafuso para sindesmose foi colocado através de mini-incisão lateral e se a sindesmose pudesse ser anatomicamente reduzida e o comprimento e a rotação da fíbula pudessem ser restaurados. No seguimento, a distância tibiofibular anteroposterior, a distância fibular lateral e a distância medial do encaixe do tornozelo e a consolidação das fraturas foram comparados e os pacientes foram avaliados clinicamente pelo sistema de pontuação da escala de tornozelo de Olerud e Molander. Resultados: A duração média do seguimento foi de 49 meses e as diminuições da distância tibiofibular anteroposterior e fibular lateral foram estatisticamente significantes. No último seguimento, a pontuação clínica média foi de 86. O encaixe do tornozelo foi reduzido em todos os casos, exceto um, que resultou em uma diástase tardia. Conclusões: A fixação apenas da sindesmose pode ser um método eficaz de tratamento de fraturas laterais Weber tipo C com lesão na sindesmose, nos casos em que o comprimento fibular intraoperatório pode ser restaurado e a redução anatômica da sindesmose possa ser obtida. ***Nível de Evidência IV, Série de Casos.***

Descritores: *Traumatismos do tornozelo. Fixação interna de fraturas. Fraturas ósseas. Seguimentos.*

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INTRODUCTION

Syndesmosis injuries occur in 10% of ankle fractures and approximately 20% of ankle fractures that require internal fixation, with an incidence of approximately 15 per 100,000 in the general population. Syndesmotic injuries are most commonly caused by pronation-external rotation, pronation-abduction and less frequently supination external rotation mechanisms. As the talus abducts or rotates externally in the mortise, one or more syndesmotic ligament disruptions can occur. Initial rupture of the deltoid ligament or fracture of the medial malleolus consequently occurs and if the trauma is severe enough may be followed by rupture of the anterior tibiofibular ligament and interosseous membrane. These events may be at the syndesmotic level (Danis-Weber type B injury) or the supra-syndesmotic level (Danis-Weber type C injury); both are associated with fracture of the fibula.[1]

All authors declare no potential conflict of interest related to this article.

This study was carried out at the Harran University Faculty of Medicine, Orthopedics and Traumatology Department, Sanliurfa, Turkey.
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To avoid diastasis of the ankle joint, an injured distal tibiofibular syndesmosis should be reduced.[1] Osteoarthritis and poor functional outcomes are more common in patients with a widened mortise.[2] Although numerous methods have described the conventional procedure, stabilization with a syndesmotic screw remains the most popular treatment. It is not possible to consistently estimate the integrity of the interosseous membrane and subsequent need for trans-syndesmotic fixation based solely on the level of the fibular fracture and an intraoperative syndesmotic stress test is consequently recommended to establish the presence or absence of syndesmotic instability. This has led to controversy over decisions related to syndesmotic fixation based on the level of the fibular fracture. Traditionally, a diastasis screw is recommended if the fibular fracture is more than 3.5 cm above the top of the syndesmosis and the deltoid ligament is injured. In cases with a medial malleolar fracture, after the fracture has been rigidly fixed a diastasis screw is used if the fibular fracture is more than 15 cm above the syndesmosis.[3]

Since the indications for syndesmotic screw application are clear, questions arise about the role of internal fixation of the fibula in an associated fibula fracture after syndesmosis reduction. When the fibular fracture is located in the middle or proximal one-third of the diaphysis, problems with performing an additional procedure may arise in cases where soft tissue is compromised. If the syndesmosis can be anatomically reduced and stable fixation is achievable, internal fixation of the fibula may not be required. This study presents the results of syndesmosis-only fixation in patients with Weber C ankle fractures with tibiofibular diastasis.

MATERIALS AND METHODS

Twenty-three patients with supra-syndesmotic fibular fractures whose distal tibiofibular syndesmotic injuries were fixed by syndesmosis alone were studied retrospectively. Patients with multiple injuries, late diagnosis and open fractures were not included. All patients underwent ankle X-rays that included bilateral anteroposterior (AP), AP 15-degree internal rotation (mortise) and lateral views for comparison and to determine whether there was a tibiofibular diastasis. Syndesmosis was determined by measuring the horizontal distance between the medial cortical border of the fibula and the radio dense line of the tibiofibular notch 1 cm above the ankle joint. We also evaluated the anteroposterior X-rays to assess the distance between the medial malleolar lateral articular side and medial talus side, designated as the medial mortise distance (medial clear space). On the lateral radiograms, the distance measured between the fractured ends of the fibula was recorded as the lateral fibular distance. Patients with a tibia-fibular clear space exceeding five millimeters were diagnosed with tibiofibular diastasis and treated with syndesmosis fixation.

Patients underwent surgery when the soft-tissue swelling decreased. Syndesmotic disruption was confirmed under fluoroscopy using the external rotation stress test; the proximal tibia was stabilized using the examiner's or an assistant's hand, the examiner held the ankle in neutral flexion at a 90 angle between the tibia and foot and consistent external rotational force was applied to the ankle mortise. The external rotation stress test was positive in all patients. Proximal fibula fractures with syndesmosis injury (Maisonneuve fracture) were excluded from the study since fibula fixation is unnecessary for these fractures.[4]

During surgery, the medial ankle structures were internally fixed first when necessary. A malleolar screw was used for medial malleolar fixation in all patients. In cases where it was possible to anatomically reduce the syndesmosis and restore fibular length, a syndesmosis screw was placed through a mini open lateral incision. Restoration of fibular length and rotation was decided using fluoroscopy and Shenton's line of the ankle was assessed. A malleolar screw was used for the tibiofibular diastasis as a syndesmotic screw; 4.0 mm stainless steel malleolar screws were used in all cases and tricortical fixation was performed using a single screw. The diastasis screws were placed parallel and 2 to 3 cm above the ankle joint, 20 to 30 degrees antero-medially after clamp stabilization of the syndesmosis was achieved. A tourniquet was used and antibiotic prophylaxis was initiated prior to surgery. A short leg plaster splint was used postoperatively in all patients. (Figures 1A-D) Non-weight-bearing mobilization using crutches was recommended for six weeks. At six weeks, the ankle was X-rayed to assess whether the ankle mortise was well-reduced and stable and if the fracture was healing. If no problems were seen, the diastasis screws were removed under local anesthesia six to eight weeks after the surgery. Ankle motion and partial weight bearing were subsequently permitted.

At follow-up, we compared X-rays including measurements of the anteroposterior tibiofibular distance, lateral fibular distance and medial mortise distance (including preoperative, postoperative and final control films). During the last follow-up visit, the patients were clinically evaluated using the Olerud and Molander[5] ankle scale (OMAS). The OMAS is a self-administered objective scoring system patients complete using a questionnaire. In this functional rating scale, the score ranges from 0 (totally impaired) to 100 (completely unimpaired). Scores are based on nine different items: pain, stiffness, swelling, stair climbing, running, jumping, squatting, supports and activities of daily living. Scores of 91-100 were graded as excellent, 61-90 as good, 31-60 as fair and 0-30 as poor.

Statistical analysis was performed using SPSS 12.0 software (SPSS Inc., Chicago, IL, USA). Preoperative and postoperative

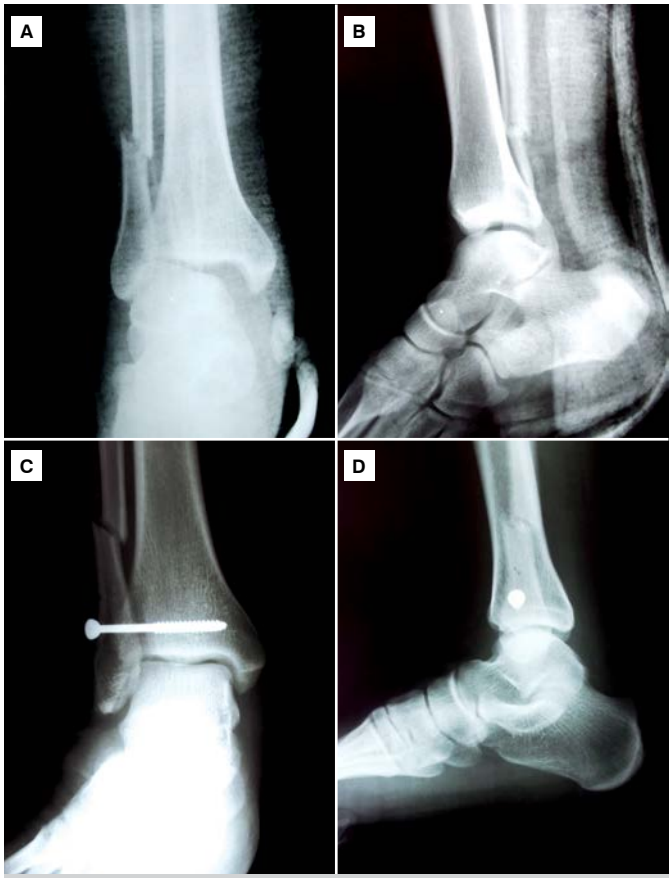

Figure 1. (A and B) Weber C ankle fracture with tibiofibular diastasis, (C and D). Postoperative radiograph with syndesmosis-only fixation.

differences were compared using the Wilcoxon signed rank test. The significance level was set at $p < 0.05$. All subjects gave informed consent to participate in the study and the protocol was approved by the institutional review board under reference number 125/2009.

RESULTS

The average patient age was 40.1 ± 11.7 years (range 20-61). Thirty percent (n= 7) of the patients were women. The mechanism of injury was a twisting sprain in 15 patients, sports-related in five patients and traffic accident in three patients. All of the fractures were in the middle third of the fibula. Seventeen fractures were pronation-external rotation (PER) injuries according to the Lauge-Hansen classification (stage 3 PER in 13 ankles and stage 4 PER in four ankles) and six were pronation-abduction type. Medial malleolar screw fixation was performed in 12 ankles and a deltoid ligament repair was performed in one case. There were no soft tissue infections. On the control examinations, delayed union was observed in two patients. Complex regional pain syndrome (CRPS) developed in one patient and he was referred to the physiotherapy department.

The average duration of follow-up was 48.3 ± 19.1 months (range 22-78 months). The average anteroposterior tibiofibular distance was 6.8 ± 2.5 mm (range 14-2 mm) preoperatively and 3.4 ± 1.0 mm (range 6-2) postoperatively. The average lateral fibular distance was 2.0 ± 1.2 mm preoperatively and 1.2 ± 0.8 mm postoperatively. The decrease in anteroposterior tibiofibular distance and lateral fibular distance was statistically significant. The average medial mortise distance was 3 ± 1.9 mm (range 2-11 mm) preoperatively and 2.1 ± 0.5 mm (range 1-3 mm) postoperatively. The change in the medial mortise distance was not statistically significant. When the last control radiographic measurements were compared with the postoperative measurements, there was no statistically significant change in their values.

At the last follow-up, the average score according to the OMAS scoring system was 85.8 ± 8.2 (range 64-94). Five patients (22%) had an excellent outcome, 16 patients (69%) had a good outcome and two patients (9%) had a fair outcome. The ankle mortise was reduced in all cases except one, which resulted in a late diastasis; revision surgery with bone grafting and internal fixation of the fibula was performed in this patient. One patient had residual ankle stiffness which responded to intensive physiotherapy. None of the syndesmotic screws broke.

DISCUSSION

The most important predictor of a good functional outcome for ankle fractures with a syndesmotic injury is the anatomical reduction of the syndesmosis.[2] Displacement greater than 1 mm of the talus on the mortise X-rays in comparison with the contralateral extremity is accepted as an indication for surgery. Restoration of fibular length and achieving correct rotation of the fibula are essential for restoring the proper tibiofibular relationship. A residual lateral displacement of the talu (exceeding 2 mm) is associated with a 49% increase in articular mean pressure and a greater than 90% chance of degenerative changes and poor outcomes. The distal fibular fragment has been shown to rotate externally relative to the proximal fragment, so internal rotation of the distal fragment is essential to achieve reduction.[6]

Lateral plating of the fibula in proximal and diaphysis fractures involves additional soft tissue dissection, which is associated with a risk for injury to the common peroneal nerve and anatomical plate incongruity. Though overall complication rates are low and outcomes are usually good, soft tissue problems are reported in up to 22% of cases. Patients with a compromised soft tissue envelope resulting from either the injury or other co-morbidities including diabetes mellitus peripheral vascular disease are prone to high complication rates.[7] To avoid compromising the thin lateral soft tissues, a dorsal approach with application of an "antiglide" plate to the posterior aspect of the fibula has been described.[8] Some reports also describe superficial peroneal nerve variations in anatomic study with the possibility of injury to the intermediate dorsal cutaneous nerve.[9] Kim et al.[10] suggested anterior transposition of this nerve to reduce the incidence of symptoms related to superficial peroneal nerve injury after fixation of the lateral malleolus. Redfern et al.[11] found significantly more symptoms associated with the superficial peroneal nerve in a surgically-treated group (21%) compared to patients who were treated conservatively (9%) 2 years after an ankle fracture. In order to avoid these problems, indirect fixation of the fibula is possible using syndesmosis fixation after the correct length and rotation of the fibula and reduction of the syndesmosis is achieved. Syndesmosis fixation alone was performed according to the level of the fibular fracture, preoperatively and only high-level fractures were selected. The surgical procedure was performed to restore fibular length and reduce the syndesmosis. If these conditions could not be obtained preoperatively or intraoperatively, additional fixations were performed.

Some investigators suggest that there are no optimal radiological parameters to assess the integrity of the syndesmosis.[12] The Hook test in the sagittal plane is considered a sensitive assessment of instability. In this study, the Hook test was used for diagnosis in addition to radiological assessment of the syndesmosis. The medial clear space, tibiofibular overlap and tibiofibular clear space should be accurately restored in the mortise view and the Shenton line of the ankle should be unbroken. Lateral imaging of the ankle is useful, together with comparison views of the normal ankle so that the required result can be achieved. The anteroposterior tibiofibular distance, lateral fibular distance and medial mortise distance were used to evaluate the reduction. Only a decrease in the medial mortise distance was not statistically significant. Because the medial malleolus was also fractured in 12 patients, the change in the medial mortise distance was not statistically significant.

In a cadaver study, Ho et al.[13] compared syndesmotic fixation alone and syndesmotic fixation with the addition of a fibular plate to determine whether the addition of a fibular plate would lead to better biomechanical properties. The results showed higher rotational stability, load to failure and stiffness with the plate compared to the syndesmotic fixation-only technique. In addition, a syndesmosis study in cadavers with stable fixation of bimalleolar fractures showed that if the fibular fracture was within 4.5 centimeters of the joint, syndesmotic fixation was not necessary.[3] However, one clinical study found a high failure rate when PE-4 fractures with deltoid ligament disruption and fibular fractures distal to this "critical zone" were treated with fibular fixation only.[14] The investigators concluded that trans-syndesmotic fixation is indicated in all PE-4 fractures with rupture of the deltoid, regardless of the location of the fibular fracture. In the case of a supra-syndesmotic stage 4 PER injury, reported by Saltzman, syndesmotic fixation alone restored the length and rotation of the distal fibular segment, thereby achieving a congruent ankle mortise,[15] which provided a buttress against lateral talar subluxation. Diaphyseal fibular fractures, in which the syndesmosis and ankle joints are congruent, are treated non-operatively with high rates of union and low complication rates. Internal fixation of such diaphyseal fibular fractures is associated with risks (e.g. infection, neurological damage, prominent metal work, peroneal tendonitis, nonunion and delayed union and hardware failure) that outweigh the benefits of such procedures. Mohammed et al.[16] performed syndesmosis fixation alone in 12 patients with Weber-C ankle fractures with syndesmotic injury and reported good to excellent outcomes in 83% of these cases. As a result,

syndesmosis-only fixation was recommended as an effective treatment option for the combination of syndesmosis disruption and Weber type-C lateral malleolar fractures.

Removal of the fixation screw is recommended at week eight or nine.[6,17] Burgert and Jones[18] reported that six weeks was not sufficient. Some investigators have reported that early mobilization and weight bearing should be encouraged.[19] Some suggest that the screw should not be removed and that any additional surgery in an incompletely healed wound may cause higher rates of infection.[20] Ebraheim et al.[17] suggested that the syndesmotic screw should not be removed until the fibular fracture shows signs of healing, especially in cases with a deltoid ligament injury. In an internal fixation series containing 32 patients with supra-syndesmotic ankle fractures, these authors found a 6% rate of delayed union and 13% rate of nonunion, as well as one late diastasis of the syndesmosis following screw removal after six weeks; as a result, fibular fracture healing should be assessed prior to screw removal. Syndesmosis-only fixation can be an effective method for treating patients with Weber type-C lateral malleolar fractures with syndesmosis disruption. However, restoration of fibular length and anatomical reduction of the syndesmosis are essential for a successful outcome. Fibular fracture healing should be assessed prior to removal of the diastasis screw at the appropriate time. We recommend fixing syndesmosis with only a screw after anatomic reduction if fibular length is restored in Weber C fractures.

CONCLUSIONS

Syndesmosis-only fixation can be an effective method of treating patients with Weber type-C lateral malleolar fractures with syndesmosis disruption in cases where intraoperative fibular length restoration and anatomical syndesmosis reduction can be achieved.

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. SS (0000-0001-5987-2813)* and SZ (0000-0003-3945-6294)* were the main contributors in drafting the manuscript. SS, SZ and EI (0000-0002-2039-8189)* performed the surgeries, followed the patients and gathered clinical data. SS evaluated the data for the statistical analysis. SZ and EI reviewed the manuscript and contributed to the intellectual concept of the study. *ORCID (Open Researcher and Contributor ID)

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SURGICAL TREATMENT RESULTS FOR DUPUYTREN'S DISEASE

RESULTADOS DO TRATAMENTO CIRÚRGICO NA DOENÇA DE DUPUYTREN

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ABSTRACT

Objective: To present the results of our cases of Dupuytren's disease treated with regional selective fasciectomy in light of the literature. Methods: Patients diagnosed with Dupuytren's contracture and surgically treated with regional selective fasciectomy at our institution with adequate follow-up data were included in the study. All patients were routinely followed after surgery to assess results and complications. QuickDASH scoring was used to evaluate the patients and recurrences and complications were recorded. Results: Twenty-one hands of 19 patients (13 males, 6 females) who underwent surgery and received adequate follow-up were retrospectively evaluated. Mean patient age was 65.8 (range: 41 to 86) and the mean follow-up period was 48.2 months (range: 24 to 86). Fourteen (66.6%) hands had excellent results, five (23%) hands had good results and two (9.4%) had fair results. The mean QuickDASH score for the patients at the final follow-up was 6.58 (range: 0 to 20.4). Conclusion: Our study results demonstrated that regional selective fasciectomy is a reliable and efficient method to treat Dupuytren's disease with low rates of complications and recurrence and the technique can be considered the gold standard. ***Level of Evidence IV, Case Series.***

Keywords: Dupuytren contracture/surgery. Dupuytren contracture/therapy. Fasciotomy.

RESUMO

Objetivo: Apresentar os resultados de nossos casos de doença de Dupuytren tratados com fasciotomia seletiva regional, à luz da literatura. Métodos: Os pacientes diagnosticados com contratura de Dupuytren e tratados cirurgicamente com fasciotomia seletiva regional em nossa instituição que tinham dados de acompanhamento adequados foram incluídos no estudo. Todos os pacientes foram rotineiramente acompanhados após a cirurgia para avaliação dos resultados e das complicações. Foi utilizada a pontuação QuickDASH na avaliação dos pacientes e as recorrências e complicações foram registradas. Resultados: Foram avaliadas retrospectivamente vinte e uma mãos de 19 pacientes (13 homens, 6 mulheres) submetidos à cirurgia e acompanhados adequadamente. A média de idade dos pacientes foi de 65,8 (intervalo: 41 a 86) e o período médio de seguimento foi 48,2 meses (intervalo: 24 a 86). Quatorze (66,6%) mãos tiveram excelentes resultados, enquanto cinco (23%) mãos tiveram bons e duas (9,4%) tiveram resultados moderados. A pontuação média no QuickDASH dos pacientes no seguimento final foi de 6,58 (intervalo: 0 a 20,4). Conclusão: Os resultados do nosso estudo demonstraram que a fasciotomia seletiva regional é um método confiável e eficiente, com baixas taxas de complicação e recorrência no tratamento da doença de Dupuytren e a técnica pode ser considerada o padrão-ouro. ***Nível de Evidência IV, Série de Casos.***

Descritores: *Contratura de dupuytren/cirurgia. Contratura de dupuytren/terapia. Fasciotomia.*

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INTRODUCTION

Dupuytren's disease is a benign fibroproliferative disorder of the palmar and digital fascia. The disease usually starts with a palpable nodule (the Dupuytren nodule) in the palm and may cause flexion contracture in the joints and functional impairment as it progresses.[1-5] The etiology of the disease remains unclear. However, male sex, advanced age, occupation, trauma, alcohol use, diabetes, smoking and epilepsy are known risk factors.[6-8] Autosomal dominant inheritance with varying penetrance has been reported in several studies and the disorder has been confirmed in positive family histories.[4,9,10] Treatment options can be categorized under four main sections; conservative approaches, collagenase injections, needle aponeurotomy and fasciectomy.[3] Fixed-flexion contractures are usually treated with surgical methods. Surgical management is recommended for cases with contracture in the PIP joint or contracture over 30 degrees in the metacarpophalangeal joint, with the limited palmar fasciectomy method the most popular and recognized option.[11,12]

This study presents the results in our cases who received surgical treatment for Dupuytren's disease, in light of the literature.

PATIENTS AND METHODS

Patients diagnosed with Dupuytren's contracture and surgically treated with regional selective fasciectomy at our institution between

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May 2006 and May 2014 who had adequate follow-up data were included in the study. All patients signed a free and informed consent form. Patients were staged according to system by Khan et al.[13] (Table 1) In addition, smoking habits, alcohol use, regular use of medications and accompanying chronic diseases were noted for each patient. Since this study is retrospective in nature, institutional review board approval was not necessary.

All surgeries were carried out using an infraclavicular block with the application of a pneumatic tourniquet. Patients were given prophylactic first-generation cephalosporin for the 24 hours before and after surgery. Zigzagplasty extending straight toward the proximal or direct incision with multiple z-plasties was employed for the surgical incision. (Figure 1A-C) Regional fasciectomy (excision of the involved fascia) was performed in all patients and all surgeries were performed under magnification. After release of the tourniquet, the site was checked for bleeding and an aspiration drain was used. Skin grafting was required for wound closure in one patient and primary closure was performed in the others.

A short arm splint was applied postoperatively to maintain the hand and fingers in extension. After the edema subsided, the splint was removed and rehabilitation initiated. All patients continued to use the extension splint at night for three months.

All patients were routinely followed after surgery to assess results and complications. QuickDASH scoring was used for patient evaluation, challenges during functional recovery and daily activities were investigated and recurrences and complications were recorded. (Figure 1D, E)

We grouped our results into four sections, as suggested by Khan et al.[13] According to this classification, full movement/function and no recurrence was considered 'excellent,' mild loss of flexion-extension in fingers with minor impact on function was considered 'good,' loss of function with joint stiffness, recurrence and limitation in daily activities was considered 'fair,' and severe loss of function and failure to recover after the first contracture was considered 'poor.' (Table 2)

Table 1. Clinical staging of the patients.

Staging	Clinical characteristics
Stage 1	Thickened nodule and band in the palmar aponeurosis; may have associated skin abnormalities
Stage 2	Limitation of finger extension in addition to Stage 1
Stage 3	Presence of flexion contracture in addition to Stage 2

RESULTS

Twenty-one hands in 19 patients (13 males, 6 females) who underwent surgery and had adequate follow-up were retrospectively evaluated. Mean patient age was 65.8 (range: 41 to 86) and mean follow-up period was 48.2 months (range: 24 to 86). Fourteen (66.6%) hands had excellent results, five (23%) hands had good results and two (9.4%) had fair results. Mean QuickDASH score for patients at the final follow-up was 6.58 (range: 0 to 20.4). (Table 3) Bilateral involvement was observed in two (10.5%) patients. Four other patients had Dupuytren nodules in the other hand (21%). All (100%) patients had either contracture of the finger or flexion contracture over 30 degrees, constituting severe involvement (Stage 3). The second digit was involved in three (14.2%) cases, the third digit in six cases (28.5%), the fourth digit in 13 cases (61%) and the fifth digit in 12 (57%) cases.

Table 2. Classification of patient outcomes.

Results	Movement/Function/Recurrence
Excellent	Full movement and function, no recurrence
Good	Mild loss of flexion-extension in fingers with minor impact on function
Fair	Loss of function with joint stiffness, recurrence, limitation in daily activities
Poor	Failed to recover, severe loss of function

Table 3. Our results.

Treatment outcome	Point score	%
Excellent	14.0	66.6
Good	5.0	23.0
Fair	2.0	9.5

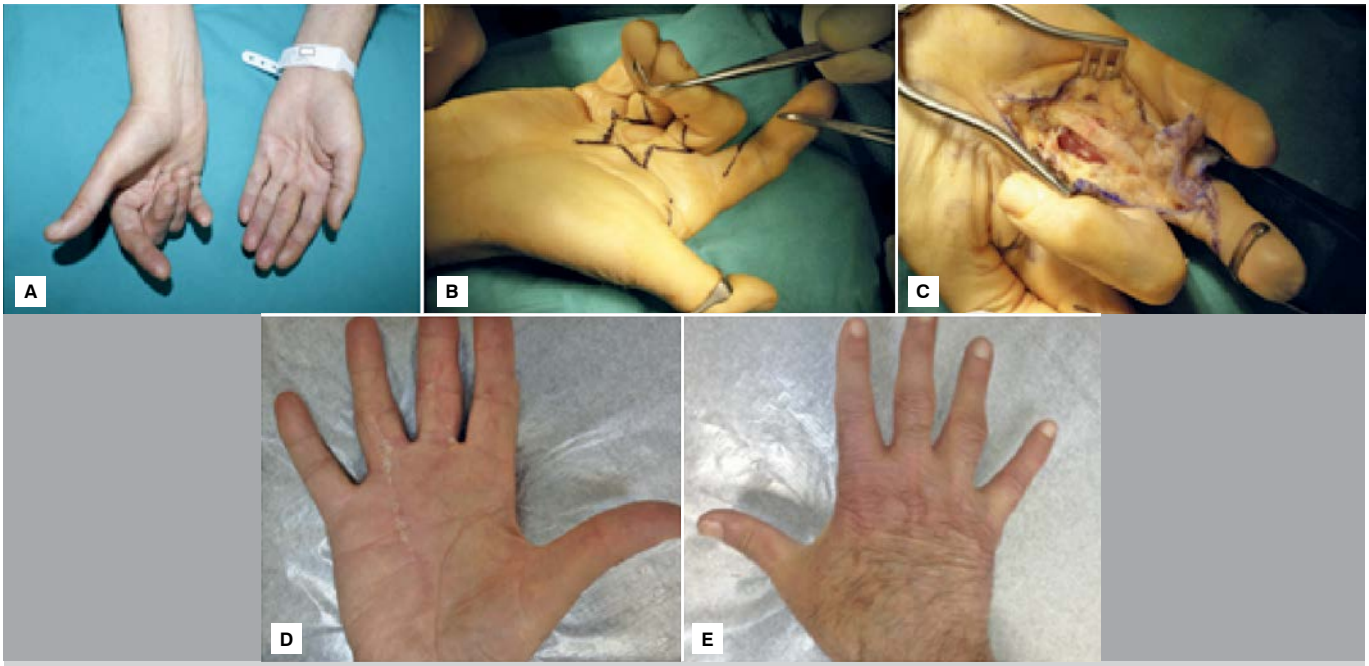

Figure 1. (A) Preoperative image of a patient with involvement in the 3rd and 4th digit of the right hand. (B) Planning for zigzagplasty. (C) Appearance of 3rd digit after removal of diseased tissue. (D, E) Functional outcome at 24th months post-procedure.

Six patients were regular smokers, three were regular drinkers and one patient used barbiturates for epilepsy. Two patients were diagnosed with diabetes.

In one patient, the digital artery at the radial side of the fifth digit was accidentally cut during surgery. Primary repair was performed in this patient and no circulation problems were observed in the follow-up examinations. Two other patients complained of numbness in their fingers and two patients experienced recurrences.

DISCUSSION

Several methods with varying rates of success, complication and recurrence have been reported in the literature to manage Dupuytren's disease.[3] A general review of these methods will lead to better recovery, clinical outcome, morbidity and recurrence rates in cases treated with aggressive tissue dissection.[3] Regional selective fasciectomy remains the gold standard in surgical treatment of Dupuytren's disease. The goal of the technique is to remove the macroscopically affected diseased fascia. Only regional selective fasciectomy was performed in our study and 90% of the patients had excellent and good results; excluding the two cases which developed recurrence.

Duthie and Chesney[14] performed percutaneous needle fasciectomy on 82 patients and followed them for 10 years. These authors observed a recurrence rate of 66%. In their series of 100 patients, Tonkin et al.[15] compared dermofasciectomy with selective fasciectomy and reported that the recurrence rate was lower in patients who had undergone dermofasciectomy. Dermofasciectomy is still a valid treatment option in patients with recurrence or extensive skin involvement.[3] Although fasciectomy and selective fasciectomy are similar in terms of functionality and recurrence rates, complication and morbidity rates are strikingly higher with radical fasciectomy.[16] Khan et al.[13] employed regional fasciectomy in 27 of their 30 patients and reported excellent and good results in 97% of the patients after five years of follow-up. Özkaya et al.[4] retrospectively evaluated patients who underwent partial selective fasciectomy over a 10-year period and observed complications in 16.6% of the patients, but no recurrence. Ribak et al.[17] compared regional selective fasciectomy and percutaneous needle fasciectomy and found no difference in terms of functionality between these techniques. These authors reported less total loss of passive extension in open selective fasciectomy.

CONCLUSION

In conclusion, selective fasciectomy is an effective technique to treat Dupuytren's disease. Key factors for higher rates of success and lower rates of complication and recurrence are a good command of anatomy and extreme attention during surgery, as well as efficient rehabilitation in the postoperative period.

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. SA (0000-0003-1028-2120)*, KO (0000-0002-7644-659X)* and AFB (0000-0003-0316-5444)* were main contributors in drafting the manuscript. SA, MB (0000-0002-1020-1207)*, IAO (0000-0002-7672-4270)*, EO (0000-0003-0765-5635)* and KO performed surgeries. SA and AFB followed patients, gathered clinical data and performed the literature search. SA and KO reviewed the manuscript and contributed to the intellectual concept of the study. *ORCID (Open Researcher and Contributor ID).

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ORIGINAL ARTICLE

OSTEOPOROSIS IN BRAZILIAN PATIENTS AWAITING KNEE ARTHROPLASTY

OSTEOPOROSE EM PACIENTES AGUARDANDO ARTROPLASTIA DE JOELHO NA POPULAÇÃO BRASILEIRA

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ABSTRACT

Objective: The primary objective of this study was to determine the prevalence of osteoporosis and osteopenia prior to total knee arthroplasty (TKA) in female patients. As a secondary objective, we evaluated the incidence of hip fractures, types of drugs to treat osteoporosis and serum vitamin D levels. Method: This is a transversal, descriptive and observational study which evaluated 60 women above age 55 prior to total knee replacement. Results: Mean patient age was 71.4 years. Osteoporosis was present in 16.7% of the sample and osteopenia in 15%. In the patients with osteoporosis, femur fracture (20%) was most frequent. Most of the group with osteopenia did not take any medication to treat this condition (55.6%), while most patients with osteoporosis took alendronate (30%) and 30% did not take any medication. Conclusion: The female population awaiting total knee replacement should be considered at risk for osteoporosis, confirming recent findings in the literature. ***Level of Evidence III, Control Case Study.***

Keywords: Osteoporosis. Climacteric. Arthroplasty.

RESUMO

Objetivo: O objetivo primário do estudo foi determinar a prevalência de osteoporose e osteopenia no pré-operatório de artroplastia total de joelho (ATJ) em pacientes do sexo feminino. Como objetivos secundários, avaliamos a incidência de fraturas de fêmur, o uso de medicações para o tratamento da osteoporose e os níveis da 25-OH vitamina D. Método: É um estudo transversal, descritivo e observacional. A amostra foi composta por 60 mulheres com idade acima de 55 anos, no climatério, em pré-operatório de ATJ. Resultados: A média de idade foi de 71,4 anos. A osteoporose estava presente em 16,7% e a osteopenia em 15% da amostra estudada. Entre os pacientes com osteoporose, a fratura de fêmur foi a mais frequente (20%). A maioria do grupo com osteopenia não usava medicação para tratar essa afecção (55,6%), enquanto a maior parte dos pacientes com osteoporose usava alendronato (30%) e 30% não usavam nenhum medicamento. Conclusão: A população do sexo feminino aguardando artroplastia total de joelho deve ser considerada em risco de acometimento pela osteoporose, confirmando dados recentes da literatura. ***Nível de Evidência III, Estudo de Caso Controle.***

Descritores: *Osteoporose. Climatério. Artroplastia.*

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INTRODUCTION

IBGE data from 1994 can be used to estimate that in Brazil there are 2.5 million osteoporotic individuals and 105,000 cases of hip fractures per year, resulting in a cost of approximately 630 million reais.[1]

In a population-based study, Pinheiro et al.[2] demonstrated that smoking was the most important risk factor for osteoporosis in men. For women, the main factors are advanced age, early menopause, higher phosphorus intake, chronic use of benzodiazepines and family history of hip fracture after age 50 (first-degree relatives). Sedentary lifestyle, worsened quality of life and diabetes mellitus (DM) were considered common risk factors in both sexes. A prevalence study reported that higher body mass index (BMI) was associated with lower risk of disease involvement.[1]

Total knee arthroplasty (TKA) is a highly successful operation for treating degenerative changes of the knee such as osteoarthritis and demand for this procedure is growing worldwide due to aging populations and the need to preserve their quality of life.[3,4] According to the National Institutes of Health Consensus, the most common long-term complications are aseptic loosening, pain and functional limitation, progressive bone loss, polyethylene wear and infection.[4] Aseptic loosening leads to nearly half of indications for revision of primary arthroplasties.[5] The cause of this complication is still the focus of much study and the current explanation is

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multifactorial, involving adaptive bone remodeling (stress shielding), micro-movement, high intra-articular pressure and individual susceptibility to microparticles.[6] Furthermore, osteolysis is a factor that contributes to loosening of the implant and in some cases is related to osteoporosis.[7]

Some authors speculate that patients with osteoporosis have increased risk for periprosthetic fractures and consequently loosening of the implant due to the presence of micro-fractures and loss of contiguity in the bone tissue in this group.[4,8]

Domingues et al.[9] found a 20.7% prevalence of osteoporosis and 37.9% for osteopenia in patients awaiting total hip arthroplasty. Additionally, the same study found a high prevalence of inadequate serum vitamin D levels, with only 16.6% of patients demonstrating levels considered normal (>30 ng/ml).

Based on the data above from the current literature, the present study aims to determine the prevalence of osteoporosis in patients undergoing TKA and also compares calcium and vitamin D levels, as well as preoperative densitometry findings. It is extremely important to understand the impact of this disease on women's health, since there are currently no studies in the literature correlating osteoporosis and TKA.

The objectives of the study were to determine the prevalence of osteoporosis prior to TKA in female patients and correlate levels of pain and functional capacity in patients with decreased bone mass in order to assess whether patients with osteoporosis and osteopenia demonstrate clinical profiles comparable to the population with normal bone density levels. The study also aimed to demonstrate if the involvement of osteoporosis had some direct or inverse correlation with the degree of functional limitation and pain prior to surgery.

METHODS

This original study is cross-sectional, descriptive and observational. We assessed 60 patients over 55 years of age prior to TKA; only female patients were selected. Data were collected from july 2015 to february 2016.

This study was approved by the institutional review board under CAAE number 49258815.9.0000.5032. The subjects involved in this study signed a free and informed consent form.

Inclusion criteria were: diagnosis of osteoarthritis of the knee confirmed by radiography, scheduled TKA procedure and consent to participate in the study.

Exclusion criteria were: previous infection, congenital diseases, neoplasms, inflammatory arthritis, secondary osteoporosis, previous orthopedic surgery, hypothyroidism, decompensated DM and use of corticosteroids.

Bone mineral density (BMD) was measured by dual-energy x-ray absorptiometry (DEXA) in the femur and hip of all patients. Only the lower bone mass values were recorded in each component of the sample.

Osteoporosis was defined as a decrease in bone mass of at least 2.5 standard deviations from the mean young adult BMD (T-score < -2.5) and osteopenia was defined in patients with BMD values between -1 and -2.5 standard deviations from the mean peak value in young adults.[2]

A comparison of pain and functional impairment was established between patients with and without osteoporosis to establish correlations between the degree of osteoarthritis and decreased bone mass. Three questionnaires were used: the Western Ontario and McMaster Universities Osteoarthritis index (WOMAC),[10] the Knee Society Score index (KSS),[11] and the Visual Analog Pain Scale (VAS).[12] The questionnaires were applied to all patients preoperatively. The Ahlback classification modified by Keyes et al. apud Galli et al.[13] was used to establish the degree to which the knee joint is compromised in knee osteoarthritis. We also compared fracture involvement in the groups with osteoporosis, osteopenia and no changes in BMD in order to identify patterns that worsen quality of life in these patients.

The angular deviation of the lower limbs (LL) was assessed in all patients via physical examination and panoramic radiography. X-rays of all patients were taken from the front and profile views, as well as an axial view of the patella at 45° knee flexion, in addition to front and profile panoramic radiography; patients were classified as genu varum or genu valgum.

The variables analyzed were age, sex, degree of deformity, comorbidities, lifestyle habits (particularly smoking and alcoholism), serum level of 25-OH-D, ionic calcium, presence of osteoporosis and osteopenia according to BMD, use of medications to treat osteoporosis/osteopenia, hormone replacement therapy, vitamin D or calcium supplementation, BMI and previous fractures.

The statistical analysis was conducted using Excel 2003 (Microsoft Corporation, Redmond, WA, USA) and SPSS 20.0 (IBM, New York, NY, USA) software. The tests were performed at a 5% significance level. The qualitative characteristics were described using absolute and relative frequencies and the quantitative measures were described in summary measures (mean, standard deviation, minimum and maximum). The quantitative characteristics were described according to the presence of osteoporosis and compared between patients with and without osteoporosis using Mann-Whitney tests.

RESULTS

Table 1 describes the sample studied. The average age was 71.4 years with standard deviation (SD) of 6.9, minimum of 58 years and maximum of 85.

Mean ionic calcium was 4.85 with SD of 0.31; mean vitamin D (25-OH-cholecalciferol) was 32 with SD of 7.12. Four patients were smokers and five used alcohol. Table 1 shows the comorbidities found in each patient through the pre-procedure diagnostic questionnaire, medical records and physical examination. Hypertension was most frequent (35%), followed by DM (18.3%), hypothyroidism (10%) and dyslipidemia (10%). No other clinically relevant comorbidities were reported by the patients.

Table 2 below shows the presence of alterations in BMD. Osteoporosis was present in 10 of the individuals surveyed (16.7%) and osteopenia in 9 (15%).

Angular deviation in the lower limbs (genus valgum, genus varum) was compared in patients with osteopenia, osteoporosis, or without BMD changes. Genus valgum was detected in 70% of patients with osteoporosis and 55.6% of patients with osteopenia. Genus varum was the most common change (61%) in patients without changes in the BMD.

We also evaluated the BMI of patients in each group based on changes in BMD (osteoporosis, osteopenia and no bone changes). The group classified as having osteoporosis had a mean BMI of 27.3 (SD 2.9), the osteopenia group had mean BMI of 27.44 (SD 3.6) and the group with no changes in the densitometry had a mean BMI of 27.15 (SD 3.0).

Table 3 contrasts the bone density classification and fracture history of the patients. We can see that the group with osteoporosis had the most fractures, most frequently femur fracture (20%).

Table 4 shows the use of biphosphonates for prevention and/or treatment and also divides patients by osteoporosis, osteopenia and no bone alterations. Most of the osteopenia group did not use any anti-resorption medication (55.6%), while most of the patients with osteoporosis used alendronate or no medication (30%).

Table 5 describes pain levels according to VAS[12] and functional capacity according to KSS[14] and WOMAC[10] in patients with

osteoporosis, osteopenia and no bone changes. Note that there was no statistically significant difference for any scale in the preoperative period and that 100% of the evaluated patients with osteoporosis showed insufficient levels of 25-OH-cholecalciferol (reference value: <30 ng/mL).

Table 1. Description of the sample.

Variable	N=60 (%)	Mean SD (min–max)
Age (years)		71.4 ± 6.9 (58–85)
Ionic calcium		4.85 ± 0.31 (4.2–5.5)
Vitamin D (25-OH-cholecalciferol)		32 ± 7.12 (22–43)
Lifestyle factors		
Tobacco user	4 (6.7)	
Alcohol user	5 (8.3)	
Non-user of tobacco or alcohol	51 (85)	
Comorbidities		
High blood pressure	21 (35)	
Hypothyroidism	6 (10)	
Diabetes mellitus	11 (18.3)	
Dyslipidemia	6 (10)	
Heart failure	1 (1.7)	
History of breast cancer	1 (1.7)	
No comorbidities	26 (43.33)	

Table 2. Changes in bone density in the sample.

Changes in bone density	N (%)
Osteoporosis	10 (16.7)
Osteopenia	9 (15)
Normal	41 (68.3)

Table 3. History of fractures in each group.

Fracture	Group of patients according to changes in bone densitometry (mean SD)			*p** (95% CI)
	Osteoporosis n=10	Osteopenia n=9	No bone changes n=41	
Spinal fractures (due to osteoporosis)	1 (10)	1 (11.1)	0	0.803 (0.796-0.811)
Fracture of proximal femur	2 (20)	0	1 (2.4)	
Fracture of distal radius	1 (10)	0	0	
No fractures	6 (60)	8 (88.9)	40 (97.6)	

*Pearson's chi-squared test with statistical significance if *p* is less than 0.05.

Table 4. Medications used in each group.

Variable	Group of patients according to changes in bone densitometry (%)		
	Osteoporosis n=10	Osteopenia n=9	Normal BMD n = 41
Medication for osteoporosis			
None	3 (30)	5 (55.6)	41 (100)
Risedronate	2 (20)	2 (22.2)	0
Alendronate	3 (30)	1 (11.1)	0
Ibandronate	0	1 (11.1)	0
Zoledronic acid	2 (20)	0	0
Denosumab	0	0	0
Teriparatide	0	0	0
Hormone replacement	0	3 (33.3)	0
Vitamin D replacement	7 (70)	6 (66.7)	0

Table 5. Comparative analysis of patients with osteoporosis, osteopenia and normal patients according to VAS, KSS and WOMAC scores*

	Group of patients according to changes in bone densitometry (mean SD)			*P** (95% CI)
	Osteoporosis n= 10	Osteopenia n= 9	No bone changes n=41	
Visual Analog Scale				
Preoperative	8.2 ± 0.79	7.8 ± 0.9	7.8 ± 0.6	0.346 (0.337-0.355)
Knee society score				
Preoperative	44.1 ± 5.67	39.8 ± 5.3	42.6 ± 6.5	0.273 (0.265/0.282)
WOMAC score				
Preoperative	60.4 ± 7.15	59.7 ± 7.0	62.2 ± 7.7	0.356 (0.346/0.365)

*VAS = Visual Analog Pain Scale, Knee Society Score, Western Ontario and McMaster Universities osteoarthritis index. *Kruskal-Wallis test with statistical significance if *p* is less than 0.05.

DISCUSSION

This is the first prevalence study that establishes a correlation between osteoporosis and TKA. Patients with osteoarthritis who need joint replacement are predominantly elderly women, a population with a high risk of developing osteoporosis,[15] which justifies the selection of only women for this study. The selected age range coincides with menopause.

In this study we found that 31.7% of patients had decreases in bone mass and 16.7% had a confirmed diagnosis of osteoporosis from BMD and 15% had osteopenia. This value can be considered low in comparison with the study conducted by Pinheiro et al.[2] on a sample of 4,332 patients in the metropolitan region of São Paulo, in which 33% of postmenopausal women showed osteoporosis of the lumbar spine or femur. Faisal-Cury and Zacchello[1] found a 32.7% prevalence of osteoporosis in a group of 999 women above 49 years of age. We can therefore speculate that the difference between the results obtained may derive from differences in sample size.

Bisphosphonates are analogous to pyrophosphates and have an anti-resorptive action; they are among the most common therapeutic options for treating osteoporosis[16] in order to prevent the occurrence

of fractures. We found that 30% of patients with osteoporosis and 55.6% of patients with osteopenia were not taking bisphosphonate medication prior to the assessment. There was no statistically significant difference between the BMI of patients with osteoporosis, osteopenia and those with no changes in bone mass. The scores for the VAS,[12] KSS,[11] and WOMAC[10] did not demonstrate a statistically significant difference between patients with and without osteoporosis. Smoking has been established in the literature as a risk factor for osteoporosis. Only 6.7% of the population studied were smokers, but 80% of the patients who smoked had osteoporosis.[17]

Hormone replacement therapy is recommended for postmenopausal patients as the best way of preventing osteoporotic fractures, especially in the first years after last menstruation, although it should be used cautiously because of the increased risk of embolism and breast cancer.[15] Based on this information, this study found that 33.3% of patients with osteopenia and no patients with unaltered bone mineral densitometry results used hormone replacement therapy. This finding may show insufficient monitoring for this disease in this group of women.

Calcitriol (1.25-dihidroxicolecalciferol) is the active form of vitamin D and plays a prominent role in bone metabolism, contributing to intestinal absorption of calcium and inhibiting resorption of the bone matrix.[18] According to Glowacki et al.[19] one of the most important factors contributing to its activation is exposure to sunlight. Serum values between 20-29 ng/mL indicate insufficient vitamin D, while levels below 20 ng/mL indicate an established deficiency of the hormone.[20] A significant difference was seen in vitamin D levels among the groups with osteoporosis or osteopenia and no changes in bone mass. All patients diagnosed with osteoporosis showed insufficient levels, which indicates the significant influence this hormone deficiency plays in the presentation of the disease.

One limitation of this study was the inclusion of the entire sample which fit the inclusion criteria, creating a convenience sample. A second limitation was the lack of a control group with patients without osteoarthritis matched for age and sex. The BMD only evaluated the hip and lumbar spine because these regions are most commonly included in assessment of the disease. Because this was a prevalence study, it was not possible to establish a causal relationship between exposure factors and outcomes.

The female population scheduled for TKA should receive special attention during the preoperative period since this group is notably susceptible to osteoporosis, in order to prevent complications such as osteoporotic and periprosthetic fractures and infection, which may lead to early loosening of the implant. We can infer that osteoarthritis does not appear to protect against osteoporosis, according to the same findings demonstrated by Domingues et al.[9] if special attention is given to diagnosis in this group of patients and appropriate treatment is established.

CONCLUSION

The prevalence of osteoporosis in the group studied was 16.7%, while the prevalence of osteopenia was 15%. The female population waiting for TKA should be considered at risk for involvement of osteoporosis in the studied population. The data we found resemble those found in the international literature.

No statistically significant difference was observed between pain levels and functional capacity among groups with osteoporosis, osteopenia, or with normal levels of bone mineral density.

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. RLT (0000-0002-5709-2714)* and AYN (0000-0002-6451-8488)* were the main contributors in writing the article. RLT, AYN, RRB (0000-0001-9581-3239)* and LP (0000-0001-9914-4327)* performed the surgery, followed the patients and gathered clinical data. RLT, AYN, MAPV (0000-0003-3675-4966)* and ETD (0000-0001-6735-1401)* evaluated the data from the statistical analysis. RLT, AYN, LP, RRB, ETD and MAPV performed the bibliographic research, reviewed the manuscript and contributed to the study's intellectual concept. *ORCID (Open Researcher and Contributor ID).

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ORIGINAL ARTICLE

SHOULDER DISORDERS IN AN OUTPATIENT CLINIC: AN EPIDEMIOLOGICAL STUDY

AFECÇÕES DO OMBRO EM AMBULATÓRIO ESPECIALIZADO: UM ESTUDO EPIDEMIOLÓGICO

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ABSTRACT

Objective: To describe shoulder disorders in patients evaluated by two shoulder and elbow surgeons. Methods: This cross-sectional study analyzed patients evaluated by two authors, excluding acute fractures and dislocations and patients with symptoms not involving the shoulder. Age and sex distribution was determined for the different diagnoses. Results: We evaluated 1001 patients. Mean age was 51.43±15.15 years and 51.0% were female. Disorders of the rotator cuff occurred in 64.3% (41.2% tendinopathy, 11.0% partial tears and 12.2% full-thickness tears). Adhesive capsulitis occurred in 13.5% of cases and glenohumeral instability in 8.1%. Rotator cuff disorders were more common in women, with a peak between 50 and 59 years for tendinopathy and partial tears and between 60 and 69 years for full-thickness tears. Glenohumeral instability was more frequent in men, with a peak between 30 and 39 years. Conclusion: The most frequent diagnosis was rotator cuff tendinopathy, followed by adhesive capsulitis, full-thickness rotator cuff tears, partial rotator cuff tears and glenohumeral instability. Rotator cuff lesions were more common in women, with a peak between 60 and 69 years for full-thickness tears. ***Level of Evidence IV, Case Series.***

Keywords: Shoulder. Prevalence. Diagnosis. Rotator cuff.

RESUMO

Objetivo: Descrever as afecções do ombro atendidas por dois membros da Sociedade Brasileira de Ombro e Cotovelo. Métodos: Estudo transversal que avaliou atendimentos de dois dos autores. Excluímos fraturas e luxações agudas e pacientes com sintomatologia que não envolvia o ombro. A distribuição etária e por sexo foi determinada para os diferentes diagnósticos. Resultados: Avaliamos 1001 pacientes. A idade foi de 51,43 ± 15,15 anos e 51,0% eram do sexo feminino. As afecções do manguito rotador ocorreram em 64,3%, sendo 41,2% de tendinopatia, 11,0% de rotura parcial e 12,2% de rotura completa. A capsulite adesiva ocorreu em 13,5% e instabilidade glenoumeral em 8,1%. As afecções do manguito rotador foram mais frequentes em mulheres, com pico entre 50 e 59 anos para tendinopatia e rotura parcial, e entre 60 e 69 anos para rotura completa. A instabilidade glenoumeral foi mais frequente em homens, com pico entre 30 e 39 anos. Conclusão: Os diagnósticos mais frequentes foram tendinopatia do manguito rotador, seguido de capsulite adesiva, rotura completa do manguito rotador, rotura parcial do manguito rotador e instabilidade glenoumeral. As afecções do manguito rotador foram mais frequentes em mulheres, com pico entre 60 e 69 anos para rotura completa. ***Nível de Evidência IV, Série de Casos.***

Descritores: *Ombro. Prevalência. Diagnóstico. Bainha rotadora.*

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INTRODUCTION

Shoulder complaints are frequent in the population, with an annual incidence of 14.7/1000[1] and prevalence of 7 to 14%[2-4] which rises to 67% in older people.[5] Few studies have epidemiologically assessed patients with shoulder pain and described the main diagnostics.[1,6-10] The most frequent causes of shoulder pain are tendinopathy of the rotator cuff and adhesive capsulitis.[8-10] To our knowledge, no studies have examined the epidemiology of the main shoulder complaints in Brazil. Establishing the national panorama is useful for stimulating public education policies, alerting doctors about the problems that most affect the population and helping define plans for prevention and treatment.

The objective of this study is to describe the various shoulder disorders treated in outpatients by two Brazilian shoulder and elbow surgeons, as well as to present the distribution of the main diagnoses by sex and age.

METHODS

This cross-sectional study was conducted using data from patients treated by the two main authors (EAM and MECG). These

All authors declare no potential conflict of interest related to this article.

Study conducted at the Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Instituto de Ortopedia e Traumatologia, Shoulder and Elbow Group, São Paulo, SP, Brazil.
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researchers have 10 and 9 years of experience, respectively, in shoulder and elbow surgery. This study was approved by the institutional review board under process number 1195.
All individuals attended between July 1, 2015 and May 25, 2016 were included. Patients with acute fractures and dislocations were excluded, as well as those with symptoms which did not involve the shoulder. MRI or X-rays in conjunction with ultrasound were taken in all patients.

Assessment methods

The database was constructed using FileMaker (FileMaker Incorporated, Santa Clara, CA, USA). This tool was used to create a spreadsheet in Excel (Microsoft Corporation, Redmond, WA, USA) containing data for age, sex and diagnosis. Age was recorded in years completed at the time of the first treatment and categorized into 10-year intervals. Diagnosis was classified as: tendinopathy of the rotator cuff, partial tear of the rotator cuff, complete tear of the rotator cuff, adhesive capsulitis, calcific tendonitis, glenohumeral instability, SLAP lesion (superior labrum anterior to posterior), glenohumeral osteoarthritis, acromioclavicular osteoarthritis, scapular dyskinesia, chronic acromioclavicular dislocation and other. The "other" category included those diagnoses which occurred in less than 0.5% of the sample. For cases with more than one diagnosis, the patient's electronic record was reviewed and only the most clinically significant diagnosis was considered. Distribution by age and by sex was determined for the most frequent diagnoses.

Statistical analysis

The data are presented in a descriptive manner with absolute numbers and percentages. The general characteristics of the sample for age, sex and comorbidities were presented as means and standard deviation for continuous data and total amount and percentages for categorical data. Calculation was performed using SPSS 21.0 software (Chicago, IL, USA).

RESULTS

We evaluated the medical records of 1338 patients. Of these, we excluded 64 with shoulder fractures, 33 with elbow fractures, 15 with acute acromioclavicular or sternoclavicular dislocation, 159 with orthopedic disorders of the elbow and 66 for orthopedic disorders in other sites, leaving 1001 patients with shoulder disorders.
Mean patient age for the sample was 51.43±15.15 years and 511 patients (51.0%) were female. The youngest patient was 10 years old and the oldest was 98.
Rotator cuff disorders accounted for 64.3% of cases, tendinopathy accounted for 41.2%, 11.0% were partial tears and 12.2% were complete tears. Adhesive capsulitis occurred in 13.5% of cases and glenohumeral instability in 8.1%. The distribution of shoulder disorders is shown in Table 1.
Rotator cuff disorders were more frequent in women, with tendinopathy and partial tears peaking between 50 and 59 years and complete tears peaking between 60 and 69 years. Adhesive capsulitis and calcific tendonitis were also more frequent in female patients, with the former peaking between 50 and 59 years and the latter between 40 and 49 years. Shoulder instability and SLAP lesion prevailed in young men, peaking between 30 and 39 years. Glenohumeral arthritis occurred mainly after 50 years of age and involved more females. Distribution of cases by the various age groups and by sex for each of the main diagnoses is presented in Figure 1.

DISCUSSION

Our results show that rotator cuff disorders were present in 64.1% of the sample, with 41.2% tendinopathy, 11.0% partial tears and

Table 1. Absolute and percentage distribution of diagnoses affecting the shoulder.

Diagnosis	n	%
Rotator cuff	644	64.3
Rotator cuff tendinopathy	412	41.2
Partial rotator cuff tear	110	11
Complete rotator cuff tear	122	12.2
Adhesive capsulitis	135	13.5
Shoulder instability	81	8.1
Calcific tendonitis	36	3.6
SLAP lesion	32	3.2
Glenohumeral arthrosis	22	2.2
Acromioclavicular joint arthrosis	14	1.4
Scapular dyskinesia	14	1.4
Chronic acromioclavicular dislocation	8	0.8
Others	15	1.5
Total	**1001**	**100**

SLAP: superior labrum anterior to posterior.

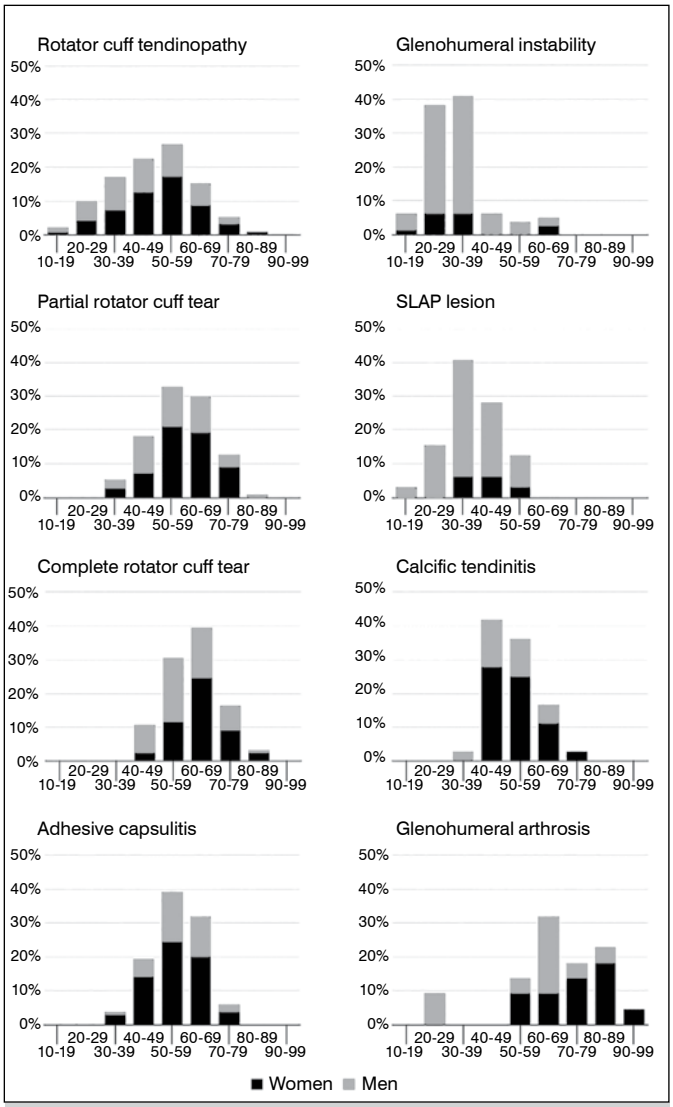

Figure 1. Percentage distribution of main diagnoses by decade of life and sex.

12.2% complete tears. Rotator cuff tendinopathy, the most frequent diagnosis in our sample, was also the most prevalent diagnosis in studies by Juel and Natvig[8] and Ostör et al.,[10] while Walker-Bone et al.[9] reported that the most frequent disorder was adhesive capsulitis. Tendinopathy and partial tear peaked at 50-59 years; tendinopathy presented a wider distribution, while partial tear was only observed after 30 years of age. Complete rotator cuff tear was most prevalent between 60 and 69 years and occurred only after 40 years of age. These findings are consistent with the progressive nature of rotator cuff injuries and the fact that complete tears increase in prevalence with age.[11] Rotator cuff disorders were more common in women, except for tendinopathy in the 20 to 39 year age group, partial tears in the 40 to 49 year group and complete tears in the 40 to 59 year group. Juel and Natvig[8] also found greater involvement in women, but more men had complete tears between ages 50 and 59. We believe that this may be at least partly explained by a greater number of men performing manual labor. Our data, however, do not allow us to draw this conclusion.

Adhesive capsulitis was present in 13.5% of patients, the second most frequent diagnosis. As with the findings by Juel and Natvig,[8] this diagnosis predominated in women and peaked between 50 and 59 years of age. It did not occur under age 30 or above age 80. Similar frequency has been reported by other authors, with a variation of 11 to 16%.[8,10] The fifth most frequent diagnosis was glenohumeral instability, occurring in 8.1% of the sample. As Juel and Natvig also found,[8] this diagnosis was predominant in young men. Our study showed that calcific tendonitis involved 3.6% of the sample and was prevalent in women 40 to 59 years old. The other studies did not individualize this diagnosis and probably included patients with this diagnosis in within rotator cuff tendinopathy or other disorders.[1,8-10] SLAP lesions caused symptoms in 3.2% of our series and also were not separated by the other authors.[1,8-10] Juel and Natvig[8] studied labral lesions and glenohumeral instability together, while the other studies did not describe this diagnosis.[1,9,10] We noted that this disease and glenohumeral instability were more prevalent in young men. Glenohumeral osteoarthritis was seen in 2.2% of the patients we studied, 4% lower than the number described by Juel and Natvig.[8] The other studies do not describe this condition in detail.[1,9,10] With the exception of 2 patients, our data demonstrate that this condition predominantly affects women after age 50, peaking between 60 and 69 years. Juel and Natvig[8] found all cases of this condition after age 40 years and a peak after age 70. We emphasize that glenohumeral osteoarthritis represents 37.5% (6/16) of the diagnoses in patients aged 80 or older. The two young patients with glenohumeral osteoarthritis in our series had a specific diagnosis of arthropathy secondary to juvenile rheumatoid arthritis and septic arthritis.

We chose to present the main diagnosis in cases with more than one disease. The purpose of this methodology was to facilitate data analysis and understanding. A similar methodology has been used by other authors[8,9] and may affect some results, especially for acromioclavicular osteoarthritis, joint degeneration that which affects up to 82% of asymptomatic individuals.[12] However, we chose to highlight clinical findings over changes in imaging. Unlike Juel and Natvig[8] but like other authors,[9,10] we chose not to consider myalgia a diagnosis in itself. We believe that myalgia is more of a symptom than a specific diagnosis[8] and that it may present concurrently with other disorders.

This study has limitations. We did not include cases of acute fractures and dislocations; we opted to exclude these patients because these injuries are generally treated in the emergency unit. Consequently, only less serious cases come to the outpatient clinic, along with those that do not remain hospitalized for surgical treatment. While this sample may not be statistically representative of the entire national population, it is larger than the majority of similar studies.[1,8,10] Additionally, the patients were seen in a private practice by specialists, so this data may not be generalized to patients in the Brazilian Unified Health System and to general orthopedists, decreasing external validity. However, we emphasize that all patients were personally assessed by one of the main authors (EAM and MECG), who are surgeons with ample experience diagnosing these disorders and imagery was confirmed via MRI or a combination of x-ray and ultrasound. These characteristics increase the internal validity of the data.

CONCLUSIONS

The most common diagnoses in the specialist clinic were tendinopathy of the rotator cuff (41.2%), adhesive capsulitis (13.5%), complete rotator cuff tear (12.2%), partial rotator cuff tear (11.0%) and glenohumeral instability (8.1%). Rotator cuff disorders were more frequent in women, with tendinopathy and partial tears peaking between 50 and 59 years and complete tears peaking between 60 and 69 years. Adhesive capsulitis was more frequent in female patients, peaking between 50 and 59 years old, while glenohumeral instability was more frequent in men and peaked between 30 and 39 years of age.

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. EAM (0000-0003-1956-6445)* and MECG (0000-0002-0214-9576)* attended the patients included in the study. EAM, JHA, (0000-0002-2566-3471)* and MECG wrote the manuscript, analyzed the data and designed the study. AZFS (0000-0002-3289-7479)* and GMRP (0000-0002-4079-3100)* carried out the bibliographic review and analyzed the medical records. AAFN (0000-0001-5097-9542)* reviewed and approved the final version of the manuscript. *ORCID (Open Researcher and Contributor ID).

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SURGICAL TREATMENT OF ACROMIOCLAVICULAR DISLOCATION USING THE ENDOBUTTON

TRATAMENTO CIRÚRGICO DA LUXAÇÃO ACROMIOCLAVICULAR COM O USO DE ENDOBUTTON

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ABSTRACT

Objective: To evaluate the clinical and radiographic results of 23 patients diagnosed with acute type III acromioclavicular dislocation treated with the Endobutton. Methods: Twenty-three patients with a diagnosis of type III acromioclavicular dislocation were treated surgically. Results: Twenty-one patients were male (91.3%) and 2 (8.7%) were female. The dominant side was affected in 15 patients (65.21%) and the non-dominant side in 8 patients (34.79%). All patients were operated on by the same surgical team within 4 weeks of the trauma. According to the UCLA score, 14 patients (60.86%) presented excellent results, 7 patients (30.43%) had good results and 2 patients (8.69%) had regular results. Conclusion: The technique was effective in treating acute type III dislocations with a high degree of patient satisfaction. ***Level of Evidence IV, Case Series.***

Keywords: Acromioclavicular joint/diagnostic imaging. Acromioclavicular joint/surgery. Ligaments, articular. Orthopedic procedures/methods. Evaluation studies.

RESUMO

Objetivo: Avaliar os resultados clínicos e radiográficos de 23 pacientes com diagnóstico de luxação acromioclavicular aguda tipo III tratados com uso de placa Endobutton. Métodos: Foram submetidos a tratamento cirúrgico 23 pacientes com diagnóstico LAC III. Resultados: O sexo masculino foi prevalente, sendo 21 (91,3%) homens e duas (8,7%) mulheres. O lado dominante foi acometido em 15 pacientes (65,21%) e o não dominante, em oito pacientes (34,79%). Todos os pacientes foram operados pela mesma equipe cirúrgica em até quatro semanas da data do trauma. Pelo escore da UCLA: 14 pacientes (60,86%) apresentaram excelentes resultados, sete pacientes (30,43%), bons resultados e em dois pacientes (8,69%) os resultados foram regulares. Conclusão: A técnica mostrou-se efetiva no tratamento das luxações agudas de grau III, com elevado grau de satisfação dos pacientes. ***Nível de Evidência IV, Série de Casos.***

Descritores*: Articulação acromioclavicular/diagnóstico por imagem. Articulação acromioclavicular/cirurgia. Ligamentos articulares. Procedimentos ortopédicos/métodos. Estudos de avaliação.*

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INTRODUCTION

Dislocation of the acromioclavicular joint (ACJ) is a common injury[1] responsible for 9% of all shoulder injuries,[2] and is one of the oldest traumatic pathologies recorded in the literature. It is 10 times more common in males[3] from 20 to 39 years of age[4] and predominant in young people since it is associated with high-impact sports and high-speed vehicle accidents.[5,6]

The Rockwood classification[7] is most commonly used to describe the degree of injury, which was initially described by Tossy et al.,[8] who divided acromioclavicular dislocations into three types: types I and II are light to moderate and are treated conservatively, while type III is severe and involves an offset of at least 1 cm or larger than the thickness of the clavicle, requiring surgical treatment. The Rockwood classification[7] modified type III and added the types IV, V and VI to Tossy's classification.

After a traumatic episode, diagnosis is made clinically and using x-rays. The clinical examination is characterized by the presence of sharp pain in the upper portion of the shoulder, algic limitation, edema, bruising, deformity and piano key sign (clavicle is reduced by pressing downward on the deformed area like pushing down a piano key, a sign present in most type III and V ACJ dislocations). Characteristic radiographic findings seen in the AP view (or in the Zanca view for better definition of the ACJ) permit the vertical stability of the ACJ to be assessed and the axillary view permits assessment of the horizontal stability of the ACJ.

ACJ dislocation has been a subject of controversy since the time of Hippocrates (460-377 BC). Treatment of Rockwood

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types I and II initially do not involve surgery;[9] treatment of type III remains controversial and may be approached using the criteria by Copeland:[10]

- Conditions in favor of: young, slim, athletic patient, manual laborer, dominant side, joint cannot be reduced.
- Conditions against surgery: elderly, obese, sedentary patient, non-manual laborer, non-dominant side, reducible joint and little apparent deformity.

Types IV, V and VI require surgical treatment.[11] The techniques may involve the use of wires, transfer of the coracoacromial ligament, fixing the coracoacromial interval with a screw, suture anchors, or suture loops, reconstruction of the acromioclavicular and coracoclavicular ligaments and using the Endobutton and may be conducted in open or minimally invasive procedures or use arthroscopy.

The open approach is most common; its advantages include direct visualization of the ACJ, the possibility to remove any degenerative material from the disk, precise identification of the origins of the coracoclavicular ligaments and shorter surgical time. Disadvantages include a more prominent scar and aggression to the insertion of the deltoid muscle.[12,13]

The objective of this study was to evaluate the clinical and radiographic results of 23 patients diagnosed with acute Rockwell type III ACJ dislocation who were treated with coracoclavicular fixation using two anchors and an Endobutton using the open approach.

MATERIALS AND METHODS

This study was approved by the institutional review board under process number 1717404. All patients participating in the study signed the terms of free and informed consent. From June 2013 to March 2015 23 patients underwent surgical treatment for ACJ dislocation. Mean patient age was 31.04 years (minimum 19 years; maximum 45 years). Males were more prevalent, with 21 patients (91.3%) compared with 2 (8.7%) females. The dominant side was affected in 15 patients (65.21%) and the non-dominant side in 8 patients (34.79%). All patients were operated by the same surgical team until 4 weeks of the date of the trauma. Minimum follow-up was 6 months.

The study included patients with clinical and radiographic diagnosis of Rockwood type III ACJ dislocation with evolution of up to 4 weeks (average of 8 days). (Figure 1) Exclusion criteria were patients with osteoarthritis in the ACJ and injuries which occurred more than 4 weeks prior.

Rockwood Classification:

Type I: sprain of the AC ligaments (35% of cases) – x-ray shows no alterations.

Type II: rupture of the acromioclavicular ligaments and sprain of the coracoclavicular ligaments (22% of cases) – x-ray shows <25% increase in acromioclavicular space.

Type III: rupture of the acromioclavicular and coracoclavicular ligaments (39% of cases) – x-ray shows 25-100% increase in acromioclavicular space.

Type IV: rupture of acromioclavicular ligaments – x-ray may show normal coracoclavicular space with posterior dislocation of the clavicle.

Type V: rupture of the acromioclavicular and coracoclavicular ligaments, desinsertion of the trapezoid and deltoid muscles in the distal half of the clavicle – x-ray shows a 100–300% increase in acromioclavicular space.

Type VI: rupture of acromioclavicular ligaments with inferior dislocation of the clavicle – x-ray shows inferior dislocation of the clavicle.

Tables 1, 2 and 3 present the distribution of the operated patients according to age, sex and affected side, respectively.

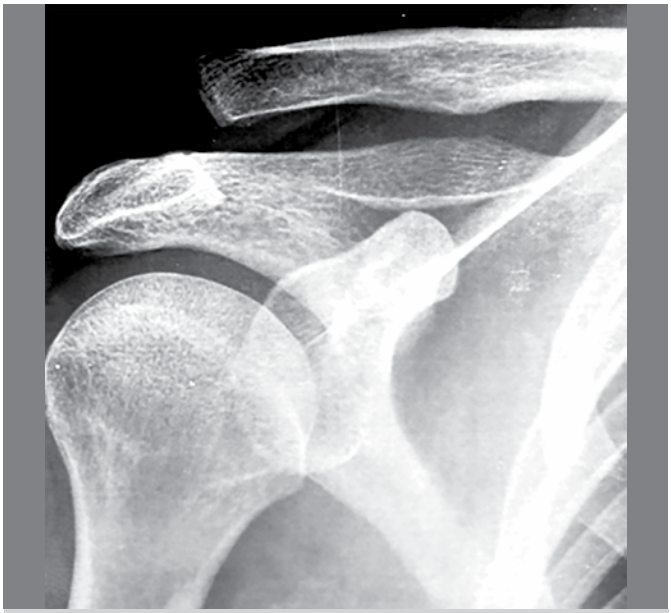

Figure 1. X-ray, AP view of right shoulder.

Table 1. Patient age, highlighting youngest, oldest and mean.

Patient age	
Age	**Years**
Youngest	19
Oldest	45
Mean	31.04

Table 2. Patient distribution according to sex.

Sex distribution		
Limb	Frequency	%
Male	21	91.3
Female	2	8.7

Table 3. Patient distribution according to side affected.

Distribution, side affected		
Limb	**Frequency**	**%**
Dominant	15	65.21
Non-dominant	8	34.79

UCLA Criteria for clinical evaluation. (Chart 1)

Surgical technique: The patient is placed in "beach chair" position under general anesthesia and brachial plexus block is applied. Access occurs through an incision (about 3 cm) made topographically along the anterior edge of the clavicle (5 mm medial to the acromioclavicular joint) to the top edge of the coracoid process. The deltotrapezoidal fascia is opened and the deltoid detached to visualize the acromioclavicular joint and coracoid process. Two anchors are fixed at the base of the coracoid process. A downward hole is made in the clavicle using a 2.5 mm drill 3 cm medial to the acromioclavicular joint and equidistant between the anterior and posterior edges of the clavicle. The anchor wires are individually passed through the hole in the clavicle from bottom to top, using No. 1 Aciflex wire. After reduction of the ACJ, the Endobutton (composed of 4 holes) is placed on the hole and the lateral anchor wires are passed through the 1st and 3rd holes (hole

order increases from lateral to medial), while the more medial anchor wires are passed through the 2nd and 4th holes The tie-off is made separately from the anchor wires and reinsertion of the deltotrapezoidal muscles uses the anchor wires which are already attached. Intraoperative arthroscopy is conducted to visualize the reduction and x-rays are taken after the procedure. (Figure 2)
Patients are immobilized using a Velpeau sling for 4 weeks with immediate release of active flexion-extension of the elbow, wrist and hand. Radiographic evaluation includes the anteroposterior, axillary and shoulder profile views to assess the comparative coracoclavicular distance and is conducted weekly during the first month and monthly until the sixth month.

Chart 1. Scoring results according to UCLA.

Pain	
Present all the time, unbearable, frequent use of strong painkillers	1
Present all the time, unbearable, occasional use of strong painkillers	2
Weak/absent at rest, present during light activity, frequent use of salicylates	4
Present during heavy/specific activities, frequent use of salicylates	6
Occasional and weak	8
Absent	10
Function	
Unable to use the limb	1
Only light activities possible	2
Able/activities at home/activities of daily living	4
Activities at home/shopping/driving/combing hair/ dressing/put on clothing that closes in the back	6
Mild restriction/able to work above shoulder level	8
Normal activities	10
Active flexion	
150 degrees or more	5
120 to 150 degrees	4
90 to 120 degrees	3
45 to 90 degrees	2
30 to 45 degrees	1
Less than 30 degrees	0
Anterior flexion strength (manual muscle test)	
Grade 5 (normal)	5
Grade 4 (good)	4
Grade 3 (average)	3
Grade 2 (weak)	2
Grade 1 (muscle contractions)	1
Grade 0 (absent)	0
Patient satisfaction	
Satisfied and better	5
Unsatisfied and worse	0
Maximum score: 35 points	
Ellmann Score (UCLA)	
34-35	Excellent
28-33	Good
21-27	Reasonable
00-20	Poor

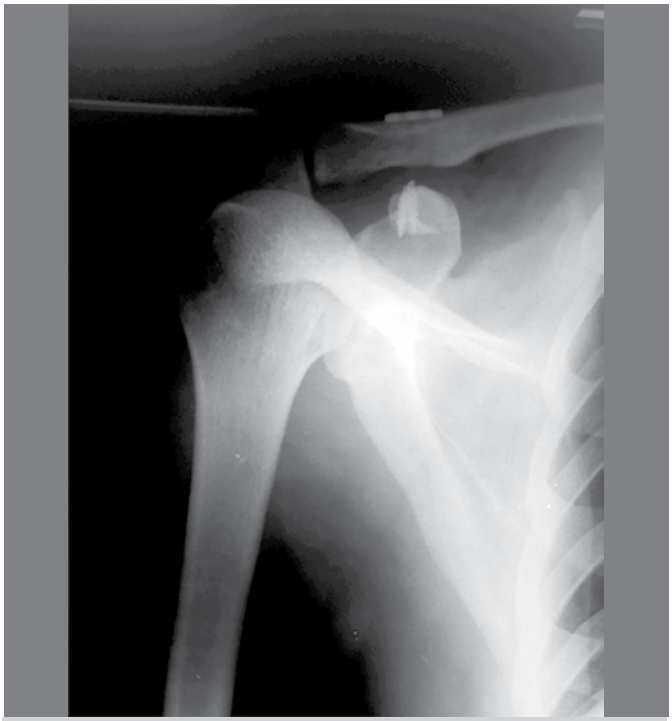

Figure 2. X-ray, post-procedure.

RESULTS

According to UCLA score and Elmann criteria: 14 patients (60.86%) presented excellent results, 7 patients (30.43%) had good results and in 2 patients (8.69%) results were reasonable. All patients reported satisfaction with the treatment.
The patients were evaluated after 6 months. Five patients (21.73%) experienced less than 30% loss of reduction, but without functional impairment. In one patient (4.3%) there was superficial infection of the surgical wound, with resolution in 7 days.

DISCUSSION

The ideal method for treating type III ACJ dislocation remains controversial in the literature. There are several surgical techniques and preferences described for treating the acromioclavicular joint.[14] Fixation with Kirschner wires is not used often at present because of high rates of complications such as breakage and material migration, infection, arthritis and loss of reduction.[15]
The coracoacromial ligament transfer described in 1972 by Weaver and Dunn consists of deinsertion of the coracoacromial ligament from the acromium and transposing it into the intramedullary region of the distal portion of the clavicle. However, a complication of this technique is loss of joint reduction.[16]
The Bosworth technique uses a screw to affix the clavicle to the coracoid process. Although it is effective and restores the reduction of the ACJ, the screw may break or loosen or the coracoid process may fracture, requiring a new procedure to remove the material and presenting high rates of osteolysis in the clavicle.[17] The subcoracoid ties with high-strength wires can cause bone erosion and anterior subluxation of the clavicle.[18]
Some authors performed arthroscopic reconstruction of the coracoclavicular ligament. The use of autologous semitendinous graft or synthetic suture[19] has the advantage of preserving the deltoid insertion and this method also permits treatment of associated injuries and uses a minimally invasive route.

The use of fixation anchors on the coracoid process reduces the risk of neurovascular injury and decreases surgical time in comparison with the subcoracoid knot and avoids displacement of this tie-off to the anterior portion of the coracoid.[20]

The technique of stabilization between the clavicle and the coracoid process using the Endobutton or anchors has been described by various authors[20] with satisfactory results. Its advantages include the fact that it is not necessary to remove synthetic material and it has been shown to be effective in restoring and maintaining the reduction of the ACJ. Complications include the cut-out of the suture, foreign body reaction (observed mainly when polytetrafluoroethylene suture is used) and potential osteolysis in the clavicle.

In our study, the technique permitted a small open approach with relatively short surgical time. The use of anchors allowed fixation at the base of the coracoid process in the region where the conoid ligament is inserted. The Endobutton was effective because there is no need to remove it; to avoid the shear effect of the wires with consequent failure of the synthesis resulting from passing through a single bone tunnel, they are tied over the Endobutton so that the knot does not come into contact with the clavicle.

The degree of satisfaction (excellent and good) among patients who underwent the Endobutton procedure in our study was 91%.

CONCLUSION

The technique proved to be effective in treating acute ACJ dislocations (Rockwood type III) with a high degree of patient satisfaction.

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. RLT (0000-0002-5709-2714)* and AYN (0000-0002-6451-8488)* were the main contributors in writing the article. RLT, AYN, RRB (0000-0001-9581-3239)* and LP (0000-0001-9914-4327)* performed the surgery, followed the patients and gathered clinical data. RLT, AYN, MAPV (0000-0003-3675-4966)* and ETD (0000-0001-6735-1401)* evaluated the data from the statistical analysis. RLT, AYN, LP, RRB, ETD and MAPV performed the bibliographic research, reviewed the manuscript and contributed to the study's intellectual concept. *ORCID (Open Researcher and Contributor ID).

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ADOLESCENT IDIOPATHIC SCOLIOSIS: SURGICAL TREATMENT AND QUALITY OF LIFE

ESCOLIOSE IDIOPÁTICA DO ADOLESCENTE: TRATAMENTO CIRÚRGICO E QUALIDADE DE VIDA

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ABSTRACT

Objectives: The purpose of this study was to determine the influence of perioperative factors and their impact on clinical and functional outcomes in Brazilian patients with adolescent idiopathic scoliosis (AIS). Methods: We performed a prospective study with 49 consecutive AIS patients who underwent spine fusion and had a minimum 2 year follow-up. Clinical and radiographic data were correlated to SRS-30 scores in order to predict postoperative results. Results: There was a negative association between patient age at the time of surgery and back pain. We also observed higher scores in the "satisfaction" domain in patients who underwent surgery after 15 years of age ($p < 0.05$). The average SRS-30 "mental health" score was significantly higher in males than in females ($p= 0.035$). Patients treated with braces had worse results than those who did not use them ($p= 0.005$). Conclusions: Posterior spine fusion led to improvement of all domains of the SRS-30 questionnaire. Clinical results were influenced by age, sex and the use of braces prior to surgery. There was no correlation between curve correction and presence of perioperative complications. ***Level of Evidence IV, Case Series.***

Keywords: Scoliosis. Adolescent. Spinal fusion. Pedicle screws. Treatment outcome.

RESUMO

Objetivo: A finalidade deste estudo foi determinar a influência dos fatores perioperatórios e seu impacto sobre os desfechos clínicos e funcionais em pacientes brasileiros com escoliose idiopática do adolescente (EIA). Métodos: Foi realizado um estudo prospectivo com 49 pacientes consecutivos com EIA submetidos à fusão da coluna vertebral, com seguimento de no mínimo dois anos. Os dados clínicos e radiográficos foram correlacionados com o escore SRS-30 para predizer os resultados pós-operatórios. Resultados: Houve uma associação negativa entre a idade do paciente no momento da cirurgia e dor nas costas. Observamos também escore mais alto no domínio "satisfação" nos pacientes operados depois dos 15 anos de idade ($p < 0,05$). O escore médio de "saúde mental" do SRS-30 foi significativamente superior em homens com relação às mulheres ($p= 0,035$). Os pacientes tratados com órteses tiveram resultados piores comparados com aqueles que não usaram ($p= 0,005$). Conclusão: Artrodese posterior levou à melhora de todos os domínios do questionário SRS-30. Os resultados clínicos foram influenciados por idade, sexo e uso de órtese antes da cirurgia. Não houve correlação entre a correção da curva e a presença de complicações perioperatórias. ***Nível de Evidência IV, Série de Casos.***

Descritores: *Escoliose. Adolescente. Fusão vertebral. Parafusos pediculares. Resultado do tratamento.*

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INTRODUCTION

Adolescent idiopathic scoliosis (AIS) is a three-dimensional disease corresponding to 70 to 80% of all spine deformity cases. The prevalence of AIS is described as 2-3%; 0.3 to 0.5% of these cases are progressive and consequently require surgical treatment.[1]
The main goals of AIS surgery are to obtain a balanced trunk and solid fusion. However, despite good clinical and radiological outcomes patient self-evaluation and quality of life may be poor after surgery. Several aspects influence postoperative outcomes for AIS, including age, ethnicity, sociocultural issues and sex. Identification of these variables before surgery procedures may therefore help predict treatment outcomes.[2-5] The authors of this present study did not find previous studies evaluating these parameters in Brazilian AIS patients in the medical literature.
The objective of this study was to determine the influence of perioperative factors and their impact on clinical and functional outcomes in Brazilian AIS patients.

All authors declare no potential conflict of interest related to this article.

Study conducted at Hospital Estadual Mario Covas, Spine Group, Santo André, SP, Brazil.
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PATIENTS AND METHODS

We performed a prospective study with forty-nine consecutive AIS patients who underwent spine fusion surgery between March 2009 and June 2011. There was no restriction to curve patterns and all AIS types according to Lenke's classification were included.[6] The same senior surgeon performed all procedures. Evaluations were performed preoperatively and 6, 12 and 24 months after the surgery. Approval was obtained from the institutional review board of our institution (process 377.252) and all patients voluntarily signed a informed consent form.

Inclusion criteria

We included AIS patients with Cobb angle >45°, age between 11 and 18 years at the time of surgery, instrumentation with pedicle screw only and minimum of two years follow-up. Patients who had no follow-up or incomplete data were excluded.

High thoracic rib hump during Adam's forward bending test and coronal translation of the trunk (evaluated with a plumb line) were measured as clinical parameters. Coronal deviations greater than 20 mm were considered to be trunk imbalance.[7]

Function was evaluated using the SRS-30 questionnaire developed by the Scoliosis Research Society. It consists of 30 questions divided into five domains (pain, function, appearance, mental health and satisfaction). Each question ranges from 1 (worst scenario) to 5 (best scenario) and the maximum score is 150. In the present study we used a culturally adapted and validated questionnaire in Brazilian Portuguese.[8] A trained nurse who was not directly involved in the study applied all the questionnaires.

The following parameters were correlated with the SRS-30 results: (1) age at time of surgery; (2) use of braces before surgery; (3) main thoracic Cobb angle; (4) main thoracic curve correction; (5) sex; and (6) complications.

The correction percentages of the main thoracic curve were established using the equation proposed by Cheung:[9]

$$\% \text{ Correction} = \frac{\text{Preoperative Cobb angle} - \text{Postoperative Cobb angle}}{\text{Preoperative Cobb angle}} \times 100\%$$

Radiographic assessments comprised posteroanterior and lateral spine x-rays in a standing position. In all cases the Cobb angle of the proximal thoracic curve and main thoracic and thoracolumbar/lumbar curves were measured.[5] The curves were classified according to Lenke's criteria.[6] Curve flexibility was assessed by means of supine lateral bending x-rays.[7,10]

Statistical analysis

The sample was characterized by frequency and percentage for categorical variables and by mean, standard deviation (SD), median, minimum and maximum values and number of valid observations for numeric variables. Domain scores for the SRS-30 questionnaire were described in each group and time by mean, SD, median, minimum and maximum values and number of valid observations.

The relationship between age and domain scores for the questionnaire in each moment was verified by Pearson's correlation. To compare questionnaire scores between groups and across time, we used analysis of variance (ANOVA) with repeated measures and a fixed factor, considering that normality and/or homogeneity of variances for variables can be assumed between each group of interest. In each ANOVA the interaction effect between time and group was tested to verify the need to compare the groups in each stage separately, in other words, to check whether the behavior of groups through time follows the same trend.

When statistical significance was observed in the coefficient test between age and domain scores of the questionnaire, linear regression analysis was used to interpret the regression coefficient. A significance level of 95% ($\alpha = 0.05$) was used to complete each test (bilateral); in other words, descriptive levels (p) of less than 0.050 were considered statistically significant. SPSS software version 19.0 was used.

RESULTS

Of the 63 patients with AIS who underwent surgical correction, 49 patients (78%) completed the SRS-30 questionnaire before surgery and 2 years after surgery. Mean participant age (±SD) at the time of surgery was 11.9 (±1.2 years), ranging from 11 to 18 years and 87.8% of them were female. Prior to surgery, 67% of patients did not use braces. The most common curve patterns were Lenke 1AN (46.9%) and 1BN (24.5%). Most patients were considered to have "coronal imbalance" before surgery (61.2%). Of all patients, 81% were classified as grade 4 or 5 Risser sign. (Table 1)

The mean proximal thoracic Cobb angle was 25.4 (±9.4). The mean main thoracic and thoracolumbar/lumbar Cobb angles were 58.5 (±11.8) and 36.0 (±10.1), respectively. Mean size of the thoracic hump was 2.2 cm (±0.9 cm). The average correction of the main thoracic and thoracolumbar/lumbar Cobb angles was 39.8.

A negative association between patient age at the time of surgery and back pain was found. Patients who underwent surgery after 15 years of age had worse outcomes compared to those who had surgery before this age. (Table 2) Higher scores were also observed in the "satisfaction" domain in patients who underwent surgery after 15 years of age ($p<0.05$). The β-regression coefficient indicated that for each year of delay from the ideal time of surgery (after age 11), there was an increase of approximately 0.5 points in the SRS-30 "satisfaction" domain. (Table 2)

The correlation between the SRS-30 "function" and "pain" domains with the use of corsets during conservative treatment are shown in Tables 3 and 4. It was possible to verify that these patients had worse results in comparison to patients without brace treatment ($p=0.005$). Furthermore, the use of braces did not influence the other SRS-30 domains after surgical treatment.

There was no correlation between degree of coronal correction of the main thoracic curve and SRS-30 scores. (Table 5) After surgery, there was significant improvement of the five domains of the SRS-30 ($p<0.001$) and these results were maintained in subsequent evaluations. (Table 6)

DISCUSSION

The impact of surgery and perioperative predictive factors remains controversial in AIS treatment. Unlike the present prospective study, most current reports that assessed the quality of life after spine fusion to treat AIS are retrospective studies.[2] Some authors have used meta-analysis to demonstrate no change in patient quality of life after surgical treatment. However, in the present study we found significant improvement in all functional SRS-30 domains two years after surgery.

Our results suggest a positive correlation between patient satisfaction and age at the time of surgery. Patients operated after 15 years of age were more satisfied with surgery than younger ones ($p<0.05$). We believe that individual factors such as education and psychological changes during adolescence may justify such findings. We also observed that age at the time of surgery had an impact on patients' back pain (dorsal and/or lumbar). Patients who received surgery at the end of adolescence had more back

Table 1. Sample features.

Age (years)		
Mean ± SD.	11.9 ± 1.2	
Median		11.0
Minimum – Maximum	11 – 18	
Total of patients		49
Sex – n (%)		
Male	6	(12.2%)
Female	43	(87.8%)
Total of patients	49	
Brace – n (%)		
No	33	(67.3%)
Yes	16	(32.7%)
Total of patients	49	
Lenke – n (%)		
1AN	23	(46.9%)
1A-	4	(8.2%)
1B+	1	(2.0%)
1BN	12	(24.5%)
1B-	2	(4.1%)
1CN	2	(4.1%)
2	2	(4.1%)
3	2	(4.1%)
5	1	(2.0%)
Total of patients	49	
Plumb line – n (%)		
Compensated	30	(61.2%)
Uncompensated	19	(38.8%)
Total of patients	49	
Risser sign – n (%)		
0, 1, 2, 3	9	(18.4%)
4, 5	40	(81.6%)
Total of patients	49	
Proximal thoracic angle		
Mean ± SD.	25.4 ± 9.4	
Median		25.0
Minimum – Maximum	8 – 56	
Total of patients		49
Main thoracic angle		
Mean ± SD.	58.5 ± 11.8	
Median		58.0
Minimum – Maximum	20 – 91	
Total of patients		49
Thoracolumbar angle		
Mean ± SD.	36 ± 10.1	
Median		37.0
Minimum – Maximum	17 – 56	
Total of patients		49
Rib hump size		
Mean ± SD.	2.2 ± 0.9	
Median		2.0
Minimum – Maximum	0 – 4	
Total of patients		49

pain. This phenomenon was not observed in younger patients. The reasons for these findings are not completely clear; we hypothesize that scoliotic deformities produce asymmetric load distribution on facet joints, which may explain early degeneration of articular cartilage and consequent pain. Unfortunately, this theory is not part of the objective of the present study and was not proven.

Male patients had higher "mental health" domain scores in comparison to female subjects ($p<0.035$). This finding was consistent with a previous report that described better results in the "appearance" and "mental health" domains as well as less postoperative pain in males.[11] In this study, patients of both

Table 2. SRS30 "Pain domain" and "satisfaction domain" versus age (in years).

	Correlation between age and SRS30 "Pain Domain"							
	Preoperative		**6 months**		**1 year**		**2 years**	
	A	**B**	**A**	**B**	**A**	**B**	**A**	**B**
Pearson correlation coefficient *(r)*	-0.11	0.11	-0.06	0.29	-0.18	0.28	-0.27	0.19
Total of patients	49	49	49	49	49	49	49	49
p value	0.454	0.449	0.682	0.044	0.22	0.047	0.064	0.194

p: Linear regression analysis. A: Correlation between age and SRS30 "Pain Domain". B: Correlation between age and SRS-30 "Satisfaction Domain".

Table 3. SRS30 "Function domain" versus "use of braces".

Use of braces	**SRS30 – "Function Domain"**			
	Preoperative	**6 months**	**1 year**	**2 years**
No				
Mean ± SD.	17.9 ± 3.7	25 ± 4.3	25.8 ± 3.9	25.7 ± 4
Median	18.0	25.0	26.0	26.0
Min – Max	11 – 23	14 – 33	20 – 32	20 – 33
Total of patients	33	33	33	33
Yes				
Mean ± SD.	20.1 ± 3.7	27.1 ± 5.1	28.5 ± 3.2	28.6 ± 3.5
Median	21.5	29.0	29.0	29.0
Min – Max	10 – 23	16 – 33	20 – 33	23 – 35
Total of patients	16	16	16	16
p value (time VS use of braces)	p= 0.873			
p value (time)	p <0.001			
p value (use of braces)	p= 0.005			

p: Analysis of variance with repeated measures and a fixed factor.

Table 4. SRS30 "Pain domain" versus "use of braces".

Use of braces	**SRS30 – "Pain Domain"**			
	Preoperative	**6 months**	**1 year**	**2 years**
No				
Mean ± SD.	19.9 ± 3.5	24 ± 4.5	24.8 ± 4.1	25.3 ± 4.1
Median	20.0	25.0	25.0	26.0
Min – Max	13 – 25	10 – 30	16 – 30	16 – 30
Total of patients	33	33	33	33
Yes				
Mean ± SD.	22.4 ± 2.4	25.7 ± 5.3	26.9 ± 2.2	27.1 ± 2.8
Median	22.5	28.0	28.0	28.0
Min – Max	15 – 25	8 – 30	21 – 30	21 – 30
Total of patients	16	16	16	16
p value (Time VS Use of Braces)	p= 0.931			
p value (Time)	p < 0.001			
p value (Use of Braces)	p= 0.038			

p: Analysis of variance with repeated measures and a fixed factor.

Table 5. SRS30 total score versus main curve correction.

Curve correction	SRS30 – Total score			
	Preoperative	6 months	1 year	2 years
< 50%				
Mean ± SD.	85 ± 11.4	122.3 ± 3.5	127 ± 6.2	121.3 ± 12
Median	80.0	122.0	125.0	122.0
Min – Max	77 – 98	119 – 126	122 – 134	109 – 133
Total of patients	3	3	3	3
51 – 70%				
Mean ± SD.	82 ± 11.8	120.5 ± 18.4	125.3 ± 12.8	121.4 ± 12.5
Median	82.0	126.0	126.0	119.0
Min – Max	61 – 107	68 – 142	95 – 142	95 – 142
Total of patients	23	23	23	23
>= 71%				
Mean ± SD.	79.3 ± 12	120.4 ± 13.1	122.7 ± 11.3	125.3 ± 12
Median	76.0	120.0	125.0	127.0
Min – Max	60 – 101	93 – 138	97 – 140	96 – 144
Total of patients	23	23	23	23
p value (time VS main curve correction)	p= 0.309			
p value (time)	p < 0.001			
p value (main curve correction)	p= 0.951			

p: Analysis of variance with repeated measures and a fixed factor.

Table 6. SRS30 total score versus time.

SRS30 Domains	SRS30 – Total score			
	Preoperative	6 months	1 year	2 years
Function				
Mean ± SD.	18.6 ± 3.8	25.7 ± 4.6	26.7 ± 3.9	26.7 ± 4
Median	19.0	27.0	27.0	27.0
Min – Max	10 – 23	14 – 33	20 – 33	20 – 35
Total of patients	49	49	49	49
Pain				
Mean ± SD.	20.7 ± 3.4	24.6 ± 4.8	25.5 ± 3.7	25.9 ± 3.8
Median	21.0	26.0	26.0	26.0
Min – Max	13 – 25	8 – 30	16 – 30	16 – 30
Total of patients	49	49	49	49
Appearance				
Mean ± SD.	17.3 ± 4.3	36.3 ± 4.8	36.9 ± 4.5	36.3 ± 4.5
Median	17.0	37.0	37.0	36.0
Min – Max	8 – 28	22 – 45	24 – 45	24 – 45
Total of patients	49	49	49	49
Mental health				
Mean ± SD.	17.5 ± 3.7	20.4 ± 4.2	21.3 ± 3.2	20.9 ± 3.4
Median	17.0	21.0	22.0	21.0
Min – Max	11 – 25	9 – 25	14 – 25	13 – 25
Total of patients	49	49	49	49
Satisfaction				
Mean ± SD.	6.8 ± 2.1	13.7 ± 2.0	13.8 ± 1.9	13.5 ± 1.8
Median	6.0	14.0	15.0	14.0
Min – Max	2 – 10	8 – 15	8 – 15	8 – 15
Total of patients	49	49	49	49
Total				
Mean ± SD.	80.9 ± 11.7	120.6 ± 15.3	124.2 ± 11.7	123.3 ± 12.2
Median	79.0	123.0	125.0	120.0
Min – Max	60 – 107	68 – 142	95 – 142	95 – 144
Total of patients	49	49	49	49

sexes showed significant improvement regarding the domain "appearance." Other studies compared AIS fusion results and showed no direct association with "mental health" and sex.[12,13] In the present study, braces exerted a negative effect on postoperative back pain, personal satisfaction and overall function (p=0.05). Our findings were consistent with those previously described by Diab et al.[14] Other studies also have found negative effects regarding the use of braces prior to surgery.[15,16] One reason could be the fact that braced patients were probably less active (in sports and daily activities) than non-braced patients and consequently presented hypotrophy of the trunk stabilization muscles. However, this outcome was not addressed in our study. Future studies about muscle activity in AIS may answer this specific question.

The impact of the amount of correction in functional outcomes of AIS patients is not well established. D'Andrea et al.[4] and Sanders et al.[16] reported a weak correlation between curve correction and functional outcomes. Despite the fact that our results do not support a direct correlation between curve correction and functional outcomes, (Table 5) additional studies showed higher rates of complications after major curve corrections (SOSORT study), including iatrogenic trunk imbalance.[17] In a longitudinal cohort study of 745 patients with AIS who underwent surgical correction, Carreon et al.[18] observed no statistically significant correlation between the 2-year postoperative SRS satisfaction score and the amount of curve correction (r= 0.07, P= 0.062). However, other studies found high levels of AIS patient satisfaction after deformity correction.[13] The degree of curve correction after surgery was a significant predictor of function/activity scores, self-image/appearance and satisfaction in 104 Chinese AIS patients.[19]

The incidence of complications was low and minor, as previously described.[20] We experienced 3 wound infections, but only one patient had a deep wound infection and needed reoperation. All patients were treated with oral antibiotics. There was no reported dural perforation, implant loosening, or neurological deficit. We did not find differences among functional outcomes of patients who presented or did not present surgical complications. This may be attributed to the low sociocultural profile of patients included in the present study, who were satisfied even when such complications were present. Moreover, the complications observed were minor and presented satisfactory resolution.

CONCLUSIONS

Posterior spine fusion to treat AIS led to improvement in all domains of the SRS-30 questionnaire. Clinical results were influenced by age, sex and the use of braces prior to the surgery. There was no correlation between functional outcomes and the amount of curve correction and the presence of minor perioperative complications.

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ORIGINAL ARTICLE

CONCORDANCE FOR CURVE TYPE IN IDIOPATHIC SCOLIOSIS AMONG FAMILY MEMBERS

CONCORDÂNCIA DO TIPO DE CURVA EM ESCOLIOSE IDIOPÁTICA ENTRE FAMILIARES

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ABSTRACT

Objective: To evaluate the concordance for the curve pattern, side and levels of the superior apical vertebrae, apex and inferior apical vertebrae of curves in patients and their relatives with idiopathic scoliosis. Methods: Concordance according to the Lenke classification for curve pattern, side and levels of the superior apical vertebrae, apex and inferior apical vertebrae were evaluated comparative and prospectively in 243 pairs of patients and respective relatives with idiopathic scoliosis. Results: The family concordance for the curve pattern and side was 51.4% (125 pairs). Among these pairs, the concordance of the levels of the vertebrae was 91.2% (114 pairs). The concordance rate for the curve pattern and side between parents/children was 51.6% and between siblings was 50.0% (p-value= 0.411). The concordance rates of the levels of vertebrae were 86.8% and 95.1%, respectively (p-value = 0.219). Conclusion: Curve shape in idiopathic scoliosis is related to family and degree of kinship, since the data showed a high concordance for the curve pattern, side and levels of the apical vertebrae and apex between patients and relatives with this deformity. The concordance was higher in those with a closer degree of kinship. ***Level of Evidence II, Lesser Quality Prospective Study.***

Keywords: Scoliosis. Genetics. Spine.

RESUMO

Objetivo: Avaliar a concordância para o padrão de curva, lado e níveis das vértebras apical superior, ápex e apical inferior das curvas de pacientes e respectivos familiares com escoliose idiopática. Métodos: A concordância, pela classificação de Lenke, para o padrão de curva, lado e níveis das vértebras apical superior, ápex e apical inferior foi avaliada em 243 pares de pacientes e respectivos familiares com escoliose idiopática. Resultados: A concordância familiar para o padrão de curva e lado foi de 51,4% (125 pares). Entre esses pares, a concordância dos níveis das vértebras foi de 91,2% (114 pares). A taxa de concordância para o padrão de curva e lado entre pais/filhos foi de 51,6% e entre irmãos foi de 50,0% (p= 0,411). As taxas de concordância dos níveis das vértebras foram respectivamente de 86,8% e 95,1% (p-valor = 0,219). Conclusão: O formato das curvas na escoliose idiopática tem relação familiar e com o grau de parentesco, uma vez que se reportou alta concordância para o padrão de curva, lado e níveis das vértebras apicais e ápex entre pacientes e familiares com a deformidade. A concordância foi maior entre aqueles com grau de parentesco mais próximo. ***Nível de Evidência II, Estudo Prospectivo de Menor Qualidade.***

Descritores: *Escoliose. Genética. Coluna vertebral.*

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INTRODUCTION

Idiopathic scoliosis (IS) is a three-dimensional deformity of the spine in which a structural lateral curvature is associated with vertebral rotation and lordosis.[1] This deformity affects otherwise healthy patients and is one of the most common pathologies involving the spine.[2] Despite many years of research, the exact cause of this condition has not yet been found. Several hypotheses have included metabolic, biomechanical, neuromuscular, developmental and genetic factors.[2] IS is often seen in several members of the same family, strongly suggesting a genetic component.[2-5] One study showed that 11% of first-degree relatives of patients with IS are also affected, as well as 2.4% and 1.4% of second and third-degree relatives, respectively.[5] Studies on twins reported higher concordance for the presence of the curve in monozygotic twins in comparison with dizygotic twins.[6,7] As early as the 1950s scientists suggested that the shape of the curve in IS was genetically determined.[8] Support for this theory was reported in other studies which identified similar curves in twins concordant for IS.[9-11]

All authors declare no potential conflict of interest related to this article.

Study conducted at Centre Hospitalier Universitaire de Toulouse, Hospital des Enfants, Department of Pediatric Orthopedic Surgery, Toulouse, France and at Universidade Federal de Pernambuco, Hospital das Clínicas, Surgery of Department, Recife, PE, Brazil.
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Curve pattern has not been widely investigated in familial IS other than in twin pairs. The aim of this study was to evaluate whether patients and respective family relatives with IS have concordant curve types. To do so, we compared the pattern, the side and the levels of the apical superior vertebrae (ASV) and the apex and apical inferior vertebrae (AIV) of curves in patients with IS and their relatives.

MATERIAL AND METHODS

The data collected followed the institutional review board standards on human experimentation (protocol number 08-0916). A total of 419 individuals with a positive family history for IS were referred to our institution between 2006 and 2015. After excluding 21 subjects who did not have spine X-rays for evaluation, 398 patients remained. The present study used only data contained in patient charts and the researchers signed an agreement to update this data.

IS was prospectively assessed using full spine standing posteroanterior X-rays analyzed by 2 observers. For diagnosis, this study considered lateral structural curvature greater than 10° according to Cobb.[12]

Concordance according to the Lenke classification for curve pattern and the side of the convexity of the curves were analyzed.[13] In this study the double major (DM) curves were not differentiated from the thoracolumbar/lumbar-main thoracic curves (TL/L-MT) and 5 different patterns were identified. The ASV, apex and AIV of each curve were subsequently identified.[14]

We compared the X-rays in pairs containing the patient and their respective family relative with IS. A total of 21 families presented more than 2 family relatives with IS and all were considered in the study. These pairs were identified with respect to type of family relationship and individual sex. First-degree family relationships were parents, siblings and children; second-degree relationships were uncles/aunts, nephews/nieces, grandparents/grandchildren; third-degree relationships were cousins.[15] A total of 243 pairs were evaluated: 225 first-degree relatives, 6 second-degree relatives and 12 third-degree relatives. The first-degree pairs were comprised of 159 siblings and 66 parents/children. The second-degree pairs contained 4 uncles/aunts/nephews/nieces and 2 grandparents/grandchildren. The third-degree pairs were comprised of 12 cousin pairs. In total, there were 174 pairs of female patients, 14 male pairs and 55 pairs with one male and one female subject. The sibling pairs were comprised of 110 female pairs, 11 male pairs and 38 female/male pairs. The parent/child pairs were comprised of 52 female pairs, 1 male pair and 13 female/male pairs.

The pairs were considered concordant if both relatives had the same curve pattern and side. They were compared with respect to the level of ASV, apex and AIV. The study considered individuals to have the same curve type when there was no difference in the position of these vertebrae in a maximum of two levels, proximal or distal. (Figure 1)

A Microsoft Excel spreadsheet using EPI INFO version 3.5.2 was used to analyze the data. To evaluate the chance of concordance of the curve pattern, side and levels of the vertebrae, the prevalence was calculated in the different pairs according to family relationship. The chance of concordance was then compared using the chi-square test. The same aspects were also verified according to sex: female/female (FxF); male/male (MxM); female/male (FxM). All conclusions were obtained using a 5% significance level.

RESULTS

The study evaluated 243 pairs of individuals, 125 (51.4%) of which were concordant for the curve pattern and side of the deformity. Among these, there was a high concordance prevalence for the levels of ASV, apex and AIV: 91.2% (114 pairs).

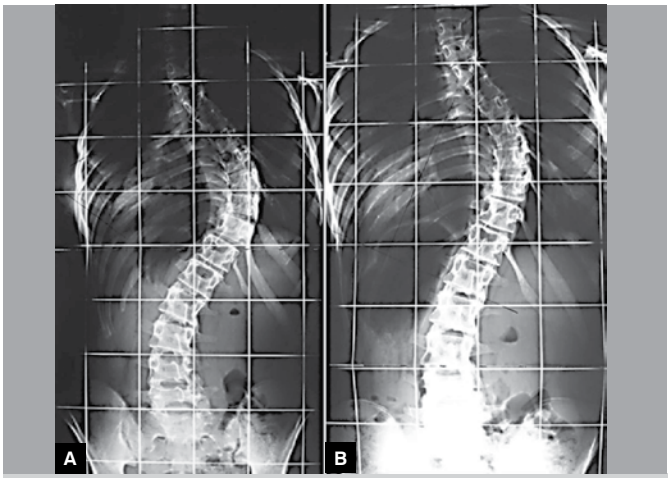

Figure 1. Radiographs of two twin sisters with concordant curve pattern, side and levels of ASV, apex and AIV. A, DM Curve; right/left; ASV T5, apex 9 and AIV T12/ASV L1, apex L4, AIV L5. B, DM Curve; right/left; ASV T5, apex T9, AIV T12/ASV L1, apex L4, AIV L5.

Distribution of the curve patterns according to family relationship is shown in Table 1. Higher concordance prevalence was seen in all groups for DM or TL/L-MT curves. The proportion comparison test was significant in all evaluated groups (all with p-value <0.05). (Table 1)

Table 2 shows the distribution of the evaluated pairs in relation to type of family relationship and concordance prevalence for each evaluated pair type. The concordance prevalence for the curve pattern and side was of 57.6% for parents/children, 51.6% for siblings and 8.3% for cousins. The proportion comparison test was not significant between the groups of siblings and parents/children (p= 0.411). However, when comparing the chance in the cousin group with the sibling and the parent/child groups, the test was significant (p= 0.004 and 0.002, respectively). The concordance evaluation of vertebrae was of 95.1% for siblings and 86.8% for parents/children. The proportion comparison test was not significant (p= 0.219).

Table 3 shows the distribution of the evaluated pairs in relation to sex and the concordance prevalence of the curb pattern, side and levels of the vertebrae. The concordance prevalence of the curve pattern and side was highest for the FxF comparison (55.8%), followed by FxM (45.6%) and MxM (21.4%). The proportion comparison test was significant for the differences found (p= 0.028). The concordance comparison found for vertebrae was of 100% among MxM pairs, followed by FxF pairs (91.7%) and FxM pairs (88.5%). The proportion comparison test was not significant (p= 0.904).

Table 4 shows the concordance prevalence for the curve pattern, side and vertebrae according to sex in the sibling and parent/child groups. In the sibling group the highest prevalence of concordance for the curve pattern and side was in the FxF pairs (59.1%), followed by FxM (36.8%) and MxM (27.3%). The proportion comparison test showed a significant difference in the percentages found (p= 0.015). In comparing vertebrae concordance, 100% of these concordant cases for MxM and FxM comparisons were also concordant. In the FxF pairs this percentage was 93.8%. Since two groups presented total concordance, the application of the proportion comparison test was not feasible. For the parent/child group, the highest prevalence of concordance for the curve pattern and side was seen in the FxM pairs (69.2%), followed by FxF (55.8%). The proportion comparison test was not significant (p= 0.378). Of the FxF pairs concordant to the curve pattern and side, 93.1% were concordant for the vertebrae. In the FxM pairs,

Table 1. Concordance prevalence of the curve pattern according to family relationship.

Curve pattern	ALL		Parent/child		Siblings		Other[2]	
	Total	Concordance	Total	Concordance	Total	Concordance	Total	Concordance
MT	31	0 (0.0%)	6	0 (0.0%)	21	0 (0.0%)	4	0 (0.0%)
DT	15	2 (13.3%)	3	0 (0.0%)	11	2 (18.2%)	1	0 (0.0%)
DM or TL/L-MT	283	184 (65.0%)[1]	93	68 (73.1%)[1]	169	106 (62.7%)[1]	21	10 (47.6%)[1]
TL/L	87	26 (29.9%)	19	6 (31.6%)	60	20 (33.3%)	8	0 (0.0%)
TM	70	38 (54.3%)	11	2 (18.2%)	57	36 (63.2%)	2	0 (0.0%)

[1]Greater concordance for DM or TL/L-MT curves in all groups (p-valor < 0.05). [2]Other refers to second – and third-degree relatives.

Table 2. Concordance prevalence of curve pattern, side and vertebrae according to family group.

Family relationship	Total	Concordance evaluated	
		Curve and side	ASV, Apex, AIV
Siblings	159 (65.4%)	82 (51.6%)[1]	78 (95.1%)[3]
Parent/Child	66 (27.2%)	38 (57.6%)[1]	33 (86.8%)[3]
Aunt-Uncle/Niece-Nephew	4 (1.6%)	2 (50.0%)	2 (100.0%)
Grandparent/Grandchild	2 (0.8%)	2 (100.0%)	1 (50.0%)
Cousin/Cousin	12 (4.9%)	1 (8.3%)[2]	0 (0.0%)
Total	243 (100.0%)	125 (51.4%)	114 (91.2%)

[1]Similar prevalence between Siblings and Parent/Child (p= 0.411). [2]Prevalence significantly lower among Cousins, compared to Siblings and Parent/Child groups (p= 0.004 and 0.002, respectively). [3]Prevalence statistically similar between Siblings and Parent/Child (p= 0.219).

Table 3. Concordance prevalence of curve pattern, side and vertebrae according to sex.

Sex	Total	Concordance evaluated	
		Curve and side	ASV, Apex, AIV
FxF	172 (70.8%)	96 (55.8%)[1]	88 (91.7%)[2]
MxM	14 (5.8%)	3 (21.4%)	3 (100.0%)[2]
FxM	57 (23.5%)	26 (45.6%)[1]	23 (88.5%)[2]
Total	243 (100.0%)	125 (51.4%)	114 (91.2%)

[1]Similar prevalence between FxF and FxM (p= 0.028). [2]Similar prevalence between FxF, MxM and FxM (p= 0.904).

Table 4. Concordance prevalence of curve pattern, side and vertebrae according to gender in the "siblings" and "parents/child" groups.

Sex	Siblings			Parent/child		
	Total	Concordance evaluated		Total	Concordance evaluated	
		Curve and side	AIS, Apex, AIV		Curve and side	AIS, Apex, AIV
FxF	110 (69.2%)	65 (59.1%)[1]	61 (93.8%)[2]	52 (78.8%)	29 (55.8%)[3]	27 (93.1%)[4]
MxM	11 (6.9%)	3 (27.3%)	3 (100.0%)[2]	1 (1.5%)	0 (0.0%)	-
FxM	38 (23.9%)	14 (36.8%)	14 (100.0%)[2]	13 (19.7%)	9 (69.2%)[3]	6 (66.7%)[4]
Total	159 (100.0%)	82 (51.6%)	78 (95.1%)	66 (100.0%)	38 (57.6%)	33 (86.8%)

[1]Higher prevalence in FxF (p= 0.015). [2]Similar prevalence between FxF, MxM and FxM. [3]Similar prevalence between FxF and FxM (p= 0.378). [4]Similar prevalence between FxF and FxM (p= 0.137).

this percentage was 66.7%. The proportion comparison test was not significant (p= 0.137).

Of the total of 21 families, 19 allowed combination of 3 pairs of individuals with IS; in 2 other families, 6 pairs were made. In 3 families (14.3%), all pairs evaluated for curve pattern and side were concordant. In 5 families (23.8%), all were discordant. The study identified 16 families (76.2%) with one or more pairs which were concordant for the curve pattern and side. Vertebrae assessment found that in 15 (93.8%) of these 16 families there were one or more concordant pairs. (Table 5)

Table 5. Number of concordant and discordant pairs in evaluating curve pattern, side and vertebrae in families.

Evaluated family	TOTAL pairs	Curve and side		Vertebrae	
		Concordant pairs	Discordant pairs	Concordant pairs	Discordant pairs
1	3	1	2	1	-
2	3	1	2	-	1
3	3	-	3	-	-
4	3	-	3	-	-
5	3	1	2	1	-
6	3	1	2	1	-
7	3	1	2	1	-
8	3	1	2	1	-
9	3	1	2	1	-
10	3	-	3	-	-
11	3	-	3	-	-
12	3	1	2	1	-
13	3	3	-	3	-
14	6	3	3	3	-
15	3	1	2	1	-
16	3	1	2	1	-
17	3	3	-	3	-
18	3	-	3	-	-
19	6	3	3	3	-
20	3	3	-	3	-
21	3	1	2	1	-

DISCUSSION

IS is a genetic disorder involving one or more genetic loci and complex interactions between them for expression.[3] Several studies have concluded that the most likely form of inheritance is multifactorial, postulating that predisposing alleles are required together with environmental factors to express this phenotype.[2,9,15] Studies have suggested a biomechanical explanation for family tendency in IS when proposing that it originates in a genetically determined spine profile. Individuals with flatter profiles would be more vulnerable to developing the deformity.[1,7,16] Other studies argue that the primary mechanical factor triggering this disorder is rotational instability. Subsequent shear forces act on certain areas of the spine and lead to rotation of the vertebral bodies, producing apical lordosis and the appearance of lateral deviation in the anteroposterior plane in X-rays.[17,18]

In the 1950s Ponseti and Friedman[8] suggested that the shape of the curve in IS was genetically determined and other studies have provided support for this theory.[3,4,7,8,10,19] Dryden et al.[20] observed that similar back shapes were more frequently found in individuals who were closer genetically and of the same sex, suggesting a relationship between deformity and sex. Kesling and Reinker[9] demonstrated that monozygotic twins tend to have more similar curves than dizygotic twins and only one segment difference in apex vertebrae position. Van Rhijn et al.[10] reported that the direction of the convexity of the curve and apex vertebrae were most commonly the same in monozygotic twins with scoliosis.

Our results demonstrate that the concordance for curve pattern and side among family relatives with IS is high. In an analysis of 100 families Sales de Gauzy et al.[3] showed a 66% concordance rate for curve pattern and side in family relatives with IS, with a concordance rate that was not statistically different between siblings (65%) and parents/children (67%).

In the present study 243 pairs of relatives were evaluated, showing a concordance rate of 51.4% for curve pattern and side, as well as a statistically insignificant (p= 0.411) concordance rate between parents/children (57.6%) and siblings (51.6%), indicating that the chance of concordance between siblings is similar to the rate in parents/children. Comparison between cousins showed a concordance rate of 8.3%, significantly lower than in siblings and parents/children (p= 0.004 and 0.002, respectively), indicating that the chance of concordance between cousins is significantly lower than in these groups. This suggests that genetically more distant family relatives are less likely to present concordance for curve pattern and side.

In this analysis, 114 of the 125 (91.2%) pairs concordant for curve pattern and side were concordant for levels of ASV, apex and AIV. When comparing the different family groups, siblings (95.1%) and parents/children (86.8%) showed no statistically significant difference (p= 0.219), demonstrating that the chance of concordance in vertebra position is similar between these two groups. Because the samples of second – and third-degree relatives were so small, a larger population should be evaluated to accurately compare these groups. We found no studies in the literature comparing vertebra position in family pairs. One study which only evaluated the level of the apex vertebrae in 68 pairs of twin siblings with IS observed that the apex vertebra only differed by one segment in most of the monozygotic pairs.[9] Another analysis in 18 twin pairs observed that nine-tenths of the apex vertebrae were the same or differed only by one segment between pairs.[10]

In analyzing sex, Sales de Gauzy et al.[3] found a concordance rate of 68% for curve pattern and side in FxF pairs and 62% in FxM pairs, with no statistically significant difference.

This analysis showed that the concordance rate for the curve pattern and side was significantly higher (p= 0.028) in FxF (55.8%) and FxM pairs (45.6%) compared with MxM pairs (21.4%), indicating a higher probability of concordance in FxF and FxM pairs than in MxM pairs. However, when vertebra levels were compared among these pair groups, the concordance was not statistically different (p= 0.904), showing that although the concordance for curve pattern and side is greater when comparing FxF and FxM pairs, vertebra position presents similar concordance among all three parameters. In the evaluating curve pattern and side in parents/children, the concordance prevalence was greater in FxM (69.2%) and FxF (55.8%) pairs, again with no statistically significant difference (p= 0.378). In the sibling group, prevalence was significantly higher in FxF pairs (p= 0.015). The analysis of the vertebrae in these groups also showed similar concordance among all pairings.

Both the DM and TL/L-MT curves have structured thoracic and thoracolumbar/lumbar curves but differ in the main curve.[13] This study opted not to differentiate these curved because it is possible that a structured curve initially identified as minor might intensify in a future assessment. Since the objective of this study was to assess whether pairs had the same curve types, we believe that differentiating DM from TL/L-MT patterns could lead to a false interpretation that similar curves are different, thereby excluding them from the second stage of the study which compared vertebra position. In the analysis by Sales de Gauzy et al.,[3] the curved patterns most commonly found were DM, followed by TL/L, MT, TL/L-MT and DT. In this study, DM or TL/L-MT patterns were significantly the most frequent in all analyzed groups ($p < 0.05$), followed by TL/L, TM, MT and DT patterns.

In only 14.3% of the 21 assessed families were all pairs concordant. Most families (76.2%) presented one or more concordant pairs and consequently the concordance for curve pattern and side did not increase when more members of the same family were affected by the deformity.

CONCLUSION

The analysis in this study showed high concordance in curve pattern and side among family relatives with IS and also showed that genetically more distant individuals have less chance of concordance than closer relatives. All evaluated pairs showed a greater frequency of concordance when at least one individual in the pair was female. When evaluating families with the deformity, the findings indicate that the pairs of individuals with IS within a single family are independent of each other. These results reinforce the hypothesis that the type of the curve is related to family and sex and opens prospects for future research including evaluating the concordance among the type of curve and the degree of family relatedness and sex.

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. CMCAO (0000-0002-3321-8255)* was the main contributor to the design and intellectual and scientific content of the study. JSG (0000-0001-6206-514X)* and PCVCA (0000-0003-1898-9139)* were responsible for designing the study and critical review. FA (0000-0001-5366-3885)* was responsible for the critical review. PEMCA (0000-0002-92382303)* helped acquire and interpret data. JLAA (0000-0002-12065368)* responsible for critical revision. *ORCID (Open Researcher and Contributor ID).

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Ginkgo biloba improves bone formation during fracture healing: an experimental study in rats

Ginkgo biloba melhora a formação dos ossos durante a consolidação da fratura: estudo em ratos

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ABSTRACT

Objectives: *Ginkgo biloba* extract (EGb 761) is a plant extract obtained from the leaves of the *G. biloba* tree. The aim of this study was to assess the histological and radiological effects of *G. biloba* extract on fracture healing in an experimental fracture model using rat femurs. Methods: Forty-eight female Sprague-Dawley rats (weight: 195–252 g; age: 20 weeks) were used in the study. The rats were randomly divided into six groups (n=8). A transverse fracture was made in the middle of the right femur of each rat and fixed with a Kirschner wire. The *G. biloba* groups received 60 mg/kg oral *G. biloba* extract once daily. No medication was given to the control groups. On days 7, 21 and 35, both sets of femurs were evaluated radiologically and histopathologically. Results: Histological evaluation revealed that the *G. biloba* groups had significant differences at 21 and 35 days ($p<0.05$). The *G. biloba* group showed a significant difference in terms of bone formation on day 21 when compared to the control group ($p<0.05$). Conclusions: This study indicated that the use of *G. biloba* extract accelerated fracture healing. Both radiological and histological differences were detected, but the histological differences were more remarkable. ***Level of Evidence I, High Quality Randomized Trial.***

Keywords: Fracture healing. Ginkgo biloba. Rats.

RESUMO

Objetivos: O extrato de Ginkgo biloba (EGb 761) é um extrato vegetal obtido das folhas da árvore Ginkgo biloba. O objetivo deste estudo foi avaliar os efeitos histológicos e radiológicos do extrato de Ginkgo biloba sobre a consolidação de fraturas em um modelo experimental de fratura em fêmures de rato. Métodos: Foram utilizados 48 ratos Sprague-Dawley fêmeas (peso: 195-252 g, idade: 20 semanas). Os ratos foram divididos randomicamente em seis grupos (n = 8). Uma fratura transversal foi feita no meio do fêmur direito de cada rato e fixada com fio de Kirschner. Os grupos G. biloba receberam 60 mg/kg de G. biloba por via oral uma vez por dia. Não foi administrada nenhuma medicação aos grupos de controle. Nos dias 7, 21 e 35, ambos os fêmures foram avaliados radiológica e histopatologicamente. Resultados: A avaliação histológica revelou que os grupos G. biloba apresentaram diferenças significativas aos 21 e 35 dias ($p < 0,05$). O grupo G. biloba mostrou uma diferença significativa em termos de formação óssea no dia 21 quando comparado com o grupo controle ($p < 0,05$). Conclusões: Este estudo indicou que o uso de extrato de G. biloba acelerou a consolidação de fraturas. As diferenças radiológicas e histológicas foram detectadas, mas as diferenças histológicas foram mais notáveis. ***Nível de Evidência I, Estudo Clínico Randomizado de Alta Qualidade.***

Descritores: *Consolidação da fratura. Ginkgo biloba. Ratos.*

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INTRODUCTION

Many factors may affect the fracture healing process and blood supply at the fracture site has a direct effect.[1-3] Blood vessels regenerate during the fracture healing process with the budding of existing blood vessels; if an adequate blood supply exists, the osteoblasts in the callus provide a matrix conductive to normal bone development. Oxygenation of the fracture site is one of the most important factors for fracture healing. Wu et al.[4] reported that hyperbaric oxygen increased the proliferation and differentiation of osteoblasts.

Ginkgo biloba extract (EGb 761) is a plant extract obtained from the leaves of the *Ginkgo biloba* tree, which has been proven to cause many metabolic effects such as vascular relaxation and increased blood volume, elimination of free radicals and reduction in secondary injury-induced tissue necrosis and cell apoptosis.[5,6] In addition as a platelet-activating factor (PAF) antagonist and antioxidant, *G. biloba* improves blood circulation and helps prevent ischemic and reperfusion damage to tissue.[7] Moreover, in patients with peripheral artery disease *G. biloba* has been shown to improve pain-free walking distance.[8]

All authors declare no potential conflict of interest related to this article.

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In this study, we investigated the histological and radiological effects of *G. biloba* on fracture healing in an experimental rat model.

MATERIALS AND METHODS

This study was approved by the institutional review board and ethics committee for animal experiments (KTU-hadyek/2010/41). Forty-eight female Sprague-Dawley rats (weight: 195–252 g; age: 20 weeks) were used; the rats were randomly divided into six groups (n= 8) after a 6-week compliance period. The first three groups were identified as Gb (*G. biloba*) 1, 2 and 3; the other three groups were classified as C (control) 1, 2 and 3. The Gb1 and C1 groups were followed for 7 days; Gb2 and C2 were followed for 21 days, while Gb3 and C3 were followed for 35 days. Patients in the Gb groups received 60 mg/kg oral *G. biloba* (EGb761) (Tebokan® Forte, Abdiibrahim, Istanbul, Turkey) once daily. No medication was administered to the control groups.

Surgical Procedure

The rats fasted for 4 hours prior to surgery and received intraperitoneal injections of 5 mg/kg xylazine hydrochloride (Rompun®; Bayer Healthcare, Leverkusen, Germany) and 50 mg/kg ketamine hydrochloride (Ketalar®; Pfizer, Istanbul, Turkey) for anesthesia, with an additional 15 mg/kg ketamine hydrochloride administered if necessary. The rats were placed in the left lateral position and the surgical area was shaved. The skin of the right thigh was cleaned with 10% povidone iodine solution and a sterile field was created using appropriate covering before the surgery. A 2-cm lateral longitudinal incision was made at the right thigh. The fascia lata was split longitudinally and the vastus lateralis muscle was separated by blunt dissection from the fascia lata and the bone. (Figure 1A) Transverse holes were created using a 0.8-mm Kirschner wire and then a transverse fracture was gently created. (Figure 1B) A 1 mm diameter Kirschner wire was placed in an antegrade manner in the intramedullary canal towards the distal femoral condyles from the fracture site and then the wire was pulled distally. (Figure 1C) After fixation of the fracture, the wire was moved in a retrograde manner towards the greater trochanter. (Figure 1D) The wire stopped 2–3 mm before the greater trochanter and was cut distally with a wire cutter and pushed into the bone using another wire. After fixation, full reduction of the fracture site was achieved. (Figure 1E-F) The fascia and muscle were closed with absorbable sutures and the skin was stitched using nonabsorbable sutures. Lastly, the wound was cleaned with povidone iodine.

During the postoperative period, the rats were not prevented from bearing weight on the broken legs. No antibiotics were given before or after surgery. For postoperative analgesia, 4.5 mg/ml (150–250 mg/kg/day) paracetamol were added to the rats' water for 3 days after the surgery. The GB groups received 60 mg/kg oral *G. biloba* at the same time of day during the predetermined periods for each group. There were no complications related to the surgery or medication and all the rats survived.

The rats in the Gb1 and C1 groups were sacrificed by cervical dislocation under general anesthesia on the seventh postoperative day. The Gb2 and C2 rats were sacrificed 21 days following surgery and the Gb3 and C3 groups were sacrificed on the 35th postoperative day. The right femurs of all rats were disarticulated from the hip and the knee. The soft tissues were stripped for radiological evaluation and anteroposterior and lateral radiographs were taken of the right femurs. (Figure 2A-F) All X-rays were assessed using the Lane-Sandhu radiological scoring system,[9] and were scored by a different orthopedic surgeon who was unaware of the study and the groups. After the X-rays were obtained, the samples were placed in different containers numbered separately for the histologic evaluation which were filled with a 10% neutral formaldehyde solution. A 10% formaldehyde solution with formic acid was used for decalcification of the fixated tissues. Paraffin was cut into 5-micrometer-thick blocks using a fully automatic microtome (Leica RM2255, Japan). Hematoxylin and eosin staining was used to show the overall structure and Masson's trichrome was employed to distinguish the connective tissue.

The sample preparations were evaluated by an experienced independent histologist under a light microscope (Olympus BX51-Japan) and were photographed with a digital camera under the light microscope. (Figure 3A-D) The histological scoring system described by Huo et al.[10] was used for to evaluate the preparations. (Figure 4A-D)

Statistical analyses

The Statistical Package for the Social Sciences (SPSS, version 20 for Windows; SPSS Inc., Chicago, Illinois, USA) was used for all statistical analyses. The Kolmogorov-Smirnov test was performed to determine if the data were normally distributed. The

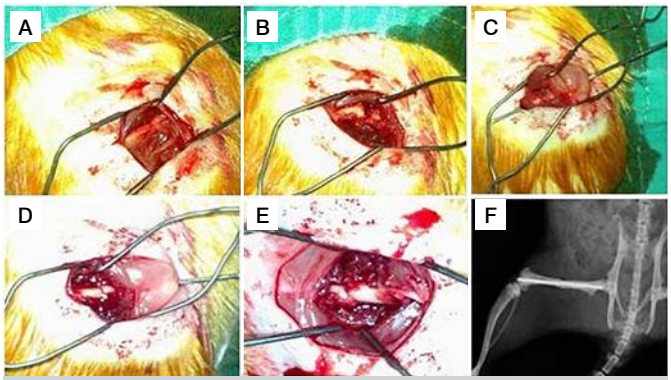

Figure 1. (A) An image of the femur after retraction of the soft tissues; (B) After the transverse fracture was obtained; (C) After placing an anterograde intramedullary K-wire from the fracture site to the knee; (D) Retrograde movement of the K-wire after reducing the fracture; (E) The last image of the fracture after pushing the K-wire inside the bone; (F) The postoperative roentgenogram of the fracture.

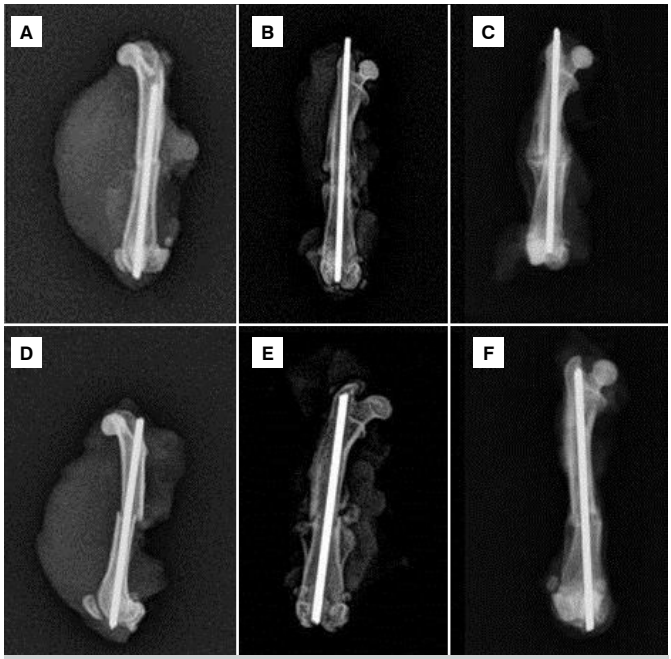

Figure 2. X-ray images of each group. (A) Gb1; (B) Gb2; (C) Gb3; (D) C1; (E) C2; (F) C3. (Gb: *Ginkgo biloba,* C: Control).

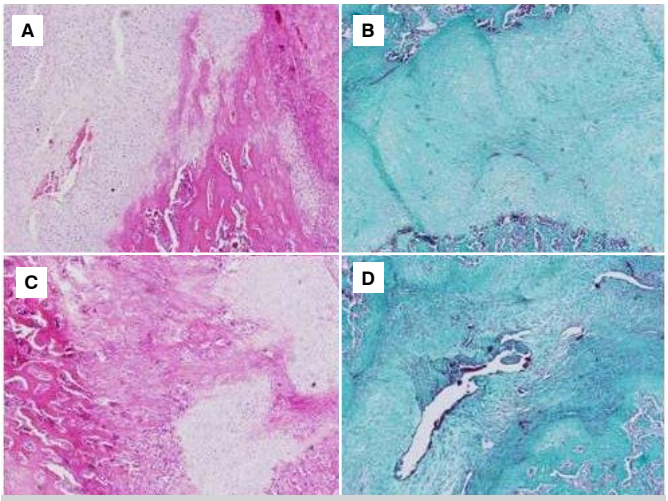

Figure 3. Abundant cartilaginous tissue was seen in the control group on day 21; (A) Hematoxylin and eosin staining x20; (B) Masson's trichrome x10). Abundant cartilaginous tissue and immature bone formation; (C) Hematoxylin and eosin staining x10) and immature bone spicules and red bone marrow; (D) Masson's trichrome x10) were seen in the Ginkgo biloba group at day 21.

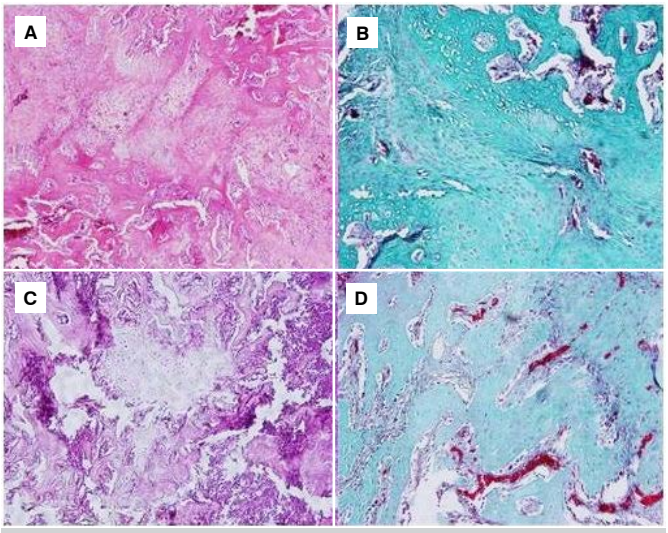

Figure 4. (A) A fracture line containing equal amounts of immature bone and cartilage tissue was observed in the control group on day 35 (Hematoxylin and eosin x10). (B) Equal amounts of cartilage and immature bone containing red bone marrow were seen in the control group on day 35 (Trichrome's Masson x20). (C) A fracture line containing abundant immature bone tissue and a small amount of cartilaginous tissue was seen in the *Ginkgo biloba* group on day 35 (Hematoxylin and eosin x20). (D) A fracture line containing abundant bone spicules, red bone marrow and a small amount of cartilaginous tissue was seen in the *Ginkgo biloba* group on day 35 (Trichrome's Masson x20).

Mann-Whitney U test was employed to compare the radiological and histopathological evaluations between the two groups. The data were summarized as median (minimum-maximum) values. A p-value <0.05 was considered statistically significant.

RESULTS

The X-ray scoring subgroups were evaluated separately. No statistically significant differences were found between the *G. biloba* and the control groups on day 7 or day 35 in terms of bone formation ($p > 0.05$), whereas a significant difference between the groups was seen on day 21 ($p<0.05$). (Table 1) There was no statistically significant difference between groups in terms of union, remodeling, or the total radiological score ($p>0.05$). (Tables 2, 3 and 4) Following the histopathological evaluation, no statistically significant difference was found between the groups on day 7 ($p>0.05$); however, there were statistically significant differences between the groups on day 21 and 35 ($p<0.05$). (Table 5)

DISCUSSION

The effects of different drugs or substances have been investigated by many researchers.[11,12] However, there have been no studies to date that have explored the effects of *G. biloba* on fracture healing. *G. biloba* is a well-known vasoregulatory agent that reduces blood viscosity and increases blood flow.[13] Ginkgolide B, one of the components of *G. biloba*, has been particularly reported to act as an antiaggregant by antagonizing PAF. In this way, *G. biloba* decreases neutrophil degranulation and the production of oxygen radicals which stimulate platelet aggregation.[14] *G. biloba* has been reported to produce a strong vasorelaxant and antiaggregant effect with its superoxide anion cleansing action, which prolongs the half-life of endothelium-derived relaxing factor (EDRF).[15] *G. biloba* has also been used to prevent neurotoxic conditions by inhibiting c-Fos translocation, which causes glutamate-induced

Table 1. The median (minimum-maximum) radiological scores of all groups according to bone formation.

	Bone formation		
	Day 7	Day 21	Day 35
Gb	3(2-4)	3(3-4)	4(1-4)
C	2,5(1-3)	3(2-3)	3(1-4)
p	0,076	0,018*	0,534

Gb: Ginkgo biloba. C: Control. * indicates statistical significance.

Table 2. The median (minimum-maximum) radiological scores of all groups according to the union.

	Union		
	Day 7	Day 21	Day 35
Gb	2(0-4)	2(2-4)	4(0-4)
C	2(0-2)	2(2-2)	2(0-4)
p	0,199	0,143	0,174

Gb: Ginkgo biloba. C: Control.

Table 3. The median (minimum-maximum) radiological scores of all groups according to the remodeling.

	Remodeling		
	Day 7	Day 21	Day 35
Gb	2(0-4)	2(2-4)	4(0-4)
C	2(0-2)	2(2-4)	2(0-4)
p	0,464	0,535	0,174

Gb: Ginkgo biloba. C: Control.

Table 4. The median (minimum-maximum) total radiological scores of all groups.

	Total radiological score		
	Day 7	Day 21	Day 35
Gb	7(2-12)	7(7-12)	12(1-12)
C	6,5(1-7)	7(6-9)	7(1-12)
p	0,124	0,063	0,377

Gb: Ginkgo biloba. C: Control.

Table 5. The median (minimum-maximum) histopathological scores of all groups.

	Histopathological score		
	Day 7	Day 21	Day 35
Gb	2(1-2)	6(5-7)	8,5(7-10)
C	2(1-2)	5(4-6)	6(6-7)
p	0,535	0,009*	0,001*

Gb: Ginkgo biloba. C: Control. * indicates statistical significance.

up-regulation of tissue plasminogen activator.[16] Yan et al. showed that administering EGb761 during the acute phase following spinal cord injury significantly reduced secondary injury-induced tissue necrosis and cell apoptosis and improved functional performance in rats.[6] *G. biloba* extract has been used for many clinical conditions such as concentration and memory problems in elderly patients, anxiety and depressive diseases, dizziness and tinnitus.[17,18] Treatment with *G. biloba* produces significant differences in cerebral insufficiency symptoms.[19] However, there have been no clinical or experimental studies that have investigated the effects of *G. biloba* on fracture healing. Our experimental fracture model revealed that this compound made significant differences in fracture healing which were demonstrated both radiologically and histopathologically in this study. Histologically, those effects were more distinctive on the 21st and 35th days following the fracture. However, radiological scoring revealed that a significant difference in bone formation only occurred on day 21. Blood supply to the fracture area is important in fracture healing; *G. biloba* extract increases oxygen uptake into cells by increasing blood circulation in tissues and allows the removal of toxins from the environment.[20] This effect occurs because *G. biloba* is a PAF antagonist, has antioxidant properties, removes free radicals from the environment, provides vascular relaxation and increases the blood supply and oxygenation of the tissues by reducing blood viscosity. Increased blood supply to the fracture site leads to higher concentrations of mediators and cytokines, which aid in the fracture healing process.

In this study, although the radiological scores of the *G. biloba* group for bone formation were higher on day 7 and day 35, there was only a significant difference on day 21 between the two groups. This may occur because the effects of revascularization are more important between days 7 and 35 for new bone formation. Union and remodeling take place after bone formation, so the radiological scores of both groups were nearly the same according to union and remodeling. Scores improved on day 35, but were not statistically significant. These findings support the suspicion that *G. biloba* causes accelerated bone formation but has no significant effects on final union or remodeling. According to the histopathological scores, there were significant differences between the *G. biloba* and control groups on days 21 and 35. Fibrous and cartilaginous tissues formed during the early stages of bone healing, leading to the subsequent development of both immature and mature bone. The effects of *G. biloba* on bone formation were significant during the late phases of healing. One limitation of our study was the lack of different dosages of *G. biloba*. Further studies with different dosages are required to obtain more information about the effects of *G. biloba*.

CONCLUSION

This study showed that use of *Ginkgo biloba* accelerated bone formation and fracture healing. Both radiological and histological differences were detected, but the histological differences were more notable.

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. NG (0000-0001-5869-8702)*, OA (0000-0002-8001-8678)* and SK (0000-0003-2190-9742)* conducted surgery, monitored the rats and gathered clinical data. ES was the main contributor in drafting the manuscript. EY (0000-0002-5405-7083)* and MT (0000-0002-0660-197X)* evaluated specimens and the data for the statistical analysis. ES (0000-0003-0733-8621)* searched the literature, reviewed the manuscript and contributed to the intellectual concept of the study. *ORCID (Open Researcher and Contributor ID).

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SUBCHONDRAL RAFT CONSTRUCTION WITH LOCKING PLATES FOR THE TREATMENT OF SCHATZKER TYPE II FRACTURES

CONSTRUÇÃO DE PLATAFORMA SUBCONDRAL COM PLACAS DE TRAVA PARA O TRATAMENTO DE FRATURAS DO TIPO II DE SCHATZKER

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ABSTRACT

Objectives: To evaluate the functional and radiological results of Schatzker type II fractures treated via subchondral raft screws combined with locking plates. Methods: Twenty-four individuals were enrolled in this study between 2010 and 2014. The depressed joint line was elevated and the defect was filled with allograft. Next, two or three subchondral screws were placed in combination with a locking plate. At the last follow-up, clinical and radiological data were recorded. Results: The mean follow-up period was 21.4 months (12–39). The mean Knee Society Score (KSS) and Rasmussen clinical scores were 91.5 (range, 77-100) and 16.75 (range, 14-18), respectively. The mean Rasmussen radiological score was 27.9 (range, 24-30) during the follow-up. There was no statistically significant difference between injured and non-injured sides with respect to the mechanical axis, the proximal medial tibial angle, and tibial slope. In addition, arthritis showed no difference on the non-injured side, although follow-up was short. Conclusions: The periarticular raft construction combined with the locking plate helps surgeon to maintain the anatomic line of the joint and the mechanical axis obtained during the surgery. Secondary arthritis seems to be major complication after fractures of the tibial plateau, although the functional results were satisfactory. ***Level of Evidence IV, Case Series.***

Keywords: Tibial fractures/classification. Fracture fixation, internal. Bone screws. Treatment outcome.

RESUMO

Objetivos: Avaliar os resultados funcionais e radiológicos das fraturas de Schatzker tipo II tratadas com parafusos de plataforma subcondral em combinação com placas de trava. Métodos: Vinte e quatro indivíduos foram selecionados para este estudo entre 2010 e 2014. A linha articular deprimida foi elevada e o defeito foi preenchido com aloenxerto. A seguir, dois ou três parafusos subcondrais foram colocados em combinação com uma placa de trava. No último acompanhamento, foram registrados os dados clínicos e radiológicos. Resultados: O período médio de acompanhamento foi 21,4 meses (12–39). A média do Knee Society Score (KSS) e dos escores clínicos de Rasmussen foram 91,5 (faixa, 77-100) e 16,75 (faixa, 14-18), respectivamente. A média do escore radiológico de Rasmussen foi 27,9 (faixa, 24-30) durante o acompanhamento. Não houve diferença estatisticamente significante entre o lado com lesão e sem lesão, com relação ao eixo mecânico, ao ângulo medial proximal da tíbia e à inclinação tibial. Além disso, a artrite não apresentou diferença no lado sem lesão, embora o acompanhamento tenha sido curto. Conclusões: A construção de plataforma periarticular combinada com placa de trava ajuda o cirurgião a manter a linha anatômica da articulação e o eixo mecânico obtido durante a cirurgia. A artrite secundária parece ser uma complicação importante depois de fraturas do platô tibial, embora os resultados funcionais sejam satisfatórios. ***Nível de Evidência IV, Série de Casos.***

Descritores: *Fraturas da tíbia/classificação. Fixação interna de fraturas. Parafusos ósseos. Resultado do tratamento.*

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INTRODUCTION

Split-depression tibial plateau fractures are the most commonly seen tibial injuries, accounting for 25-33% of tibial plateau fractures.[1] Over the past three decades, many surgical techniques to treat this injury have been published; minimally invasive methods such as arthroscopy and/or C-armed fluoroscopy assisted osteosynthesis or traditional methods have been successfully used by many physicians.[2-5]

However, Schatzker type II fractures with comminuted osteochondral fragments are at the point of joint line collapse. Consequently, many authors have performed biomechanical studies to evaluate postoperative reduction loss. Subchondral raft construction is one popular methods under investigation for this purpose.[6-12]

In this study, we aimed to evaluate the clinical and radiological results of Schatzker type II fractures treated using subchondral raft screws combined with anatomical lateral plateau locking plates.

All authors declare no potential conflict of interest related to this article.

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PATIENTS AND METHODS

In this retrospective study, 24 consecutive Schatzker type II tibial plateau fractures treated over a three-year period were reviewed. The series consisted of only isolated tibial plateau fractures confirmed by plain x-rays and computerized tomography. (Figures 1, 2, 3A, 3B, 3C) Patients with other associated injuries, pathologic fractures, or younger than 18 years were excluded to create a uniform group.

The sample was comprised of 19 male and 5 female patients with an average age of 45 years (range, 20–69 years). The etiology of injuries was as follows; 16 motor vehicle collisions and 8 falls from height. Mean time from hospitalization to operation was 4 days (range, 2-10 days). All patients signed an informed consent form. Because this is a retrospective study, approval was not sought from the institutional review board.

An anterolateral incision was made over the proximal tibia, using a pneumatic tourniquet and spinal anesthesia. After the anterolateral part of the proximal tibia was exposed, fracture line was made more visible using the open book maneuver. The depressed joint line was elevated, the defect was filled with allograft and joint line congruency was observed via the submeniscal approach. Then 2 or 3 5 mm locking screws for raft construction were placed through the anatomic lateral locking plate. After C-arm fluoroscopy control, the last screws were placed and osteosynthesis was completed. Active and passive rehabilitation was begun after suction drains were removed. Partial and full weight bearing were encouraged at 6 and 10 weeks, respectively, at the outpatient clinic.

The Knee Society and Rasmussen clinical scores were used for functional evaluation.[13,14] The Rasmussen radiological score, tibiofemoral anatomical angle, proximal tibial medial angle and tibial slope were used for radiological evaluation. (Figure 4) Student's t test and the Chi-squared tests were used for statistical analysis using SPSS version 20 software.

RESULTS

The mean follow-up period was 21.4 months (range: 12–39 months). The mean Knee Society Score (KSS) and Rasmussen clinical scores were 91.5 (range: 77–100) and 16.75 (range: 14–18), respectively. Anatomical or near-anatomical joint line reconstruction was achieved in all cases but one. A 2 mm depression was measured in the postoperative x-ray in this case. The mean Rasmussen radiologic score was 27.9 (range: 24–30) at follow-up.

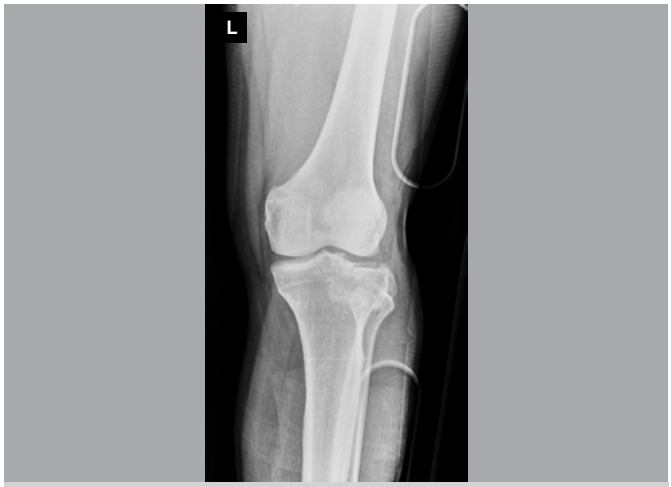

Figure 1. Male, 47 years, preoperative AP X-ray.

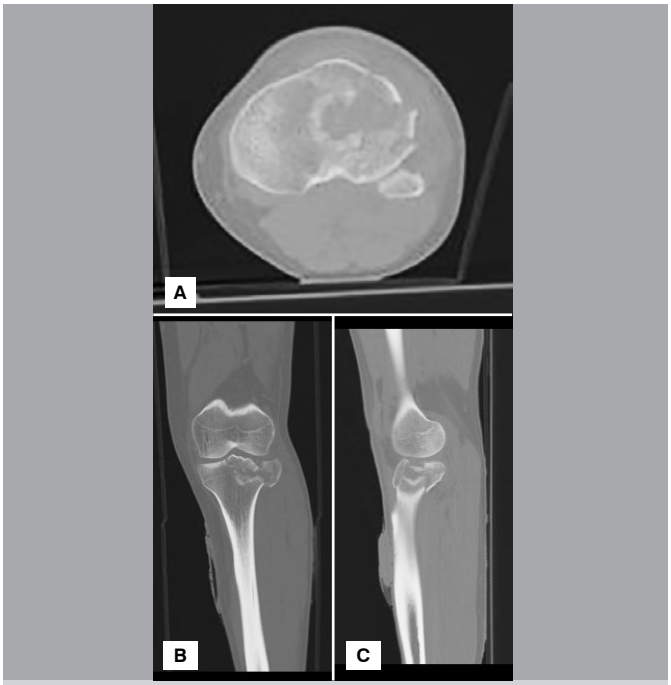

Figure 3. (A) Preoperative horizontal CT view; (B) preoperative frontal CT view; (C) preoperative sagittal CT view.

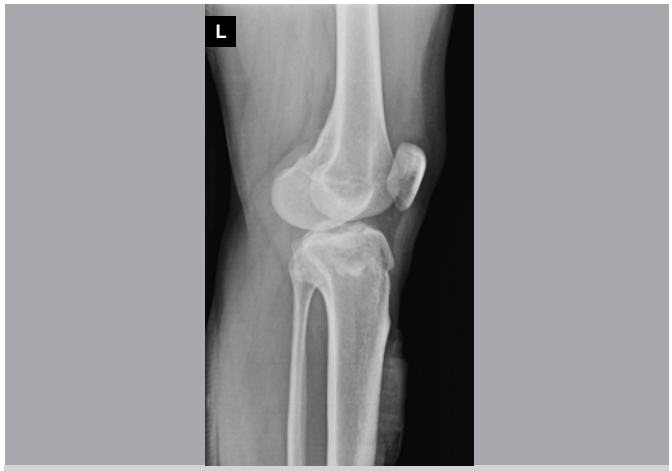

Figure 2. Preoperative lateral X-ray.

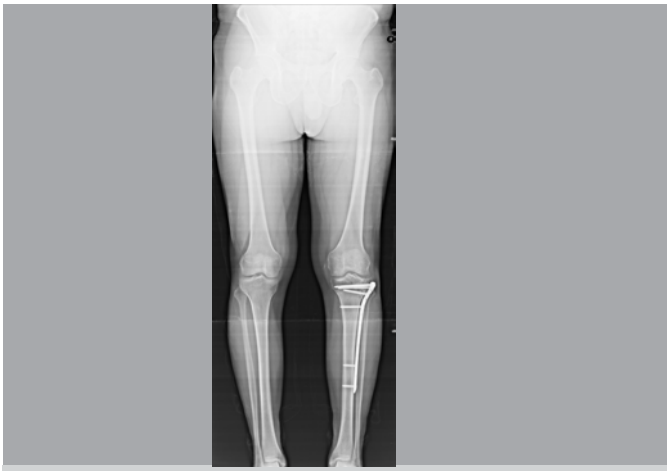

Figure 4. Ortho roentgenogram at last visit.

The tibio-femoral anatomical axis, proximal tibial medial angle and tibial slope angles of both the injured and uninjured sides in x-rays from the last visit were measured, recorded and compared statistically to evaluate the effectiveness of subchondral raft construction. These parameters are shown in Table 1. In summary, we found no statistical difference between the values for the injured and uninjured sides (p_{TFAA}=0.265, p_{PTMA}=0.574, p_{TSA}=0.57).

The range of motion (ROM) for the knee joint for both injured and uninjured sides was measured using a goniometer at the last visit. The mean ROM for the injured and uninjured sides were 133.75° (range: 120°–145°) and 137° (range: 130°–145°), respectively. There was no significant difference with respect to knee joint ROM at last visit (p=0.121).

Tibio-femoral osteoarthritis was defined using Ahlbäck classification criteria as stage 0: no radiographic sign of arthritis; stage I: narrowing of the joint space (JSN) (with or without subchondral sclerosis). JSN is defined by a space inferior to 3 mm, or inferior to the half of the space in the other compartment (or in the homologous compartment of the other knee); stage II: obliteration of the joint space; stage III: bone defect/loss <5 mm; stage IV: bone defect/loss 5–10 mm; and stage V: bone defect/loss >10 mm, often with subluxation and arthritis of the other compartment.[15] There were 6 cases with grade 0, 13 cases with grade 1 and 5 cases with grade 2 arthritis. For comparison we evaluated the degree of arthritis in the contralateral uninjured knee. There were 10 cases with grade 0, 10 cases with grade 1 and 4 cases with grade 2 arthritis. When these groups were analyzed statistically using the greater contingency table (chi-squared test) no significant difference was observed (p=0.471). No severe osteoarthritis was seen.

No superficial or deep infection was observed, no peroneal paralysis was recorded before or after the procedure and no hardware was removed from any patient. All patients except one returned to their pre-injury level of activity, work, or recreational activities; in this case, a 33 year old male moved from heavy labor to a desk job. His functional status was good according to KSS and Rasmussen criteria.

DISCUSSION

Schatzker type II fractures are the most common tibial plateau injuries resulting from axial and bending forces. Type II fractures usually contain more than 1 fracture fragment because the lateral plateau is convex to the femur and features a substantial proportion of cancellous bone. Articular surface depression is widely seen in older patients because of osteoporosis. Consequently, both minimally invasive and conventional approaches are used to treat type II fractures.[1,9]

Cross et al. described the debate on ideal internal fixation for preventing subsequent loss of reduction during postoperative rehabilitation. Adequate maintenance in the postoperative period is important to avoid this outcome, due to the risk of posttraumatic arthritis. The subchondral raft technique is a well-known method to resist depression and loss of reduction and can be performed using a Kirschner wire, lag screw, conventional screw and locking screw either through the plate or individually.[10]

Raft construction has also been addressed by other authors. Cole reported that comminuted, unstable areas could be supported in their reduced position by placing a raft of parallel smaller-diameter screws close below and parallel to the articular surface. After elevation and support using a bone void filler, fixation of the lateral cortex is then achieved with a buttress plate or periarticular "raft" plate. This author recommended that the subchondral raft of screws be placed through the plate so the screws are fixed laterally at the plate and medially in the intact medial column of bone.[16]

Karunakar et al. compared biomechanical characteristics of 4 fixation options: the L-buttress plate, four 3.5 mm subchondral raft

Table 1. The summary of demographic, functional and radiological data of the cases. DM: Diabetes Mellitus, KSS: Knee Society Score, contr: data from contralateral uninjured side, MA: Mechanical Axe ((-) means varus), TS: Tibial Slope, PTMA: Proximal Tibial Medial Angle.

Gender	Op. day	Side	Medical history	Follow up (months)	KSS	Rass. rad.	Rass. clin.	Contr. MA	MA	Contr. T. S.	T. S.	Contr. PTMA	PTMA	Contr. arthrosis	Arthrosis
M	2	L	-	12	93	29	18	-1	-1	4	4	88	88	grade 0	grade 0
M	4	R	DM	10	87	29	16	-1	-2	5	4	87	87	grade 1	grade 1
M	3	L	-	36	90	26	16	-1	-1	4	4	87.5	87.5	grade 0	grade 1
M	2	L	-	18	100	30	18	0	0	5	5	88	88	grade 1	grade 0
F	4	R	DM	19	90	24	16	-3	-4	4	4	88	88	grade 2	grade 2
M	10	R	Alcohol	18	88	26	16	-2	-2	4	4	89	89	grade 2	grade 2
M	5	R	Smoke, Alcohol	15	87	27	16	-2	-3	4	4	86.5	86	grade 0	grade 1
M	3	R	Smoke	8	87	27	18	0	0	4	4	88	88	grade 2	grade 2
M	3	L	Smoke	28	93	29	18	0	0	5	5	86.5	86.5	grade 0	grade 0
M	2	R	Smoke, Alcohol	28	93	30	18	-1	-1	5	5	87,5	87.5	grade 1	grade 0
M	6	R	Smoke	26	90	29	18	-2	-3	5	5	87	87	grade 1	grade 1
M	4	L	-	30	77	24	18	-1	-1	4	4	86.5	86.5	grade 0	grade 1
M	5	R	-	26	93	30	18	0	0	6	6	87	87	grade 1	grade 1
M	5	L	-	24	90	26	14	-1	-1	5	5	86	86	grade 1	grade 2
M	4	L	Alcohol	11	93	25	14	-3	-2	4	3	86	86.5	grade 2	grade 2
M	2	R	Smoke	28	97	28	18	0	0	4	4	87	87	grade 0	grade 0
M	4	R	-	30	93	29	14	0	1	5	5	88	88	grade 1	grade 1
M	2	R	-	36	100	30	18	-1	-1	5	5	88.5	88.5	grade 0	grade 0
F	2	L	-	24	95	29	18	-3	-3	4	4	88	88	grade 1	grade 1
M	5	L	Smoke	21	90	26	18	-1	-1	4	4	87	87	grade 1	grade 1
F	3	L	Smoke	18	93	29	18	-1	-1	6	6	88	88	grade 2	grade 1
M	3	L	Smoke, Alcohol	18	91	29	14	-2	-3	4	5	86.5	86	grade 0	grade 1
M	5	L	-	7	93	29	18	-3	-3	3	3	87	87	grade 2	grade 1
F	7	R	DM	24	93	30	14	-3	-3	5	5	88	88	grade 1	grade 1

screws with an antiglide plate, an L-buttress plate with cancellous allograft and four 3.5 mm subchondral raft screws through a periarticular plate for type II fractures. These authors found no significant differences between these constructions, but the raft of subchondral screws demonstrated more resistance to local depression loads.[9]

In another biomechanical study, Cross et al. evaluated three different raft alternatives: raft construction outside the plate, non-locking raft screws through the plate and locking raft screws through the plate. These authors reported achieving statistically significant stability with the raft through plate over screws outside the plate. However, they did not find that locking screws were superior to non-locking screws and recommended considering raft construction through the plate versus outside the plate.[10]

In our study we applied 5 mm raft screws through the locking plate to support comminuted osteochondral fragments against collapse. The radiological and functional results are promising. Among the radiological parameters (tibio-femoral anatomic angle, proximal medial tibial angle and posterior tibial slope), there was no significant difference between injured and uninjured knees at the last visit.

The functional results were all good or excellent according to KSS and Rasmussen criteria. There was no significant loss of knee ROM at the last follow-up. The only issue is the stage of arthrosis detected. Post traumatic arthrosis is the most concerning complaint after tibial plateau fractures.[17,18]

Parkkinen et al. reported that factors predicting the development of early arthritis are postoperative articular congruity and normal mechanical axis. They found valgus malalignment ≥5° and articular depression >2 mm lead to severe arthritis.[19]

Another study comprised of 109 plateau fractures after a long-term follow-up (5 to 27 years) reported that cases with malalignment exceeding 5° have more moderate to severe arthritis than cases with anatomic axes. In that study, 31% of the patients had post-traumatic arthritis.[4]

Two points are important to lower arthritis rate: obtaining the anatomic joint line and normal mechanical axis during surgery and maintaining this reduction throughout the healing period.[4,19] In addition to all initial articular cartilage damage was accused for the development of arthritis.[20]

In our study we had 18 cases with grade 1 or 2 arthritis at last visit. However, 4 cases had grade 1 arthritis in the injured knee and grade 0 arthritis in the uninjured contralateral knee and only one case had grade 2 arthritis in the injured knee and grade 1 arthritis in the uninjured knee. Arthritis developed in 4 cases and progressed one level in one case due to a plateau fracture. At this point 21% of patients have secondary arthritis which developed at a mean of 21.4 months.

This study poses some shortcomings, namely the fact that it was a retrospective analysis with no comparative group. Although the study group seems small, it was identical, with only Schatzker type II fractures. In addition, the same surgical team was used in all cases.

CONCLUSION

In conclusion, periarticular raft construction through the locking plate helps surgeons achieve and preserve the anatomic joint line and normal mechanical axis. Secondary arthritis seems to be the major complication after tibial plateau fractures although superior functional results were obtained in the short term.

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. CK (0000-0002-6260-0744)* and CC (0000-0003-1812-0863)* were the main contributors in drafting the manuscript. CK, CC, TA (0000-0002-6917-934X)* and ZK (0000-0002-4885-545X)* performed surgery, followed patients and gathered clinical data. CK and CC evaluated the data for the statistical analysis. CK, CC and TA performed the literature search, reviewed the manuscript and contributed to the intellectual concept of the study. *ORCID (Open Researcher and Contributor ID).

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MULTIFOCAL OSTEONECROSIS SECONDARY TO OCCUPATIONAL EXPOSURE TO ALUMINUM

OSTEONECROSE MULTIFOCAL SECUNDÁRIA À EXPOSIÇÃO OCUPACIONAL AO ALUMÍNIO

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ABSTRACT

Multifocal osteonecrosis is a rare disease; chronic use of corticosteroids is considered the main risk factor. Patients with chronic renal failure can develop aluminum toxicity, which can lead to osteomalacia and encephalopathy. An association between osteonecrosis and aluminum toxicity has been reported among patients with dialytic renal insufficiency. Occupational exposure to aluminum rarely causes lung disease and no cases of bone lesions resulting from exposure to this metal have been reported. In this manuscript, we describe a novel case of a patient with multifocal osteonecrosis associated with chronic occupational exposure to aluminum. ***Level of Evidence IV, Case Report.***

Keywords: Osteonecrosis. Occupational injuries. Shoulder. Hip. Knee.

RESUMO

A osteonecrose multifocal é uma doença rara. O uso crônico de corticoides é considerado seu principal fator de risco. Em pacientes com insuficiência renal crônica é descrita a intoxicação por alumínio, causando osteomalácia e encefalopatia. A relação entre osteonecrose e toxicidade pelo alumínio já foi relatada em estudos que envolveram pacientes com insuficiência renal dialítica. A exposição ocupacional ao alumínio pode, raramente, ocasionar doenças pulmonares. Não existem casos relatados de lesões ósseas decorrentes da exposição a esse metal. Descrevemos neste artigo, o relato inédito de um paciente com osteonecrose multifocal associada à exposição ocupacional crônica ao alumínio. ***Nível de Evidência IV, Relato de Caso.***

Descritores: *Osteonecrose. Doenças ocupacionais. Ombro. Quadril. Joelho.*

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INTRODUCTION

Osteonecrosis is a common orthopedic disease[1] and tends to affect the hip.[2] Multifocal involvement has a prevalence of only 3%.[3] Prominent among occupational causes is dysbaric disease.[4] Occupational exposure to aluminum is a rare cause of disease,[5] and its relationship with pneumoconiosis has been established.[5,6] In this paper we report an unprecedented case of multifocal osteonecrosis secondary to chronic occupational exposure to aluminum.

METHODS

Black male patient, 39 years old, was evaluated for the first time in our service in 2008. He presented polyarthralgia involving knees, hips and shoulders, which started four years prior. At the time of the consultation, the pain was debilitating. He worked for eight years in a plant refining bauxite and producing aluminum. His job was to open packages containing solid material and empty them into a tank, where a chemical reaction occurred. During his work, he used glasses, a filter mask, ear plugs, boots and a uniform with long cotton sleeves and gloves. He states he did not use a helmet. He did not come into contact with ionizing radiation or a hyperbaric chamber.

X-rays of the hips, knees and shoulders did not show alterations. (Figure 1) MRI scans showed signs of osteonecrosis. (Figures 2-4) In the hips and shoulders, the location was subchondral, while in the knees it was predominantly located in the metaphysis of the femur as well as the tibia. Collapse was not observed in any of the joints. According to the visual analogue pain scale (VAS), the patient scored nine points in the right hip, knee and shoulder and seven in the left hip, knee and shoulder. Range of motion was complete in all joints except the patient's right shoulder, which had 150° elevation, internal rotation to L5 and external rotation of 40°.

The patient was subjected to extensive laboratory testing. No changes were seen in kidney, liver, thyroid, pancreatic, or parathyroid function. Electrolytes (sodium, potassium, calcium, phosphorus and magnesium) were at normal concentrations, as well as vitamin D, cholesterol,

All authors declare no potential conflict of interest related to this article.

Study conducted at the Universidade de São Paulo, Faculdade de Medicina, Hospital das Clínicas, Instituto de Ortopedia e Traumatologia, Grupo de Ombro e Cotovelo, São Paulo, SP, Brazil.
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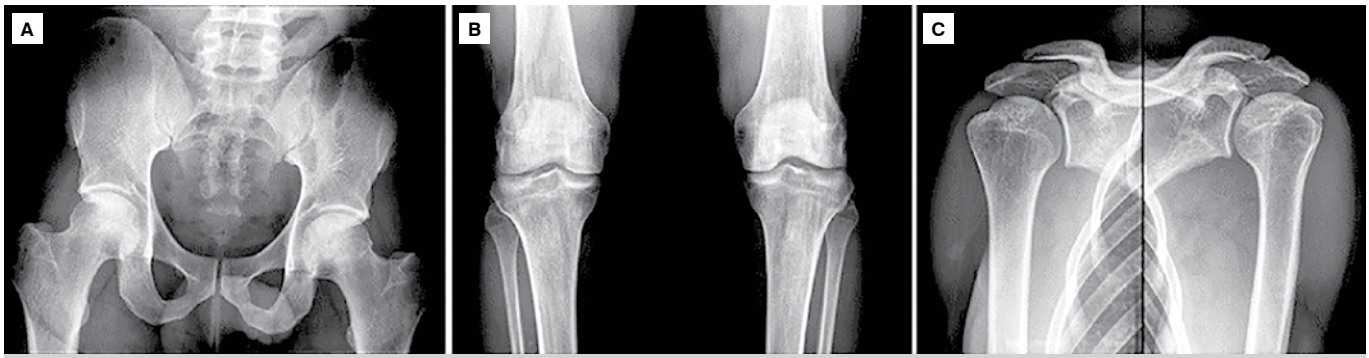

Figure 1. X-rays of hips (A), knees (B) and shoulders (C) showing preserved joint congruity.

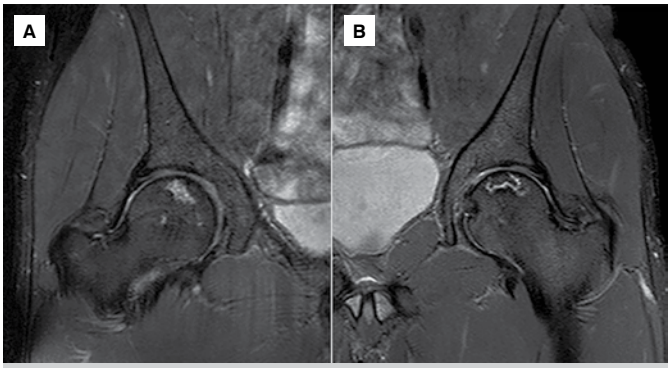

Figure 2. MRI of the hips showing bilateral involvement without joint collapse: (A) right, (B) left.

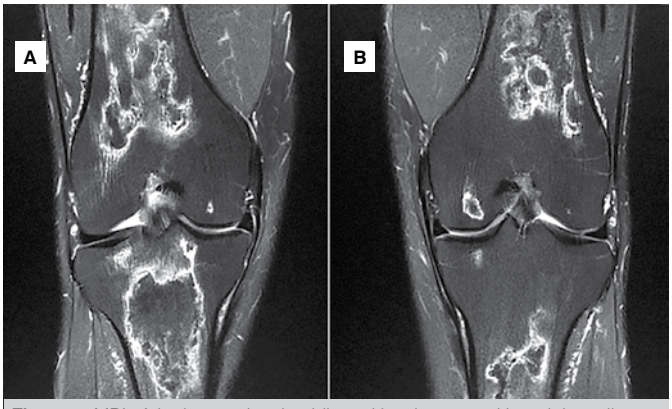

Figure 3. MRI of the knees showing bilateral involvement without joint collapse: (A) right, (B) left.

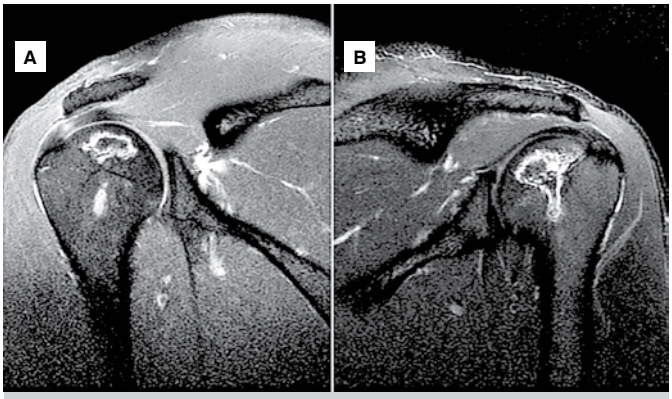

Figure 4. MRI of the shoulders showing bilateral involvement without joint collapse: (A) right, (B) left.

triglycerides and plasma proteins. The blood count did not show any abnormalities. Inflammatory and rheumatological tests were negative. Predisposing factors for thromboembolic phenomena (coagulation, platelet concentration, antiphospholipid syndrome, factor V Leiden, anti-cardiolipin) were also normal. Serology for hepatitis, HIV and HTLV was negative.

Bone marrow biopsy showed no alterations. Electrophoresis of hemoglobin showed 62.1% hemoglobin A1, 2.3% hemoglobin A2 and 35.6% hemoglobin S (sickle cell trait). The bone lesion present in the metaphyseal region of the left femur was biopsied, showing bone infarction.

The patient had plasma aluminum above normal levels in all samples. (Figure 5) A new biopsy was performed in the iliac crest, which showed a high concentration of aluminum and a low calcium concentration in relation to a healthy sample control. X-ray fluorescence spectrometry was employed. (Figure 6)

The patient did not report respiratory symptoms. Tomography of the chest revealed the presence of centrilobular micronodules, (Figure 7) both calcified and uncalcified. A lung biopsy collected via bronchoscopy showed normal tissue and bronchoalveolar lavage did not show the presence of fungi or mycobacteria.

Conservative treatment was indicated, with pain relief and physiotherapy. The patient currently exhibits level five pain in the lower limbs and four in the upper limbs and full range of motion in the involved joints. The patient uses analgesics regularly and chose not to undergo decompression in the foci of osteonecrosis. X-rays still show no signs of collapse after six years of follow-up. The patient has remained on disability leave from his work since 2008. The study was approved by the institutional review board under process number 1113.

DISCUSSION

A variety of causes have been described for osteonecrosis. Among extrinsic or iatrogenic causes are decompression sickness,[1,4] alcohol consumption[1,2] and chronic use of corticosteroids.[1,2]

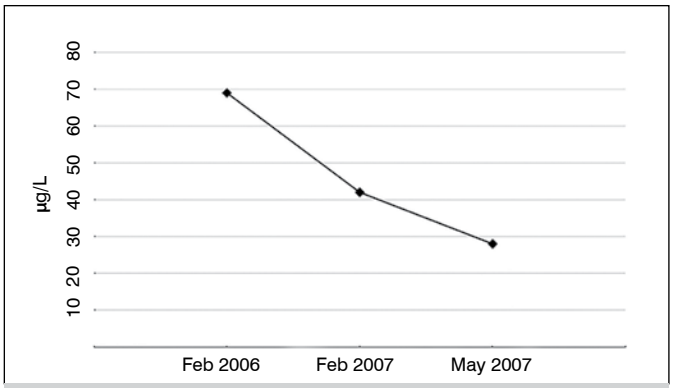

Figure 5. Graph showing patient's plasma aluminum concentration.

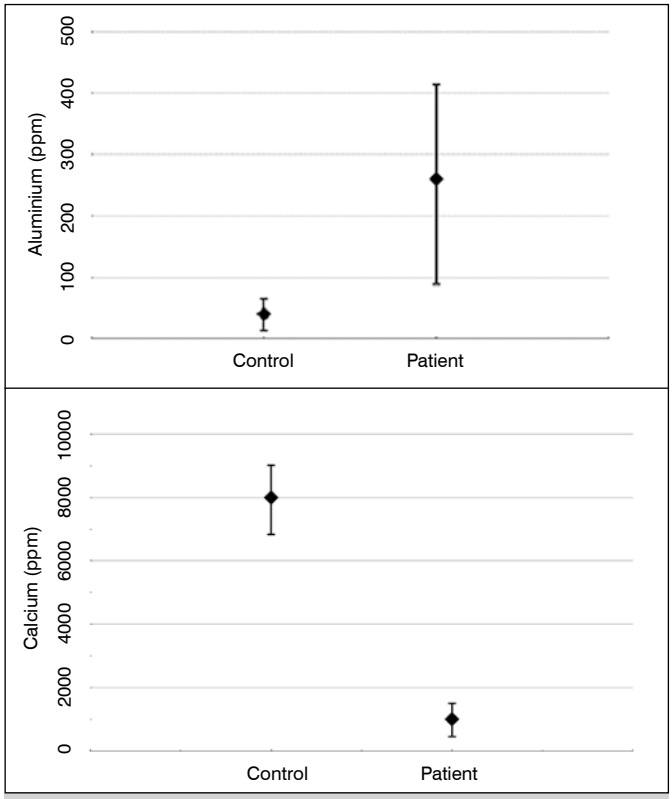

Figure 6. Graph showing high concentration of aluminum and low concentration of calcium in the bone tissue compared to a healthy sample control.

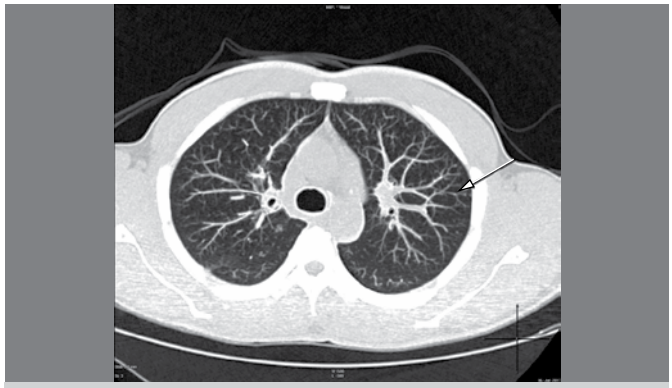

Figure 7. CT scan of the chest showing centrilobular micronodules (arrows).

Multifocal involvement, defined as occurring in three or more places, is rare. In a study involving 1056 patients with osteonecrosis, LaPorte et al.[3] found only 3% with multifocal involvement. The average number of affected sites was 6.3 and 77% of the joints did not collapse. Another multicenter study[7] involving 101 patients with osteonecrosis found progressive involvement of the femoral head in 100% of cases, the knee in 96%, the shoulder in 80% and the ankle in 44%. Bilaterality was commonly found in the hip (98%), knees (86%) and shoulder (83%). Most of the injuries (69%) were diagnosed in pre-collapse stage. The case described here presented involvement in six joints (hips, knees and shoulders), all without collapse.

Previous use of corticosteroids represents 91% of the causes of multifocal osteonecrosis.[7] Other less common causes are alcoholism,[1] chemotherapy,[8] sickle cell disease,[9] rheumatological diseases,[3] coagulation disorders,[10] inflammatory bowel disease,[11] and HIV infection.[12] In the case described here, the patient was negative for all these risk factors.

The presence of the sickle cell trait, as seen in our patient, has been reported in association with osteonecrosis of the hip.[13] However, the evidence is insufficient to determine a significant association.[14] Dorwart et al.,[15] in a larger study on this subject, observed that the occurrence of osteonecrosis was not higher in the 114 patients evaluated in comparison with controls. We believe that the sickle cell trait was not a determining factor in the development of the multiple osteonecrotic foci.

In patients with chronic renal failure, aluminum poisoning resulting from hemodialysis fluids and/or oral prophylactic use of phosphate chelating agents has been described as causing osteomalacia and encephalopathy.[16] The relationship between osteonecrosis and aluminum toxicity has been reported in only two studies involving patients with dialytic renal failure.[17,18] However, we found no reports associating the occurrence of osteonecrosis with occupational exposure to aluminum. In 2007, Krewsky et al.[5] published a systematic review of the risks aluminum poses to health. These authors did not refer to any bone complications resulting from occupational exposure in their study. Willhite et al.[6] updated this systematic review, also without reporting osteonecrosis as a complication.

The relationship between aluminum exposure and pneumoconiosis is well established, however.[5,6,19] Kraus et al.[19] reported data on 62 workers involved with the production of aluminum powder with median exposure of 123 months. These authors found nodular centrolobular opacity in tomography in 24.2% of their sample and 6.5% reported effort dyspnea. They also observed that plasma and urine concentrations of aluminum are correlated to labor risks. Our case presented calcified and non-calcified centrilobular micronodules in tomography. Despite these findings, the patient denied present or past respiratory discomfort. We believe that the high concentration of aluminum in the bloodstream, after inhalation or skin absorption, could be the cause of osteonecrosis in the case in question. Aluminum inhibits osteoid tissue calcification of the trabecular bone,[17,18] and consequently the resulting osteomalacia makes the bone tissue more fragile and susceptible to osteonecrosis from microtrauma.[18] The patient was exposed to aluminum until 2005, when he took disability leave from his work. Three plasma aluminum levels were taken, one in 2006 and two in 2007. In all tests the concentrations were high and gradually decreased. Another factor that contributes to our hypothesis was the high aluminum level seen in the patient's bone tissue via x-ray fluorescent spectrometry.

Pre-collapse osteonecrosis can be treated conservatively or with surgery in order to relieve pain and prevent collapse.[20] Decompression of the focus of the osteonecrosis is an effective procedure for treating early stages of osteonecrosis of the hip, knee and shoulder,[3] although there is no consensus on the indications for this procedure.[20] When joint collapse or secondary arthrosis has already occurred, joint arthroplasty is the recommended treatment.[3] The case reported herein was treated conservatively, with partial improvement of pain and no collapse in 6 years of follow-up. Nevertheless, the patient uses opioids regularly. Surgical decompression was indicated for the foci of the osteonecrosis, but the patient opted for non-surgical treatment despite the severity of painful symptoms.

CONCLUSION

In this article we describe an unpublished report of a patient with multifocal osteonecrosis associated with chronic occupational exposure to aluminum.

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. JHA (0000-0002-2566-3471)*, EAM (0000-0003-1956-6445)* and MECG (0000-0002-0214-9576)* were the main contributors in writing the manuscript and carried out the bibliographic review. RZF (0000-0002-1250-0876)* performed the analysis and interpreted the data. AAFN (0000-0001-5097-9542)* conducted the review and final approval of the manuscript version. *ORCID (Open Researcher and Contributor ID).

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Contraindicação: Hipersensibilidade a qualquer dos componentes da fórmula. Interação Medicamentosa: A administração concomitante de glicocorticóides e outros agentes anti-inflamatórios não-esteróides pode levar ao agravamento de reações adversas gastrintestinais.

TANDRILAX é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas.

TANDRILAX (cafeína 30 mg / carisoprodol 125 mg / diclofenaco sódico 50 mg / paracetamol 300 mg) Comprimidos. USO ORAL. USO ADULTO. Indicações: Tratamento de reumatismo nas suas formas inflamatório-degenerativas agudas e crônicas; crises agudas de gota, estados inflamatórios agudos, pós-traumáticos e pós-cirúrgicos. Exacerbações agudas de artrite reumatóide e osteo-artrose e estados agudos de reumatismo nos tecidos extra-articulares e como coadjuvante em processos inflamatórios graves decorrentes de quadros infecciosos. **Contraindicações: Nos casos de úlcera péptica em atividade; hipersensibilidade a quaisquer dos componentes de sua fórmula; discrasias sanguíneas; diáteses hemorrágicas (trombocitopenia, distúrbios da coagulação), porfiria; insuficiência cardíaca, hepática ou renal grave; hipertensão grave. É contra-indicado em pacientes asmáticos nos quais são precipitados acessos de asma, urticária ou rinite aguda pelo ácido acetilsalicílico e demais inibidores da via da cicloxigenase da síntese de prostaglandinas. Precauções e Advertências: O uso em pacientes idosos, geralmente mais sensíveis aos medicamentos, deve ser cuidadosamente observado. Desaconselha-se o uso do TANDRILAX durante a gravidez e lactação. A possibilidade de reativação de úlceras pépticas requer anamnese cuidadosa quando houver história pregressa de dispepsia, hemorragia gastrintestinal ou úlcera péptica. Nas indicações do TANDRILAX por períodos superiores a dez dias, deverá ser realizado hemograma e provas de função hepática antes do início do tratamento e, periodicamente, a seguir. A diminuição da contagem de leucócitos e/ou plaquetas, ou do hematócrito requer a suspensão da medicação. Em pacientes portadores de doenças cardiovasculares, a possibilidade de ocorrer retenção de sódio e edema deverá ser considerada. Observando-se reações alérgicas pruriginosas ou eritematosas, febre, icterícia, cianose ou sangue nas fezes, a medicação deverá ser imediatamente suspensa. Não use outro produto que contenha paracetamol. Não é indicado para crianças abaixo de 14 anos, com exceção de casos de artrite juvenil crônica. Interações medicamentosas:** O diclofenaco sódico, constituinte do TANDRILAX, pode elevar a concentração plasmática de lítio ou digoxina, quando administrado concomitantemente com estas preparações. Alguns agentes antiinflamatórios não-esteróides são responsáveis pela inibição da ação de diuréticos da classe da furosemida e pela potenciação de diuréticos poupadores de potássio, sendo necessário o controle periódico dos níveis séricos de potássio. A administração concomitante de glicocorticóides e outros agentes antiinflamatórios não-esteróides pode levar ao agravamento de reações adversas gastrintestinais. A biodisponibilidade do TANDRILAX é alterada pelo ácido acetilsalicílico quando este composto é administrado conjuntamente. Recomenda-se a realização de exames laboratoriais periódicos quando anticoagulantes forem administrados juntamente com TANDRILAX, para aferir se o efeito anticoagulante desejado está sendo mantido. Pacientes em tratamento com metotrexato devem abster-se do uso do TANDRILAX nas 24 horas que antecedem ou que sucedem sua ingestão, uma vez que a concentração sérica pode elevar-se, aumentando a toxicidade deste quimioterápico. **Reações adversas: Distúrbios gastrintestinais como dispepsia, dor epigástrica, recorrência de úlcera péptica, náuseas, vômitos e diarréia. ocasionalmente, podem ocorrer cefaléia, sonolência, confusão mental, tonturas, distúrbios da visão, edema por retenção de eletrólitos, hepatite, pancreatite, nefrite intersticial. Foram relatadas raras reações anafilactóides urticariformes ou asmatiformes bem como síndrome de stevens-johnson e síndrome de lyell, além de leucopenia, trombocitopenia, pancitopenia, agranulocitose e anemia aplástica. o uso prolongado pode provocar necrose papilar renal. TANDRILAX é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas. Posologia:** A dose mínima diária recomendada é de um comprimido a cada 12 horas e a duração do tratamento deve ser a critério médico e não deverá ultrapassar 10 dias. Tratamentos mais prolongados requerem observações especiais (vide "Precauções"). Os comprimidos do TANDRILAX deverão ser ingeridos inteiros (sem mastigar), às refeições, com auxílio de líquido. "SE PERSISTIREM OS SINTOMAS O MÉDICO DEVERÁ SER CONSULTADO." VENDA SOB PRESCRIÇÃO MÉDICA - MS - 1.0573.0055 - MB 08 - SAP 4104203

ALÍVIO COM[1,2]

dorene pregabalina

Rápido, eficaz e seguro no tratamento da fibromialgia.[3]

Redução da dor
a partir da primeira semana de tratamento na fibromialgia[4]

A pregabalina é eficaz
em reduzir a dor dos pacientes com fibromialgia[5]

Melhora da disfunção do sono
relacionada à fibromialgia.[6]
Grande parte desse benefício foi devido:[6]

- Efeito da pregabalina na insônia[6]
- Atividade analgésica do medicamento[6]

Referências Bibliográficas: 1) TOLLE, T. et al. Pregabalin for relief of neuropathic pain associated with diabetic neuropathy: a randomized, double-blind study. European Journal of Pain, v. 12, n. 2, p. 203-213, 2008. 2) OHTA, H. et al. A randomized, double-blind, multicenter, placebo-controlled phase III trial to evaluate the efficacy and safety of pregabalin in Japanese patients with fibromyalgia. Arthritis Research & Therapy, v. 14, N. 217, 2012. 3) BOOMERSHINE, C. S. Pregabalin for the management of fibromyalgia syndrome. Journal of Pain Research, v. 3, p. 81-88, 2010. 4) PAUER, L. et al. An international, randomized, double-blind, placebo-controlled, phase III trial of pregabalin monotherapy in treatment of patients with fibromyalgia. J Rheumatol, v. 38, n. 12, p. 2643-2652, 2011. 5) HEYMANN, R.E. et al. Consenso Brasileiro do tratamento da fibromialgia. Rev Bras Reumatol, v. 50, n.1, p.56-66, 2010. - A pregabalina é eficaz em reduzir a dor dos pacientes com fibromialgia (grau de recomendação A, nível de evidência 1b. Página 60, coluna 1, 5º parágrafo. - Consenso brasileiro do tratamento da fibromialgia, que inclui a pregabalina no tratamento da fibromialgia com grau de recomendação A e nível de evidência 1B. 6) RUSSELL, I.J. et al. The effects of pregabalin on sleep disturbance symptoms among individuals with fibromyalgia syndrome. Sleep Med., v. 10, n. 6, p. 604-610, 2009.

DORENE (pregabalina) 75 mg e 150 mg. Cápsula. USO ORAL. USO ADULTO E PEDIÁTRICO ACIMA DE 12 ANOS (vide Indicações). Indicações: Dor Neuropática; Epilepsia; Transtorno de Ansiedade Generalizada (TAG); Fibromialgia. Contraindicações: Dorene é contraindicado a pacientes com hipersensibilidade conhecida à pregabalina ou a qualquer componente da fórmula. Precauções e advertências: **Pacientes com problemas hereditários raros de intolerância a galactose, deficiência de lactase ou má- absorção de glicose-galactose não devem utilizar pregabalina cápsulas. Alguns pacientes diabéticos sob tratamento com pregabalina que obtiverem ganho de peso podem necessitar de ajuste da medicação hipoglicêmica. Houve relatos de reações de hipersensibilidade, incluindo casos de angioedema. Pregabalina deve ser descontinuado imediatamente se ocorrerem sintomas de angioedema, tais como edema facial, perioral ou da via aérea superior. O tratamento com pregabalina está associado com tontura e sonolência, que pode aumentar a ocorrência de acidentes (queda) na população idosa. Pacientes devem ser alertados para ter cautela até que os efeitos potenciais de pregabalina sejam familiares. Visão borrada transitória e outras alterações na acuidade visual foram reportadas por pacientes tratados com pregabalina. A descontinuação da pregabalina pode resultar na resolução ou melhora desses sintomas visuais. Foram observados sintomas de retirada em alguns pacientes após a descontinuação do tratamento prolongado e de curto prazo com pregabalina. Os seguintes eventos foram mencionados: insônia, dor de cabeça, náusea, ansiedade, hiperidrose e diarreia (vide item Reações Adversas). Como é o caso com qualquer droga ativa do SNC, deve-se avaliar cuidadosamente o histórico de pacientes quanto ao abuso de drogas e observá-los quanto a sinais de abuso da pregabalina. Foi relatada melhora da função renal após a descontinuação ou redução da dose de pregabalina. Houve relatos pós-comercialização de insuficiência cardíaca congestiva em alguns pacientes recebendo pregabalina. Devido aos dados limitados de pacientes com insuficiência cardíaca congestiva grave, Dorene deve ser administrado com cautela nesses pacientes (vide item 9. Reações Adversas).** Efeitos sobre a Habilidade de Dirigir e Operar Máquinas: Dorene pode produzir tontura e sonolência que, portanto, podem prejudicar a habilidade de dirigir e operar máquinas. Os pacientes devem ser aconselhados a não dirigir, operar máquinas complexas, ou se engajar em outras atividades potencialmente perigosas até que se saiba se este medicamento afeta a sua capacidade de executar tais atividades. Uso em Idosos, Crianças e Outros Grupos de Risco: Vide item Posologia **Gravidez e lactação: Uso durante a Gravidez:** Não há dados adequados sobre o uso de pregabalina em mulheres grávidas. Estudos em animais mostraram toxicidade reprodutiva. O risco potencial a humanos é desconhecido. Portanto, Dorene não deve ser utilizado durante a gravidez. Métodos contraceptivos eficazes devem ser utilizados por mulheres com potencial de engravidar. **A pregabalina é um medicamento classificado na categoria C de risco de gravidez. Portanto, este medicamento não deve ser utilizado por mulheres grávidas sem orientação médica ou do cirurgião-dentista. Uso durante a Lactação:** Não se sabe se a pregabalina é excretada no leite materno de humanos. Entretanto, está presente no leite de ratas. Portanto, a amamentação não é recomendada durante o tratamento com Dorene. **Interações medicamentosas:** A pregabalina provavelmente não inibe o metabolismo de fármacos ***in vitro*** e nem se liga a proteínas plasmáticas. A pregabalina pode potencializar os efeitos do etanol e lorazepan. A pregabalina parece ser aditiva no prejuízo da função cognitiva e coordenação motora grosseira causado pela oxicodona. Em experiência pós-comercialização, houve relatos de insuficiência respiratória e coma em pacientes sob tratamento de pregabalina e outros medicamentos antidepressivos do SNC. Há relatos pós-comercialização de eventos relacionados à redução da função do trato gastrintestinal inferior (por ex. obstrução intestinal, íleo paralítico, constipação) quando a pregabalina foi coadministrada com medicamentos que têm o potencial para produzir constipação, tais como analgésicos opioides. Não foram conduzidos estudos de interação farmacodinâmica específica em voluntários idosos. Reações adversas: **As reações adversas mais comuns foram tontura e sonolência, em geral, de intensidade leve a moderada. As reações adversas comuns foram: Aumento de apetite, Confusão, desorientação, irritabilidade, humor eufórico, diminuição da libido, insônia, Ataxia, coordenação anormal, transtorno de equilíbrio, amnésia, distúrbios de atenção, dificuldade de memória, tremores, disartria, parestesia, sedação, letargia, Visão turva, diplopia, Vertigem, Vômitos, distensão abdominal, constipação, boca seca, flatulência, disfunção erétil, edema periférico, edema, marcha anormal, sensação de embriaguez, sensação anormal, fadiga e aumento de peso. As seguintes reações adversas foram relatadas durante a pós-comercialização: Sistema imune: angioedema, reação alérgica, hipersensibilidade. Sistema nervoso: dor de cabeça, perda de consciência, prejuízo mental.** Oftalmológicos: cegueira. Cardíacos: insuficiência cardíaca congestiva. Respiratório e torácico: edema pulmonar. Gastrintestinais: edema de língua, diarreia, náusea. Pele e tecido subcutâneo: inchaço da face, prurido. Renais e urinários: retenção urinária. Reprodutor e mamas: ginecomastia. Geral: mal-estar. Idosos (acima de 65 anos de idade). Num total de 998 pacientes idosos, não foram observadas diferenças quanto a segurança geral, em comparação aos pacientes com menos de 65 anos de idade. Posologia: Dorene deve ser utilizado por via oral, com ou sem alimentos. Cada cápsula de Dorene contém 75 mg ou 150 mg de pregabalina. Dor Neuropática: A dose inicial recomendada de Dorene é de 75 mg duas vezes ao dia (150 mg/dia), com ou sem alimentos. Para a maioria dos pacientes, 150 mg duas vezes ao dia é a dose ideal. Com base na resposta individual e na tolerabilidade do paciente, a dose poderá ser aumentada para 150 mg duas vezes ao dia após um intervalo de 3 a 7 dias e, se necessário, até uma dose máxima de 300 mg duas vezes ao dia após mais uma semana. Epilepsia: A dose inicial recomendada de Dorene é de 75 mg duas vezes ao dia (150 mg/dia), com ou sem alimentos. Com base na resposta e tolerabilidade individuais do paciente, a dose poderá ser aumentada para 150 mg duas vezes ao dia após 1 semana. A dose máxima de 300 mg duas vezes ao dia pode ser atingida após mais 1 semana. Transtorno de Ansiedade Generalizada (TAG): A dose varia de 150 a 600 mg/dia, divididas em duas ou três doses. A necessidade para o tratamento deve ser reavaliada regularmente. Fibromialgia: A dose recomendada de Dorene é de 300 a 450 mg/dia. A dose deve ser iniciada com 75 mg duas vezes ao dia (150 mg/dia), com ou sem alimentos, e a dose pode ser aumentada para 150 mg duas vezes ao dia (300 mg/dia) em uma semana baseado na eficácia e tolerabilidade individuais. Descontinuação do Tratamento: Se Dorene for descontinuado, recomenda-se que isto seja feito gradualmente durante no mínimo 1 semana. Uso em Pacientes com Insuficiência Renal: A redução da dosagem em pacientes com a função renal comprometida deve ser individualizada de acordo com o clearance de creatinina. Para pacientes submetidos à hemodiálise, a dose diária de Dorene deve ser ajustada com base na função renal. Além da dose diária, uma dose suplementar deve ser administrada imediatamente após cada tratamento de 4 horas de hemodiálise. Uso em Pacientes com Insuficiência Hepática: Nenhum ajuste de dose é necessário para pacientes com insuficiência hepática. Uso em Crianças: A segurança e a eficácia de pregabalina em pacientes pediátricos abaixo de 12 anos de idade ainda não foram estabelecidas. O uso em crianças não é recomendado. Uso em Adolescentes (12 a 17 anos de idade): Pacientes adolescentes com epilepsia podem receber a dose como adultos. A segurança e a eficácia de pregabalina em pacientes abaixo de 18 anos de idade com dor neuropática não foram estabelecidas. Uso em Pacientes Idosos (acima de 65 anos de idade): Pacientes idosos podem necessitar de redução da dose de Dorene devido à diminuição da função renal. Dose Omitida: Caso o paciente esqueça de tomar Dorene no horário estabelecido, deve tomá-lo assim que lembrar. Entretanto, se já estiver perto do horário de tomar a próxima dose, deve desconsiderar a dose esquecida e tomar a próxima. **Este medicamento não pode ser partido, aberto ou mastigado.** SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO. **VENDA SOB PRESCRIÇÃO MÉDICA. SÓ PODE SER VENDIDO COM RETENÇÃO DA RECEITA.** MS - 1.0573.0457. MB 02_VP SAP 4475900.

Contraindicações: Dorene não deve ser utilizado se você tem hipersensibilidade (alergia) conhecida à pregabalina ou a qualquer componente da fórmula.
Interações medicamentosas: A pregabalina pode potencializar o efeito da oxicodona (analgésico), bebidas alcoólicas e de lorazepam (tranquilizante).

DORENE é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas.

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REVISTAS ACTAS DORENE CL.4 2017

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HÁ 13 ANOS CONSTRUINDO

histórias de sucesso[1]

ARTROLIVE

sulfato de glicosamina+sulfato de condroitina

PIONEIRISMO* & LIDERANÇA[1,2]
NO TRATAMENTO DA OSTEOARTRITE[3,4]

Novas evidências

Estudo demonstrou que os participantes **que tomaram sulfato de glucosamina + sulfato de condroitina reduziram a perda de volume de cartilagem após 24 meses**, argumentando para um efeito modificador da doença.[5]

*Pioneirismo refere-se ao lançamento do produto à classe médica.

Referências Bibliográficas: 1. 1. Internal Report. Dados de auditoria IMS Health. Fevereiro/2017. **2.** Internal Report. Dados de auditoria IMS-PMB. Fevereiro/2017. **3.** Bula do produto ARTROLIVE: cápsulas. Farmacêutica Responsável: Gabriela Mallmann. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A. **4.** Bula do produto ARTROLIVE: granulado em sachê. Farmacêutica Responsável: Gabriela Mallmann. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A. **5.** MARTEL-PELLETIER, J. et al. First-line analysis of the effects of treatment on progression of structural changes in knee osteoarthritis over 24 months: data from the osteoarthritis initiative progression cohort. Ann Rheum Dis, v. 74, n. 3, p. 547-556, 2015.

Contraindicação: Pacientes que apresentem hipersensibilidade a quaisquer dos componentes de sua fórmula. Interação medicamentosa: É recomendável que pacientes diabéticos monitorem seus níveis sanguíneos de glicose mais frequentemente durante o tratamento com Artrolive.

ARTROLIVE CAPS. sulfato de glicosamina + sulfato de condroitina. MS – 1.0573.0286. **INDICAÇÕES: ARTROLIVE** é indicado para osteoartrite, osteoartrose ou artrose em todas as suas manifestações. **CONTRAINDICAÇÕES: ARTROLIVE** É CONTRAINDICADO EM PACIENTES QUE APRESENTEM HIPERSENSIBILIDADE A QUAISQUER DOS COMPONENTES DE SUA FÓRMULA, GRAVIDEZ E LACTAÇÃO. **PRECAUÇÕES E ADVERTÊNCIAS:** SÃO NECESSÁRIOS O DIAGNÓSTICO PRECISO E O ACOMPANHAMENTO CUIDADOSO DE PACIENTES COM SINTOMAS INDICATIVOS DE AFECÇÃO GASTRINTESTINAL, HISTÓRIA PREGRESSA DE ÚLCERA GÁSTRICA OU INTESTINAL, DIABETES MELLITUS, OU A CONSTATAÇÃO DE DISTÚRBIOS DO SISTEMA HEMATOPOIÉTICO OU DA COAGULAÇÃO SANGUÍNEA ASSIM COMO PORTADORES DE INSUFICIÊNCIA DAS FUNÇÕES RENAL, HEPÁTICA OU CARDÍACA. SE OCORRER EVENTUALMENTE ULCERAÇÃO PÉPTICA OU SANGRAMENTO GASTRINTESTINAL EM PACIENTES SOB TRATAMENTO, A MEDICAÇÃO DEVERÁ SER SUSPENSA IMEDIATAMENTE. DEVIDO À INEXISTÊNCIA DE INFORMAÇÕES TOXICOLÓGICAS DURANTE O PERÍODO GESTACIONAL, **ARTROLIVE** NÃO ESTÁ INDICADO PARA SER UTILIZADO DURANTE A GRAVIDEZ. NÃO EXISTEM INFORMAÇÕES SOBRE A PASSAGEM DO MEDICAMENTO PARA O LEITE MATERNO SENDO DESACONSELHADO SEU USO NESSAS CONDIÇÕES E AS LACTANTES SOB TRATAMENTO NÃO DEVEM AMAMENTAR. PODE OCORRER FOTOSSENSIBILIZAÇÃO EM PACIENTES SUSCETÍVEIS, PORTANTO PACIENTES COM HISTÓRICO DE FOTOSSENSIBILIDADE A OUTROS MEDICAMENTOS DEVEM EVITAR SE EXPOR À LUZ SOLAR. FORAM DESCRITOS NA LITERATURA, ALGUNS CASOS DE HIPERTENSÃO SISTÓLICA REVERSÍVEL, EM PACIENTES NÃO PREVIAMENTE HIPERTENSOS, NA VIGÊNCIA DO TRATAMENTO COM GLICOSAMINA E CONDROITINA. PORTANTO, A PRESSÃO ARTERIAL DEVE SER VERIFICADA PERIODICAMENTE DURANTE O TRATAMENTO COM **ARTROLIVE**. FORAM RELATADOS POUCOS CASOS DE PROTEINÚRIA LEVE E AUMENTO DA CREATINO-FOSFOQUINASE (CPK) DURANTE TRATAMENTO COM GLICOSAMINA E CONDROITINA, QUE VOLTARAM AOS NÍVEIS NORMAIS APÓS INTERRUPÇÃO DO TRATAMENTO. **INTERAÇÕES MEDICAMENTOSAS:** O tratamento concomitante com antiinflamatórios não-esteroidais pode incorrer no agravamento de reações adversas do sistema gastrintestinal, sendo recomendado um acompanhamento médico mais rigoroso nesses casos. Alguns autores da literatura médica descrevem que o uso de glicosamina e condroitina pode incorrer em um aumento da resistência à insulina, porém, esses estudos foram realizados com doses muito superiores às indicadas na terapêutica clínica normal e sua validade ainda é discutida por vários outros autores. Estudos recentes demonstraram que a associação condroitina e glicosamina, quando empregada em pacientes portadores de diabetes mellitus tipo II, não levou a alterações no metabolismo da glicose. Os resultados destes estudos não podem ser extrapolados para pacientes com diabetes mellitus descompensado ou não-controlado. É recomendável que pacientes diabéticos monitorem seus níveis sanguíneos de glicose mais frequentemente durante o tratamento com **ARTROLIVE**. O uso concomitante de **ARTROLIVE** com os inibidores da topoisomerase II (etoposídeo, teniposídeo e doxorrubicina) deve ser evitado, uma vez que a glicosamina induziu resistência in vitro a estes medicamentos em células humanas cancerosas de cólon e de ovário. O tratamento concomitante de **ARTROLIVE** com anticoagulantes como o acenocoumarol, dicumarol, heparina e varfarina, pode levar ao aumento das chances de sangramento, devido a alterações nos valores de INR (International Normalized Ratio). Há relato de um caso na literatura de potencialização do efeito da varfarina, com consequente aumento dos valores sanguíneos de INR. Portanto, o uso concomitante de **ARTROLIVE** com anticoagulantes orais deve levar em conta avaliações rigorosas do INR. **Reações adversas: SISTEMA CARDIOVASCULAR:** EDEMA PERIFÉRICO E TAQUICARDIA. JÁ FORAM RELATADOS COM O USO DA GLICOSAMINA, PORÉM NÃO FOI ESTABELECIDA UMA RELAÇÃO CAUSAL. FORAM DESCRITOS NA LITERATURA, ALGUNS CASOS DE HIPERTENSÃO SISTÓLICA REVERSÍVEL, EM PACIENTES NÃO PREVIAMENTE HIPERTENSOS, NA VIGÊNCIA DO TRATAMENTO COM GLICOSAMINA E CONDROITINA. PORTANTO, A PRESSÃO ARTERIAL DEVE SER VERIFICADA PERIODICAMENTE DURANTE O TRATAMENTO COM **ARTROLIVE**. **SISTEMA NERVOSO CENTRAL:** MENOS DE 1% DOS PACIENTES EM ESTUDOS CLÍNICOS APRESENTARAM CEFALEIA, INSÔNIA E SONOLÊNCIA NA VIGÊNCIA DO TRATAMENTO COM A GLICOSAMINA. **ENDÓCRINO-METABÓLICO:** ESTUDOS RECENTES DEMONSTRARAM QUE A ASSOCIAÇÃO CONDROITINA E GLICOSAMINA, QUANDO EMPREGADA EM PACIENTES PORTADORES DE DIABETES MELLITUS TIPO II, NÃO LEVOU A ALTERAÇÕES NO METABOLISMO DA GLICOSE. OS RESULTADOS DESTES ESTUDOS NÃO PODEM SER EXTRAPOLADOS PARA PACIENTES COM DIABETES MELLITUS DESCOMPENSADO OU NÃO-CONTROLADO. É RECOMENDÁVEL QUE PACIENTES DIABÉTICOS MONITOREM SEUS NÍVEIS SANGUÍNEOS DE GLICOSE MAIS FREQUENTEMENTE DURANTE O TRATAMENTO COM **ARTROLIVE**. **GASTRINTESTINAL:** NÁUSEA, DISPEPSIA, VÔMITO, DOR ABDOMINAL OU EPIGÁSTRICA, CONSTIPAÇÃO, DIARREIA, QUEIMAÇÃO E ANOREXIA TÊM SIDO RARAMENTE DESCRITOS NA LITERATURA NA VIGÊNCIA DE TRATAMENTO COM GLICOSAMINA E CONDROITINA. **PELE:** ERITEMA, PRURIDO, ERUPÇÕES CUTÂNEAS E OUTRAS MANIFESTAÇÕES ALÉRGICAS DE PELE FORAM REPORTADAS EM ENSAIOS CLÍNICOS COM GLICOSAMINA. PODE OCORRER FOTOSSENSIBILIZAÇÃO EM PACIENTES SUSCETÍVEIS, PORTANTO PACIENTES COM HISTÓRICO DE FOTOSSENSIBILIDADE A OUTROS MEDICAMENTOS DEVEM EVITAR SE EXPOR À LUZ SOLAR. **POSOLOGIA: Adultos:** Recomenda-se iniciar a terapêutica com a prescrição de 1 cápsula via oral 3 vezes ao dia. Como os efeitos do medicamento se iniciam em média após a terceira semana de tratamento deve-se ter em mente que a continuidade e a não-interrupção do tratamento são fundamentais para se alcançar os benefícios analgésicos e de mobilidade articular. **SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO. VENDA SOB PRESCRIÇÃO MÉDICA.** MB03a SAP4470700. **ARTROLIVE**. 1,5 g sulfato de glicosamina + 1,2 g sulfato de condroitina. MS – 1.0573.0286. **INDICAÇÕES: ARTROLIVE** é indicado para osteoartrite, osteoartrose ou artrose em todas as suas manifestações. **CONTRAINDICAÇÕES: ARTROLIVE** É CONTRAINDICADO EM PACIENTES QUE APRESENTEM HIPERSENSIBILIDADE A QUAISQUER DOS COMPONENTES DE SUA FÓRMULA, GRAVIDEZ E LACTAÇÃO. **PRECAUÇÕES E ADVERTÊNCIAS:** SÃO NECESSÁRIOS O DIAGNÓSTICO PRECISO E O ACOMPANHAMENTO CUIDADOSO DE PACIENTES COM SINTOMAS INDICATIVOS DE AFECÇÃO GASTRINTESTINAL, HISTÓRIA PREGRESSA DE ÚLCERA GÁSTRICA OU INTESTINAL, DIABETES MELLITUS, OU A CONSTATAÇÃO DE DISTÚRBIOS DO SISTEMA HEMATOPOIÉTICO OU DA COAGULAÇÃO SANGUÍNEA ASSIM COMO PORTADORES DE INSUFICIÊNCIA DAS FUNÇÕES RENAL, HEPÁTICA OU CARDÍACA. SE OCORRER EVENTUALMENTE ULCERAÇÃO PÉPTICA OU SANGRAMENTO GASTRINTESTINAL EM PACIENTES SOB TRATAMENTO, A MEDICAÇÃO DEVERÁ SER SUSPENSA IMEDIATAMENTE. DEVIDO À INEXISTÊNCIA DE INFORMAÇÕES TOXICOLÓGICAS DURANTE O PERÍODO GESTACIONAL, **ARTROLIVE** NÃO ESTÁ INDICADO PARA SER UTILIZADO DURANTE A GRAVIDEZ. NÃO EXISTEM INFORMAÇÕES SOBRE A PASSAGEM DO MEDICAMENTO PARA O LEITE MATERNO SENDO DESACONSELHADO SEU USO NESSAS CONDIÇÕES E AS LACTANTES SOB TRATAMENTO NÃO DEVEM AMAMENTAR. PODE OCORRER FOTOSSENSIBILIZAÇÃO EM PACIENTES SUSCETÍVEIS, PORTANTO PACIENTES COM HISTÓRICO DE FOTOSSENSIBILIDADE A OUTROS MEDICAMENTOS DEVEM EVITAR SE EXPOR À LUZ SOLAR. FORAM DESCRITOS NA LITERATURA, ALGUNS CASOS DE HIPERTENSÃO SISTÓLICA REVERSÍVEL, EM PACIENTES NÃO PREVIAMENTE HIPERTENSOS, NA VIGÊNCIA DO TRATAMENTO COM GLICOSAMINA E CONDROITINA. PORTANTO, A PRESSÃO ARTERIAL DEVE SER VERIFICADA PERIODICAMENTE DURANTE O TRATAMENTO COM **ARTROLIVE**. FORAM RELATADOS POUCOS CASOS DE PROTEINÚRIA LEVE E AUMENTO DA CREATINO-FOSFOQUINASE (CPK) DURANTE TRATAMENTO COM GLICOSAMINA E CONDROITINA, QUE VOLTARAM AOS NÍVEIS NORMAIS APÓS INTERRUPÇÃO DO TRATAMENTO. **INTERAÇÕES MEDICAMENTOSAS:** O tratamento concomitante com antiinflamatórios não-esteroidais pode incorrer no agravamento de reações adversas do sistema gastrintestinal, sendo recomendado um acompanhamento médico mais rigoroso nesses casos. Alguns autores da literatura médica descrevem que o uso de glicosamina e condroitina pode incorrer em um aumento da resistência à insulina, porém, esses estudos foram realizados com doses muito superiores às indicadas na terapêutica clínica normal e sua validade ainda é discutida por vários outros autores. Estudos recentes demonstraram que a associação condroitina e glicosamina, quando empregada em pacientes portadores de diabetes mellitus tipo II, não levou a alterações no metabolismo da glicose. Os resultados destes estudos não podem ser extrapolados para pacientes com diabetes mellitus descompensado ou não-controlado. É recomendável que pacientes diabéticos monitorem seus níveis sanguíneos de glicose mais frequentemente durante o tratamento com **ARTROLIVE**. O uso concomitante de **ARTROLIVE** com os inibidores da topoisomerase II (etoposídeo, teniposídeo e doxorrubicina) deve ser evitado, uma vez que a glicosamina induziu resistência in vitro a estes medicamentos em células humanas cancerosas de cólon e de ovário. O tratamento concomitante de **ARTROLIVE** com anticoagulantes como o acenocoumarol, dicumarol, heparina e varfarina, pode levar ao aumento das chances de sangramento, devido a alterações nos valores de INR (International Normalized Ratio). Há relato de um caso na literatura de potencialização do efeito da varfarina, com consequente aumento dos valores sanguíneos de INR. Portanto, o uso concomitante de **ARTROLIVE** com anticoagulantes orais deve levar em conta avaliações rigorosas do INR. **Reações adversas: SISTEMA CARDIOVASCULAR:** EDEMA PERIFÉRICO E TAQUICARDIA JÁ FORAM RELATADOS COM O USO DA GLICOSAMINA, PORÉM NÃO FOI ESTABELECIDA UMA RELAÇÃO CAUSAL. FORAM DESCRITOS NA LITERATURA, ALGUNS CASOS DE HIPERTENSÃO SISTÓLICA REVERSÍVEL, EM PACIENTES NÃO PREVIAMENTE HIPERTENSOS, NA VIGÊNCIA DO TRATAMENTO COM GLICOSAMINA E CONDROITINA. PORTANTO, A PRESSÃO ARTERIAL DEVE SER VERIFICADA PERIODICAMENTE DURANTE O TRATAMENTO COM **ARTROLIVE**. **SISTEMA NERVOSO CENTRAL:** MENOS DE 1% DOS PACIENTES EM ESTUDOS CLÍNICOS APRESENTARAM CEFALEIA, INSÔNIA E SONOLÊNCIA NA VIGÊNCIA DO TRATAMENTO COM A GLICOSAMINA. **ENDÓCRINO-METABÓLICO:** ESTUDOS RECENTES DEMONSTRARAM QUE A ASSOCIAÇÃO CONDROITINA E GLICOSAMINA, QUANDO EMPREGADA EM PACIENTES PORTADORES DE DIABETES MELLITUS TIPO II, NÃO LEVOU A ALTERAÇÕES NO METABOLISMO DA GLICOSE. OS RESULTADOS DESTES ESTUDOS NÃO PODEM SER EXTRAPOLADOS PARA PACIENTES COM DIABETES MELLITUS DESCOMPENSADO OU NÃO-CONTROLADO. É RECOMENDÁVEL QUE PACIENTES DIABÉTICOS MONITOREM SEUS NÍVEIS SANGUÍNEOS DE GLICOSE MAIS FREQUENTEMENTE DURANTE O TRATAMENTO COM **ARTROLIVE**. **GASTRINTESTINAL:** NÁUSEA, DISPEPSIA, VÔMITO, DOR ABDOMINAL OU EPIGÁSTRICA, CONSTIPAÇÃO, DIARREIA, QUEIMAÇÃO E ANOREXIA TÊM SIDO RARAMENTE DESCRITOS NA LITERATURA NA VIGÊNCIA DE TRATAMENTO COM GLICOSAMINA E CONDROITINA. **PELE:** ERITEMA, PRURIDO, ERUPÇÕES CUTÂNEAS E OUTRAS MANIFESTAÇÕES ALÉRGICAS DE PELE FORAM REPORTADAS EM ENSAIOS CLÍNICOS COM GLICOSAMINA. PODE OCORRER FOTOSSENSIBILIZAÇÃO EM PACIENTES SUSCETÍVEIS, PORTANTO PACIENTES COM HISTÓRICO DE FOTOSSENSIBILIDADE A OUTROS MEDICAMENTOS DEVEM EVITAR SE EXPOR À LUZ SOLAR. **POSOLOGIA: Adultos:** Recomenda-se iniciar a terapêutica com a prescrição de 1 envelope por dia, dissolvido em um copo com água. Como os efeitos do medicamento se iniciam em média após a terceira semana de tratamento deve-se ter em mente que a continuidade e a não-interrupção do tratamento são fundamentais para se alcançar os benefícios analgésicos e de mobilidade articular. **SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO. VENDA SOB PRESCRIÇÃO MÉDICA.** MB03a SAP4406702.

Material técnico-científico de distribuição exclusiva à classe médica. 7021020 - Maio/2017

A ação eficaz[1] no tratamento da Osteoartrite.

Glicolive
sulfato de glicosamina

Qualidade Aché e preço acessível para o tratamento da OA.[2-5]

Referências Bibliográficas: 1) MATHESON, A. J; PERRY, C. M. Glucosamine: a review of its use in the management of osteoarthritis. Drugs Aging, v. 20, n. 14, p. 1041-60, 2003. **2)** Kairos Web Brasil. Disponível em: http://brasil.kairosweb.com Acesso em: Agosto/16. **3)** Programa Cuidados pela Vida (" O Programa Cuidados pela Vida pode alterar ou interromper esta campanha sem aviso prévio". Desconto calculado sobre o Preço Máximo ao Consumidor)". **4)** Bula do produto GLICOLIVE: pó para solução oral. Farmacêutica Responsável: Gabriela Mallmann, Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A. **5)** BRASIL. ANVISA. Agência Nacional de Vigilância Sanitária. Resolução - RE nº 1.101, de 9 de abril de 2015. Concede Certificação de Boas Práticas de Fabricação ao Aché. Diário Oficial da União, Brasília DF, p. 133, 9 abr 2015. **6)** Internal Report.

Contraindicações: hipersensibilidade a glicosamina ou a qualquer outro componente da fórmula. Interações medicamentosas: o sulfato de glicosamina pode favorecer a absorção gastrintestinal de tetraciclinas e reduzir a de penicilina e cloranfenicol.

GLICOLIVE é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas.

GLICOLIVE (sulfato de glicosamina) 1500 mg pó para solução oral. USO ORAL. USO ADULTO. **Indicações:** GLICOLIVE é indicado no tratamento deartrose ou osteoartrite primária e secundária e suas manifestações. Contraindicações: **GLICOLIVE é contra-indicado em pacientes com hipersensibilidade a glicosamina ou a qualquer outro componente da fórmula. Não deve ser utilizado durante a gravidez, lactação ou em fenilcetonúricos. Cuidados e advertências: informar ao médico caso esteja utilizando outros medicamentos. Recomenda-se cautela em pacientes com sintomas indicativos de distúrbios gastrintestinais, história de úlcera gástrica ou intestinal, diabetes mellitus, portadores de insuficiência renal, hepática ou cardíaca. Caso ocorra ulceração péptica ou sangramento gastrintestinal a medicação deverá ser suspensa imediatamente. Recomenda-se evitar a ingestão de bebidas alcoólicas, durante o tratamento.** Gravidez e lactação: não há dados com relação ao uso de GLICOLIVE na gravidez e lactação humana, portanto, seu uso não é recomendado nestes casos. Interações medicamentosas: o sulfato de glicosamina pode favorecer a absorção gastrintestinal de tetraciclinas e reduzir a de penicilina e cloranfenicol. Não existe limitação para administração simultânea de analgésicos ou anti-inflamatórios esteroides e não esteroides. **Reações adversas: os efeitos colaterais mais comuns são de origem gastrintestinal, de intensidade leve a moderada, consistindo em desconforto gástrico, diarreia, náusea, prurido e cefaléia. Reações hematológicas: não foram observadas alterações clínicas significativas.Testes laboratoriais: não se observaram diferenças significativas nos valores médios nem nos dados individuais das provas laboratoriais e constantes vitais. Glicolive é um medicamento. "Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas."** Posologia: GLICOLIVE apresenta-se na forma de pó branco a levemente amarelado, com odor e sabor de abacaxi. Dispensar o conteúdo do envelope em um copo com água. Aguardar entre 2 a 5 minutos, mexer a solução com o auxílio de uma colher e consumir. Consumir 1 envelope por dia antes das refeições ou segundo indicação médica. A duração do tratamento fica a critério do médico. Para informações completas, consultar a bula na íntegra através da Central de Atendimento ao Cliente.VENDA SOB PRESCRIÇÃO MÉDICA. MS - 1.0573. 0403. MB05 SAP 4423401. "Material técnico científico de distribuição exclusiva à classe médica." SE PERSISTIREM OS SINTOMAS, O MÉDICO DEVERÁ SER CONSULTADO.

Artrosil
lisinato de cetoprofeno

SMR
SMART MODULATED RELEASE[1]

O ÚNICO lisinato de cetoprofeno[1] com **TECNOLOGIA SMR[2,3]**

SEGURANÇA[2]
- Tolerabilidade gástrica 3 a 4 vezes maior comparado ao cetoprofeno comum.[2]

RÁPIDO INÍCIO DE AÇÃO[2]

EFICÁCIA[2]
- **Potência** anti-inflamatória, analgésica e antipirética superior ao cetoprofeno.[2]
- **Liberação prolongada:** Níveis plasmáticos mantidos por até 24h.[2,4]

Apresentações[4]
Cápsulas de liberação prolongada
de 160 e 320 mg com 10 e 20 cápsulas

Referências Bibliográficas: 1) ANVISA. Consulta de produtos. Disponível em: <http://www7.anvisa.gov.br/datavisa/Consulta_Produto/consulta_medicamento.asp>. Acesso em: Abr/2016. **2)** PELOGGIA, C.C.N.; BRITO NETO, A.J.; CUNHA, J. Avaliação da eficácia terapêuta e da tolerância do antiinflamatório lisinato de cetoprofeno, na forma cápsulas. Estudo multicêntrico aberto e não comparativo. Revista Brasileira de Medicina, v.57, n.6, p.617-624, 2000. **3)** Internal Report. **4)** Bula Do Produto ARTROSIL: Cápsulas. Farmacêutica Responsável: Gabriela Mallmann. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A.

Contraindicações: Úlcera péptica na fase ativa. Interações medicamentosas: Devido à elevada ligação de cetoprofeno com proteínas plasmáticas, é necessário reduzir a dosagem de anticoagulantes, fenitoínas ou sulfamidas quando administrados concomitantemente.

ARTROSIL (lisinato de cetoprofeno) - 160 mg e 320 mg - Cápsulas de liberação prolongada - Uso oral - Uso Adulto - Indicações: Artrose, coxartrose, espondiloartrose, artrite reumatóide, bursite, flebite e tromboflebite superficial, contusão, entorse, luxação, distensão muscular. **Contraindicações: Úlcera péptica na fase ativa, anamnese positiva de úlcera péptica recorrente, dispepsia crônica, gastrite, insuficiência renal grave, leucopenia e plaquetopenia, grave distúrbio de hemocoagulação.** Hipersensibilidade a quaisquer componentes de sua fórmula. Existe a possibilidade de hipersensibilidade cruzada com ácido acetilsalicílico ou outros fármacos anti-inflamatórios não-esteroidais. Portanto, o cetoprofeno não deve ser administrado a pacientes nos quais o ácido acetilsalicílico ou outros fármacos antiinflamatórios não-esteroidais tenham provocado sintomas de asma, rinite, urticária. O uso de lisinato de cetoprofeno é contra-indicado durante o primeiro e o último trimestre de gestação, pois pode causar hipertensão pulmonar e toxicidade renal no feto, característica comum aos inibidores da síntese de prostaglandinas. Pode também levar ao aumento do tempo de sangramento das gestantes e fetos e conseqüentemente eventuais manifestações hemorrágicas no recém-nascido. Há risco de retardar o trabalho de parto. **Precauções e advertências: O uso de cetoprofeno em pacientes com asma brônquica ou com diáteses alérgicas pode provocar uma crise asmática. Em pacientes com função renal comprometida, a administração de cetoprofeno deve ser efetuada com particular cautela levando-se em consideração a eliminação essencialmente renal do fármaco.** Embora não tenha sido observada experimentalmente toxicidade embriofetal com cetoprofeno nas doses previstas para uso clínico, a administração em mulheres grávidas, durante a amamentação ou na infância não é recomendada. **Interações medicamentosas: Devido à elevada ligação de cetoprofeno com proteínas plasmáticas, é necessário reduzir a dosagem de anticoagulantes, fenitoínas ou sulfamidas quando administrados concomitantemente.** O uso com ácido acetilsalicílico reduz o nível sérico de cetoprofeno e aumenta o risco de distúrbios gastrintestinais. No caso da administração com lítio há aumento de seu nível sérico podendo levar à intoxicação. Foi observado aumento da toxicidade do metotrexato em decorrência da diminuição de seu "clearance" renal. A probenecida reduz as perdas de cetoprofeno e aumenta seu nível sérico. A metoclopramida reduz a biodisponibilidade do cetoprofeno e pode ocorrer uma pequena redução de sua absorção no uso simultâneo com hidróxidos de magnésio ou alumínio. **Reações adversas: Assim como com outros antiinflamatórios não-esteroidais, podem ocorrer distúrbios transitórios, no trato gastrintestinal, tais como gastralgia, náusea, vômito, diarréia e flatulência.** Excepcionalmente foram observadas hemorragia gastrintestinal, discinésia transitória, astenia, cefaléia, sensação de vertigem e exantema cutâneo. O produto pode ser tomado às refeições ou com leite, a fim de evitar possíveis distúrbios gastrintestinais. **Posologia:** ARTROSIL 160 mg: Uma cápsula duas vezes ao dia durante ou após às refeições. A duração do tratamento deve ser a critério médico. ARTROSIL 320 mg: Uma cápsula ao dia durante ou após às refeições. A duração do tratamento deve ser a critério médico. SE PERSISTIREM OS SINTOMAS O MÉDICO DEVERÁ SER CONSULTADO. VENDA SOB PRESCRIÇÃO MÉDICA. MS – 1.0573.0128. MB_08 SAP 4057006.

Material técnico-científico de distribuição exclusiva a profissionais de saúde habilitados à prescrição e/ou dispensação de medicamentos.

REVANGE®

cloridrato de tramadol + paracetamol

A escolha certa no combate à dor

Vários estudos **confirmam** que a associação de **Revange®** (cloridrato de tramadol + paracetamol) é **superior** ao **tratamento isolado**, oferecendo[1,2,3]:

- **Efeito sinérgico[1]**
  Redução em torno de 30% a 40% na requisição de opioides
- **Menos efeitos adversos[2]**
- *17 MINUTOS* [3]
  Rápido início de ação*[3]
- **Maior tempo de ação*[3]**

PREÇO ACESSÍVEL

*** Trata-se de estudo realizado em modelo de dor de dente.**

Referências Bibliográficas: 1. ELIA, N.; LYSAKOWSKI, C.; TRAMER, M.R. Does multimodal analgesia with acetaminophen, nonsteroidal anti-inflammatory drugs, or selective cyclooxygenase-2 inhibitors and patient-controlled analgesia morphine offer advantages over morphine alone? Meta-analyses of randomized trials. Anesthesiology, v. 103, p. 1296-304, 2005. **2.** PERROT, S. et al. Efficacy and Tolerability of Paracetamol/Tramadol (325 mg/37.5 mg) Combination Treatment Compared with Tramadol (50 mg) Monotherapy in Patients with Subacute Low Back Pain: A Multicenter, Randomized, Double-Blind, Parallel-Group, 10-Day Treatment Study. Clinical Therapeutics, v. 28, n. 10, p. 1592-1606 , 2006. **3.** MEDVE, R.A.; WANG, J .; KARIM, R. Tramadol and acetaminophen tablets for dental pain. Anesth Prog, v.48, n.3, p.79-81 , 2001. **4.** Kairos Web Brasil. Disponível em: <http://brasil.kairosweb.com> Acesso em: Agosto/2016.

Contraindicações: hipersensibilidade ao tramadol, paracetamol ou a qualquer componente da fórmula ou aos opioides; intoxicações agudas pelo álcool, hipnóticos, analgésicos de ação central, opioides ou psicotrópicos; pacientes em tratamento com inibidores da monoaminoxidase (MAO) ou tratados com estes agentes nos últimos 14 dias. Interações medicamentosas: REVANGE® comprimido revestido não é recomendado como medicação pré-operatória obstétrica ou na analgesia pós-parto em lactantes, pois a segurança em lactentes e recém-nascidos não foi estudada.

REVANGE® é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas.

REVANGE®. cloridrato de tramadol e paracetamol. 37,5 MG + 325 MG comprimidos revestidos. USO ORAL. USO ADULTO. Indicações: dores moderadas a severas de caráter agudo, subagudo e crônico. **Contraindicações: hipersensibilidade ao tramadol, paracetamol ou a qualquer componente da fórmula ou aos opioides; intoxicações agudas pelo álcool, hipnóticos, analgésicos de ação central, opioides ou psicotrópicos; pacientes em tratamento com inibidores da monoaminoxidase (MAO) ou tratados com estes agentes nos últimos 14 dias. Cuidados e advertências:** convulsões foram relatadas em pacientes recebendo tramadol na dose recomendada. Relatos espontâneos pós-comercialização indicam que o risco de convulsões está aumentado com doses de tramadol acima das recomendadas. A administração de tramadol pode aumentar o risco de convulsão em pacientes tomando inibidores da MAO, neurolépticos ou outros fármacos que reduzem o limiar convulsivo. REVANGE® comprimido revestido não deve ser administrado à pacientes dependentes de opioides. O tramadol reinicia a dependência física em alguns pacientes previamente dependentes de outros opioides. REVANGE® comprimido revestido deve ser usado com cautela e em dose reduzida em pacientes recebendo depressores do SNC como álcool, opioides, agentes anestésicos, fenotiazinas, tranquilizantes ou sedativos hipnóticos. REVANGE® comprimido revestido deve ser usado com bastante cautela em pacientes sob tratamento com inibidores da monoaminoxidase pois os estudos em animais mostraram aumento da incidência de óbito com a administração combinada de inibidores da MAO e tramadol. Precauções e advertências: REVANGE® comprimido revestido não deve ser administrado em conjunto com outros produtos à base de tramadol ou paracetamol. REVANGE® comprimido revestido deve ser administrado com cautela em pacientes sob risco de depressão respiratória. REVANGE® comprimido revestido deve ser usado com cautela em pacientes com pressão intracraniana aumentada ou traumatismo craniano. Alterações da pupila (miose) provocadas pelo tramadol podem mascarar a existência, extensão ou curso da patologia intracraniana. Gravidez e lactação: uso na gravidez e lactação: REVANGE® comprimido revestido somente deverá ser utilizado durante a gravidez se o potencial benefício justificar o potencial risco para o feto. Interações medicamentosas: REVANGE® comprimido revestido não é recomendado como medicação pré-operatória obstétrica ou na analgesia pós-parto em lactantes, pois a segurança em lactentes e recém-nascidos não foi estudada. Reações adversas: efeitos sobre a capacidade de dirigir e operar máquinas: mesmo quando usado de acordo com as instruções, REVANGE® comprimido revestido pode afetar a habilidade mental ou física necessária para a realização de tarefas potencialmente perigosas como dirigir ou operar máquinas, especialmente ao início do tratamento, na mudança de outro produto para REVANGE® comprimido revestido e na administração concomitante de outras drogas de ação central e, em particular, do álcool. **REVANGE® é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas.** Os eventos adversos relatados com maior freqüência ocorreram no sistema nervoso central e gastrintestinal, sendo que os relatos mais comuns foram vertigem, náusea e sonolência. **Posologia:** a dose diária máxima de REVANGE® comprimido revestido é 1 a 2 comprimidos a cada 4 a 6 horas de acordo com a necessidade para alívio da dor, até o máximo de 8 comprimidos ao dia. A administração dos comprimidos pode ser feita independentemente das refeições. Nas condições dolorosas crônicas, o tratamento deve ser iniciado com 1 comprimido ao dia e aumentado em 1 comprimido a cada 3 dias, conforme a tolerância do paciente, até atingir a dose de 4 comprimidos ao dia. Depois disso, REVANGE® comprimido revestido pode ser administrado na dose de 1-2 comprimidos a cada 4-6 horas, até o máximo de 8 comprimidos ao dia. Nas condições dolorosas agudas, o tratamento pode ser iniciado com a dose terapêutica completa (1-2 comprimidos a cada 4-6 horas), até o máximo de 8 comprimidos ao dia. Pacientes com disfunção renal: em pacientes com "clearance" de creatinina inferior a 30 mL/min, recomenda-se aumentar o intervalo entre as administrações de REVANGE® comprimido revestido de forma a não exceder 2 comprimidos a cada 12 horas. VENDA SOB PRESCRIÇÃO MÉDICA. SÓ PODE SER VENDIDO COM RETENÇÃO DA RECEITA. Farmacêutica Responsável: Gabriela Mallmann CRF-SP 30.138. MS - 1.0573.0440. MB02 SAP 4389200.

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Oxotron
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A NOVA OPÇÃO NO TRATAMENTO ANTI-INFLAMATÓRIO.[1,2]

RÁPIDO INÍCIO DE AÇÃO

Início de ação em aproximadamente 15 minutos[2]

- **Atividade preferencial sobre a COX-2[3,4]**
- **Fármaco seguro[3,5]**
- **Boa tolerabilidade[3]**
- **Tão eficaz quanto celecoxibe, ibuprofeno e naproxeno na redução da dor e inflamação em pacientes com dor pós-operatória, osteoartrite e ombro congelado[6]**

Referências Bibliográficas: 1) BRASIL. ANVISA. Agência Nacional de Vigilância Sanitária. Consulta de produtos. Disponível em: <http://www7.anvisa.gov.br/datavisa/Consulta_Produto/consulta_produto_detalhe.asp>. Acesso em: Out. 2016. 2) Bula do produto OXOTRON: comprimidos. Farmacêutica Responsável: Gabriela Mallmann. Guarulhos, SP. Aché Laboratórios Farmacêuticos S.A. 3) DUTRA, F.G.; ENGELKE, F. O uso do loxoprofeno sódico nos processos inflamatórios comuns em reumatologia e ortopedia: Estudo colaborativo. RBM, v. 58, n. 1/2, p. 39-48, 2001. 4) MARONE, S.; ENGELKE, F. Loxoprofeno sódico no tratamento complementar das infecções agudas das vias aéreas superiores: Estudo colaborativo. RBM, v. 58, n. 3, p. 171-178, 2001. 5) LEDERMAN, R.; GUIMARÃES, S.; VERZTMAN, J.F. Eficácia clínica e segurança do loxoprofeno sódico (Loxonin®) no tratamento da gonartrose. RMB, v. 58, v. 4, p. 263-271, 2001. 6) GREIG, S.L.; GARNOCK-JONES, K.P. Loxoprofen: A review in pain and inflammation. Clin Drug Investig, v. 36, n. 9, p. 771-81, 2016.

Oxotron é um medicamento. Durante seu uso, não dirija veículos ou opere máquinas, pois sua agilidade e atenção podem estar prejudicadas

Oxotron está contraindicado em: Crianças e jovens menores de 18 anos de idade, gestantes no último trimestre da gravidez e durante o período de lactação; pessoas que apresentaram reações de hipersensibilidade ao loxoprofeno ou a qualquer um dos componentes da fórmula; portadores de úlcera péptica, graves distúrbios hematológicos, hepáticos ou renais.INTERAÇÕES MEDICAMENTOSAS: Coadministração cautelosa: Anticoagulantes cumarínicos, hipoglicemiantes sulfoniluréicos, antibacteriano fluoroquinolona, metotrexate, sais de lítio, diuréticos benzotiazídicos, anti-hipertensivos.

Oxotron. Loxoprofeno sódico. MEDICAMENTO SIMILAR EQUIVALENTE AO MEDICAMENTO DE REFERÊNCIA. 60 mg. Comprimido. USO ORAL. USO ADULTO. Oxotron. Loxoprofeno sódico. APRESENTAÇÕES. Comprimidos 60 mg: embalagens com 8, 15 ou 30 comprimidos. USO ORAL. USO ADULTO. **COMPOSIÇÃO.** Cada comprimido de Oxotron contém: Loxoprofeno sódico anidro (como loxoprofeno sódico di-hidratado) 60 mg. Excipientes: lactose monoidratada, estearato de magnésio, hipromelose de baixa substituição, óxido férrico vermelho. **INFORMAÇÕES TÉCNICAS AOS PROFISSIONAIS DE SAÚDE. INDICAÇÕES.** Oxotron está indicado como anti-inflamatório e analgésico no tratamento de artrite reumatoide, osteoartrite, periartrite escapuloumeral, processos inflamatórios osteomusculares do pescoço, ombro, braço e lombalgias; como analgésico e anti-inflamatório em pós-cirurgia, pós-traumatismo e pós-exodontia; como analgésico anti-inflamatório e antitérmico em processos inflamatórios agudos do trato respiratório superior (acompanhados ou não de bronquite aguda). **CONTRAINDICAÇÕES.** Oxotron está contraindicado em: Crianças e jovens menores de 18 anos de idade; gestantes no último trimestre da gravidez e durante o período de lactação; pessoas que apresentaram reações de hipersensibilidade ao loxoprofeno ou a qualquer um dos componentes da fórmula; portadores de úlcera péptica; graves distúrbios hematológicos, hepáticos ou renais; portadores de disfunções cardíacas graves; indivíduos com asma induzida por AINE. Este medicamento é contraindicado para menores de 18 anos. Categoria de risco na gravidez: D (terceiro trimestre): este medicamento não deve ser utilizado por mulheres grávidas sem orientação médica. Informe imediatamente seu médico em caso de suspeita de gravidez. **ADVERTÊNCIAS E PRECAUÇÕES:** Oxotron deve ser administrado com cautela em: Pessoas com histórico de úlcera péptica; pessoas portadoras ou com histórico de distúrbios hematológicos; pessoas portadoras ou com histórico de disfunção hepática; pessoas portadoras ou com histórico de disfunção renal; pessoas com úlcera associada ao tratamento prolongado com anti-inflamatórios não esteroides, ainda que estejam em uso de misoprostol como medida profilática; pessoas com asma brônquica de qualquer causa; pessoas com disfunção cardíaca; pessoas com história de hipersensibilidade; pessoas com colite ulcerativa; pessoas com doença de Crohn; pessoas idosas. Durante tratamento prolongado com Oxotron, exames laboratoriais, tais como urina tipo I, hemograma completo e enzimas hepáticas devem ser realizados periodicamente. Se forem observadas alterações, recomenda-se redução da dose ou interrupção do tratamento. O uso de Oxotron, bem como de outros anti-inflamatórios, pode provocar alteração do controle da pressão arterial em indivíduos hipertensos sob tratamento. Alguns efeitos indesejáveis como tontura e sonolência têm sido relatados durante o uso de Oxotron. Para segurança do paciente, solicitar cuidado ao dirigir e ao operar máquinas. A segurança do uso de loxoprofeno sódico na gestação não foi estabelecida, portanto, Oxotron somente deverá ser administrado a gestantes se os benefícios terapêuticos justificarem os riscos potenciais para o feto (particularmente no terceiro trimestre) bem como durante a lactação. Categoria de risco na gravidez: B (primeiro e segundo trimestres): Este medicamento não deve ser utilizado por mulheres grávidas sem orientação médica ou do cirurgião-dentista. **INTERAÇÕES MEDICAMENTOSAS:** Coadministração cautelosa: Anticoagulantes cumarínicos, hipoglicemiantes sulfoniluréicos, antibacteriano fluoroquinolona, metotrexate, sais de lítio, diuréticos benzotiazídicos, anti-hipertensivos. **REAÇÕES ADVERSAS.** Oxotron pode causar os seguintes efeitos indesejados: rash cutâneo, urticária, sonolência, edema, dor abdominal, desconforto gástrico, anorexia, náusea e vômito, diarreia e aumento das transaminases hepáticas, prurido, úlcera péptica, constipação intestinal, pirose, estomatite, urticária, dispepsia, cefaleia, anemia, leucopenia, eosinofilia, aumento da fosfatase alcalina, palpitação, fogachos, febre, sede, distensão abdominal, úlcera no intestino delgado e/ou grosso, aumento da pressão arterial, enterpecimento, tontura, trombocitopenia, hematúria, proteinúria, disúria, dor no peito e mal estar. Outras reações adversas clinicamente significantes: choque, sintomas anafiláticoides, crise asmática, Stevens-Johnson, síndrome de Lyell (necrose epidérmica tóxica), agranulocitose, anemia hemolítica, leucopenia, trombocitopenia, insuficiência renal aguda, síndrome nefrótica, nefrite intersticial, insuficiência cardíaca congestiva, pneumonia intersticial, sangramento gastrintestinal, estenose e/ou obstrução do intestino delgado e/ou grosso, perfuração gastrintestinal, disfunção hepática, icterícia, meningite asséptica e rabdomiólise. Estes casos devem ser observados cuidadosamente. A terapia com Oxotron deve ser descontinuada imediatamente e adotadas medidas de tratamento apropriadas. Foi reportado que anemia aplástica pode ocorrer com o uso de drogas anti-inflamatórias não esteroides. Em caso de eventos adversos, notifique ao Sistema de Notificações em Vigilância Sanitária - NOTIVISA, disponível em www.anvisa.gov.br/hotsite/notivisa/index.htm, ou para a Vigilância Sanitária Estadual ou Municipal. **POSOLOGIA E MODO DE USAR.** Em geral recomenda-se para o adulto a posologia de um comprimido (60 mg de Loxoprofeno sódico), três vezes ao dia, por via oral. Em casos agudos poderá ser realizada uma única administração de um a dois comprimidos (60-120 mg de Loxoprofeno sódico), por via oral, ajustando-se a dose de acordo com a idade e os sintomas. Não ultrapassar a dose diária de 180 mg, bem como evitar a administração em jejum. A segurança em pacientes pediátricos não foi estabelecida. VENDA SOB PRESCRIÇÃO MÉDICA. MS - 1.0573.0495. Código EDG 321605 00 "Material técnico científico de distribuição exclusiva à classe médica".

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