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Surgical & Cosmetic Dermatology

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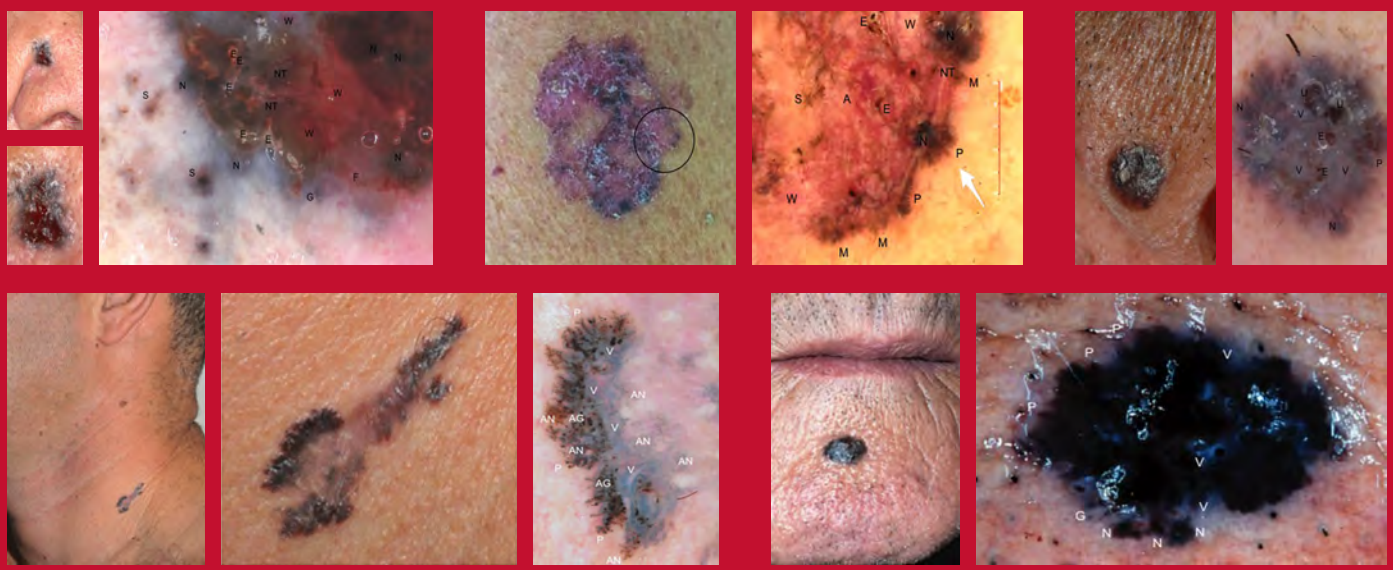
Which is the melanoma? Black lesion matters!



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A/C SURGICAL & COSMETIC DERMATOLOGY

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A *Surgical & Cosmetic Dermatology* é uma publicação oficial da Sociedade Brasileira de Dermatologia (SBD) em parceria com a Sociedade Brasileira de Cirurgia Dermatológica. O conteúdo técnico-científico apresentado nesta publicação é de co-propriedade da Sociedade Brasileira de Dermatologia.

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A revista consta no Depósito Legal, na Biblioteca Nacional, de acordo com o Decreto nº 1.825, de 20 de dezembro de 1907.

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A Surgical & Cosmetic Dermatology (S&CD), editada em 2009, constitui publicação médica destinada a difundir conhecimento e experiência nas áreas de Cirurgia Dermatológica, Oncologia Cutânea, Estudo de Imagens, Tecnologia em Dermatologia e Cosmiatria. É uma publicação trimestral da Sociedade Brasileira de Dermatologia (SBD) que conta com o apoio científico da Sociedade Brasileira de Cirurgia Dermatológica e do Colégio Íbero Latino de Dermatologia, que baseia sua política ética e editorial nas regras emitidas pelo The International Committee of Medical Journal Editors (ICMJE), www.icmje.org. A revista está disponível na íntegra online e adota a política de acesso aberto. A S&CD não cobra aos autores para que submetam ou publiquem manuscritos, não havendo qualquer tipo de custo ou taxas aos autores. A revista adota também a licença de uso da Creative Commons CC BY, https://creativecommons.org/licenses/by/3.0/br/.

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Serão produzidos exemplares impressos da versão em língua portuguesa, com resumos e títulos em inglês. A versão da língua inglesa estará disponível nos websites da SBD e da S&CD, no link: www.surgicalcosmetic.org.br.

Nomes de autores e de pareceristas são mantidos em sigilo; a revista adota o sistema de double blind review. Todos os artigos propostos à publicação serão previamente submetidos à revisão anônima e confidencial de no mínimo dois membros do Conselho Editorial ou dos Conselhos Nacional e Internacional de Revisores, seguindo as diretrizes do COPE (Committee on Publication Ethics).

Quando aceitos, estarão sujeitos a pequenas correções ou modificações que não alterem o estilo do autor.

A S&CD segue o Guia para o registro e publicação de retratação e também o Guia para registro e publicação de errata elaborados pela SciELO, disponível no endereço eletrônico http://www.scielo.org/php/level.php?lang=pt&component=56&item=57

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Se o trabalho envolver seres humanos, o autor deve cerificar que o trabalho descrito foi realizado de acordo com a Declaração de Helsinque para experimentos envolvendo seres humanos. O manuscrito também deve estar de acordo com as Recomendações para a Elaboração e Publicação de Trabalhos Acadêmicos em Periódicos Médicos e incluir populações humanas representativas (sexo, idade e etnia) de acordo com essas recomendações.

O manuscrito deve conter a informação de que o consentimento informado foi obtido em experimentos envolvendo seres humanos. Os direitos de privacidade dos envolvidos na pesquisa devem sempre ser observados.

Todos os experimentos com animais devem estar em conformidade com as diretrizes ARRIVE e devem ser realizados de acordo com a Lei dos Animais (Procedimentos Científicos) do Reino Unido, 1986 e diretrizes associadas, com a Diretiva 2010/63/EU para experimentos em animais, ou com as orientações do National Institutes of Health para cuidado e uso de animais de laboratório (NIH Publications No. 8023, revisada em 1978).

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O processo de avaliação dos artigos submetidos à S&CD ocorre nas seguintes etapas:

- Verificação preliminar: a secretaria editorial verifica a consistência dos dados cadastrais e observância das normas de submissão. Se aprovados os manuscritos são direcionados para a próxima fase, o desk-review.

- Desk-review: nesta fase o Editor analisa o formato científico do manuscrito quanto aos objetivos, marco teórico, linguagem e metodologia, verificando o enquadramento do artigo ao escopo editorial da revista e o potencial de contribuição da pesquisa. Essa tarefa é dividida entre o editor geral e os editores adjuntos, cada qual em sua área de especialidade. Se aprovados pelos editores os artigos são direcio- nados para o double blind review.

- Double blind review: o artigo e demais documentos suplementares são encaminhados a pelo menos dois avaliadores,

especialistas nacionais ou estrangeiros reconhecidos no assunto dos manuscritos que avaliam, e que não possuam qualquer espécie de vinculação com o trabalho em revisão.

- Após o trabalho receber os pareceres oriundos do estágio double blind review, o editor envia aos autores o resultado pelo sistema de submissão, que poderá referir-se a uma das três situações seguintes:

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• Revisão: os autores deverão realizar as adequações sugeridas, ou apresentarem as devidas argumentações para não procederem. As versões dos autores visando atender as revisões solicitadas pelos pareceristas deverão sempre ser acompanhadas de uma respectiva minuta esclarecendo as alterações atendidas e explicando as razões das não atendidas. O prazo de entrega do artigo revisado é determinado pelo editor e informado aos autores em função da revisão solicitada. Após a entrega do artigo revisado, o mesmo é novamente submetido aos pareceristas para verificação das alterações. A revisão poderá envolver várias rodadas até que se chegue ao parecer final de aprovação ou rejeição do manuscrito.

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A preparação correta do manuscrito torna os processos de revisão e publicação mais eficientes. Assim, recomendamos alguns cuidados que podem facilitar significativamente a preparação dos manuscritos.

1. Os artigos devem ser inéditos e redigidos no idioma de origem do autor (português, espanhol ou inglês): a equipe editorial providenciará as versões necessárias. A escolha da fonte deve ser Times New Roman ou Arial, de número 12.

2. O título do trabalho deve ser curto e conciso, informado em português e inglês, com até 150 caracteres sem espaços, acompanhado de um título resumido.

3. Os resumos em português e inglês devem acompanhar o formato adequado ao tipo de artigo.

4. Os autores devem informar o nome com suas abreviaturas, e as suas afiliações institucionais, seguidos de cidade, estado e país. Os vínculos às instituições devem ser citados em ordem hierárquica (ex.1º Departamento, 2º Universidade) e não são permitidas a inclusão dos mini-currículos. Quando um autor é afiliado a mais de uma instituição, cada uma deve ser identificada separadamente. Quando dois ou mais autores estão afiliados à mesma instituição, a sua identificação é feita uma única vez. É obrigatório mencionar o número ORCID, utilizado para a identificação de pesquisadores. O autor deve assumir pelo menos uma responsabilidade na elaboração do trabalho e deverá informar a contribuição de cada um na submissão. Um dos autores deve ser designado como autor correspondente, com endereço de e-mail. Deve também ser citado o local de realização do trabalho.

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6. s palavras-chave devem ser citadas em português e em inglês (Keywords), totalizando 3 a 10 por idio- ma, devendo ser incluídas em todos os tipos de artigos. É recomendável que estas palavras deverão estar contidas no DeCS (Descritores em Ciências da Saúde) e MeSH (Medical Subject Headings) que podem ser acessados na internet.

7. O número limite de palavras para os textos deve ser obedecido segundo o tipo de artigo, e computado excluindo as referências e os resumos em português e inglês.

8. Devem ser evitadas informações introdutórias extensas e repetitivas, dando-se preferência às mais recentes, ainda não publicadas. Evite textos com repetição da mesma informação no resumo, introdução e discussão.

9. Pesos e medidas devem ser expressos no sistema métrico decimal, e temperaturas em graus centígrados.

10. Drogas devem ser mencionadas por seus nomes genéricos, seguidos da dosagem e posologia empregadas, evitando-se a citação de termos comerciais ou marcas. Descrições de quaisquer equipamentos, instrumentos, testes e reagentes devem conter o nome do fabricante e o local de fabricação.

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Hallal AH, Amortegui JD, Jeroukhimov IM, Casillas J, Schulman CI, Manning RJ, *et al*. Magnetic resonance cholangiopancreatography accurately detects common bile duct stones in resolving gallstone pancreatitis. J Am Coll Surg. 2005;200(6):869-75.

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Reppert SM. Circadian rhythms: basic aspects and pediatric implications. In: Styne DM, Brook CGD, editors. Current concepts in pediatric endocrinology. New York: Elsevier; 1987. p .91-125.

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Fugh-Berman A. PharmedOUT [Internet]. Washington: Georgetown University, Department of Physiology and Biophysics; c2006 [cited 2007 Mar 23]. Available from: https://www.pharmedout.org/. Ex. quando o autor é uma organização: International Union of Biochemistry and Molecular Biology. Recommendations on Biochemical & Organic Nomenclature, Symbols & Terminology etc. [Internet]. London: University of London, Queen Mary, Department of Chemis- try; [updated 2006 Jul 24; cited 2007 Feb 22]. Available from: https://www.chem.qmul.ac.uk/iubmb/.

d- Apresentação prévia em eventos:

Bruhat M, Silva Carvalho JL, Campo R, Fradique A, Dequesne J, Setubal A, editors. Proceedings of the 10th Congress of the European Society for Gynaecological Endoscopy; 2001 Nov 22-24; Lisbon, Portugal. Bologna (Italy): Monduzzi Editore, International Proceedings Division; c2001. 474 p.

13. Ilustrações (figuras, quadros, gráficos e tabelas) devem ser referidas em ordem numérica sequencial no texto em números arábicos (exemplo: Figura 3, Gráfico 7), cabendo ao Editor suprimir as redundantes. As legendas das figuras e gráficos e os títulos e notas de rodapé das tabelas devem descrever precisamente seu conteúdo com frases cur- tas, porém suficientes para a compreensão ainda que o arti- go não seja totalmente lido. Todos devem ser inseridos no passo correspondente a ilustrações no sistema, evitando que use o campo destinado ao texto para que não contabilizem as palavras dentro das ilustrações.

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16. Os gráficos deverão ser elaborados em Microsoft Excel. As tabelas dispensam sua descrição no texto tendo a finalidade de suplementá-lo e não a de aumentá-lo. As unidades utilizadas para exprimir os resultados (m, g, g/100, mL etc.) figurarão no alto de cada coluna. Os pacientes devem ser identificados por números ou letras, e nunca pelos nomes, iniciais ou número de registro hospitalar.

17. O limite máximo de autores aceitável é de 5; só haverá exceção para trabalhos de maior complexidade (ex. Artigo Original, Revisão) mediante justificativa e aprovação dos editores.

18. As opiniões e declarações contidas na revista são de responsabilidade única e exclusiva de seus autores, não sendo, necessariamente, coincidentes com as da Equipe Editorial, do Conselho de Revisores ou da Sociedade Brasileira de Dermatologia.Os autores deverão submeter seu manuscrito para avaliação do Conselho Editorial da revista no endereço eletrônico que se segue: https://www.sgponline.com.br/scd/ sgp/.

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A revista aceita trabalhos inéditos e não publicados das seguintes categorias:

1– ARTIGOS DE REVISÃO

Poderão ser aprofundados os temas específicos nas áreas de interesse da S&CD, algoritmos, compilações e estatísticas. Estes trabalhos têm formato livre, porem devem conter resumo não estruturado de até 100 palavras e conclusões ou considerações finais. Limite: texto até 6000 palavras, 10 ilustrações e 60 referências. Os artigos de revisão sistemática ou metanálises devem seguir orientações pertinentes (https://www.cochrane.org/)

2– ARTIGO ORIGINAL

É o relato de uma pesquisa investigativa original nas áreas de Cirurgia Dermatológica, Oncologia Cutânea, Tecnologia em Dermatologia e Cosmiatria. Exemplos: estudos experimentais, estudos clínicos, comparações e descrições de técnicas ou de métodos de avaliação, estudos de áreas afins (ex: estudos farmacêuticos em cosmiatria). O texto deverá conter até 4000 palavras, 10 ilustrações e 35 referências e seguir o formato IMRDC (Introdução e objetivo, Métodos, Resultados, Discussão, Conclusão)

Resumo: deverá conter no máximo 200 palavras e ser estruturado seguindo os itens: Introdução, Objetivo, Métodos, Resultados e Conclusões. Não é permitido afirmar que os resultados ou outros dados serão apresentados ou discutidos.

Introdução: citar as razões que motivaram o estudo, descrevendo o estado atual do conhecimento sobre o tema. Utilizar o último parágrafo para especificar a principal pergunta ou objetivo do estudo, e a principal hipótese testada, se houver.

Métodos: Explicar como o estudo foi feito:

a- Tipo de estudo: descrever o seu desenho especificando a direção temporal (retrospectivo ou prospectivo), o tipo de randomização quando utilizada (pareamento, sorteio, sequenciamento, etc), se o estudo foi cego, comparativo, controlado por placebo, etc.

b- Local: indicar onde o estudo foi realizado (instituição privada ou pública), citar que a pesquisa foi aprovada pelo Comitê de Ética em Pesquisa de sua instituição, os procedimentos de seleção, os critérios de inclusão e exclusão, e o número inicial de pacientes.

c- Procedimentos: descrever as principais características das intervenções realizadas, detalhando a técnica e lembrando que o estudo de investigação deverá ser reprodutível.

d- Descrição dos métodos utilizados para avaliação dos resultados.

e- Inclusão da análise estatística descritiva e/ou comparativa com descrição do planejamento da amostra (representativa do universo a ser estudado), a análise e os testes estatísticos e apresentação dos níveis de significância adotados. A utilização de análises estatísticas não usuais é incentivada, porém neste caso, deve-se fazer uma descrição mais detalhada da mesma.

Resultados: descrever os principais resultados que devem ser acompanhados de estimativas pontuais e medidas de dispersão (p.ex., média e erro padrão) ou de estimativas intervalares (p.ex., intervalos de confiança), bem como os níveis descritivos dos testes estatísticos utilizados (p.ex. "p-value"). Os achados também devem ser interpretados sob o ponto de vista clínico.

Discussão: enfatizar os novos e importantes resultados encontrados pelo estudo e que farão parte da conclusão. Relatar observações de outros estudos relevantes. Mencionar as limitações dos achados e as implicações para pesqui- sas futuras.

Conclusões: devem ser concisas e responder apenas aos objetivos propostos. A mesma ênfase deve ser dada para estudos com resultados positivos ou negativos.

3- COMUNICAÇÕES

Artigos originais, breves, abordando resultados preliminares de novos achados de interesse nas áreas focadas pela revista. Texto com formatação semelhante ao artigo original, resumo estruturado de até 200 palavras. Limite: texto até 2000 palavras, 8 ilustrações e 15 referências.

4– DIAGNÓSTICO POR IMAGEM

Abordagem de temas ou casos clínicos, em que os exames de imagens (dermatoscopia, microscopia confocal, ultrassom e outros métodos) são fundamentais no diagnóstico ou tratamento. Resumo não estruturado de até 100 palavras, texto até 1200 palavras, 6 ilustrações e 5 referências.

5– COMO EU FAÇO?

Descrição de novas técnicas ou detalhes de técnicas. Resumo não estruturado de até 100 palavras, introdução com revisão de literatura, métodos, resultados, discussão e conclusão. Limite: 1200 palavras, 8 ilustrações e 30 referências.

6– RELATO DE CASO

Descrição de casos ou serie de casos de relevância nas áreas de interesse da S&CD, com descrição de tratamentos, complicações, etc. Resumo não estruturado de até 100 palavras, introdução com revisão de literatura, métodos, resultados, discussão e conclusão, sempre que pertinentes. Limite: texto até 1200 palavras, 8 ilustrações e 30 referências.

7– CARTAS

Comentários objetivos e construtivos sobre matérias publicadas. Texto até 600 palavras, e no máximo 5 referências.

Surgical & Cosmetic Dermatology

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Study of the histological characteristics of the different body anatomical regions and their importance in Mohs micrographic surgery

Estudo das características histológicas das diferentes regiões anatômicas corporais e sua importância na cirurgia micrográfica de Mohs

DOI: http://www.dx.doi.org/10.5935/scd1984-8773.20201222574

ABSTRACT

To accurately interpret intraoperative findings in Mohs Micrographic Surgery, it is essential to know the normal tissue histology of different anatomical sites. The freezing sections evaluated by the technique are obtained horizontally, unlike the vertical sections of conventional anatomopathological analysis. According to the literature review, the frozen sections of interest in topographic histology were digitized and detailed from a training Dermatology service case collection.

Keywords: Histology; Mohs Surgery; Skin Neoplasms

RESUMO

Para a interpretação precisa dos achados intraoperatórios na cirurgia micrográfica de Mohs, é fundamental conhecer a histologia normal dos tecidos nas diferentes regiões anatômicas. Os cortes de congelamento avaliados pela técnica são obtidos na horizontal, diferentemente dos cortes verticais da análise anatomopatológica convencional. A partir do acervo de casos de um serviço de formação em Dermatologia, os cortes de congelamento de interesse em histologia topográfica foram digitalizados e detalhados, conforme revisão da literatura.

Palavras-chave: *Cirurgia de Mohs; Histologia; Neoplasias Cutâneas*

Review

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INTRODUCTION

Mohs micrographic surgery (MMS) requires the dermatological surgeon to have extensive knowledge of normal tissue histology and pathological anatomy. The accurate interpretation of the freezing sections usually performed horizontally (in contrast to the vertical sections of conventional anatomopathological analysis), and the knowledge of histological peculiarities of the different anatomical regions are essential for the differentiation between typical structures and intraoperative tumor findings.[1] The case collection of an MMS training reference service was reviewed, and the freezing sections of interest in topographic histology were digitized using a Leica DM-1000 microscope and a Leica ICC-50 camera (Leica Microsystems, Wetzlar, Germany).

TOPOGRAPHIC HISTOLOGY

Scalp

The scalp presents a high density of follicular units, with anagenic terminal follicles implanted deep in the subcutaneous tissue (Figure 1a).[2] In horizontal sections, the hair follicle's cross-section results in rounded or oval basophilic structures, which may resemble basal cell carcinoma (BCC) nests. Knowing the characteristics of the different portions of the hair follicle helps in this differentiation.[1] A series of layers from the bulb form the hair follicle, often showing a central hair shaft, and, unlike the BCC, it does not usually present a gap between its structure and the adjacent dermis. The outer epithelial layer is composed of monomorphic cells, with a moderate amount of eosinophilic cytoplasm surrounded by fibrous stroma. At the height of the reticular dermis, sebaceous glands are associated with the follicular unit, and its duct marks the division of the upper (infundibulum) and middle (isthmus) hair segment. The follicular unit's connection with the hair erector muscle delimits the division between the middle and lower hair segments (or bulb, which will contain the papilla) and is called a bulge. In the transition between the infundibulum and the isthmus, arciform epithelial cords protrude laterally in relation to the follicle and are called the mantle.[2,3]

In cases of deeper tumor involvement, it is possible to identify, below the subcutaneous and the galea aponeurotica), dense connective tissue, with collagen fibers and fibroblasts, representing the periosteum (Figure 1b).[4]

Ear canal

The auricle has its shape determined by the structure of elastic cartilage (Figures 2b and 2d). It is covered by thin skin, hair follicles, sebaceous glands, and eccrine sweat glands, the latter being replaced by cerumen glands at the level of the external acoustic meatus.[5,6] The density of attachments is heterogeneous in the different portions of the canal, being more prominent in the area of the auricle (Figures 2a and 2c).

Parotid region

The skin over the parotid region is also a frequent site of tumors treated by MMS. In the case of tumor involvement in the deep margins, parotid and lymph node tissues can be identified in the freezing sections.

The parotid is the largest salivary gland in the body. It is considered a compound, tubule-acinar, merocrine and exocrine gland. In adults, serous acini form it entirely (Figure 3a). The superficial portion of the gland is closely related to the superficial musculoaponeurotic system (SMAS) of the face, which is formed from an aponeurotic extension of the platysma muscle. Some terminal branches of the great auricular nerve are also located there.[7]

The region is also a place of high lymph nodes concentration; small lymph node fragments can simulate basaloid tumor nests (Figure 3b) or peritumoral inflammatory infiltrate. This occurs mainly if the freezing sections are thick, causing overlapping cells, a common situation in specimens with high adipose tissue content.

Eyelid

The eyelid is divided into anterior and posterior lamellae. The anterior lamella consists of skin (the thinnest of the body, 0.4 mm thick) and orbicularis muscle, while the tarsus and the conjunctiva form the posterior lamella (Figure 4a).[8,9]

The tarsus, a dense fibroelastic tissue, is responsible for providing structural support, which is essential to the eyelid's function. Inside, we find modified sebaceous glands, called Meibomian glands, which produce lipid secretion. Its content flows directly through eyelid openings to form the outer layer of the tear film. They are known as the most frequent site of sebaceous carcinoma.[9]

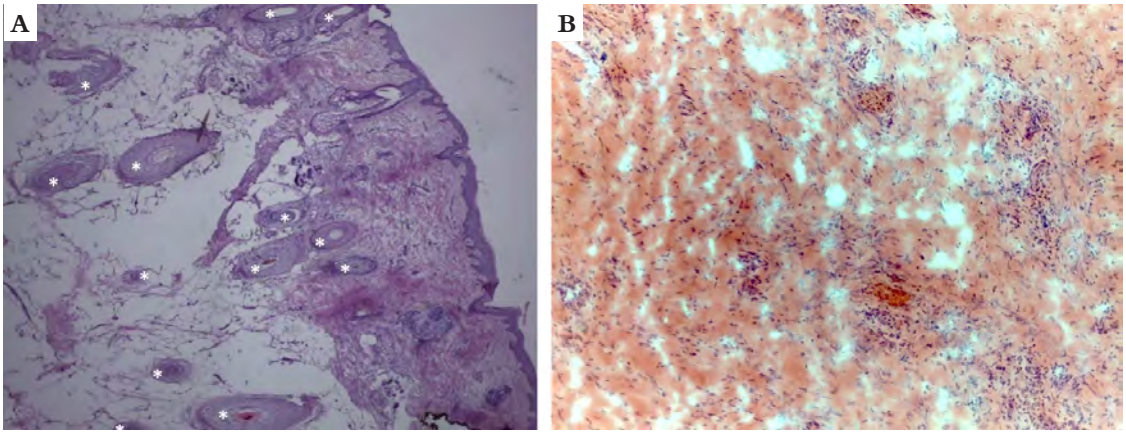

Figure 1: A) Large number of hair follicles (white asterisks), present even in the depth of subcutaneous cell tissue (vertical section, Hematoxylin & eosin, 40x). **B)** Periosteum. Dense collagen and presence of fibroblasts in large quantities (horizontal section, Hematoxylin & eosin, 100x)

Zeiss's sebaceous glands present in the dermis, in turn, are associated with the hair follicles of the eyelashes on the eyelid edge. Also, in the dermis, there are Moll glands (apocrine sweat glands), which have openings for both hair follicles and directly on the anterior palpebral margin, being more numerous on the lower eyelid (Figure 4b). Unlike Moll's glands, the eccrine sweat glands are not confined to the eyelid margins and can be found throughout the eyelid region.[9]

The conjunctival epithelium is non-keratinized and has about five layers of cells in thickness (Figure 4c). Goblet cells, which produce mucus, can be found inside the epithelium, being more frequent in the fornix region.[9]

The upper and lower lacrimal canaliculi, often seen in MMS histological sections in tumors of the medial portion of the eyelids, are lined with stratified squamous epithelium (Figure 4d). In the region of common canaliculus, formed by the union of the two canaliculi, the epithelium becomes pseudo-stratified, non-ciliary, and columnar.[10]

Nose

The nasal surface is rich in glandular and follicular structures, and their density varies according to the subunit assessed (Figures 5a and 5d). Much of the nose's shape - especially the nasal wings, and thus the patency of the nasal vestibule - depends on cartilage

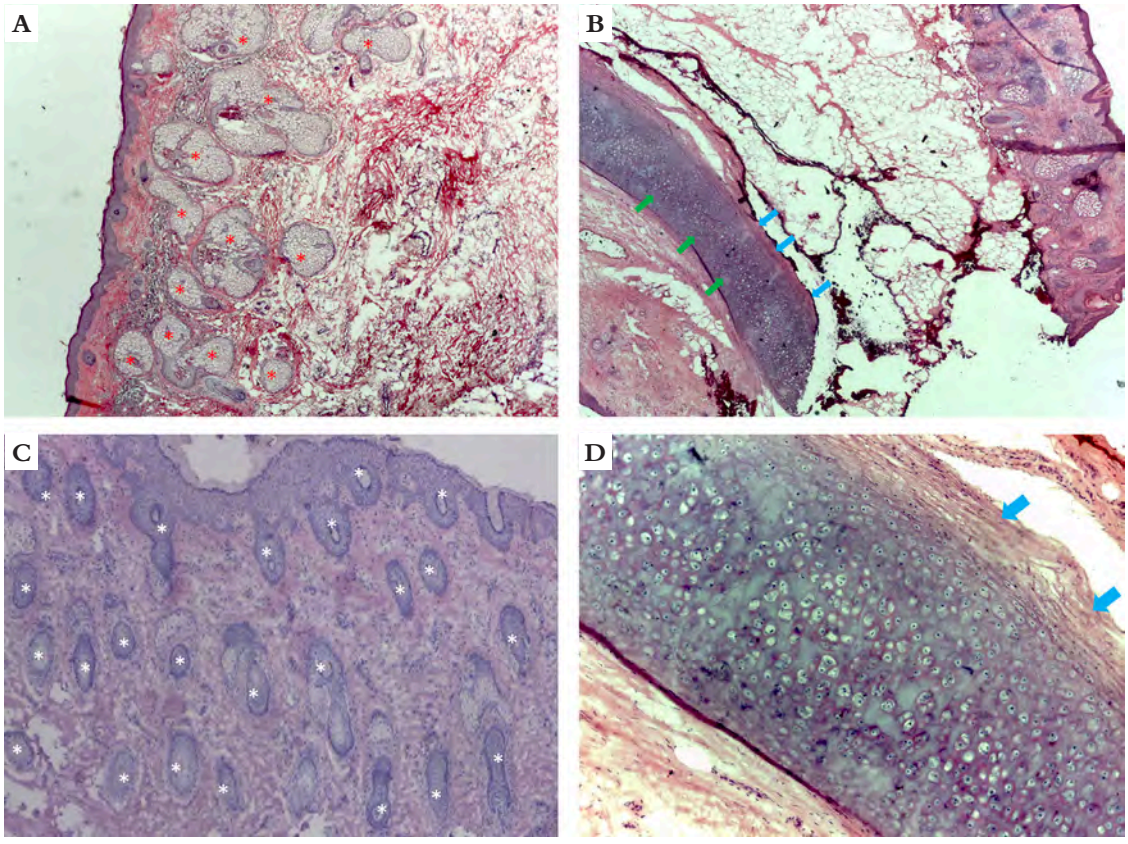

Figure 2: Ear canal.
a) Helix. Large amount of sebaceous glands (red asterisks) (horizontal section, Hematoxylin & eosin, 40x).
b) Full-thickness helix section. Helix cartilage (green arrows) under subcutaneous tissue. Perichondrium attached to cartilage (blue arrows) (vertical section, Hematoxylin & eosin, 25x).
c) Histology of the auricle. Large amount of hair follicles (white asterisks) (vertical section, Hematoxylin & eosin, 40x).
d) Detail of chondrocytes and perichondrium attached to the cartilage (blue arrows) (vertical section, Hematoxylin & eosin, 100x)

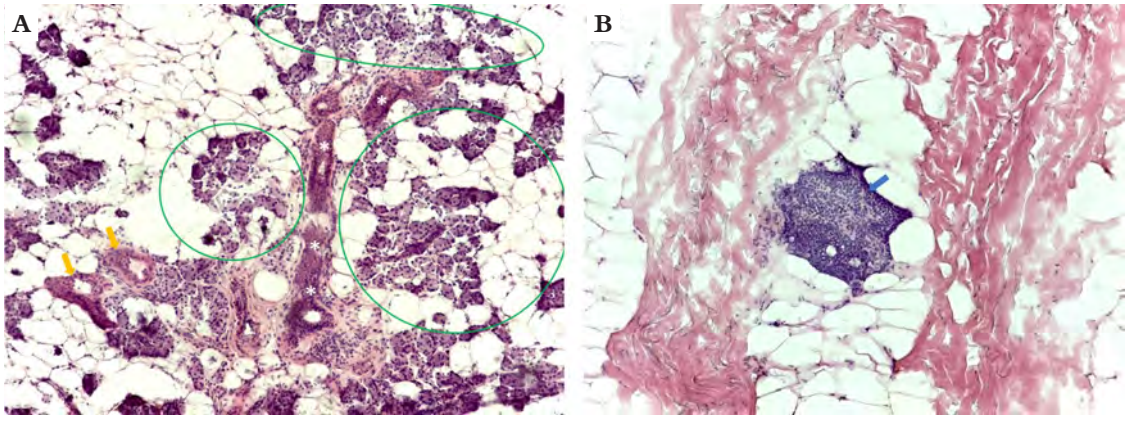

Figure 3: Parotid region.
a) Parotid tissue; serous acines interspersed with subcutaneous cell tissue (green circles); striated ducts (yellow arrows); excretory duct (white asterisks) (horizontal section, Hematoxylin & eosin, 100x).
b) Lymph node tissue in deep margin section (blue arrow) (horizontal section, Hematoxylin & eosin, 100x).

support (Figure 5c). In full-thickness sections, the mucous lining with ciliated cylindrical pseudostratified epithelium can be identified as well as the nasal mucous glands (Figures 5d and 5e).

The differentiation between BCC and hair follicles is a constant in the routine of the micrographic surgeon. The multicentric growth of the basaloid epithelium adjacent to the hair follicle characterizes the folliculocentric basaloid proliferation (FBP). This benign histological finding can occur in this topography and can be confused with BCC (Figure 5f).

If not recognized, this entity can lead to unnecessary excision of additional stages by the Mohs surgeon. Criteria such as the folliculocentric and radial disposition, in addition to the presence of a prominent hyaline basal membrane and normal adjacent stroma in the FBP, help differentiate the two entities.[11,12]

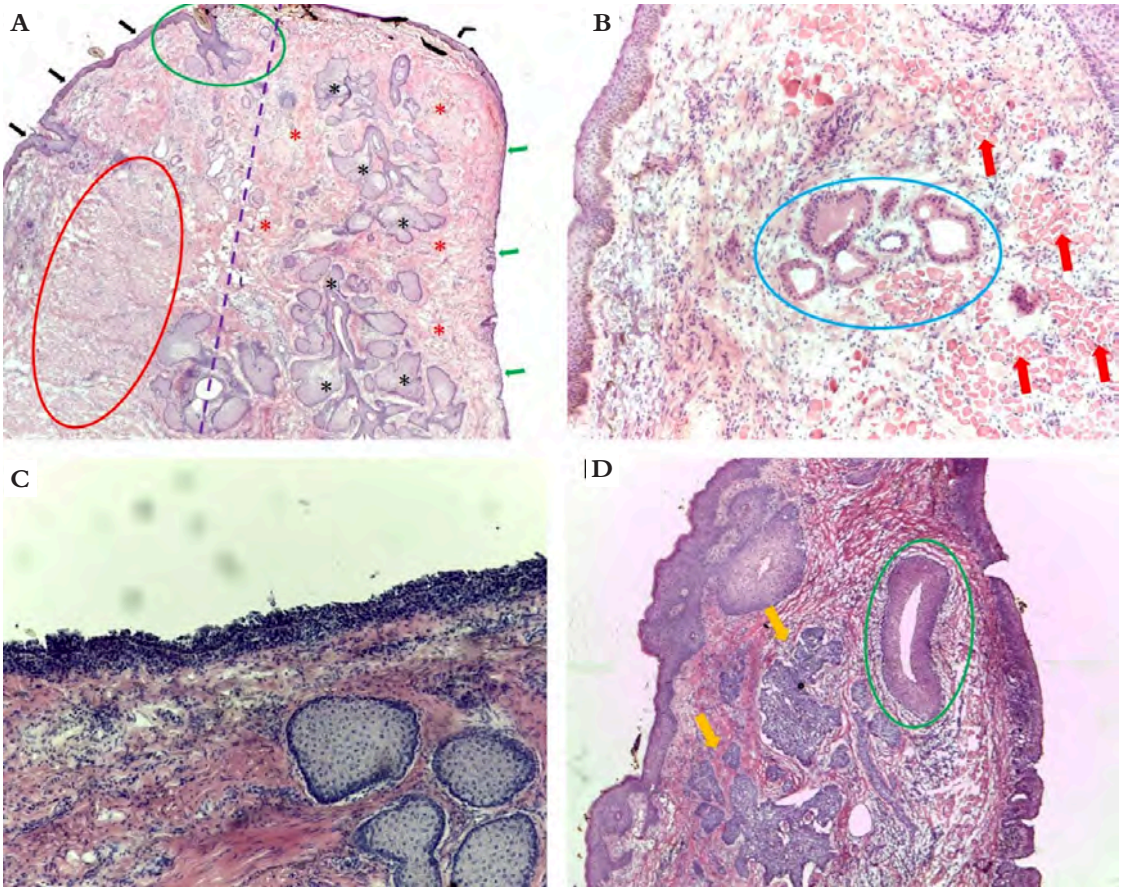

Figure 4: Eyelid histology. **a)** Division of the anterior and posterior lamellae (dashed violet line); fibers of the orbicularis oculi muscle in the anterior lamella (red circle); glands of Zeiss adjacent to a hair follicle (green circle); Meibomian glands (black asterisks); tarsus (red asterisks); conjunctival epithelium (green arrows); pre-tarsal epidermis (black arrows). Eyelid (cross-section, Hematoxylin & eosin, 25x). **b)** Moll's glands (blue circle); orbicularis oculi muscle (red arrows) (cross section, Hematoxylin & eosin, 40x). **c)** Detail of the conjunctival epithelium (cross section, Hematoxylin & eosin, 40x). **d)** Margin compromised by nodular basal cell carcinoma (yellow arrows), close to the lacrimal canaliculus (green circle) (cross section, Hematoxylin & eosin, 25x).

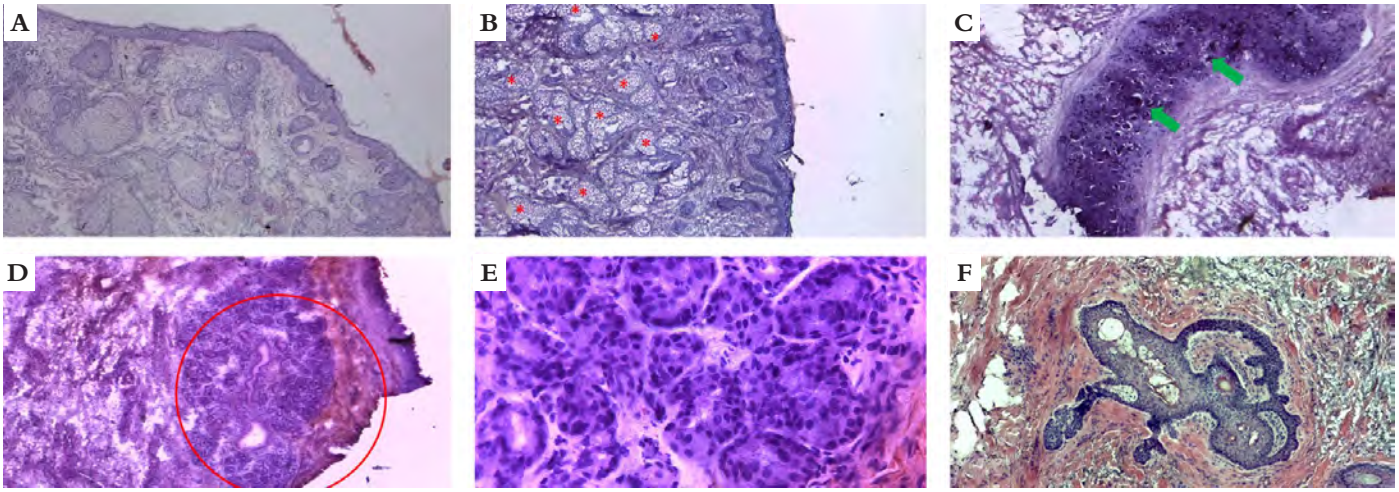

Figure 5: Nose: **a)** Nasal dorsum (horizontal section, Hematoxylin & eosin, 40x). **b)** Nasal wing. Higher density of sebaceous glands (red asterisks) (vertical section, Hematoxylin & eosin, 40x). **c)** Alar cartilage (detail) (green arrows) (horizontal section, Hematoxylin & eosin, 100x). **d)** Nasal mucosa lining epithelium (black arrows) with mucous glands (red circle) (vertical section, Hematoxylin & eosin, 25x). e) In detail, nasal mucous glands (vertical section, Hematoxylin & eosin, 100x). f) Peripollollicular basaloid proliferation (horizontal section, Hematoxylin & eosin, 100x).

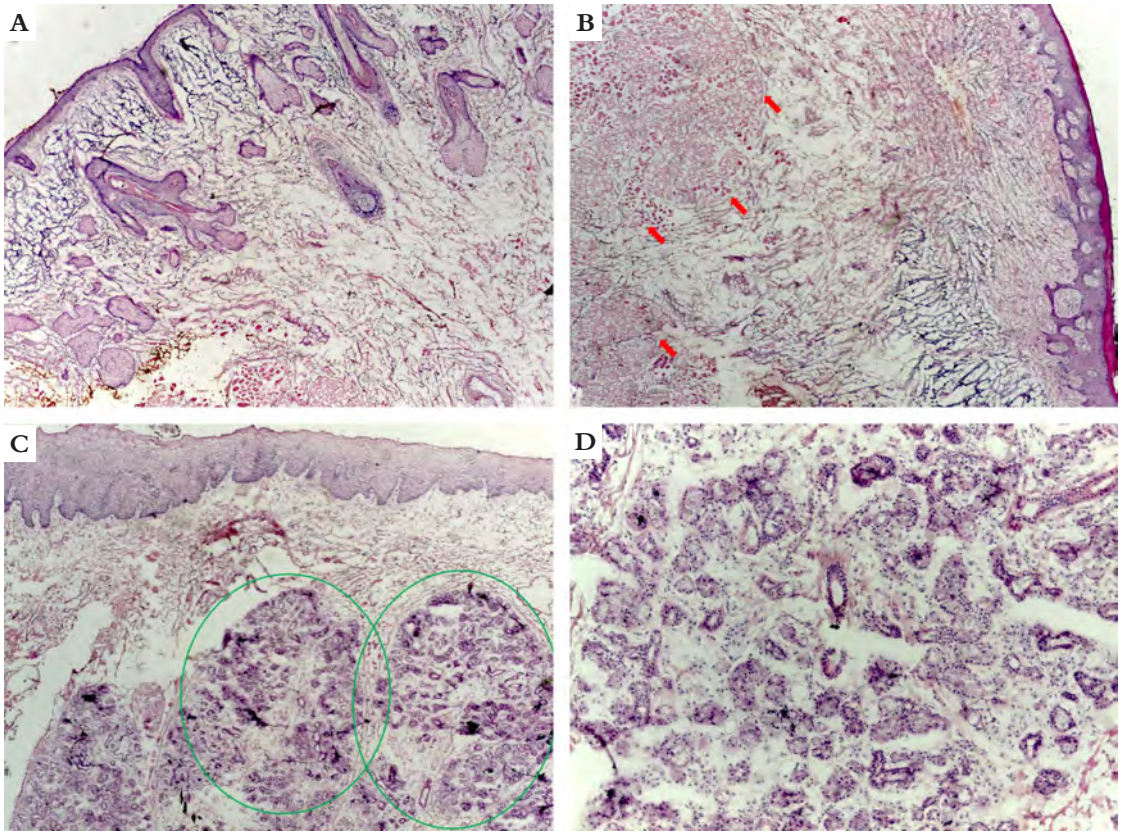

Figure 6: Lower lip.
a) Cutaneous lip. Presence of attachments in the section (black asterisks) (vertical section, Hematoxylin & eosin, 25x).
b) Lip vermilion. Note the absence of hair follicles. Fibers of the orbicularis oris muscle in depth (red arrows) (vertical section, Hematoxylin & eosin, 25x).
c) Epithelium of the labial mucosa and minor salivary glands (green circles). Note the absence of keratinization and granular layer (vertical section, Hematoxylin & eosin, 25x).
d) Detail of the minor salivary glands (vertical section, Hematoxylin

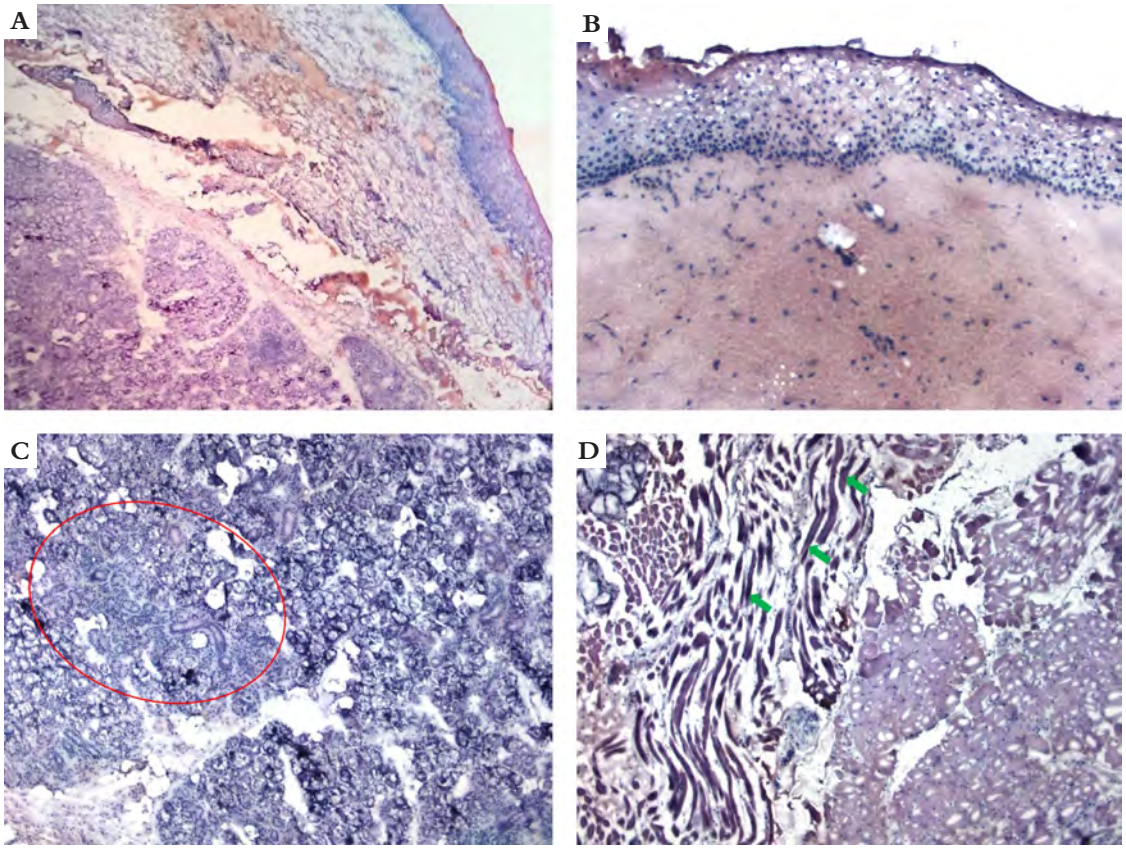

Figure 7: Tongue:
a) Fragment of the tongue (vertical section, Hematoxylin & eosin, 40x).
b) Lingual epithelium (vertical section, Hematoxylin & eosin, 100x).
c) Salivary glands, in detail (red circle) (vertical section, Hematoxylin & eosin, 100x).
d) Detail of striated muscle fibers (green arrows) (vertical section, Hematoxylin & eosin, 100x)

Lip

The lips consist of two movable musculomembranous folds, covered by mucosa, on the inner surface, and cutaneous integument, on the outside (Figure 6a). The area of the mucocutaneous union constitutes the vermilion (Figure 6b). Stratified keratinized squamous epithelium covers the cutaneous portion and preserves the cutaneous attachments. On the other hand, the mucous portion is not keratinized, and its pink color, absence of protection structures, and the presence of salivary glands differentiate it from the skin (Figures 6c and 6d). Even now, ectopic sebaceous glands can be identified, and are called Fordyce granules.[6]

Tongue

The tongue is predominantly composed of striated skeletal muscle fibers, in addition to adipose tissue, blood vessels, salivary glands, and mucous lining (Figure 7).

The mucosa that covers the back of the tongue has keratinized epithelium and, due to the taste buds' presence, makes the tongue a sensory and specialized structure. The lingual papillae (filiform, fungiform, and goblet) cover the anterior two-thirds of the tongue's back, and a smooth mucosa, rich in lymphoid aggregates (lingual tonsillar tissue), covers the tongue's base.[6,13]

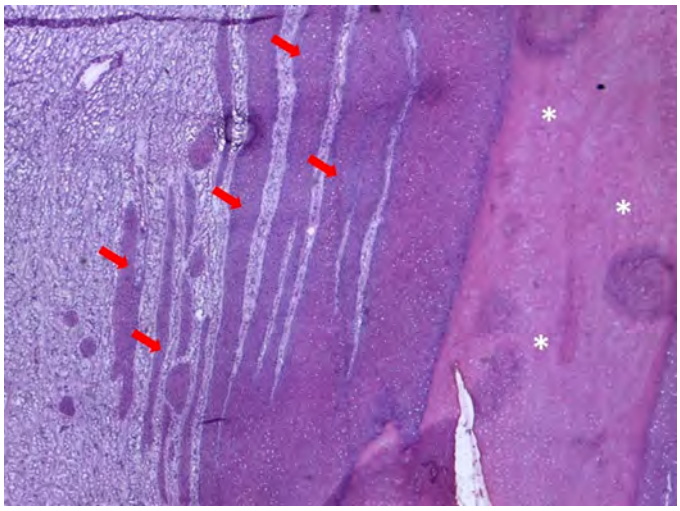

Figure 8: Nail apparatus: the pleated aspect of the nail matrix (red arrows), progressing towards the nail plate (white asterisks) (vertical cut, Hematoxylin & eosin, 40x)

Nail apparatus

In a longitudinal section of the nail apparatus, the proximal nail fold, nail plate, matrix, bed, and hyponychium are seen.[14] When addressing tumors located in the distal phalanx, it is possible to identify one or more of these structures on the surgical margins.

The proximal nail fold has dorsal epithelium (with sweat glands and no pilosebaceous units) and ventral epithelium (without cutaneous attachments, cornified, and which will originate the cuticle). The matrix is composed of a thick germinal epithelium without a granular layer, with few melanocytes. As the matrix cells progress to the upper layers, their cytoplasm becomes more eosinophilic and the nucleus, pycnotic, until it forms the nail plate, consisting of cornified cells of lamellar arrangement (Figure 8).

Below the lamina is the nail bed, delimited distally by the hyponychium and proximally by the matrix. Its epithelium is thin, without granules, and attached to the underlying dermis by long and narrow epidermal cones. The hyponychium and the volar skin have a granular and thick and compact corneal layer. The dermis rests directly on the distal phalanx, without the interposition of subcutaneous tissue.[15]

Breast

Eventually, when dealing with cutaneous lesions in breast topography, it is possible to identify mammary gland tissue in the specimen's deep margins. The secretory portion of the mammary gland includes lobules and ducts, interspersed by the interlobular stroma (dense connective tissue, fat cells, and blood vessels) (Figure 9).

The lobes are circular structures made of acids (formed by an inner layer of epithelial cells and an outer layer of myoepithelial cells) and loose connective tissue - the intralobular stroma. In this, the presence of chronic inflammatory cells, mainly lymphocytes, is physiological and variable according to the menstrual cycle period.

A layer of epithelial cells and another layer of myoepithelial cells form the mammary ducts, and they drain the lobules.6

Depending on the section's incidence, such structures may form basophilic clusters that must be differentiated from tumor infiltration at the subcutaneous level.

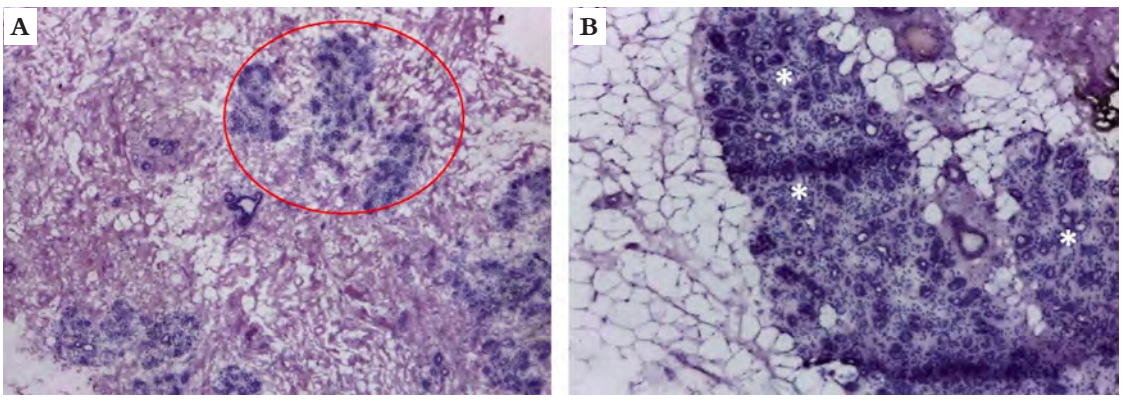

Figure 9: Breast: **a)** Breast tissue, fibroglandular area, prominent glandular lobes (circles) (horizontal section, Hematoxylin & eosin, 40x). **b)** Breast tissue, an area with a predominance of adipose tissue interspersing glandular clusters (asterisks) (horizontal section, Hematoxylin & eosin, 100x).

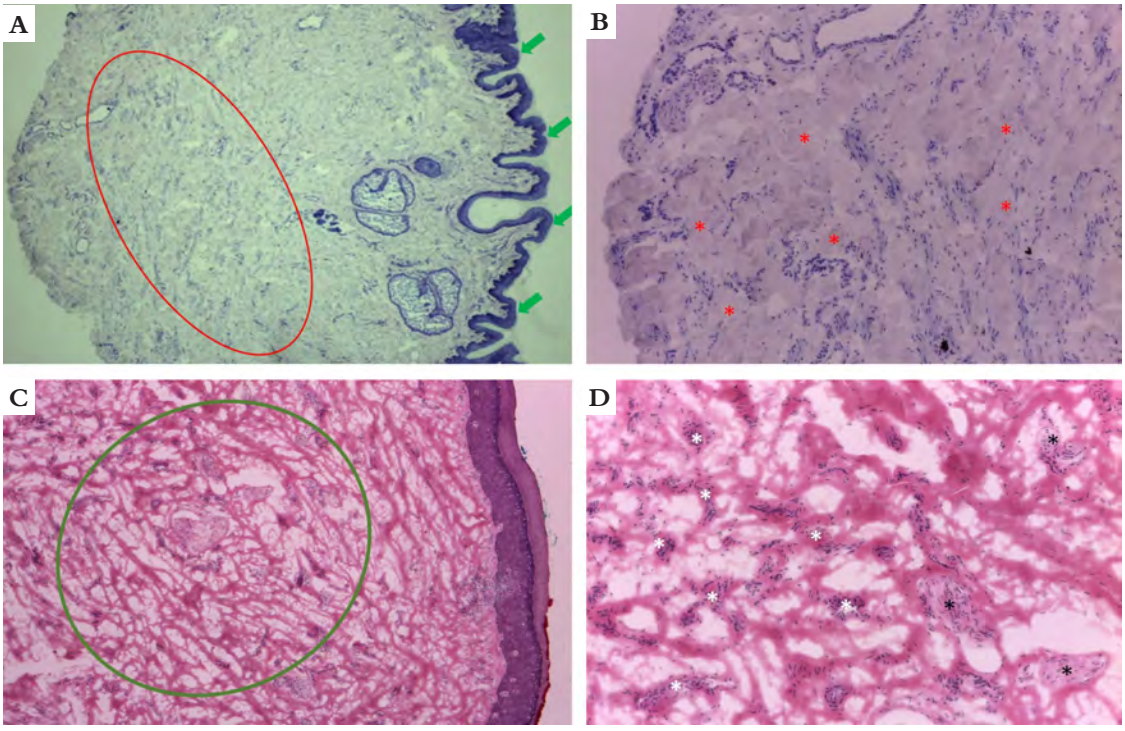

Figure 10: Male genitalia: **a)** Fragment of the scrotum, with stratified keratinized epithelium (green arrows), dermis with sebaceous glands and rich in vessels and smooth muscle fibers (arrows) (red circle) (horizontal section, Toluidine Blue, 40x). **b)** Smooth muscle fibers (arrows) (red asterisks), in detail (horizontal section, Toluidine Blue, 100x). **c)** Glans penis showing epithelial alterations suggestive of lichen sclerosus, with preserved and richly vascularized and innervated dermis (green circle) (horizontal section, Hematoxylin & eosin, 40x). **d)** In detail, density of vessels (white asterisks) and nerves (black asterisks) in the dermis at the level of the glans (horizontal section, Hematoxylin & eosin, 100x). Courtesy: Dr. Gabriel Gontijo

Male genitalia

A thin epidermis, a dermis rich in sebaceous glands and blood vessels, forms the penis and scrotum's skin envelope. This dermis is closely related to the tunica darts, composed of smooth muscle fibers (Figure 10). At the glans level, there is a transition from keratinized epithelium to the mucous epithelium.[5,13]

CONSIDERATIONS

Histological differentiation between benign and malignant entities is essential in CMM, aiming at precise removal of the tumor and preservation of healthy tissue. Dense inflammation, scar tissue, hair follicles, and other normal skin structures can resemble tumor aggregates. Knowing the histological particularities of the body's different areas through freezing sections contributes to the correct interpretation of the slides.●

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Biostimulators and their mechanisms of action

Bioestimuladores e seus mecanismos de ação

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ABSTRACT

In the skin aging process, both intrinsic alterations, secondary to cell regeneration capacity loss resulting from chronological action, and extrinsic alterations, caused by to ultraviolet radiation exposure, can be observed. Treatments that restore collagen production and stimulate fibroblasts to synthesize and organize extracellular matrix are critical for morphogenesis, angiogenesis, and skin healing. Potential uses of products that stimulate collagen production, a component that plays a fundamental role in the extracellular matrix, represents a promising perspective for improving skin quality and its mechanical properties by introducing a new concept of therapeutic approach when treating changes caused by skin aging.

Keywords: Collagen; Hydroxyapatite; Skin Aging

RESUMO

No envelhecimento da pele, as alterações intrínsecas, secundárias à perda da regeneração celular, e extrínsecas, causadas pela exposição à radiação ultravioleta, podem ser observadas e alteram a arquitetura tecidual e as propriedades fisiológicas da pele. Tratamentos que restauram a produção de colágeno e estimulam os fibroblastos a sintetizar e organizar a matriz extracelular são críticos para a morfogênese, angiogênese e cicatrização. Potencial utilização de produtos que estimulam a produção de colágeno, que desempenha papel fundamental na matriz extracelular, representa perspectiva promissora para a melhoria da qualidade da pele e das propriedades mecânicas, introduzindo um novo conceito de abordagem terapêutica no tratamento de alterações causadas pelo envelhecimento da pele.

Palavras-chave: *Colágeno; Hidroxiapatita; Rejuvenescimento*

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INTRODUCTION

The maintenance of the tissue architecture and skin physiological properties is attributed to the extracellular matrix of connective tissue, which comprises a large number of components including collagen and elastic fibers, proteoglycans and glycosaminoglycans macromolecules, as well as several non-collagen glycoproteins.[1]

In the skin aging process, both intrinsic and extrinsic changes occur. The intrinsic changes are secondary to cell regeneration capacity loss due to chronological action, with the dermis becoming relatively more acellular and avascular in senescence. Moreover, the extrinsic changes are caused mainly by chronic exposure to ultraviolet radiation.[1,2]

In chronological aging, there is a thinning of the dermal thickness, which occurs due to biochemical and structural changes in collagen, elastic fibers, and the ground substance.[3,4] The collagen synthesis decreases and its degradation increases due to higher levels of collagenase. The collagen content reduces throughout adulthood, and the remaining fibers appear disorganized, more compact, and granular, with a higher number of crosslinks. The rate of collagen types also changes, with a predominance of type I collagen in young individuals and type III collagen in the elderly. The elastic fibers decrease in number and diameter. The number of mucopolysaccharides in the ground substance decreases, especially that of hyaluronic acid. These changes negatively influence the skin's turgor and also impact on deposition, orientation, and size of collagen fibers.[4,5]

In extrinsic aging, the alterations caused mainly by solar radiation affect the dermal cellular components and the extracellular matrix, with the accumulation of disorganized elastic fibers, fragmentation of collagen fibers, and reduction in the proportion between type I and type III collagens,[6,7] which occur both by the direct action of radiation on collagen fibers and by the increase in metalloproteinases (mainly collagenase). The altered interaction of the fibroblast with the extracellular matrix also causes an interruption in the synthesis of new collagen, exerting an inhibitory mechanism on collagenesis.[6,7]

The ability of resident cells, such as fibroblasts, to synthesize and organize the extracellular matrix is critical for morphogenesis, angiogenesis, and skin healing. One of the most important modulators of connective tissue gene expression is the transforming growth factor type β (TGF-β), a member of the family of growth factors released by macrophages. It stimulates the expression of several genes in the extracellular matrix, including those encoding collagens I, III, IV, and V, apparently transforming TGF-β into connective tissue growth factor (CTGF) in the fibroblast. These growth factors have their levels reduced in the aging process.[8] The release of these factors by macrophages would be the proposed mechanism for stimulating collagen production, both in the healing process and after treatments with the biostimulators application, which act by inducing a tissue inflammatory response.[5,9,10]

Biostimulation is the polymer's ability to generate cellular benefit or tissue response in a particular clinical application through a desired controlled inflammatory response, leading to slow degradation of the material. It culminates in collagen deposition in the tissue, conditioned by biomaterial properties and by the technique that injected the polymer into the tissue.[11] The materials used as biostimulators will have different biocompatibility according to various physicochemical factors such as their chemical composition, particle size, physical shape, contact angles, structure, surface tension, and surface charges. For example, particles with pores or an uneven surface are potentially more reactive and can initiate an inflammatory response, while the smooth ones are encapsulated by fibrous tissue and induce the foreign body response regulated by the Protease Activated Receptor 2 (PAR 2), a protein involved in cell proliferation and regulation of the acute inflammatory response.[12] Microspheres with diameters between 0.5 μm and 20 μm are phagocytized by a variety of cells, resulting in a cascade of cytokines characterized by the production of tumor necrosis factor α (TNF-α) and interleukins IL-1 and IL, while the particles with larger diameters are not phagocytized and do not induce TNF-α production.[13,14]

The process of polymer degradation that constitutes the implant must also be considered, as it varies with its molar mass, composition, thermal story, crys-

talline structure, and amount of polymer applied. The corresponding monomers or the products generated from them, in an aqueous environment, also undergo metabolic action in living organisms and can generate a biological response.[12-15] The degradation of the biomaterial should result in non-reactive molecules, as their degradation products cannot cause stimulation of inflammatory cells, especially macrophages and giant cells, or interfere with their biocompatibility.[12] The search for substances for soft tissue fillers that do not evoke an important inflammatory response has led to the use of a variety of biomaterials.

The formation of a capsule and inflammatory cell infiltration are characteristic of the foreign body reaction to the biomaterial and, depending on their surface properties, distinct extracellular proteins can be attached.[16,17] The combination of these proteins and their concentrations determines cell behavior.[18] Host proteins that are absorbed by the biomaterial surface include albumin, complement fragments, fibrinogen, fibronectin, immunoglobulin G, and vitronectin.[19,20] Fibrinogen, complement, and vitronectin are recognized by macrophage and neutrophil receptors.[21] To stimulate inflammatory cell migration, mast cells release histamine.[20,22] Monocytes and Th2 helper cells infiltrate the tissue. Monocytes turn into macrophages releasing chemoattractants that attract more macrophages around the biomaterial. Platelets and macrophages produce platelet-derived growth factor (PDGF) and transforming growth factor beta (TGF-β), which promote the fibroblasts migration.[22] TGF–β seems to be the mediator for collagen synthesis, as well as for the differentiation of fibroblasts from myofibroblasts, the alpha-smooth muscle actin (aSMA)-rich, its contractile form. PDGF promotes myofibroblast proliferation.[23] Macrophages fuse under the influence of IL-4 and IL-13 to form foreign body giant cells, in case the material cannot be phagocyted. In an alternative condition, macrophages produce pro-fibrotic factors, such as TGF-β1 and PDGF, which stimulate fibroblasts to produce collagen, leading to the formation of a capsule that surrounds the material.[23,24]

There is initially the deposition of collagen type III fibers around the biostimulator microspheres, with a fibroblastic tissue response and type I collagen deposition in the periphery. Over the months, there is a remodeling process of type III collagen, resulting in the predominance of type I collagen in the newly formed tissue.[25,26] The maturation phase begins with the collagen crosslinking, which will cause its contraction and adjustment of the network, with the return of the tensile force to the tissue.[26]

Cell fusion and the formation of giant cells is an adaptation to the difficulties in eliminating the foreign body. In the expected and physiological foreign body reaction, the host, with activation of circulating monocytes, recognizes the biomaterial. Once activated, they adhere firmly to the substrate, releasing proteins that initiate specific recognition at cell surface receptors, determining an expected inflammatory response. However, some factors can modify this physiological response, attracting Langerhans cells and lymphocytes, causing a pathological foreign body reaction: chemical composition; particle size and volume; implant morphology (irregularly shaped particles activate more prostaglandins E2 and tumor necrosis factor); surface area; electrical load, and implantation site, including the individual response of the host.[16]

The potential use of products that stimulate the collagen production, a fundamental component for the properties of the extracellular matrix, currently represents a vital treatment perspective for improving the skin quality and its mechanical properties, opening a new concept for the therapeutic approach to changes caused by skin aging. Among biomaterials, poly-L-lactic acid and hydroxyapatite stand out due to their biocompatibility and bioreabsorption characteristics. They also have the most studied and well-known mechanisms of action and are, therefore, the most widely used products.

For implants, in general, the characteristics of the host also contribute to the variable responses in the interaction between biomaterial and organism response,[13] which will determine the amount of collagen, variable according to age, sex, general health, concomitant diseases, lifestyle, and pharmacological status of the patient.

OBJECTIVE

Review the articles on poly-L-lactic acid (PLLA) and calcium hydroxyapatite (CaHA),

highlighting their different mechanisms of action and their therapeutic indications.

MATERIAL AND METHODS

We searched for articles published in English on the PUBMED, with the keywords: poly-l-lactic acid, calcium hydroxyapatite, biostimulator, neocollagenesis, and collagen.

RESULTS

Twenty-nine articles were selected, specifically on biostimulators. Of these, ten were related to the clinical use of poly-L-lactic acid and nine to the clinical use of calcium hydroxyapatite. Only one article cited the clinical indications of the two products together, but not in a comparative way. Regarding the mechanisms of action, three articles on PLLA and five articles on CaHA were published. In the introduction to this article, we discussed the biological response to biostimulators, in a review of 10 articles relevant to the topic.

DISCUSSION

Poly-L-lactic acid

Injectable PLLA has been applied as a cosmetic filler since 1999 to correct facial and cutaneous volume losses caused by aging in a gradual, progressive, and prolonged manner, promoting natural and harmonious results, with low risks of adverse events.[15,27]

It is a high molecular weight organic polymer (140 kD), of the family of α-hydroxide acids, derived from lactic acid. It presents self-organization property and formation of colloidal micelles in aqueous solution, in the form of spherical particles with a smooth surface, dispersed as lyophilized powder in sterile flask, added to 4.45% of carmellose sodium and 2.67% of non-pyrogenic mannitol. It must be diluted in 8 ml of distilled water for 24 to 72 hours before implantation. The aqueous vehicle will be absorbed in 24 to 48 hours.[23,26]

PLLA microspheres have more uniform sizes, between 40 μm to 63 μm in diameter. They act as a substrate that promotes appropriate cell activity, inducing or facilitating molecular and mechanical signaling to optimize tissue regeneration without causing any local or systemic harmful response to the host.

PLLA is considered to have superior biocompatibility. Although tissue enzymes and other chemical species, such as superoxides and free radicals, can affect it, its degradation pathway occurs through non-enzymatic hydrolysis. They initially form water-soluble monomers and dimers, which are phagocytized by macrophages, metabolized in CO2 (eliminated by the respiratory route), H2O, or incorporated into glucose. Its estimated half-life is 31 days and is eliminated from the body after 18 months.[15,28] It is considered a bioresorbable material, as its degradation occurs by decreasing the size of the molecule, and its metabolites are absorbed in vivo and completely eliminated by metabolic routes.

After PLLA implantation in the deep reticular dermis or superficial hypodermis, the normal reaction begins with the injection wound, although minimal. The release of platelets in the extracellular matrix releases homeostatic and chemotactic factors that attract fibroblasts, in addition to neutrophils and monocytes from the circulation. Two hours after the injection, the inflammatory phase begins. Activated neutrophils begin to phagocytize the foreign body and secrete cytokines and proteolytic enzymes. Edema appears to facilitate cell migration. Monocytes are transformed into macrophages to eliminate apoptotic neutrophils and particles too large to be phagocyted. Between seven and ten days after the implant introduction, the level of macrophage fusion increases with the associated reduction in the number of apoptotic cells. There is a slight initial inflammatory response with foreign body reaction, in which the macrophages fuse into giant cells to try to phagocytize the particles. Macrophages also secrete growth factors to initiate the proliferative phase of reconstruction.[23,28]

Fibroblasts secrete components of the extracellular matrix, initially type I collagen, the most abundant structural protein in the dermal extracellular matrix, which plays a significant role in skin tension and resilience, accompanied by a smaller production of type III collagen. This neocollagenesis is followed by marked fibroblast activity and proliferation, with gradual deposition of more collagen fibers and the formation of mature vascularized fibrous tissue, accompanied by PLLA degradation, with no indication of acute inflammatory response.[28]

Thus, fibroblasts isolate the implant with a fibrous collagen capsule, which will gradually be replaced by fibrocytes, and each foreign particle will finally be encapsulated independently of the others. As the PLLA is degraded, the connective tissue's response around the implant results in a gradual filling with new collagen fibers at the site that it formerly occupied. This fibroplasia produces the desired cosmetic result, with increased dermis thickness.[23,28]

The new collagen begins to form after one month and continues to increase for nine months to a year. PLLA-induced tissue augmentation was based on capsule formation, orchestrating macrophages, myoblasts and fibroblasts, and substantial deposition of type III collagen close to particles and type I collagen in the periphery of the encapsulated PLLA. There is an expression of genes related to collagen metabolism, with the presence of CD68(+) macrophages next to PLLA particles, as well as CD 90(+) and α-SMA-positive fibroblasts, indicating the presence of myofibroblasts and neovascularization. MRNA expression for types I and III collagen transcription and growth factors TGF-β1 and TIMP1 are significantly elevated.[23]

In the sixth month, many particles become porous, due to enzymatic degradation, and surrounded by macrophages. At the end of this period, due to the remodeling process, there is a predominance of type I collagen, and α-SMA-positive fibroblasts, as well as PLLA particles, disappears.[15,23] Quantitatively, there is a statistically significant increase in type I collagen, without a significant increase in type III collagen after treatment. The inflammatory response after treatment is absent or with low intensity after three and six months and absent at 12 months.[20] The effect of neocollagenesis continues many months after the injection of the product.[18] The maturation phase begins with the collagen crosslinking, which will cause its contraction and adjustment of the network, with the return of the tensile force to the tissue.[28]

Calcium hydroxyapatite

The use of calcium hydroxyapatite (CaHA) as a biostimulator was approved by the US Food and Drug Administration (FDA) in 2006 to correct facial wrinkles and folds and to replace volume in patients with facial lipodystrophy associated with the HIV.[29] In 2009, the FDA approved a protocol that included lidocaine to the compound with CaHa for better comfort during application. Since 2016, the CaHA implant already added to lidocaine has become a formulation available for use in Europe.[30]

CaHA is a synthetic substance composed of calcium and phosphate ions, biodegradable, biocompatible, non-mutagenic, with no evidence of local and systemic toxicity. Its chemical composition is similar to that of inorganic constituents of bones and teeth. It decomposes in the same way as bone debris after fractures, which guarantees its biocompatibility and safety.[30,31]

CaHA corresponds to a group of compounds with the chemical formula Ca10(PO4)6(OH)2, which vary significantly in their three-dimensional structure and their biological behavior in tissues. Biologically active CaHA particles are generally subdivided into macroporous and microporous. The synthetic macroporous CaHA molecules have a highly organized structure with pore sizes ranging between 10 μm and 500 μm. Larger pores can be osteoconductive and allow fibrovascular growth within the particles. Microporous CaHA particles, on the other hand, have smaller pores that vary between 2 μm and 5 μm, which do not allow this fibrovascular growth.[25]

The CaHA particles with micropores, in the compound used commercially as a biostimulator, have diameters between 25 μm and 45 μm and correspond to 30% of the formulation. They are suspended in a sterile, non-pyrogenic carrier gel composed of highly purified water, glycerin, and sodium carboxymethyl cellulose, equivalent to 70% of the final volume.[26,31]

The carrier gel is cohesive and has high viscosity and elasticity, properties that allow a high integration into the tissues and guarantee easy manipulation. The final product made up of the gel and the particles of CaHA has demonstrated efficacy, safety and good tolerability.[25,26]

After implanting the product, its immediate action is to produce a filling effect for soft tissue volumizing, with a defect correction rate of 1:1, which avoids overcorrections. Over a few months after application (about two to four months), the carboxymethyl cellulose particles gradually collapse until phagocytosis promotes their complete resorption.[26,30,31] The im-

mediate volumizing effect is not necessary to induce neocollagenesis.

The newly formed collagen will gradually replace the initial volume of the gel. [31-32] The small deposited CaHA microspheres act as a foundation, which activates the fibroblasts by stretching and supporting the new tissue in with subsequent new collagen formation.[26,30,31] This process starts in up to four weeks and lasts for about 12 months. However, the clinical effects of CaHA can last from one to three years. [29,30]

The mechanism of stimulating the initial macrophage activity, associated with the sodium carboxymethyl cellulose gel, determines the formation of the fibrous capsule around the individual microspheres and appears to be of minimal intensity, with no significant inflammatory response.[34] In addition to this mechanism, others are described in response to the implantation of CaHA microspheres, such as fibroblast stretching, local tissue destruction, and increased cytokine production, such as TGF-β.[29] The microspheres would stabilize the extracellular matrix's three-dimensional structure, facilitating the adhesion of fibroblasts to dermal fibers, making it similar to that of young skin. Thus, the original collagen architecture and layout would be restored, which supports the growth of fibroblasts and the formation of new collagen without calcifications, physiologically inducing neocollagenesis by a process in which type I would gradually replace the type III collagen.[31]

Elastin deposition was also demonstrated four and nine months after implantation. There was a significant and progressive increase in Ki-67 (a marker of cell proliferation of collagen-producing cells with the consequent remodeling of the extracellular matrix).[26,28,29]

There was an increased CD34 density (a marker of angiogenesis), which suggests that increased blood flow and better delivery of nutrients to the skin accompany the formation of new tissue - which are vital for the dermis supply in repairing and remodeling without accentuating an inflammatory response.[28,30]

We gradually visualize a more uniform dermal structure, with a more dense and linear arrangement of fibers in the superficial and deep layers, which produces an improvement in the skin quality, which becomes more elastic and firm, in addition to the increase in the skin dermis thickness. As a result, we have greater effectiveness in the treatment of folds and wrinkles with more extended durability of the aesthetic clinical effects.[26,29,30]

At this stage, there is a small amount of type III collagen and a predominance of type I collagen due to tissue remodeling, which, associated with the increase in elastic fibers, results in higher tissue tensile strength and greater elasticity.[26,34]

Also, during natural skin aging, collagen fibers become irregular and disorganized. The accumulated collagen fragments combined with the lack of three-dimensional structure of these fibers interfere negatively in their adherence, affecting the function of the fibroblast.31 Clinically, this can be seen by the accentuation of facial folds and skin atrophy.[29] After the application of CaHA, the microspheres stabilize the adhesion of the fibroblast, making it similar to that of young skin. Thus, the original collagen architecture and layout is restored.

Regarding CaHA application plan, n comparative histological studies conducted on animals and analyzing intradermal and subdermal injection as to the resulting collagen production, it was found that intradermal applications produce a greater amount of collagen, it was found that intradermal applications produce a more significant amount of collagen. However, there is also a higher nodulation index than in the subdermal plane.[31] Nevertheless, there is still no evidence that this leads to better clinical efficacy.

In a study conducted to assess the quantitative production of collagen on weeks 4, 16, 32, 52, and 78 after application of CaHA, an immediate increase was observed at week four, higher than at week 16, explained by scar formation initial or tissue edema. Then there is a progressive increase until week 78.[31]

Immunohistochemical and histomorphological analyzes of skin biopsies treated with CaHA with two applications (at baseline and at four months) demonstrated a significant increase in the collagen type I expression in the analysis of four and seven months after the first application compared to the baseline. As for type III collagen, an increase was observed in four months with a subsequent decrease in its concentration at seven months, but still above the baseline.[29]

These findings were associated with improved skin elasticity and flexibility measured through cuto-

metry, a technique that uses a non-invasive suction instrument that measures the vertical deformity of the skin surface and quantifies its extensibility, delayed distention, deformity, and final retraction.[29]

Ultrasound images showed a statistically relevant increase in the dermis thickness, from 1462.3 mm at the baseline to 1642.8 mm after four months ($p<0.01$), with progressive growth after the second treatment, reaching values of 1865.9 mm at seven months.[29]

About six months after biomaterial injection, next to the deposition of the new collagen around and eventually inside the microspheres, the surface of the particles becomes slightly uneven. Over time, after the carrier gel is fully metabolized, the microspheres become particulate and distributed in the intra and extracellular space. CaHA is metabolized through a standard homeostatic mechanism that naturally occurs in the organism via macrophage phagocytosis, similar to the breakdown of small bone fragments. This results in calcium and phosphate ions, which are eliminated by regular metabolic routes, leading to the total disappearance of the particles after about 18 months.

CONCLUSION

Clinical implications of the mechanism of action of biostimulators

The mechanism of action of biostimulators has important practical implications, including the application form, the results optimization, and the adverse events minimization.[35] Its application on the skin allows the correction of sagging skin and wrinkles by the gradual increase of tissue volume.[36,37] Each treatment will lead to collagen formation, and the magnitude will depend on the concentration and volume used, which must be individualized. Subsequent injections promote continuous stimulation of tissue response, with deposition of more extracellular matrix and the resulting improvement in skin flaccidity and facial contour.

Unlike poly-L-lactic acid, CaHA, when applied, has immediate effects due to the carrier gel.[35] The glycerin present in the gel can cause a pronounced, but temporary, edema from 24 to 72 hours.[36] As the carrier gel presents high viscosity, density, and cohesiveness, it becomes an adequate product for tissue elevation and immediate improvement of the facial contour. It is also considered an ideal agent for supraperiosteal application, and can be used to restore volume in areas of bone resorption.[36,37]

As the biomaterial implantation results may not be evident for weeks, it is essential to wait for the biological response between applications to happen. The use of additional treatments should be conduct at intervals of at least four weeks so that there is no overcorrection.[35] Response time and degree of correction depend on each patient's characteristics, which vary according to age, sex, skin quality, phototype, and diet.

Regarding the application plan of both products, histological studies conducted in animals, comparing the resulting collagen production after intradermal and subdermal injections of the biostimulators, demonstrated that intradermal applications produce a more significant amount of collagen; 2 however, they also determine a higher rate of undulations and nodule formation due to product accumulation, generally palpable and not visible, which respond well to conservative treatment with digital massage or infiltration of saline or lidocaine.[37,38] When comparing the two products, PLLA must be hydrated hours in advance, while CaHA can be applied directly or with the addition of lidocaine at the time of use. CaHA has an immediate and sustained volumizing effect. However, it can present significant edema in the first 24 to 48 hours due to reaction to glycerin present in the carrier gel, while in PLLA, the effect presented immediately after application is due to the diluent volume and disappears with its absorption in 24 to 48 hours. Its effect is late and gradual, only reappearing when the dermal thickening resulting from neocollagenesis starts. Both products have good clinical results proven and maintained for long periods, with the formation of type I collagen and, in a smaller amount, type III collagen. ●

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Excisional biopsy of primary and well-defined basal cell carcinoma diagnosed by clinic and- dermoscopy: diagnostic and therapeutic accuracy

Biópsia excisional do carcinoma basocelular primário e bem delimitado diagnosticado pela clínica e dermatoscopia: acurácia diagnóstica e terapêutica

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ABSTRACT

Introduction: Basal cell carcinoma (BCC) is the most common malign neoplasm. It corresponds to 70-80% of skin tumors. The diagnosis is made based on clinical suspicion combined with dermoscopy, which also allows defining its limits.

Objective: To assess whether clinical and dermoscopic criteria are sufficient for the diagnosis and treatment of primary and well-defined BCC.

Materials and methods: Review of suspected cases of well-defined primary BCC surgically approached by excisional biopsy (3 mm margin) at the Dermatology Service of the University of Mogi das Cruzes (2017 to 2019). The Chi-square test was applied to assess the significance of the margins.

Results: 169 injuries were assessed, with a predominance of women in the 8th decade. The histopathological examination concluded on 141 BCCs. When evaluating the excision margins for BCC cases, there was 95% of free margins (p = 0.0004998).

Discussion: There are common dermoscopic elements between BCC and other neoplasms and benign lesions, which justifies other diagnoses found. The 3 mm surgical margin was accurate for well-defined primary BCCs, speeding up healing time and reduces costs.

Conclusion: For clinical-dermatoscopic suspicions of well-defined BCC, an excisional biopsy was effective in the diagnosis and clinical safety margins.

Keywords: Dermatoscopy; Diagnosis; Free margins

RESUMO

Introdução: *O carcinoma basocelular (CBC) é a neoplasia maligna mais comum. Corresponde a 70-80% dos tumores cutâneos. É diagnosticado pela suspeita clínica aliada à dermatoscopia, que permite definir os seus limites.*

Objetivo: *Avaliar se critérios clínicos e dermatoscópicos podem ser suficientes para diagnóstico e tratamento do CBC primário e bem delimitado.*

Materiais e métodos: *Revisão de suspeitas de CBCs primários, bem delimitados, operados por biópsia excisional (margem de 3mm) no serviço de Dermatologia da Universidade de Mogi das Cruzes (2017 a 2019). Aplicado o teste qui-quadrado para avaliar a significância das margens.*

Resultados: *Foram 169 lesões avaliadas. Predominaram: sexo feminino, 8a década de vida. Resultaram no exame histopatológico 141 CBCs. Avaliando-se as margens de segurança para os casos de CBC houve 95% de margens livres (p=0,0004998).*

Discussão: *Existem elementos dermatoscópicos comuns entre o CBC e outras neoplasias e lesões benignas, o que justifica outros diagnósticos encontrados. A margem cirúrgica de 3mm foi apropriada para CBCs primários bem delimitados, agilizando o processo de cura e reduzindo custos.*

Conclusão: *Para suspeitas clínico-dermatoscópicas de CBC bem delimitados, a biópsia excisional mostrou-se eficaz quanto ao diagnóstico e às margens de segurança.*

Palavras-chave: *Dermatoscopia; Diagnóstico; Margens de segurança*

INTRODUCTION

Basal cell carcinoma (BCC) is the most common malignant neoplasm in humans. It corresponds to 70-80% of cutaneous tumors. Exposure to ultraviolet radiation (UVR) is its main risk factor. Constitutional risk factors are Fitzpatrick's skin phototypes I and II, freckles in childhood, and family history (30% to 60%). It affects more men than women (probably due to factors of occupational exposure). Still, but studies reveal a recent increase in the proportion of women (odds ratio = 1.5), even under 40 years old. This can be attributed to the higher demand for dermatological care, laser treatments, photo exposure, and the use of tanning beds. BCC incidence has been increasing at a rate of 10% per year. Depletion of the ozone layer and increased longevity are other factors involved.[1]

Clinically, BCC has the following variants: nodular/ ulcerative (the most common type, located in the head and neck in general), superficial (found in trunk and shoulders), sclerodermiform (the one presenting the worst prognosis, situated in the face in general), pigmented (more frequent in melanoderms), and fibroepithelioma (located in lumbosacral, pubic, and genitocrural regions). Histologically, its variants are solid, adenoid, pigmented, micronodular, sclerodermiform, infiltrative, metatypical (basal squamous). The first three are considered of low risk, while the others present worse prognosis.[1]

The diagnosis of BCC is based on clinical suspicion. Dermoscopy increases diagnostic accuracy. Test performance studies have shown that dermoscopy, compared to the naked eye, improves sensitivity from 66.9% to 85%. Specificity, on the other hand, increases from 97.2% to 98.2%.[2]

There is a classification to define BCC as high or low risk. Low-risk tumors are primary tumors, with well-defined margins, low-risk histological subtypes, presented in immunocompetent individuals, without previous radiotherapy or perineural involvement. Any opposite parameter defines the high-risk tumor.[3]

As for topography, areas L (low risk), M (medium risk), and H (high risk) are defined. L area is composed of limbs and trunk, except for the pre-tibial area, hands, and feet. M area is composed of the forehead, cheeks, scalp, neck, and pre-tibial area. H area is composed of the central region of the face (perioral, chin, nose, periorbital), and temples and ears, hands, feet, and genitalia. Defining the area's risk and tumor's size of the tumor in each of these areas is determinant to classify it as high or low risk. The low-risk tumor is less than 20mm, if located in an L area, less than 10mm in an M area, and does not affect the H area by definition. Values higher than or equal in the respective areas mentioned or the H area's involvement define the high-risk tumor.[3]

There are incisional biopsy techniques that can be performed to confirm or exclude the diagnosis: shaving biopsy (more comprehensive, but it can generate perilesional erythema that overestimates the tumor margin *a posteriori*), and punch biopsy (although without the previous inconvenience, may not incorporate other histological patterns that would modify the lesion risk). Retrospective analyzes also show a 60.9% agreement between pre-surgical biopsies and the result after final excision.[3]

Given the dermoscopy diagnostic accuracy, which allows the identification of BCC's subclinical structures in apparently healthy skin,[4] it is possible to establish its limits, especially if the tumor is well delimited. From these limits, the desired incision margin is implemented. For small tumors (less than 2cm), 3mm to 4mm are usually sufficient to achieve a cure. Recurrence rates over five years are 0.7% to 5% for low-risk lesions.[3]

The literature is scarce when researching the excisional biopsy method of BCC, given the accuracy of dermoscopy for its diagnosis[2] and definition of margins.[4]

OBJECTIVE

To assess whether clinical and dermoscopic criteria can be sufficient for the resolution in a single surgical procedure (excisional biopsy) for the diagnosis and treatment of primary and well-defined BCC. The secondary objective is to assess the epidemiological profile of these patients.

MATERIALS AND METHODS

Review of suspected cases of primary, well-limited BCCs (clinical-dermoscopic criteria, using the "Chaos and Clues" algorithm), operated by excisional biopsy (3mm margin from the dermoscopy mark) (Figure 1) at the Dermatology Service of the University of Mogi das Cruzes in the years 2017, 2018 and 2019.

Data collection was based on the information present in the Excel table containing the numbers of patients' medical records, in addition to data such as age, gender, location of lesions, diagnoses found, BCC subtypes, wound closure method, and free margins.

This study had a quantitative nature, descriptive statistical method, anonymous character, exploratory-descriptive approach, and cross-section. We obtained the approval from the Research Ethics Committee (CEP) no: 2,991,936 and Certificate of Presentation for Ethical Appreciation (CAAE) no: 011515118.0.0000.5497.

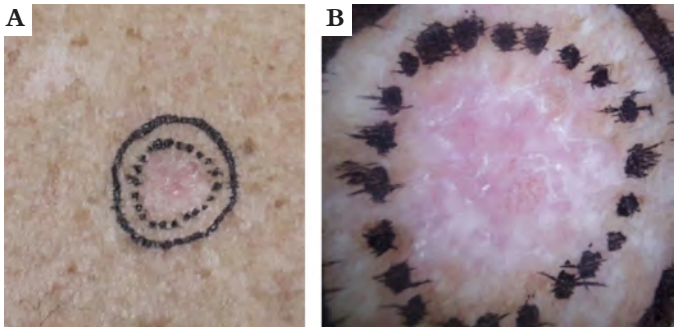

Figure 1: a) External tumor limits (internal circumference) and 3 mm surgical margin (external circumference)**; b)** Dermoscopic details: clear safety margin regarding the lesion morphology (pinkish-orange background, arboriform telangiectasias and white lines)

The dependent variables of interest were the margins of the BCC through the dermatoscope and the anatomopathological examination (AP). The independent variables were: gender, year of collection, age of the patient, location of the BCC through the AP exam, and subtype (AP). As qualitative variables, contingency tables were made, and the chi-square test (c2) was applied with a 95% significance level (20,000,000 bootstraps to estimate the p-value) to verify the relationships between them. Such analyzes were performed in the statistical software R (R Core Team, 2019) with the "gplots" (Warnes *et al.,* 2020) and "corrplot" (Wei & Simko, 2017) packages.

RESULTS

We assessed 169 injuries. Most of the patients were women (55%) (Figure 2). The predominant age group was the 8th decade (37%) (Figure 3). As for the location, 63 lesions (37%) were detected in the H area, 42 (25%) in the M area, and 64 (38%) in the L area (Figure 4). Histopathological examination detected 141 cases of BCC (Figure 5), corresponding to a positive predictive value of 83.4% with the use of dermoscopy.

The nodular histological subtype (considering the "solid" variant as a synonym) was the most common finding among BCCs, with 82 cases found (58%) (Figure 6). The following proportion is classified into high x low histological risk subtypes: 21 cases (14.1%) x 120 cases (85%), respectively. Considering the BCC cases, there is an increase to 95% of cases with free margins (134/141) (Figure 7), with statistical significance by the chi-square test (p = 0.0004998). Of the six cases with compromised margins, four were located in the nasal region, one in the chin (in which reconstruction using a skin flap was adopted), and one in the neck. Simple closures (including edge to edge and secondary intention) corresponded to 150 cases (88.7%) (Figure 8).

DISCUSSION

In this study, 83.4% of suspected cases of BCC were histologically confirmed (Figure 5). Considering other keratinocytic neoplastic lesions (squamous cell carcinoma - SCC, keratoacanthoma - KA, actinic keratosis - AK), this index reaches 95.8% (Figure 5).

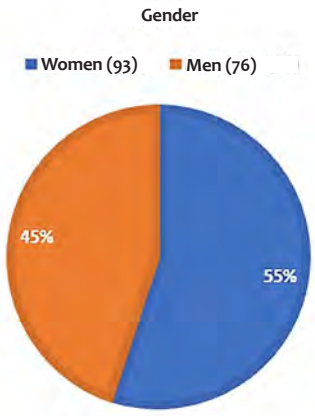

FIGURE 2: Gender distribution of the patients assessed

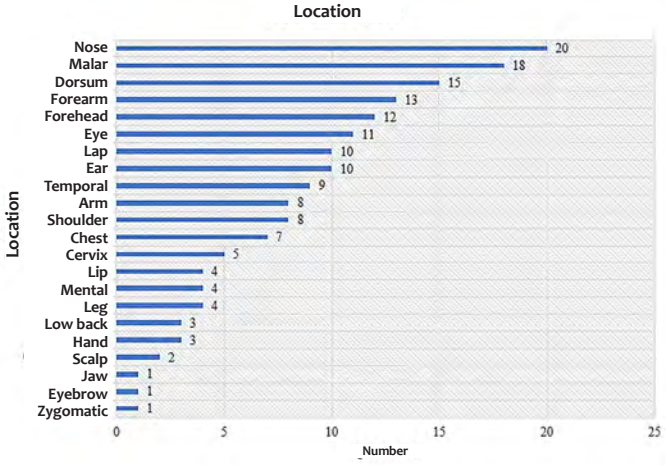

FIGURE 4: Distribution of lesion location

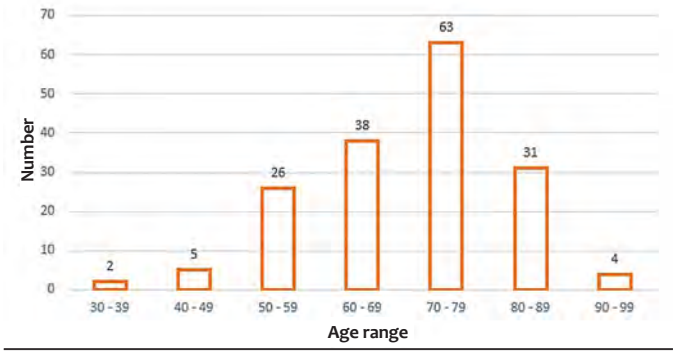

FIGURE 3: Distribution of the age range of the patients assessed

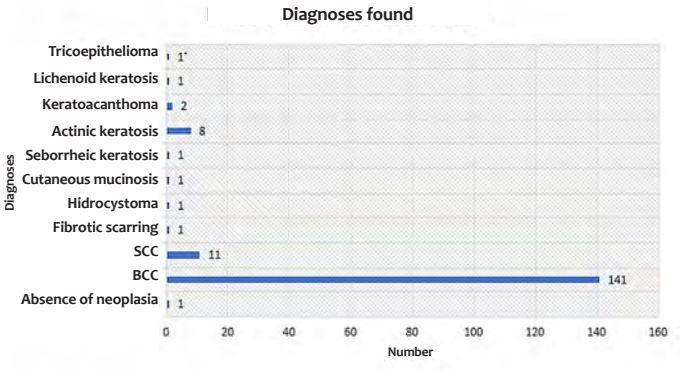

FIGURE 5: Diagnoses found by anatomopathological examination

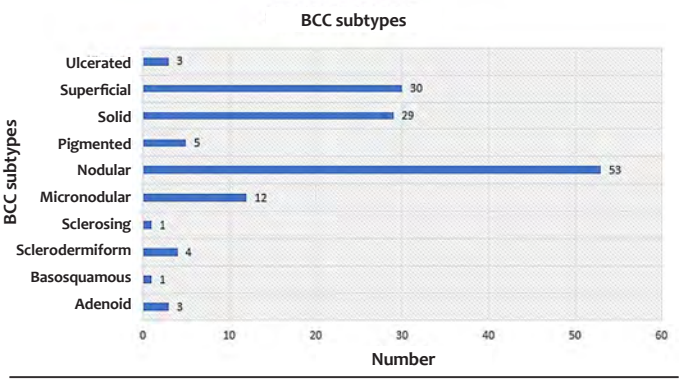

FIGURE 6: Histological subtypes of patients diagnosed with BCC

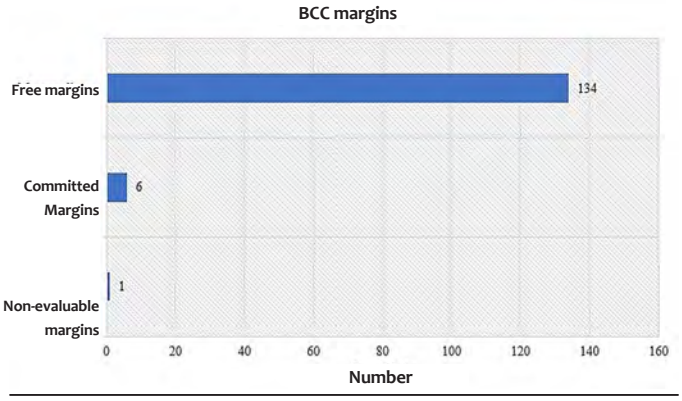

FIGURE 7: Analysis of margins of the lesions diagnosed with BCC

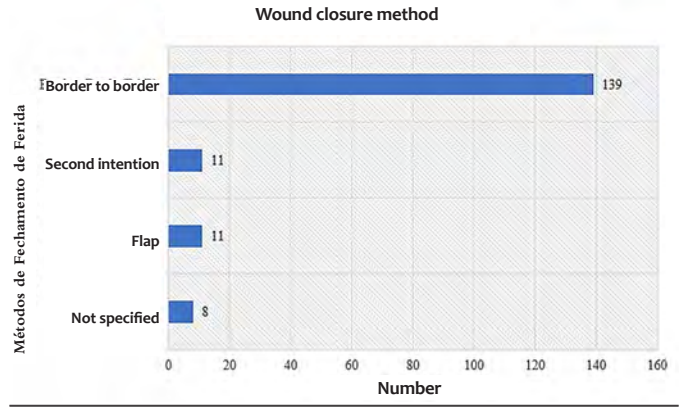

FIGURE 8: Wound closure methods used

This index is defined as a positive predictive value (true--positive/ true - positive + false-positive). Therefore, although there are classic dermoscopic criteria for BCC in some cases, in others there is an overlap of differential diagnoses.

The dermoscopic "Chaos and Clues" method recommends starting the assessment by the "chaos" of the lesion analyzed, suggesting malignancy. From then on, clues are searched for a maximum approximation of the diagnosis. However, there are common elements between BCC and other neoplasms and benign lesions:[5] ulceration (BCC x SCC), white lines (BCC x lichenoid keratosis-LK), polymorphic vessels (CBC x seborrheic keratosis-SK x LK), vessels in points/ twisted /serpentine (BCC x scarring), radial vessels (ulcerated BCC x SCC).[5] It is important to remember the possibility of lesion collisions such as BCC and SK.[6]

The 3mm surgical margins were appropriate for well--defined primary BCCs. With adequate logistical management (low-risk stratification, little personal impact of a patient's scar, simple closing technique, availability for an agile margin enlargement, if necessary), the excisional biopsy in these cases has a positive impact. It can streamline the healing process and reduce the patient's anguish[7] when waiting for a pre-result of the incisional biopsy and surgery, given the stigmatization of cancer. Also, there is a tendency of economic benefit for the assistance service (lower cost of surgical materials and optimized use of the surgical-dermatological sector).[8] Considering a small lesion, there would be an additional advantage of performing an excisional biopsy: evaluating of all histological subtypes present in the lesion.

Despite having essential characteristics for low-risk BCC, many lesions were in the H area (Figure 4). Even five of the six lesions with margin involvement were found in this region. Also, this study doesn't mention the lesions' dimension to classify them as high or low risk. Even in high-risk lesions, this excisional biopsy method is considered interesting with some caveats: small and well-defined lesions in H area, reconstruction method that does not generate significant anatomical distortion (edge-to-edge or secondary intention) and the availability for early re-approach, with the appropriate technique (example: Mohs micrographic surgery in the H area) if the margins are compromised.

The result of less aggressive histological types (85%) composing most of the results confirms the clinical-histological correlation for most well defined cases.

The preponderance in women (against the data in the literature, which, however, points to an upward incidence in women) suggests a current gender survey for low-risk tumors or general BCC epidemiology. It was observed that the face, even with well-defined lesions, is an area of significant involvement (46% of biopsied lesions), with a higher emphasis on the nasal region.

CONCLUSION

For very limited clinical-dermoscopic suspicions of BCC, excisional biopsy with a 3 mm margin proved effective in terms of diagnosis and safety margins. ●

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Efficacy of a new generation of shampoos in controlling seborrheic dermatitis of the scalp

Eficácia de uma nova geração de xampus no controle da dermatite seborreica do couro cabeludo

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ABSTRACT

Introduction: Seborrheic dermatitis is a chronic inflammatory disease in areas with a higher concentration of sebaceous glands and the participation of the fungi of the genus Malassezia sp.
Objective: To assess the effectiveness of treating moderate to severe seborrheic dermatitis using two shampoo formulations in monotherapy.
Methods: Patients with moderate to severe seborrheic dermatitis of the scalp, with or without chemically processed hair, were grouped according to the degree of affection and used one of two versions of shampoo monotherapy for four weeks. Relapse after treatment cessation was also evaluated.
Results: There was a significant reduction ($p < 0.05$) of oiliness since the first application. The other signs (erythema and peeling) showed significant improvement for both treatments. Participants also reported a considerable improvement in pruritus, erythema, and peeling. The effect on the hair strands was considered positive with both procedures. After one week of suspension, the relapse rate was considered non-significant ($p < 0.05$).
Conclusions: Both versions of shampoos were able to promote effective control of moderate to severe seborrheic dermatitis. These formulations also demonstrated not to harm the hair strands, even when chemically processed, a fundamental fact to treatment adherence.

Keywords: Dermatitis Seborrheic; Inflammation; Keratolytic Agents; Malassezia; Sebum

RESUMO

Introdução: *A dermatite seborreica é uma doença inflamatória crônica sobre áreas com maior concentração de glândulas sebáceas, com participação de fungos do gênero Malassezia sp.*
Objetivo: *Avaliar a eficácia do tratamento da dermatite seborreica moderada a intensa com o uso de duas formulações de xampu em monoterapia.*
Métodos: *Pacientes portadores de dermatite seborreica de couro cabeludo moderada à intensa, com cabelos processados quimicamente ou não, foram agrupados de acordo com o grau da afecção e usaram uma das duas versões de xampus em monoterapia, por quatro semanas. Também foi avaliada a ocorrência de recidivas após a suspensão do tratamento.*
Resultados: *Houve redução significativa ($p<0,05$) da oleosidade desde a primeira aplicação. Os demais sinais (eritema e descamação) apresentaram melhora significativa para ambos os tratamentos. Também foi relatada uma melhora significativa do prurido, eritema e descamação pelos participantes. O efeito sobre os fios foi considerado positivo com ambos os tratamentos. Após uma semana da suspensão, o índice de recidivas foi considerado não significativo ($p<0,05$).*
Conclusões: *As duas versões de xampus foram capazes de promover um controle efetivo da dermatite seborreica moderada à intensa. Essas formulações demonstraram também não agredirem os fios, mesmo quando processados, fato considerado fundamental para a adesão ao tratamento.*

Palavras-chave: *Ceratolíticos; Dermatite Seborreica; Inflamação; Malassezia; Sebo*

Original article

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INTRODUCTUON

Seborrheic dermatitis (DS) is a chronic superficial inflammatory disease of the skin characterized by erythematous--scaly, itchy areas over areas with a higher concentration of sebaceous glands, such as scalp, face, and ears.[1] Its prevalence in the general population is estimated between 3% and 10%, being more frequent in men.[2]

The scalp is the most frequently affected area, where dry pityriasis desquamation, a condition known as dandruff, is the most common manifestation. Although it is a benign condition, it is a frequent cause of embarrassment, especially when accompanied by other signs of seborrheic dermatitis, such as pruritus and erythema, as it is a visible area.[3]

Seborrheic dermatitis has an unknown etiology and pathogenesis.[1] Nevertheless, it is known as a multifactorial condition that can include environmental factors, such as humidity and solar radiation variation, and lifestyle factors, such as emotional stress and food.[2] It is also known that there is a participation of fungi of the genus Malassezia sp., especially the species Malassezia globosa and Malassezia restrita. They cause an inflammatory reaction that appears to be mediated by free fatty acids released from sebaceous triglycerides by fungal enzymes, such as lipases. The Malassezia lipid layer can also modulate the production of pro-inflammatory cytokines by keratinocytes.[2]

The treatments available for the control of seborrheic dermatitis of the scalp can have antifungal, keratolytic, or anti--inflammatory action. Most of the commercialized treatments contain some active antifungal against Malassezia. Zinc pyrithionate also acts as an antifungal and seborregulator, and salicylic acid has keratolytic action. Topical corticosteroids are also used for their anti-inflammatory action.[4]

Although seborrheic dermatitis of the scalp can vary in intensity, the first step in therapy, regardless of severity, is adopting an appropriate shampoo, capable of removing excess oil and peeling, and controlling fungal proliferation. Many actives principles have been used for this purpose, usually in association. Among the most studied, are antifungals, such as ciclopirox olamine, and zinc pyrithione,[4,5] and keratolytics, such as salicylic acid.[5,6,7]

However, the shampoo effectiveness depends on the adherence, which, in turn, can be affected if it impairs the appearance of the hair, especially in women. The occurrence of long and processed hair (dyed, straightened) is a reality in our country, and when choosing a shampoo, this question must be considered. In other words, the surfactant (cleaning) system, as well as the introduction of active principles that control inflammation and repair or protect the hair strands, greatly assist treatment adherence. Shampoos with these characteristics promote the control of SD per se and even favor the reduction of other topical drugs, such as corticosteroids.[5]

Another expected action of shampoo for seborrheic dermatitis is the control of relapses. It should not irritate or dry out the scalp too much, preventing the rebound effect when the use of the product is interrupted.

This study aimed to assess two new formulations of shampoos to control seborrheic dermatitis with differentiated vehicles, in which the anti-inflammatory and antifungal actions are associated with the innovative proposal to prevent capillary damage and recurrences while still maintaining an optimal profile of efficacy and tolerability from the first application.

METHODS

This is a prospective, randomized, blind study conducted at a Private Clinical Research Center (MEDCIN Research, MEDCIN Group - Osasco, SP). An independent ethics committee approved the study protocol (CAAE: 08031319.0.0000.5514 and 08033219.2.0000.5514), including the free and informed consent form.

We invited 133 patients of both sexes, between 18 and 60 years old, with clinical features of seborrheic dermatitis of the scalp classified as moderate to severe, without treatments for three months after inclusion. Patients using anti-inflammatories, immunosuppressants, antifungals, and antibiotics were excluded, as well as pregnant women and lactating mothers.

The determination of the degree of seborrheic dermatitis in patients was made based on a clinical evaluation by a dermatologist, using the classification Adherent Scalp Flaking Score (ASFS)8 in which: 0 = no flaking, 2 = very mild flaking, 4 = mild flaking, 6 = moderate flaking, 8 = severe flaking, and 10 = very severe flaking. Only those with grades above 6 were included. Erythema intensity (absent/ mild/moderate/intense) and symptoms of pruritus (absent/ mild/moderate/intense) were also evaluated.

From this inclusion, they were grouped, according to the peeling score, in two groups: Group 1, with score 06, to use Shampoo 1 in monotherapy (Celamina Zinco®), and Group 2, with scores 8-10, to use Shampoo 2 in monotherapy (Celamaina Ultra®).

Within both groups, patients were also included, in a balanced way, according to their type of hair:

- Hair subjected to straightening;
- Hair subjected to dye;
- Unprocessed blond hair (virgin);
- Hair not fitting fit the above criteria (other shades, including white, without processing, etc.).

This measure aimed to make each group represent more reliably the varieties of hair processing and textures that we currently find, mainly in women.

All were instructed not to wash their hair for two days and attend the Center on the third day, for the following evaluations.

Step 1: Immediate effect
Oil reduction after the first application

The patients of both groups were acclimated for the collection of sebumetric measurements, with Sebumeter® SM 815 equipment (Courage & Khazaka), which measures the sebum content on the capillary surface, in previously standardized areas: right and left frontoparietal region. Then, each half-head was washed randomly: one side with the treatment product of its respective group (Celamina Zinco® and Celamina Ultra®), and the control frontoparietal region with no application of cleaning

agents, being washed only with water.

After washing, the hair dried naturally, and subsequent measurements were taken in the treated area and in control area at 2, 3, 4, 6, and 8 hours after the single application.

Step 2: Effect on time

For assessment of Celamina Ultra® and Celamina Zinco® shampoos effect over time, participants were instructed to use the products in their homes, using them to wash their hair twice a week. The method of use was oriented as described: apply the shampoo to wet hair, massaging the scalp until obtaining an abundant foam, then wait for it to act for five minutes and rinse.

Reduction of scaling under conditions of use

For assessment of the shampoo's effect in terms of scaling reduction, on the first visit, before washing the hair at the Center, patients were referred for standardized scalp scaling collection. This collection was performed with a standardized comb, passed through the hair of the frontoparietal area 10 times in a row. This material was collected in a standardized dark plate and photographed (Canon T3i digital camera), also in a standardized way, for image analysis (Image software Pro®) of the scale area.

This procedure was repeated 24 hours after the first use of the product and two and four weeks after the start of use of shampoos.

Reduction of pruritus and erythema under conditions of use

Patients in both study groups were asked to answer a questionnaire about pruritus. They were assessed for investigation of adverse events within 24 hours, two weeks, and four weeks after the start of the study.

Cosmetic effect on the hair

Patients in both study groups were asked to answer a questionnaire about the effects of using shampoos in monotherapy, considering their cosmetic effects on the hair strands (shine, combability, and other hair qualities). This questionnaire was applied after the first washing with the products and was repeated four weeks after continuous use.

Relapse prevention

After four weeks of use and data collection, the patient received a neutral shampoo sample and was instructed not to use any other product for a week. Patients returned at the end of this period, performing a new clinical, sebumetric evaluation, and photographic record of the scaling, in the same previous models, to assess a possible relapse.

RESULTS

Of the 133 recruited patients, 96 were selected according to the inclusion and exclusion criteria, entering group 1 or group 2, according to the intensity of seborrheic dermatitis (score). Group 1 started with 48 patients and ended with 44 patients; four were discontinued for reasons unrelated to the study (violation of the protocol, failure to attend evaluations), and their data were not considered. Group 2 also started with 48 patients, ending with 47. In this group, only one patient had his data excluded due to violation of the protocol. The mean age was 42.4 years for group 1 and 48 years for group 2. Regarding gender, the study was completed with 76% of female patients and 24% of male patients in both groups.

Safety assessment

No patient, in both groups, reported worsening of the condition or other adverse events, related or not to the use of the products, throughout the study.

Effectiveness assessment

Step 1: Immediate effect

Oil reduction after the first application

Group 1: Celamina Zinco® (moderate SD)

As shown in graph 01, there was a significant reduction in sebumetry at all times of assessment, statistically significant ($p<0.001$) when compared to the control area.

Group 2: Celamina Ultra® (intense SD)

As shown in graph 02, there was also a significant reduction in sebumetry at all times of assessment, statistically significant ($p<0.001$) when compared to the control area:

Ultra (n=47) *$p<0,001$ for times 2h, 3h, 4h, and 6h;

**$p<0,003$ for time 8h.

Both treatments demonstrated effective oil control within 8 hours after the first use of the products.

Both treatments also demonstrated effective oil control at all collection times, up to 8 hours after a single application.

Step 2: Effect on time

Reduction of scaling under conditions of use

Group 1: Celamina Zinco® (moderate SD)

The quantification of scales by image analysis showed a decrease of 54.5% of scales ($p<0.001$) after two weeks of using the product in monotherapy, which progressed to 74.7% ($p<0.001$) in four weeks of use.

In the subjective evaluation, 79.5% of the patients reported significant improvement in scaling after the first application. After four weeks of use, 88.6% of patients reported a substantial improvement.

Group 2: Celamina Ultra® (intense SD)

The quantification of scales by image analysis showed a reduction of 64.7 [FA2] [FA4]% of scales ($p<0.001$) after two weeks using the product as monotherapy, which remained at 62.5% ($p <0.001$) after four weeks of use.

In the subjective evaluation, 91.5% of the patients reported significant improvement of the scaling right after the first application. After four weeks of use, 97.87% of the patients reported significant improvement.

Both treatments demonstrated control of pityriasis scaling of the scalp, in the prescribed regimen (twice/week) in mo-

notherapy.

Reduction of pruritus and erythema under conditions of use

Group 1: Celamina Zinco® (moderate SD)

The improvement in pruritus and erythema was reported by 86.36% of patients shortly after the first application. The improvement in pruritus was maintained with the use of the product in monotherapy twice a week, with this improvement reported by 95.45% of patients after four weeks of use.

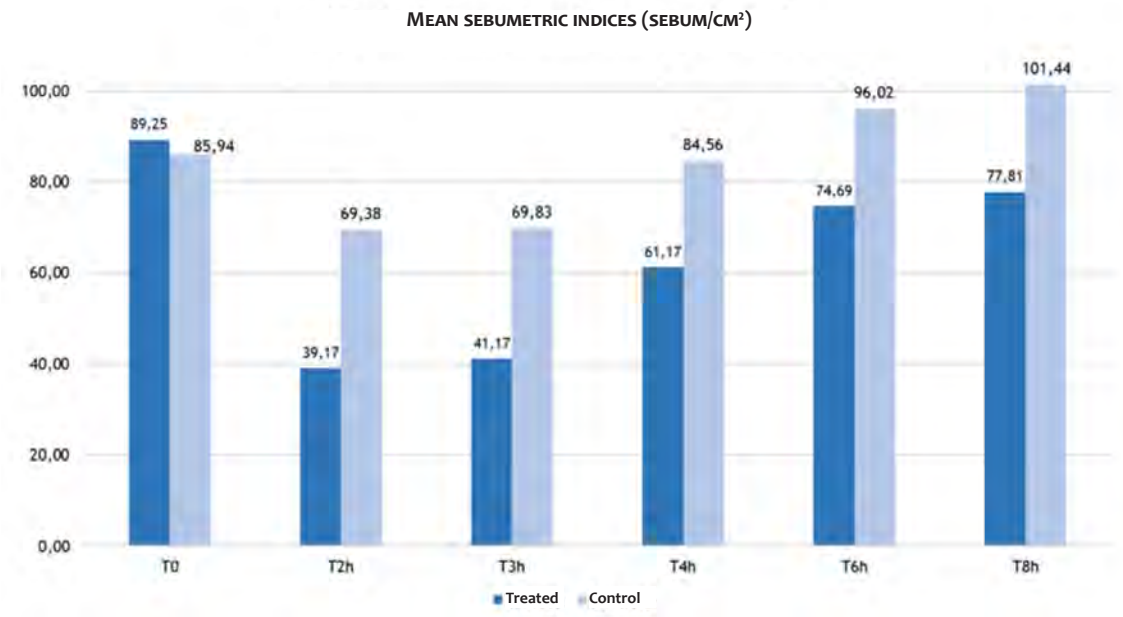
Group 2: Celamina Ultra® (intense SD)

Improvement in pruritus and erythema was reported by 97.87% of patients shortly after the first application. The improvement in pruritus was maintained with the use of the product in monotherapy twice a week, and this improvement was reported by 93.62% of patients after four weeks of use.

Cosmetic effect on the hair

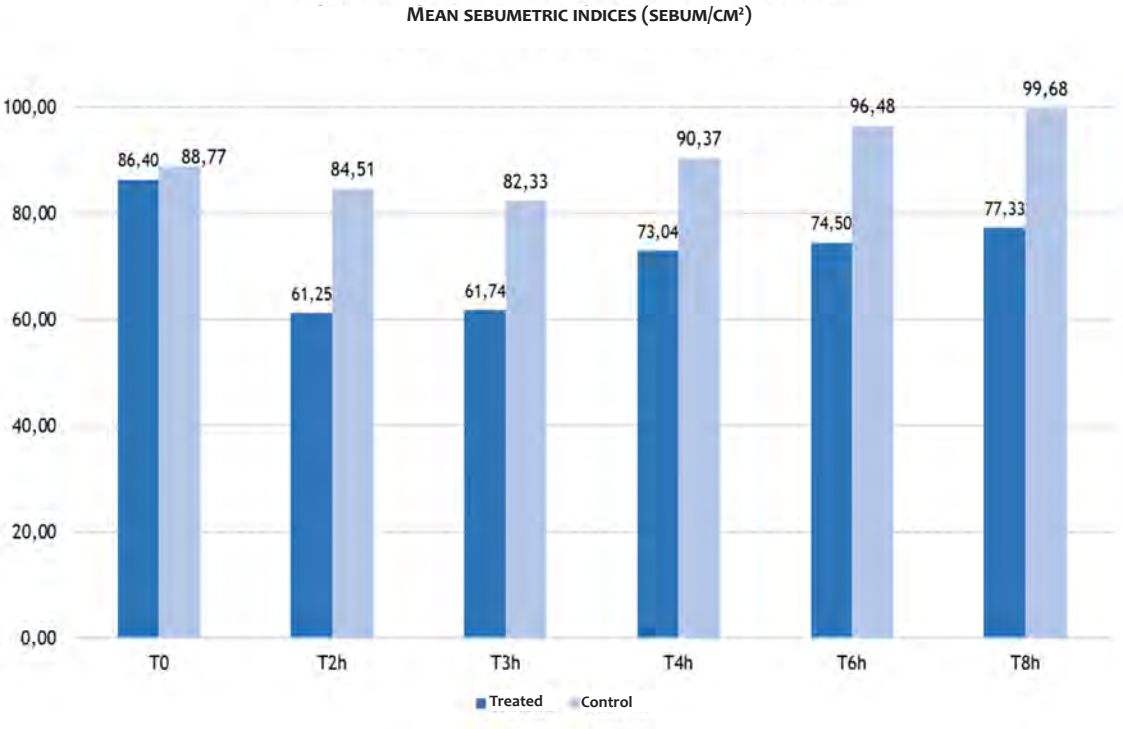
Group 1: Celamina Zinco® (moderate SD)

Box1 shows the subjective results obtained from the



GRAPH 1: Mean sebumetric indices of the treated and control temporal region before (T0) and after 2h (T2h), 3h (T3h), 4h (T4h), 6h (T6h) and 8h (T8h) hours of application of the Celamina Zinco shampoo (n = 48)

*p<0.001 for all times.



GRAPH 2: Mean sebumetric indices of the treated and control temporal region before (T0) and after 2h (T2h), 3h (T3h), 4h (T4h), 6h (T6h) and 8h (T8h) hours of application of the Celamina Ultra shampoo (n = 47)

*p <0.001 for times 2h, 3h, 4h and 6h; **p<0.003 for 8h time.

questionnaire submitted to the study participants, to assess the cosmetic effect of the products on the hair strands after the first application and prolonged use (four weeks).

Group 2: Celamina Ultra® (intense SD)

Box 2 shows the subjective results obtained from the questionnaire submitted to the study participants to assess the cosmetic effect of the products on the hair strands after the first application and prolonged use (four weeks).

Relapse prevention

This study considered relapse as any of the signs and symptoms related to seborrheic dermatitis: pruritus, scaling, and erythema.

Group 1: Celamina Zinco® (moderate SD)

After suspending the use of the products under evaluation, participants were instructed to clean the scalp with a neutral shampoo. After seven days of shampoo removal, it was observed that the percentage of relapse subjectively assessed was 13.6% in the group; regarding pruritus, 9% reported worsening when compared to the period of continuous use of the product.

Compared to the last evaluation after four weeks of use, the increase in possible relapses was not statistically significant ($p < 0.05$).

Cosmetic effect on the hair

Group 1: Celamina Zinco® (moderate SD)

Box1 shows the subjective results obtained from the questionnaire submitted to the study participants, to assess the cosmetic effect of the products on the hair strands after the first application and prolonged use (four weeks).

Group 2: Celamina Ultra® (intense SD)

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Group 1: Celamina Zinco® (moderate SD)

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Compared to the last evaluation after four weeks of use, the increase in possible relapses was not statistically significant ($p < 0.05$).

Regarding the quantitative evaluation of the scaling, it remained 17.7% lower than in the initial measurement, differing significantly from the period before treatment ($p < 0.001$) and without significant difference from the analysis obtained after four weeks of use. These data demonstrate that the product's action in moderate seborrheic dermatitis persisted statistically significant even after a week of shampoo suspension.

Box 1: Percentage of positive responses to cosmetic parameters of the shampoo used in monotherapy after the first application and after 4 weeks in patients with moderate seborrheic dermatitis (n = 48)

Parameter	% of perceived improvement after first application	% of perceived improvement after 4 weeks of use in monotherapy
Improved scalp oiliness	90,91%	79,55%
Hair has more vitality without oily appearance throughout the day	95,45%	88,64%
Better shine (cleaning) of the hair	88,64%	65,91%
Improved brush/comb slip	70,45%	52,27%
Improved hair softness	79,55%	61,36%
Improved hair silkiness	77,27%	61,36%
Improved frizz	72,73%	54,55%
Cleaner hair and scalp	93,18%	95,45%
Conditioning action	60,47%	56,82%
Refreshing action	79,55%	81,82%

Box 2: Percentage of positive responses to cosmetic parameters of the shampoo used in monotherapy after the first application and after 4 weeks in patients with moderate seborrheic dermatitis (n = 47)

Parameter	% of perceived improvement after first application	% of perceived improvement after 4 weeks of use in monotherapy
Improved scalp oiliness	93,62%	89,36%
Hair has more vitality without oily appearance throughout the day	87,23%	89,36%
Better shine (cleaning) of the hair	95,74%	82,98%
Improved brush/comb slip	87,23%	74,47%
Improved hair softness	93,62%	82,98%
Improved hair silkiness	95,74%	82,98%
Improved frizz	91,49%	72,34%
Cleaner hair and scalp	78,72%	100,00%
Conditioning action	68,09%	76,60%
Refreshing action	93,32%	76,60%

Group 2: Celamina Ultra® (intense SD)

In the assessment of seven days after suspension of the shampoo under evaluation, the percentage of relapse subjectively assessed was 14.9% in the group; regarding pruritus, 4% reported worsening when compared to the period of continuous use of the product.

Compared to the last evaluation after four weeks of use, the observed increase was not statistically significant ($p<0.05$).

Regarding the quantitative evaluation of the scaling, it remained 31.8% lower than in the initial measurement, differing significantly from the period before treatment ($p<0.001$) and with no significant difference from the analysis obtained after four weeks of use.

These data demonstrate that the product's action on intense seborrheic dermatitis persisted statistically significant even after a week of shampoo suspension.

DISCUSSION

Although it is a dermatosis with benign evolution, the patient's quality of life with seborrheic dermatitis can suffer a great negative impact due to the embarrassment caused by the itching, the visible lesions on the scalp, and the scaling itself that is also visible on the hair and clothes.[9]

Adequate hygiene products, popularly known as anti-dandruff shampoos, can provide relief from itching and scaling, being adjuvant to pharmacological treatment, regardless of the intensity of the condition.

Nowadays, formulations of anti-dandruff shampoos use combinations of anti-inflammatory, antifungal, keratolytic, and anti-seborrheic active principles, which interfere with the natural history of acne, and can have a sparing effect on drugs such as topical corticosteroids.

This review article demonstrates that ciclopirox olamine, a known antifungal agent, provides clinical and symptom improvement in rinse formulations when compared to placebo and can reduce relapses up to 12 weeks after the initial treatment phase; although zinc pyrithione has fewer studies, it also demonstrates significant effectiveness against placebo in the control of seborrheic dermatitis, due to its seborregulatory action.[2]

Its fungistatic effect for Malassezia is widely used. The combination of both active principles promotes a synergy that demonstrated superiority in the antifungal effect over topical ketoconazole.[10]

Salicylic acid, intended for more scaly conditions, promotes a keratolytic effect by improving scaling, being used in both lotions and shampoos.[11]

The combination of several classes of active principles is one of the options that produce greater effectiveness and less chance of relapses.[12]

The vehicle's impact on adherence to the use of shampoo

Although the combination of active principles is crucial for the effectiveness in reducing the signs of dermatitis and preventing relapses, care in formulating the vehicle is essential. They must be specially developed for the particularities of seborrheic dermatitis, such as:

a) an irritated scalp: the association of mild surfactants should not interfere with the skin barrier;

b) hair with chemical processing, such as hair subjected to straightening or dye, whose damaged cortex is more susceptible to the eventual dryness of surfactants to remove the oil from the strands.

The chance of adhering to treatment depends directly on the quality of the vehicle, especially in women. In these patients, the predominance of processed and long hair aggravates dryness and trichotillosis, requiring effective cleansing, but not aggressive to the strands.[13]

The main element of a shampoo is the surfactant molecule, also called detergent molecule. It is a chemical class with an apolar or hydrophobic portion, capable of binding to sebum lipids and other oily impurities, and a polar or hydrophilic part, which interacts with water, allowing the product to be removed and rinsed. Currently, a tendency to achieve a cleaning efficacy without harming the hair is the association of surfactants with silicones and lipids, minimizing the aggression to the strands.[14]

In both groups studied, the surfactant system associated with panthenol and tocopherol seems to have exerted an effective cleansing without irritating the scalp. While panthenol assumes a moisturizing role for the scalp and conditioning for the hair,[15] tocopherol is an antioxidant, protecting hair and scalp from environmental oxidative stress.[16] In the shampoo intended for group 2 (Celamina Ultra®), the presence of olive oils provides a conditioning effect with a mild effect, no leaving residues on the hair and not compromising the cleanliness,[17] while the shea butter, in addition to conditioning action, has anti-inflammatory properties.[18]

The results obtained here in both groups, using Celamina Zinco® or Celamina Ultra® shampoos in monotherapy, demonstrated effective control of moderate to severe seborrheic dermatitis in all its signs: seborrhea, desquamation, and erythema, in addition to pruritus, the most prevalent symptom. The dosage of only twice a week was sufficient to improve oiliness and flaking. The residual effect evaluated positively after a week of suspension of the product, demonstrated the action on the mechanisms of seborrheic dermatitis, reducing its recurrence, even in monotherapy.

The positive assessment on the immediate effect and over time on the hair strands showed comfort of use, improving the softness and combability, reducing oil without drying the hair, in both groups.

CONCLUSION

Both versions of shampoos studied, combining active principles with proven efficacy with vehicles that do not harm the skin barrier or the hair shaft, were able to promote effective control of the signs and symptoms of moderate to severe seborrheic dermatitis. These formulations have also demonstrated that they do not harm the hair strands, even when processed, providing comfort during use, which is considered fundamental to treatment adherence.●

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Original article

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Acral melanoma - Clinical and epidemiological study

Melanoma acral - Estudo clínico e epidemiológico

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ABSTRACT

Introduction: The characteristics of acral melanoma (MA) diagnosed in Brazil are poorly studied.

Objectives: To evaluate the MA characteristics of patients diagnosed at the Dermatology Service in a referral hospital and to verify whether the possible differences between them would be important in determining the diagnosis, treatment, and prognosis. Methods: The series was divided into localized and advanced disease. The patients were compared according to sex, color, age, thickness and level of invasion of the primary lesion, staging, and time from the tumor perception and doctor attendance.

Results: Data analysis showed an increased frequency of MA in non-white patients, with a higher age range, but without significant differences. There were also no significant differences regarding sex and staging, as well as regarding the time from the tumor perception and doctor attendance.

Conclusions: MA occurs mainly in patients who are normally not aware of skin cancer (non-whites) and belong to a higher age group. This form of cancer is unknown to the general public; and in the medical population, the acral region, especially the feet, is overlooked on physical examination.

Keywords: Melanoma; Prognosis; Survival Analysis

RESUMO

Introdução: *As características do melanoma acral (MA) diagnosticado no Brasil são pouco estudadas.*

Objetivos: *Avaliar as características do MA dos pacientes diagnosticados no Serviço de Dermatologia em um hospital de referência e verificar se as possíveis diferenças entre eles teriam importância na determinação do diagnóstico, tratamento e prognóstico.*

Métodos: *A casuística foi subdividida em doença localizada e doença avançada. Os pacientes foram comparados quanto ao sexo, cor, idade, espessura e nível de invasão da lesão primária, estadiamento, tempo decorrido entre a percepção do tumor e o atendimento pelo médico.*

Resultados: *A análise dos dados mostrou frequência aumentada do MA em pacientes não brancos, com faixa etária mais elevada, porém sem diferenças significativas. Não ocorreram diferenças significativas também quanto ao sexo e estadiamento, bem como com relação ao tempo decorrido entre perceber a neoplasia e procurar o médico.*

Conclusões: *O MA ocorre, principalmente, em pacientes que normalmente não são alertados para câncer da pele (não brancos) e pertencem a uma faixa etária mais elevada. Essa forma de câncer é desconhecida do público em geral; e na população médica a região acral, especialmente pés, é esquecida no exame físico.*

Palavras-chave: *Análise de Sobrevida; Detecção Precoce de Câncer; Melanoma*

INTRODUCTION

In the last decades, the incidence of cutaneous melanoma has increased worldwide. It is considered the fifth most common cancer in the United States. There has been a constant annual increase in melanoma, since 1950, of 6% in incidence and 2% in mortality.[1] In Brazil, according to the National Cancer Institute (INCA) statistics for the 2018-2019 biennium, approximately 2,920 new cases in men and 3,340 new cases in women are expected each year. This incidence is relatively low, but with high lethality rates.[2]

An anatomical-clinical classification subdivides cutaneous melanoma into four types: superficial spreading, nodular, lentigo maligna, and acral lentiginous.[1] Acral melanoma (AM) affects palmoplantar regions, digital extremities, mucosal and submucosal regions. It is more frequent in non-whites (35% to 60%). It has no preference for sex and, in general, occurs in the seventh decade of life. In the digital extremities, it may present as brownish subungual tumor lesion, striated melanonychia, longitudinal fragmentation of the nail plate, in addition to chronic and persistent paronychia.[5]

Current knowledge about melanoma risk factors, epidemiology, and prevention, in general, is based on studies in whites and the most common melanoma subtypes. Thus, there are not many studies explicitly aimed at the study of acral melanoma, which is more common in the black, Asian and elderly populations. Also, based on the literature's descriptions, AM is the subtype with the worst prognosis and where the affected patients present the lowest survival rates. So, there is a need for new studies that highlight the clinical and epidemiological aspects of AM.[3]

For patients with acral melanoma, the recommendation is similar to that of melanoma in other locations: to perform a biopsy, almost always excisional, followed by complete excision of the lesion with margins according to the Breslow thickness assessment. The goals of resection are to cure and prevent local recurrence. Insufficient margins are related to a higher rate of recurrence and lower survival. In this sense, acral melanoma is a major surgical challenge, since the closure of the primary wound is more difficult in this location and in extensive cases. Sometimes it needs reconstruction. Amputation should not be performed if possible. Functional surgeries are currently suggested. It is recommended to avoid the mutilations of the past.[8] Second intention healing is recommended to facilitate follow-up, aiming to early detect the recurrence. This is because hyperchromia is observed in melanodermic patients undergoing reconstruction using a flap or graft.

There are different distributions of genetic changes in the main genes among the melanoma subtypes. They are classified according to anatomical location and sun exposure. This indicates strong involvement of different molecular pathways in tumorigenesis. In particular, an increased prevalence of activation of cKIT mutations, mainly accompanied by gene overexpression and/or amplification and, to a lesser extent, BRAF and NRAS mutations, has been described in a specific subset of mucous and acral melanomas.[4]

Therefore, this study's objective is to evaluate the clinical and epidemiological characteristics of acral melanoma in patients treated at a Dermatology reference unit and compare

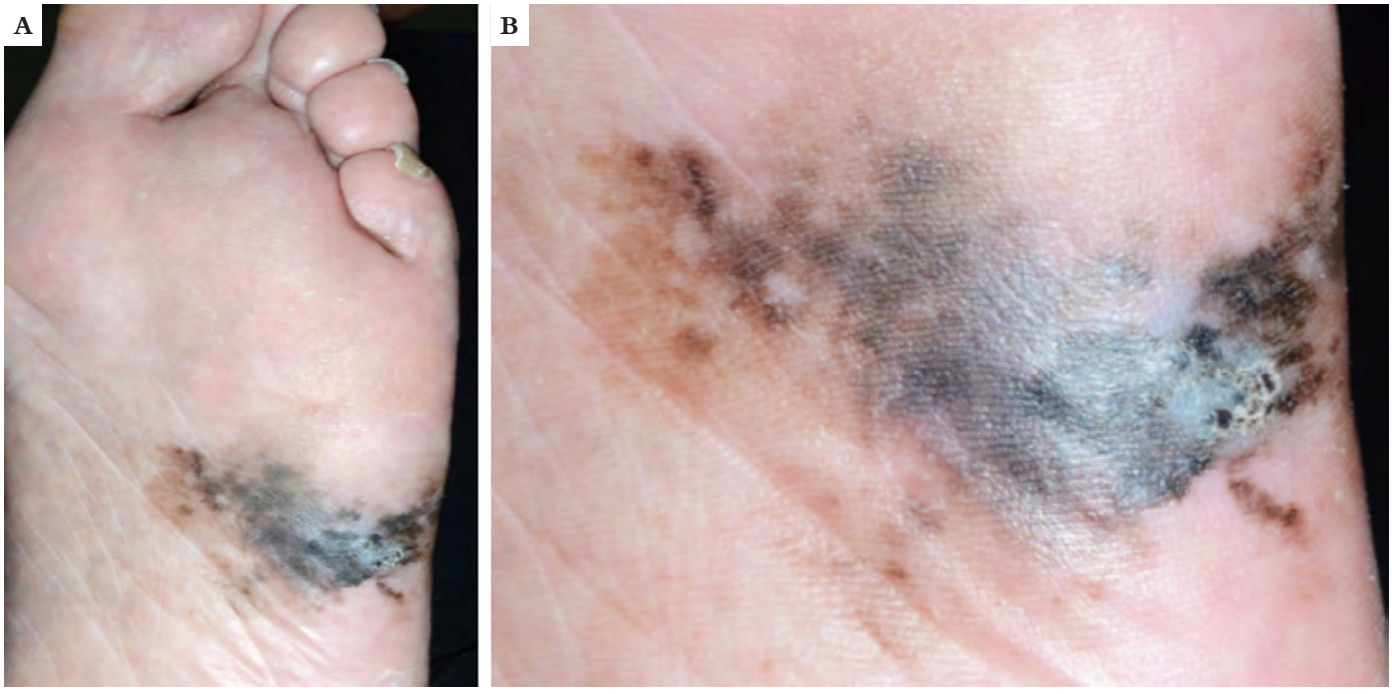

Figure 1: Acral lentiginous melanoma **A)** Blackened macula with the characteristics of: Asymmetry, Irregular margins, Varied colors, Large diameter and Progressive radial growth; **B)** Detail of the macula of imprecise limits - Illustrative iconography: from the photographic archive of the Department of Dermatology of UNESP - Botucatu

the results with those already described in the national and international literature.

METHODS

This is a retrospective, cross-sectional, and descriptive study conducted at the Reference Service in Dermatology. Ten cases of acral melanoma were recorded in this Service from January 1990 to October 2019.

The present project was sent to the Research Ethics Committee, and the data collection started after its approval. All ethical-legal precepts are following the rules of the 196/96 resolution of the National Health Council.

The study included patients previously diagnosed with melanoma in palmoplantar locations, digital extremities, mucosal and submucosal regions. They were diagnosed and followed up at the Dermatology Clinic, regardless of age, sex, Breslow index, or instituted therapy. This study excluded patients who did not agree to participate or who did not sign the Free and Informed Consent Form (ICF), or who did not present anatomopathological material available for study at the Pathological Anatomy Service.

All patients were assessed for the variables sex, color, age, tumor location, histological subtype, Clark level, Breslow thickness, growth phase, presence of perineural and perivascular invasion, metastasis, and treatment outcome. We also assessed the time elapsed between the patient noticing the lesion and attending the medical consultation.

Regarding age, the mean and median were used, in addition to separating patients by age group (<40 years and >40 years); regarding color, they were classified as white and non-white. Breslow index was divided into two groups: <1 mm and >1 mm. We then categorized the patients into two groups: localized disease and advanced disease, according to clinical and pathological staging TNM 9th edition AJCC-2019. The "localized disease" group comprised patients in stage IIC; and the "advanced disease" group included those with disease above stage III.

The statistical evaluation was performed using the chi-square test and the Mann-Whitney U test, establishing a significance level of 5% (alpha=0.05). We calculated 95% confidence intervals (95% CI) for the estimates used.

RESULTS

The distribution of cases regarding gender showed three men (30%) and seven women (70%). There was no statistical difference when comparing the two groups (p=0.500). Regarding color, the group presented four cases of white patients (40%) and six cases of non-white patients (60%).

As for age, the data showed an average of 53.2 years and a standard deviation of 14.7 years. Concerning location, 80% of the patients had lesions on their feet and 20% on their hands; no mucosal lesions were identified. As for the subtype, 40% were acral lentiginous type, 30% extensive superficial, and 30% was not described in the anatomopathological study.

The determination of the average thickness of the Breslow index of primary lesions was possible in seven cases: 30% with Breslow <1mm, 50% with Breslow higher than or equal to 1mm, and 20% were not described in the medical record. The mean thickness was 3.89mm, and the standard deviation was 5.45. In the localized disease group, the mean was 1.02mm, with a standard deviation of 0.64. In the advanced disease group, the mean Breslow index was 11.05, with a standard deviation of 5.73. There was no significant difference between the two groups (Mann-Whitney U test, p = 0.053).

Regarding the proposed staging, in case series and methods, no statistical differences were found between the groups of localized disease and advanced disease, especially the location in the feet, acral lentiginous subtype, Clark level, radial growth phase, death/loss to follow-up, and duration of evolution >5 years as markers of worse prognosis. Female gender was also not considered a risk factor, using the chi-square test.

DISCUSSION

The literature already describes a higher frequency of AM in black patients and patients aged between 60 and 70 years. There is no difference described between the sexes, in agreement with the data obtained here.

The sample of the present study was small, therefore, possibly, the difficulty in calculating statistical significance. Also, the review of medical records is not always enlightening: data such as race, education, difficulty in accessing the health system are essential in the diagnosis (late vs. early) and interfere in the prognosis of these patients, but they are not always well described. The data included a long collection period (20 years). There was a difficulty in standardizing the anatomopathological report's description because of the difference in describing the data collection at the beginning compared to the end of the period. This difference impairs the power of correlating data such as ulceration, number of mitoses, perivascular and perineural invasion with the disease outcome.

In this sense, a prospective study, with a defined and duly completed questionnaire, in addition to standardizing the description of pathological findings, could be more successful in determining risk and prognostic factors. On the other hand, medium- and long-term follow-up could verify whether there will be evolutionary differences concerning metastases and survival among patients in the advanced versus localized disease group. In case it is not possible, another work would have to be considered to differentiate the biological behavior of the various types of growth, mainly when analyzing molecular and genetic factors and mutations.

For example, from a pathogenic point of view, BRAF mutations are the most common oncogenic changes in melanoma. Mucous and acral melanomas often have a wild-type BRAF, but they may have mutations in the cKIT gene. Recent evidence suggests that mucosal melanomas with cKIT activation may respond to KIT inhibitors available for use, such as imatinib, sunitinib, dasatinib, and nilotinib.

And that possibility could change the prognosis and survival in patients with advanced disease. The role of these changes in the genesis of melanoma still needs to be better defined.[4]

Regarding the age and location of the lesions, older patients could have greater difficulty in self-examination. For this reason, they could be diagnosed later and contribute to a possible worse outcome.

Campaigns for skin cancer prevention emphasize low phototype as a risk factor and recommend photoprotection as the main measure. The AM affects, as demonstrated in the literature, preferably non-white patients, with primary lesions located mainly in the plantar region, areas without any influence of solar radiation. Also, risk factors for MA are currently unknown.

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CONCLUSIONS

This study allows us to extract the following observations regarding acral melanoma (AM) patients diagnosed at the Dermatology Service:

- There are no statistically significant differences between genders; there is a predominance of elderly patients (>40 years old), non-whites, and plantar location; a higher Breslow index is generally related to late diagnosis and worse outcome;
- Public campaigns for the prevention and diagnosis of skin cancer should emphasize the possibility that this form of cancer is not linked to sun exposure, skin color, and preferential age;
- For the AM, there is no form of prevention. Its risk factors are still unknown; therefore, we must prioritize early diagnosis;
- Immunogenic studies could help correlate tumor behavior, aggressiveness, recurrence possibility, and response to treatment to increase disease-free survival in these patients. ●

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Experience with the lip filling technique: lip tenting

Experiência com a técnica de preenchimento labial: lip tenting

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ABSTRACT

Introduction: The lips have a huge importance in facial aesthetics, and the use of fillers to improve the region is growing with a variety of different techniques described.
Objective: To report the experience with the "lip tenting" lip filling technique.
Methods: 20 female patients between 18 and 60 years of age obtained lip filling through vertically serial punctures from the lip vermilion border, depositing a small amount of product by retroinjection, in the superficial muscular plane.
Results: All treated patients reported a high degree of aesthetic satisfaction with the result of the procedure, with edema and local ecchymosis transiently present in most patients.
Conclusions: This is an easy execution technique compared to other filling techniques, presenting very satisfactory aesthetic results.

Keywords: Anatomy; Lip; Rejuvenation

RESUMO

Introdução: *Os lábios possuem grande importância na estética facial, sendo crescente o uso de preenchedores para melhorias da região, com uma variedade de diferentes técnicas descritas.*
Objetivo*: Relatar a experiência com a técnica de preenchimento labial Lip Tenting.*
Métodos*: 20 pacientes do sexo feminino entre 18 e 60 anos obtiveram preenchimento labial por meio de puncturas seriadas verticalmente a partir da borda do vermelhão do lábio, depositando pequena quantidade de produto por retroinjeção no plano muscular superficial.*
Resultados*: Todas as pacientes tratadas relataram alto grau de satisfação estética com o resultado do procedimento, sendo edema e equimose local presentes de forma transitória na maioria das pacientes.*
Conclusões*: Técnica de fácil execução e menor risco comparada a outras técnicas de preenchimento, apresentando resultados estéticos muito satisfatórios.*

Palavras-chave: *Ácido Hialurônico; Anatomia; Estética; Lábio*

Original article

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INTRODUCTION

The lips play an essential role in the aesthetic perception of the face. Historically, bulky lips are associated with youth and beauty, especially in women. Aesthetic patterns vary between cultures and over time. Currently, there is a preference for thick, natural-looking lips, proportional to other facial features, with a well-defined red border and balance between the dimensions of the upper and lower lips.[1,2,3] Filling materials are used to increase soft tissues, improve unsightly characteristics, and replace lost volume in the aging process.[4] There is a growing demand for lip filling procedures, using different techniques and substances.

In the international literature, Eijik *et al.* described a lip filling technique called Lip Tenting, which consists of injecting the filler almost vertically into the lips from the outline (the white line that borders the top of the upper). This technique allows increasing the volume, elevation, and projection of lips contour, simultaneously, with each "stroke" of the injection.5 We report the experience with this technique.

METHODS

This is a prospective, interventional study, in a series of cases, developed with selected participants at the Dermatology Clinic of the Hospital Padre Bento of Guarulhos. It was conducted respecting the ethical principles established by Resolution 466/12 of the National Health Council, including analysis by the Research Ethics Committee - CEP/ Hospital Padre Bento de Guarulhos (CHPBG) through the Brazil Platform, approved under number 3.039.220 on 09/18/2014. We requested authorization to patients through the free and informed consent term and authorization term for the use of images.

This was a self-financed research. The researchers funded all products used.

The inclusion criteria were: women; age between 18 and 60 years; with the desire to increase lip volume or correct unsightly asymmetries and disproportions. The exclusion criteria were: prior lip filling; participants with unrealistic expectations of treatment; psychiatric disorders; pregnant women; decompensated autoimmune or metabolic diseases; immunosuppression; and anticoagulants use.

EVALUATION OF PATIENTS

Initially, an evaluation of each patient's individual characteristics was conducted to establish a treatment plan, aiming to improve the contour, volume, and asymmetries of each case. The patients were evaluated in an orthostatic position, with demarcation of the lips parallel to the line drawn between the pupils. As for the spatial location, the upper lip must be 18-20mm from the nose and the lower lip 36-40mm from the chin. The desired relationship in the lip-chin complex is the upper lip projecting approximately 2mm more than the lower lip in relation to the vertical facial plane. In women, the chin's most protruding point should be in a position slightly posterior to the lower lip. In men, on the contrary, in a slightly anterior projection. The lips need to maintain a natural profile. The nasolabial angle should be approximately 95° to 100° in women and 90° to 95° in men.6

Photographs were taken before, immediately after, and 30 days after the application of lip filling. Also, patients were interviewed before and 30 days after treatment, to establish the degree of satisfaction. The data were analyzed comparing the volumization improvement and the lips contour definition subjectively by the patient, based on the interviews, and by the injectors, through the photos taken throughout the study.

FILLING TECHNIQUE

The procedure initiated by local asepsis with 2% aqueous chlorhexidine, followed by anesthetic nerve block with 2% lidocaine without vasoconstrictor, from the branches of the infraorbital nerve, right and left, and the branches of the right and left mental nerves. The hyaluronic acid filler without lidocai-

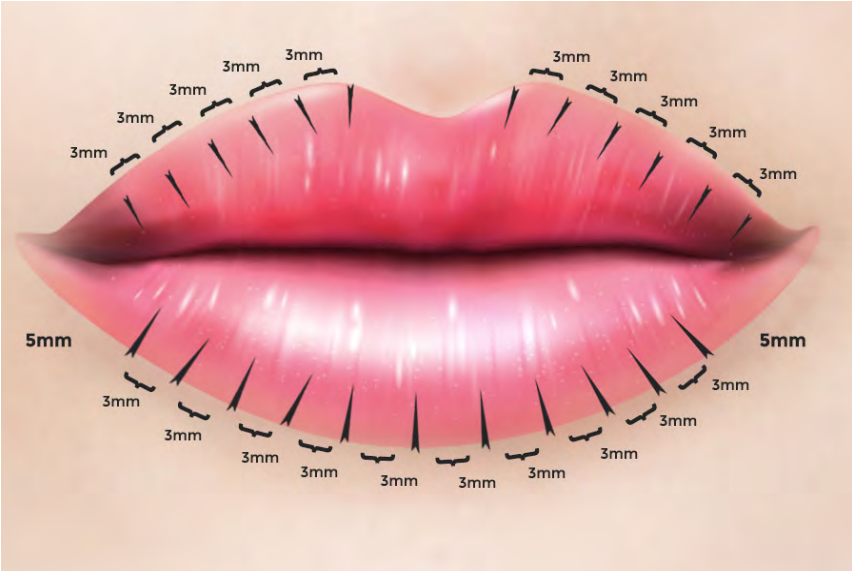

FIGURE 1: Injections along the upper and lower lip, every 2-3 mm, from the oral commissure in the medial direction

ne (Restylane® | Galderma) was injected using a 29G needle (0.33x12 mm). The puncture started at the contour (the structure that insinuates between the labial vermilion and the skin junction), inserting the needle vertically towards the transition between dry and wet mucosa. The product was retro-injected, depositing 0.01 ml to 0.02 ml of volume per stroke, in the superficial muscular plane. The injections were repeated along the upper and lower lips, every 2-3 mm, from the oral commissure in the medial direction, except for the lip filter. (Figure 1). A total of 1 ml of hyaluronic acid was injected into each patient.

After the end of the procedure, local cleaning was performed with 0.9% saline. Participants were instructed not to manipulate the site, perform ice packs for five minutes, five times a day, for five days, and not to practice physical activity, as well as immersion bath, pool, or sea in the first 48 hours. Patients were photographed before the procedure and immediately after.

RESULTS

Twenty female patients, aged between 18 and 58 years, were treated. Of the sample, 60% reported mild discomfort/pain at the time of the maxillary nerve block, with comfort after the anesthetic effect started; 40% reported comfort to perform the entire procedure. Some degree of edema, erythema, and pain were observed in 100% of patients on the first and second days after the procedure, although tolerable. They all returned to their routine activities promptly.

Eighty percent of patients presented ecchymosis in some puncture site, with complete resolution within seven days. There was no case of vascular occlusion or other adverse events. At the end of the study, 100% of the sample reported a high degree of satisfaction and stated that they would repeat the procedure when necessary. One hundred percent reported that they would indicate lip filling for a friend or relative (Images 1, 2, 3, 4: before and after [immediately after] of the procedures in four selected patients).

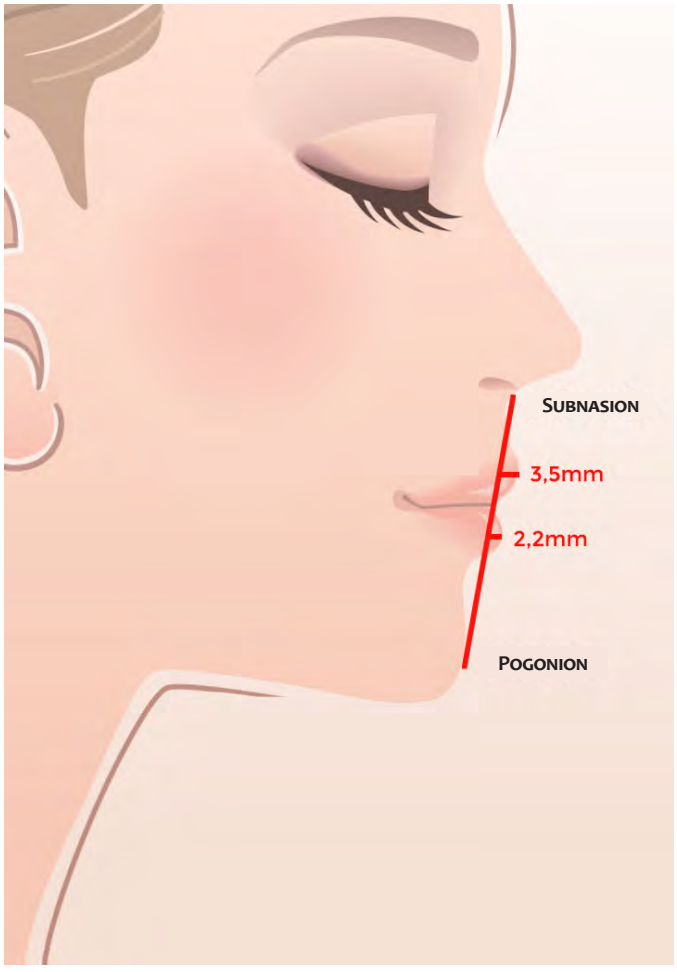

FIGURE 2: Ideal lip proportion for the profile. If a straight line is drawn from the subnasion to the pogonion, the upper lip must protrude 3.5 mm anterior to the line, and the lower lip must protrude 2.2 mm; the upper lip should protrude approximately 1.3 mm more than the lower lip.

DISCUSSION

Lip filling is a procedure with increasing demand, aiming to improve unsightly characteristics and/or replace lost volume in the aging process. The reasons for dissatisfaction with each individual's labial aspects vary from intrinsic causes, such as lips considered small, thin, asymmetrical, disproportionate, changes resulting from aging, even external influences, such as the aesthetic pattern of fashion, media, or celebrities. However, the result is often not satisfactory, leading to the discouragement of both professionals and patients to perform such a procedure. Thus, there are challenges for professionals to develop appropriate and safe techniques that adjust to the specific concerns, desires, and anatomy of each patient.

Hyaluronic acid is the substance of choice when used by qualified and adequately trained injectors. It stands out for being moldable, safe, producing immediate and lasting results, but not permanent, and being reversible with the use of hyaluronidase. The duration of the result depends on the product used, with several presentations available with different degrees of cohesiveness and viscosity. This guarantees great versatility in the application. It is biologically pure, with low protein loads, biocompatible, and biodegradable. The absence of animal proteins eliminates the need for skin tests.[6,7] To obtain an aesthetically pleasing result in lip filling, it is essential to understand the proper architecture of the face in relation to the lips. Although there is no ideal technique for obtaining a "perfect" lip or a "standard" approach to lip augmentation, there are some basic concepts that lead to natural and aesthetically pleasing results.

From hundreds of years ago, basic artistic principles still apply today, and are based on the structure of Phi - the Divine Proportion - 1:1.618, which reveals the ideal balance and symmetry relationship.

Leonardo DaVinci in his anatomical studies used corpses to measure the proportions of the human body and found that nothing else obeys the divine proportion as much as the human body. According to DaVinci, in the perfect man, dimensions follow the golden ratio.[8]

Therefore, when studying and performing measures for ideal aesthetic procedures, these proportions are used.

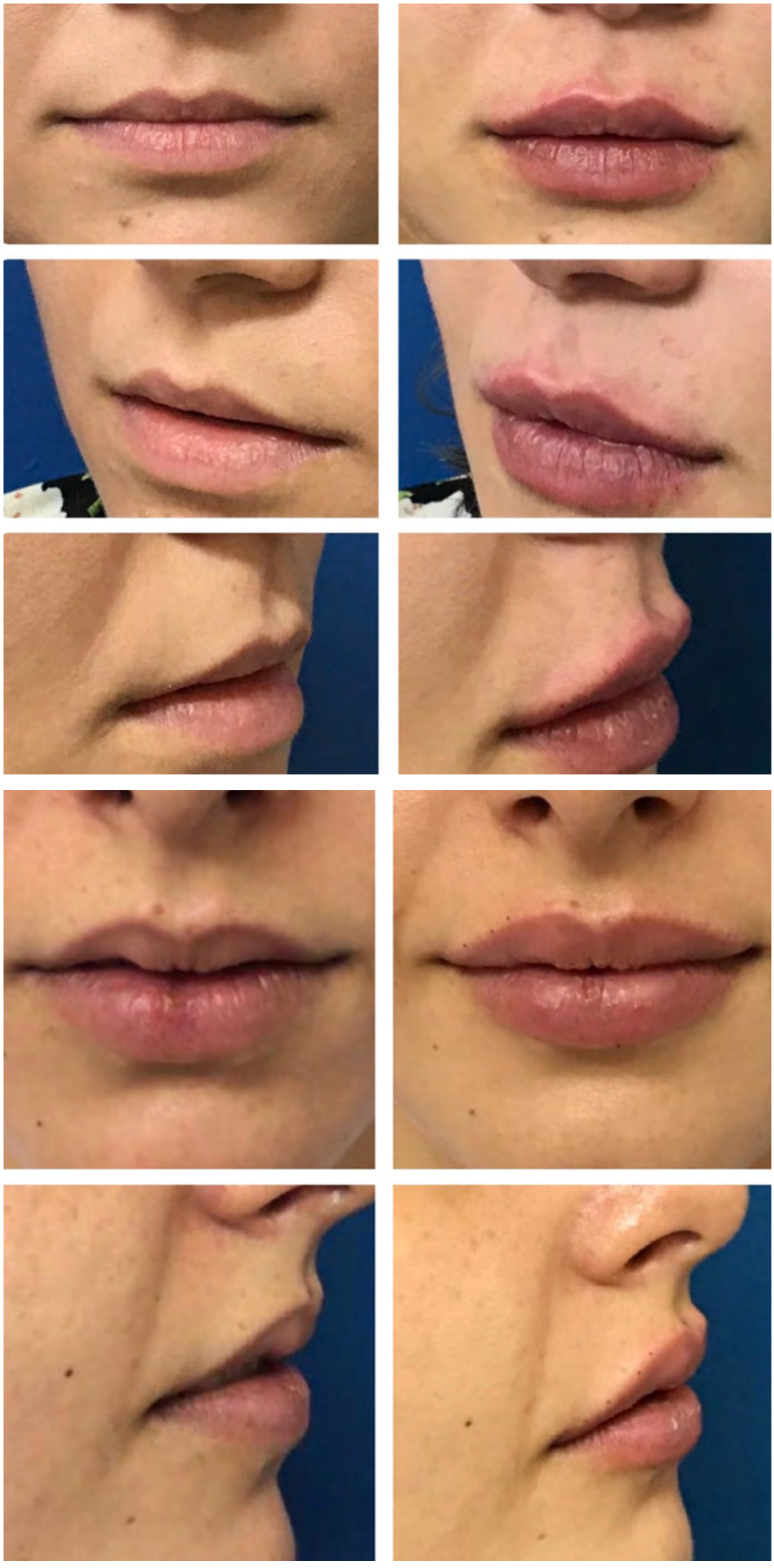

Image 1: Photos of before and immediately after lip filling with 1ml of hyaluronic acid. Front and side view

Image 2: Photos of before and immediately after lip filling with 1 ml of hyaluronic acid. Front and side view

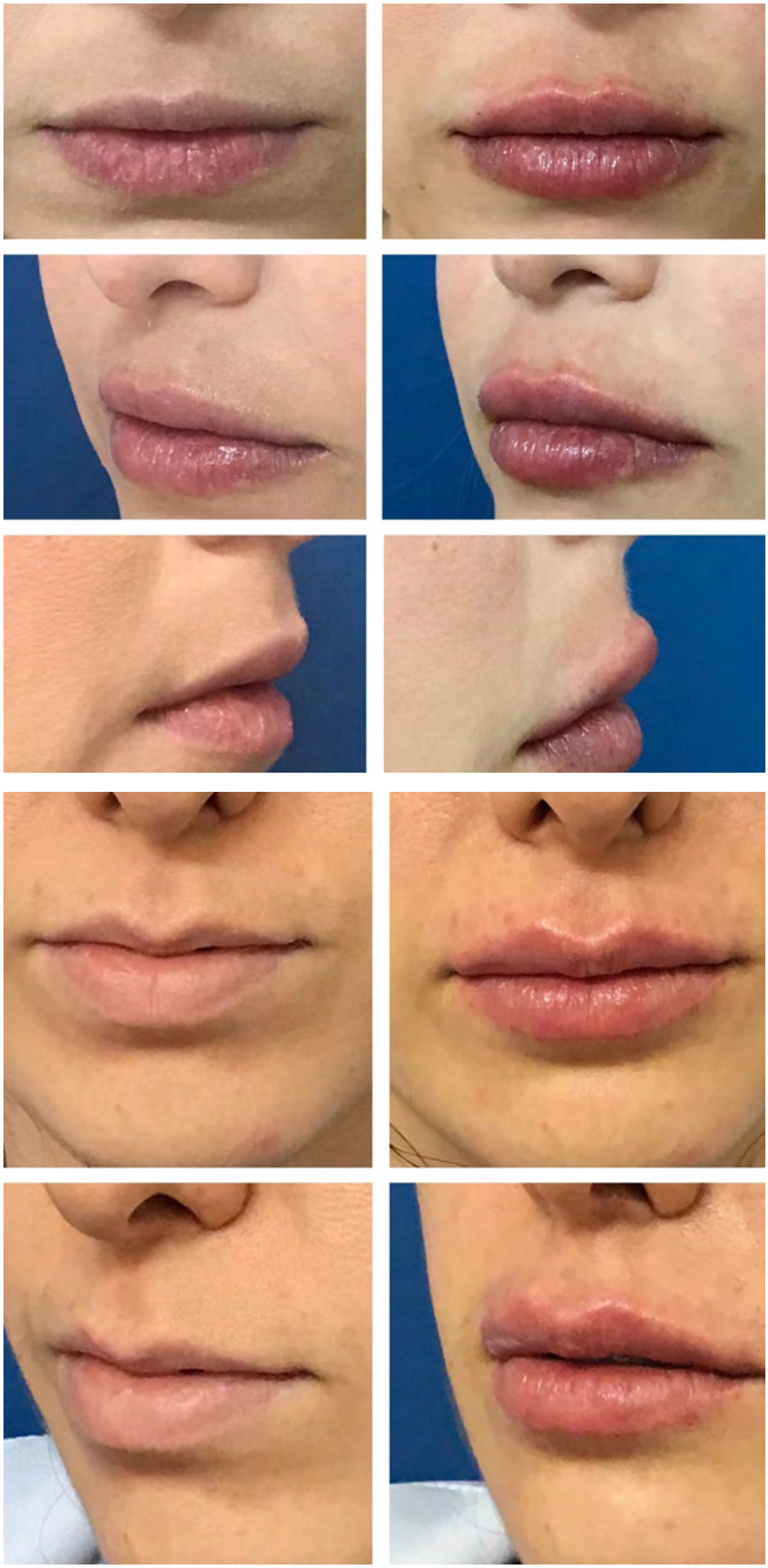

Image 3: Photos of before and immediately after lip filling with 1 ml of hyaluronic acid. Front and side view

Image 4: Photos of before and immediately after lip filling with 1ml of hyaluronic acid. Front and side view

The face is divided horizontally into thirds: upper third, middle third, and lower third, all equal in vertical height. The lower third of the face is also horizontally divided into thirds: upper third corresponding to the upper lip and the lower two-thirds corresponding to the lower lip and chin. The ideal lip ratio in Caucasians in the frontal view is 1:1.6, which translates to about 40% of the volume in the upper lip and 60% of the lower lip volume. Also, the width of the mouth horizontally must be equal to one and a half times the nose's width.[9] In the lateral view, if a straight line is drawn from the subnasion to the pogonion (the most anterior point of the chin), the upper lip should protrude 3.5mm anterior to the line, and the lower lip should protrude 2.2mm; the upper lip should protrude approximately 1.3mm more than the lower lip[10] (Figure 2). An exaggeration of these proportions or the wrong proportion can lead to a "duck mouth" or "sausage lips" appearance. Arterial vascularization of the lips, originating in the external carotid system, is supplied by the upper and lower labial arteries that emerge from the facial artery, laterally to the commissure. The labial artery presents significant variations regarding the pattern of the dominant side, trajectory, and tortuosity, remaining, in most cases, in a posterior plane to the orbicularis oris muscle[11] (Figure 3).

A large multicenter anatomical study was conducted to identify the position of the labial arteries in relation to the orbicularis oris muscle. Three distinct artery positions were identified: submucosa (between the oral mucosa and the orbicularis oris muscle in 78.1% of cases), intramuscular (between the superficial and deep layers of the orbicularis oris muscle in 17.5%), and subcutaneous (between the skin and the orbicularis oris muscle in 2.1%). The plane variability where the artery is located along the labial course was 29% for the upper lip and 32% for the lower lip. The midline was identified on the upper and lower lips as the most variable (Figure 4).[12]

Based on the results of this investigation, a safer location for the application of the volumizing material is the subcutaneous plane in the paramedian location. The artery can be identified more frequently in superficial positions on the midline, especially on the upper lip.[11] Injection into the lips at a depth of less than 3mm at the cutaneous edge of the vermilion can be considered safe for the lips' projection.[13]

The lips are abundantly provided with sensitive nerve endings. The infraorbital nerve, a branch of the maxillary division of the trigeminal nerve, innervates the upper lip, and the mental nerve, a branch of the mandibular nerve, innervates the lower lip.[14] The most commonly described technique for lip augmentation involves inserting a needle or cannula parallel to the horizontal axis of the lips. The instrument is inserted into the lateral mucosa of the lip and directed medially. This provides volume to the lip on the horizontal axis, using either an anterograde, bolus or retrograde injection. It is not uncommon to obtain unsightly results due to the deposit of a considerable amount of material horizontally across the upper and lower lip.[5]

The Lip Tenting technique reproduced in the reported patients allows good control over the filling's shape and volume. It is possible to increase the volume, elevate, and edge eversion of the upper and lower lips, resulting in a more natural appearance than often obtained with other methods. Its main indications are patients who want to have increased lip volume, defined contour, correction of asymmetrical lips or anterior suboptimal filling.[5]

If any asymmetry is detected, you can reinsert the needle vertically at the point of asymmetry and inject a small amount of material to correct it. For example, if the patient wants a more prominent cupid's bow, simply perform a retroinjection vertically on the upper lip's vermilion at the top of the cupid's bow towards the transition between the dry and wet border of the lip.[5]

The authors observed as a significant differential that the volumization of the lips does not occur horizontally only, but the "strokes" performed form structures similar to pillars that promote an increase in volume vertically together with the projection of the vermilion border, defining the contour and eversing the edges of the lips, which gives the lip an attractive shape, hence the name of the technique, "Lip tenting". Another important aspect is that the lips, thus filled, show a significant improvement in the "gingival smile", also justified by the increase in vertical volume.[5]

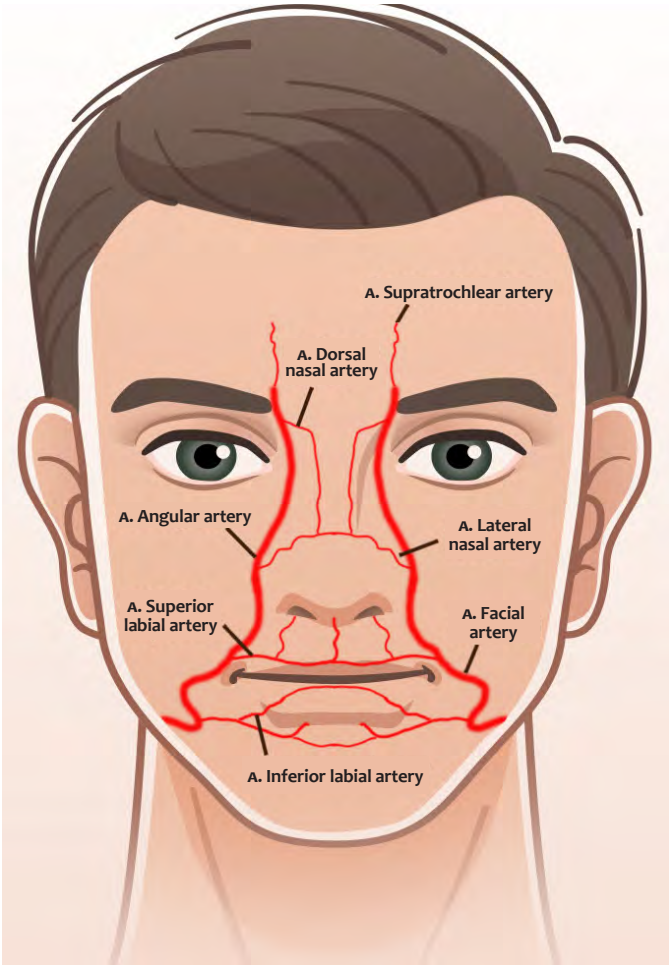

Figure 3: Upper and lower labial arteries emerge from each facial artery laterally to the commissure

A great benefit was observed in restoring the lower third of the face's proportionality, as it is possible to restore the nasolabial angle and distance. When promoting the eversion and projection of the upper lip, there is a decrease in the distance between the nose's base and the cutaneous-labial mucosa transition line and a reduction in the nasolabial angle. The increase in volume only inside the vermilion prevents the filling above or below the lips, under the perioral skin, promoting a more natural aspect. The result is a nasolabial facelift, non-surgical, with redness enhancement.

We highlight the importance of performing punctures starting at the vermilion border of the lip vertically, always towards the junction of the mucous/submucous, remaining on the superficial muscular plane. As the technique is based on multiple injections, the risks of large localized filler volumes, which give rise to palpable or even visible nodules, are minimal, as well as the risk of vascular occlusion. Thus, it is possible to reduce the risk of both visible artifacts (small nodules) and vascular involvement, whose anatomical topography is posterior to the injected plane (Figure 4). As a disadvantage, we agree with the authors of the technique that it is necessary to perform maxillary nerve block, as patients cannot tolerate multiple punctures with only topical anesthesia. We emphasize that if there are doubts since with the punctures, edema starts during the procedure, it is more appropriate to leave corrections of small asymmetries for the reevaluation after seven to 14 days.

CONCLUSION

As previously described by Eijik *et al.*, Lip Tenting is a relatively easy technique to be taught and performed, especially for novice injectors who quickly gain the ability to provide the patient with symmetrical lip and with more satisfactory results when compared to other techniques. We agree with this statement; however, we emphasize that more than the manual skill, which is acquired with the learning curve, professionals need a critical aesthetic notion applied to each patient's demands, not only before but also during and after the execution of the procedure.

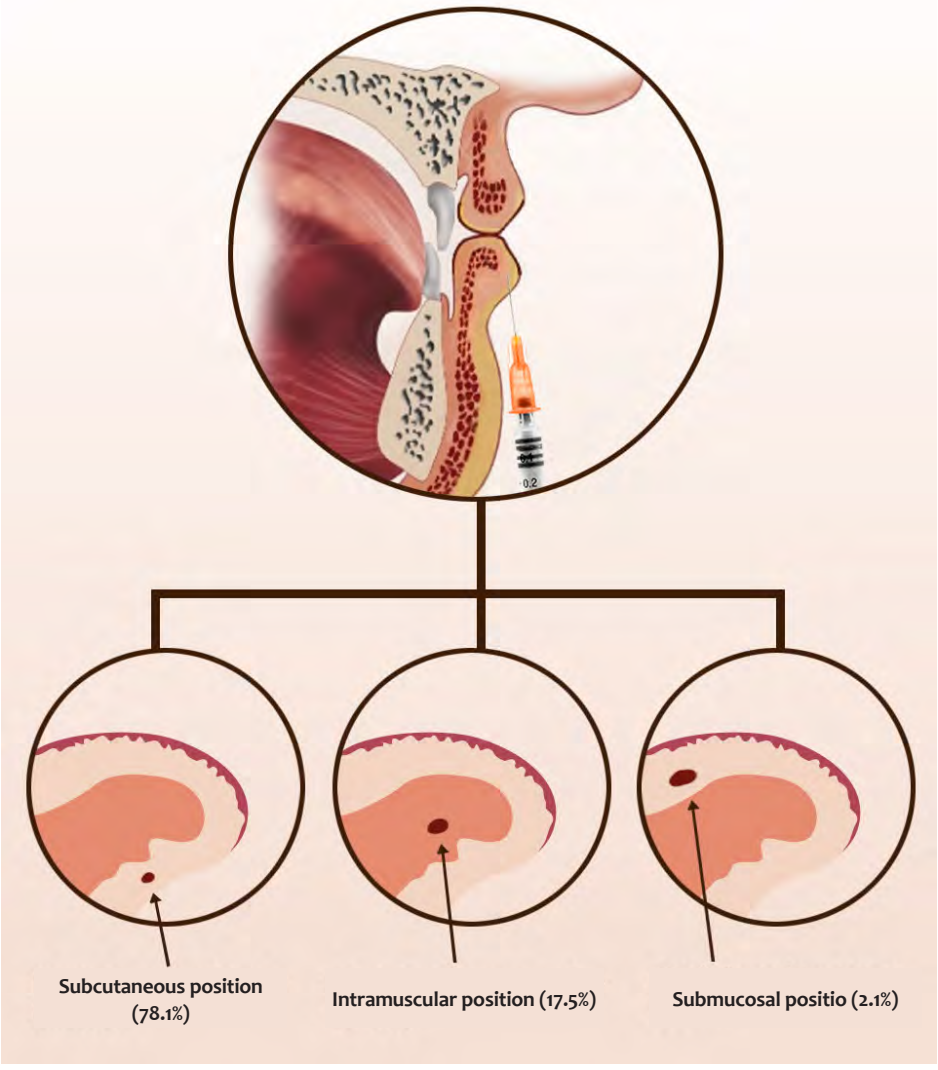

Figure 4: Position of the labial arteries in relation to the orbicularis oris muscle, respectively: subcutaneous (78.1%), intramuscular (17.5%), submucosa (2.1%)

We emphasize that the technique covered in this publication is a good option for lip filling, but due to the great diversity of techniques, there is no consensus on which is the best of them. When choosing the filler's application method, one must consider the skill of the physician combined with each patient's needs, always aiming at good aesthetic results and greater safety. Medical knowledge and technical training are essential for the management of possible complications. Further studies should be conducted to corroborate these findings.●

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CO_2 laser enhanced with modified CROLL technique optimizing results in the perioral region rejuvenation

Laser de CO_2 potencializado com técnica de CROLL modificada otimizando resultados no rejuvenescimento da região perioral

DOI: http://www.dx.doi.org/10.5935/scd1984-8773.20201222562

ABSTRACT

Introduction: The rejuvenation of the perioral region is considered a significant challenge. Numerous therapeutic modalities are used; however, there is no specific single gold standard, and the literature agrees that the best option is to associate techniques. Fractional lasers provide excellent results, and the CO_2 laser is described as quite effective.

Objective: To increase the efficiency of fractional CO_2 laser for the perioral region rejuvenation, using the modified CROLL technique.

Methods: We selected 12 female patients, between 50 and 68 years, who underwent application of the CO_2 laser in two moments. Initially, the modified CROLL technique was applied to the perioral rhytids, and later the laser was used, with less power, on the entire face, including the perioral area. Three sessions were conducted with an interval of 45-60 days.

Results: There was an improvement in tissue elasticity and rhytids superficialization, and the degree of satisfaction of all patients was in line with the clinical evaluation and photographic records.

Conclusions: The CO_2 laser offers excellent results for the perioral region rejuvenation, especially when enhanced with the modified Croll technique.

Keywords: Laser Therapy; Lip; Rejuvenation; Research and New Techniques

RESUMO

Introdução: *O rejuvenescimento da região perioral é considerado um grande desafio. Inúmeras modalidades terapêuticas são utilizadas, porém não há um procedimento específico ideal, sendo consenso da literatura a associação de técnicas, considerada a melhor opção. Os lasers fracionados proporcionam excelentes resultados sendo o de CO2 descrito como bastante eficaz.*

Objetivo: *Aumentar a eficácia do laser fracionado de CO2 para o tratamento de rejuvenescimento da região perioral, utilizando a técnica de CROLL modificada.*

Métodos: *Selecionaram-se 12 pacientes do sexo feminino, com idades entre 50 e 68 anos, com aplicação do laser de CO2 em dois momentos. Inicialmente, foi aplicada a técnica de CROLL modificada sobre as rítides periorais e, posteriormente, o laser foi aplicado, com menor potência, em toda a face, incluindo a área perioral. Foram realizadas três sessões com intervalo de 45-60 dias.*

Resultados: *Houve melhora na elasticidade tecidual e superficialização das rítides, e o grau de satisfação de todas as pacientes esteve em consonância com a avaliação clínica e os registros fotográficos.*

Conclusões: *O laser de CO2 oferece excelentes resultados para o tratamento do rejuvenescimento da região perioral, sobretudo quando potencializado com a técnica de CROLL modificada.*

Palavras-chave: *Lábio; Pesquisa e Novas Técnicas; Rejuvenescimento; Terapia a Laser*

Original article

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INTRODUCTION

The aging process reduces collagen and elastin, resulting in significant changes in the face. In the perioral region, smoking can aggravate this condition. In this location, the changes seen in senescence are increased distance between the base of the nose and the lip, shortening of the visible mucosa surface with flattening of the lip and vertical wrinkles that originates from the vermilion, known as "barcode" lips. It is also worth mentioning the decrease in lip prominence due mainly to the resorption of the jaw bone and, sometimes, changes in the dentition.[1,2]

In general, with senility, the perioral region changes from a young three-dimensional protuberance to a flat, elongated, and two-dimensional structure.[1,2]

Countless factors contribute to the changes observed in this region aging, thus no therapeutic modality in isolation is described as a "gold standard", capable of reversing the process, with a global improvement of the perioral region. The best treatment is the sum of several procedures that work synergistically, such as surgical techniques, fillers, botulinum toxin, dermabrasion, chemical peels, microneedling, and different types of lasers, which present quite satisfactory results.[3]

Fractional lasers are described as extremely effective in the treatment of this region, and, among them, those with the most significant scientific evidence are the ones using CO2 or Erbium YAG. Despite having different wavelengths, they present a similar chromophore and the same target of action, promoting a significant collagen remodeling. In the literature, comparing the effectiveness between them is a real duel. Some authors advocate the idea of the superiority of the CO2 laser, which is capable of causing more profound damage and better results despite the higher downtime. Others, however, believe in the greater effectiveness of the Erbium YAG laser, with the advantage of a shorter healing time.[4,5]

More recently, a new variety of ErbiumYag laser has been used. Although fractionated, they are non-ablative and performed with intraoral application. In this modality, the handle is inserted into the patient's oral cavity. The laser emanates its energy on the surface of the oral mucosa without damaging the skin surface, and is considered a safe, painless, and effective technique.[6]

For a better result of the perioral region rejuvenation, we propose to optimize the use of the ablative fractional CO2 laser enhanced with the application of the modified CROLL technique (surgical reconstruction with localized laser), located in the perioral rhytids. The CROLL technique was described in 2010 and is used to treat acne scars. It consists of reducing the equipment's spot, bringing the distance between the points closer and increasing the depth of the shots, optimizing the results and minimizing complications.[7]

METHODS

Twelve female patients, with ages varying between 50 and 68 years, with Fitzpatrick skin phototypes II to IV, from Belém (PA), were selected to receive the procedure. Besides presenting facial aging process, they haven't undergone previous rejuvenation treatments, and they had no comorbidities that compromised the procedure.

One month before the procedure, the patients started using sunscreen SPF 50 with color, associated with the manipulated formulation of tretinoin 0.03%, tranexamic acid 3%, hydroquinone 4%, and green tea 3%. On the day of the procedure, patients signed the free and informed consent form (ICF). Photographic documentation was performed, as well as asepsis with alcohol 70%. An hour before the procedure, they took a sublingual tablet of trometamol (Toragesic®, EMS, Brazil). Topical anesthesia was applied with the combination of tetracaine and lidocaine (Pliaglis®, Galderma, Brazil) occluded with gauze.

Anesthesia was then removed, and the procedure was conducted with the ablative fractional CO2 laser (SmartXide, DEKA, Calenzano, Italy) associated with the chiller (Freddo, Fabbinject) in two stages. Initially, the laser was applied with the modified CROLL technique, located only on the perioral rhytids, that is, the equipment spot was directed linearly on the rhytids, with a distance between the points of 200μm and depth of 2000μs and 30w of power (Figure 1). Subsequently, the laser was applied to the entire face, including the area previously treated with the modified CROLL technique, but with lower parameters. We used a distance of 650μm between the points, with a depth of 1300 μs, energy of 15w and stack 2.

For ten days after the procedure, patients were instructed to use Cicaplast baume B5® (La Roche Posay), thermal water and to maintain color SPF 50 with color. After 10 days, the manipulated formulation was reintroduced until the day of the next procedure.

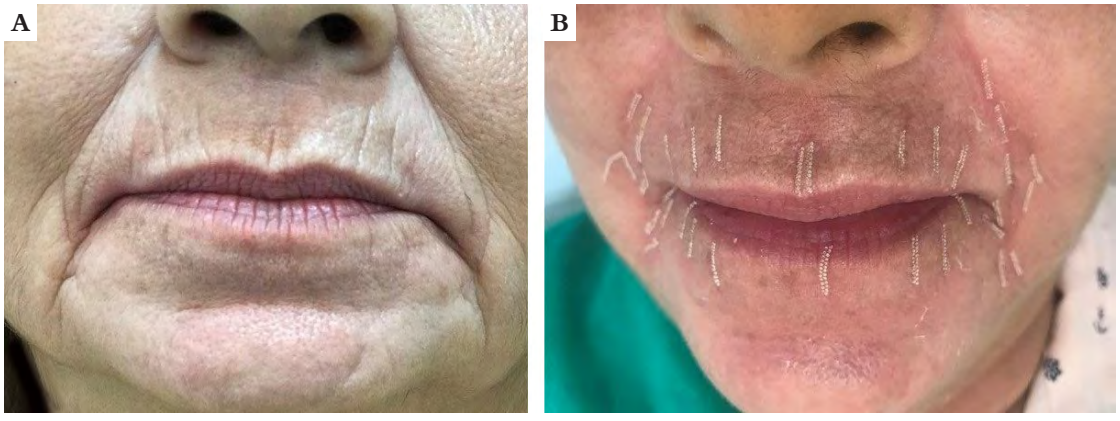

FIGURE 1: Patient 1.
a) Pre-procedure;
b) Immediate post-application of the modified CROLL technique in the perioral rhytids

The protocol was performed in three sessions, with an interval of 45 to 60 days. The analysis of the final result, with photographic documentation, was conducted 45 days after the last procedure.

The work was guided according to the rules issued by the Declaration of Helsinki.

RESULTS

Patients treated with the proposed method obtained satisfactory results as early as the 10th day after the first CO2 laser session. However, the best results were obtained 45 days after the third laser application (Figures 2, 3, and 4). On the day after the application, the patients presented linear crusts located on the rhytids, where the modified CROLL technique was applied, associated with edema and global erythema of the face, which faded until the 4th day after the procedure (Figure 5), which is why the patients were removed from their usual activities during this period. We observed no hypo or hyperchromias after the procedures.

In the global analysis of the perioral region, we found that the rhytids were superficialized, and the elasticity was improved. The degree of patient satisfaction coincided with our clinical assessment and photographic records.

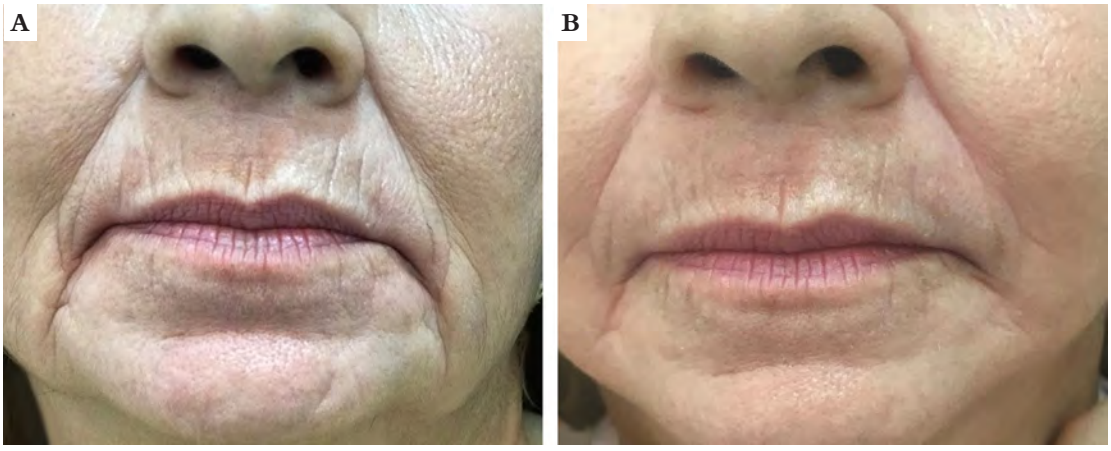

Figure 2: Patient 1, woman, 64 years.
a) Before applying the procedure;
b) 45 days after the application of the 3rd session of the CO2 laser enhanced with the modified CROLL technique

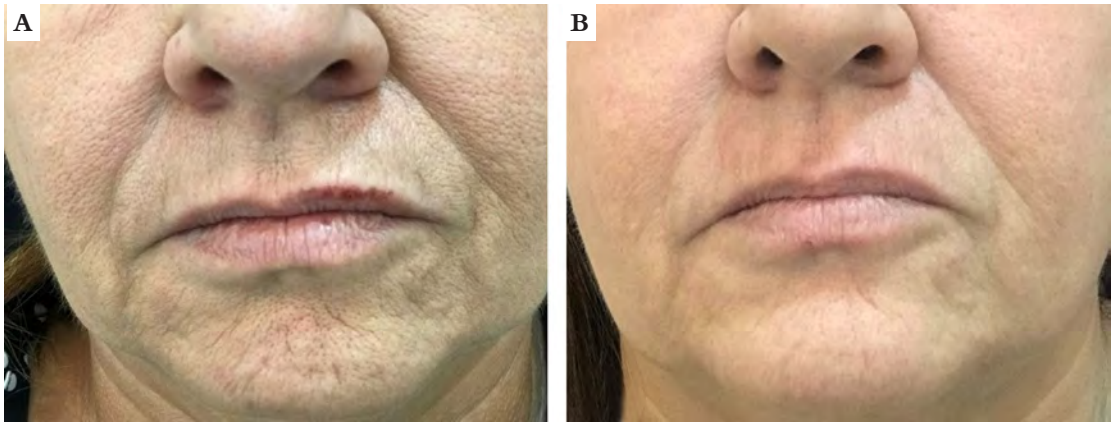

Figure 3: Patient 2, woman, 59 years.
a) Before applying the procedure;
b) 45 days after the application of the 3rd session of the CO2 laser enhanced with the modified CROLL technique

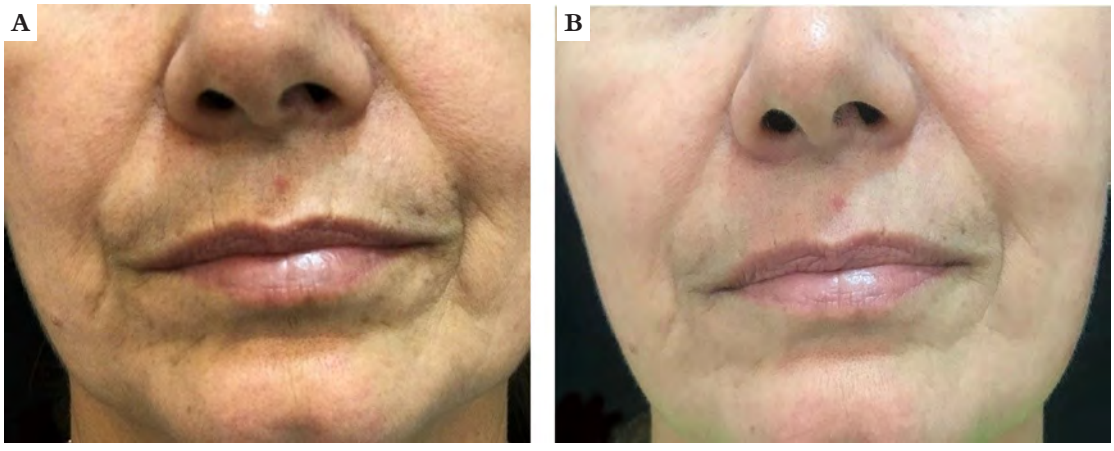

Figure 4: Patient 3, woman, 54 years.
a) Before applying the procedure;
b) 45 days after the application of the 3rd session of the CO2 laser enhanced with the modified CROLL technique

DISCUSSION

The perioral region's aging process is the result of numerous intrinsic and extrinsic factors, such as photodamage, loss of volume and elasticity of soft tissues, retraction of the redness of the lips, dental alteration, bone resorption, and smoking, among others.[8,9,10]

The changes observed in this area resulting from senescence are represented by fine perioral lines, flattening of the cupid's bow, and decreased lip prominence. The filter is poorly defined and longer, and the upper lip gets thinner.[8]

The perioral region treatment is a challenge with a lot of complexity, as it also depends on the individual and cultural concept of beauty.[11]

The literature mentions numerous techniques capable of minimizing the damage caused by aging in the perioral region. Surgical approaches, which can provide impressive results, are not the most chosen by professionals and patients because preference is for less invasive procedures, without a higher risk of scarring.[6,12,13]

Among the non-invasive procedures, many options can be used: chemical peels, dermabrasion, microneedling, fillers, botulinum toxin, biostimulators, lasers, etc., which favor improvement, but act in different ways. Because the causal factors of aging in the perioral region are multiple, the ideal therapeutic method is to associate various techniques with cohesive actions.[8,10,14,15]

Treatments with ablative lasers provide an important increase in collagen I and III, improving the appearance of the perioral complex. In clinical trials, the best results in this area are the Erbium YAG and CO_2 lasers. The comparative effectiveness between both varies between authors.

Some references describe that the ErbiumYAG laser is superior, with the advantage of shorter recovery time. On the other hand, many authors report that the CO_2 laser is a powerful ablative weapon, capable of leading to more dramatic results for the perioral rhytids than those seen with the Erbium YAG laser.[1,5,16]

For more than two decades, the CO_2 laser has been used to treat facial rejuvenation, rhytids, acne scars, blepharoplasty, surgical removal of lesions, etc. Initially, in the form of ablative resurfacing, it led to many complications such as hypertrophic scars, persistent dyschromias, risk of infection, prolonged recovery time, and reasons for which it fell into disuse the 1990s. The emergence of fractionated CO_2 lasers, which lead to a faster recovery with fewer complications, provided the resumption of this technology in the medical therapeutic arsenal.[7,17]

The fractional CO_2 laser emanates its energy in thermal columns, which are called thermal microzones. This thermal injury leads to localized dermal necrosis with collagen denaturation. It is an area of healthy, unaffected skin around, stimulating the production of new collagen, with faster healing and better tolerated postoperative than traditional ablative resurfacing, providing significant tissue remodeling. Regarding the mechanism of action, thermal damage occurs by vaporization. In the first 48/72 hours, there is edema, release of chemical mediators, and shortening of collagen fibers, so it requires downtime in this period. The best results are observed 30 days after the procedure with the recruitment of fibroblasts, new dermal matrix, resolution of the inflammatory process, among others.[17,18]

The risk of hyperchromias is higher during the recovery period and may be a limiting factor described by some authors.[17,18] The CROLL technique aims to optimize results and minimize adverse events, using the fractional CO_2 laser in a localized way, only on acne scars, with intense parameters, providing expressive results, less discomfort and greater adherence to treatment.[7]

In this approach, to enhance the CO_2 laser's effectiveness, we used the modified CROLL technique. Instead of using it on acne scars, it was applied to the perioral rhytids, reducing the equipment spot, bringing the points closer, and increasing the shots' depth.

Further studies are necessary to consolidate the results. Still, the association of the modified CROLL technique located in the perioral rhytids and subsequent application of fractional

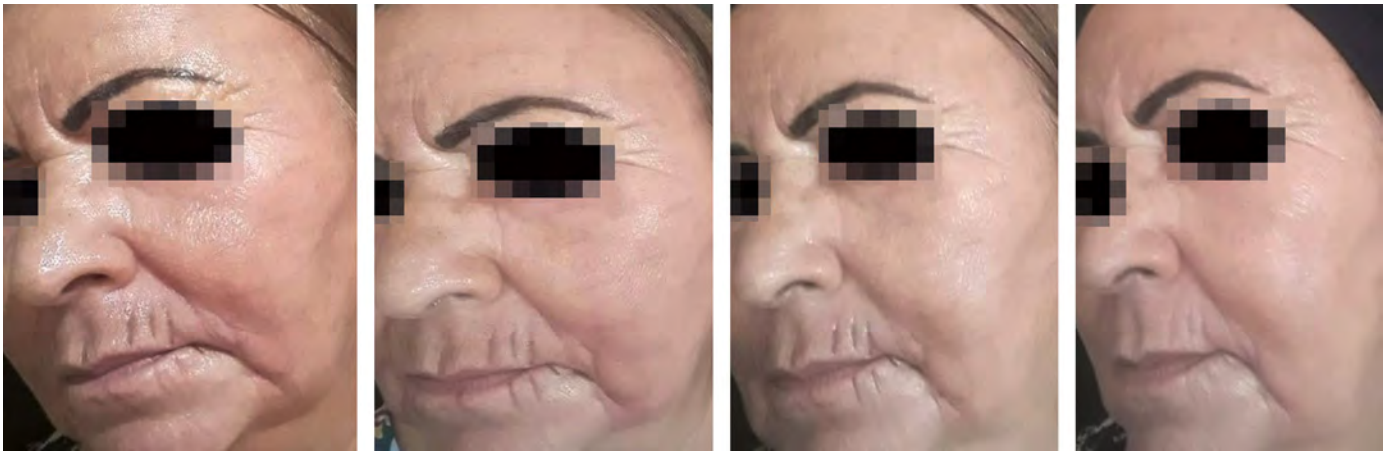

Figure 5: Patient 1 in the immediate post-procedure showing the linear crusts located in the perioral rhytids, where the modified CROLL technique was applied, associated with edema and global erythema of the face, aspects that faded until the 4th day after the procedure, which is why the patients were removed from their usual activities during this period

CO_2 laser across the face, including the area previously treated in a localized way, in this study, optimized the effectiveness of this therapeutic modality and provided entirely satisfactory results.

CONCLUSION

Although the rejuvenating treatment of the perioral region has a better result with the association of techniques with a different mechanism of action, fractional lasers have excellent efficiency in this area and the CO_2 laser, even in isolation, has shown satisfactory results, especially when enhanced with the modified CROLL method. ●

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Statistical analysis; approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Original Article

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Use of topical tyndallized probiotic bacteria in the treatment of acne vulgaris

Uso de bactéria probiótica tindalizada tópica no tratamento da acne vulgar

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ABSTRACT

Introduction: Acne vulgaris, considered a chronic inflammatory and multifactorial disease, presents several therapeutic options. The use of probiotics is a good adjunctive treatment option due to its anti-inflammatory effect.
Objective: Based on the promising character of these studies, which derive mostly from oral probiotic therapy, we decided to investigate what results could come from the topical use of a probiotic bacterium that has undergone the tyndallization process.
Methods: In this study, we demonstrated the topical use of Lactobacillus plantarum GMNL06, alone, for three months.
Results: We obtained a therapeutic response considered good or very good in 90% of mild or moderate acne cases.
Conclusions: Vulgar acne, considered a chronic inflammatory and multifactorial disease, presents several therapeutic options. The use of probiotics has become an adjunct treatment due to its anti-inflammatory effect. In this study, we demonstrated that the use of topical probiotics, in monotherapy, for three months obtained therapeutic response considered good or very good in 90% of mild or moderate acne cases.
Keywords: Probiotics; Bacteria; Acne; Treatment

RESUMO

Introdução: *A acne vulgar, considerada doença crônica inflamatória e multifatorial, apresenta diversas opções terapêuticas. O uso de probióticos tem se apresentado como uma boa opção de tratamento coadjuvante devido a seu efeito anti-inflamatório.*
Objetivo*: Com base no caráter promissor destes estudos, que são em sua grande maioria oriundos da probioticoterapia de uso oral, decidiu-se investigar quais resultados poderiam advir de seu uso tópico, utilizando-se uma bactéria probiótica que passou pelo processo de tindalização.*
Métodos*: Neste trabalho, demonstramos o uso tópico do Lactobacillus plantarum GMNL06, em monoterapia, por três meses.*
Resultados*: Obtivemos resposta terapêutica considerada boa ou muito boa em 90% dos casos de acne grau leve ou moderado.*
Conclusões*: O uso tópico de bactéria probiótica demonstrou ser eficaz no tratamento da acne, mesmo em monoterapia.*
Palavras-chave: *Probiótico; Bactéria; Acne; Tratamento*

INTRODUCTION

Acne is an inflammatory dermatosis of the pilosebaceous follicle. It has the following fundamental characteristics: the hyperproduction of glandular sebum, quantitative and qualitative changes in sebum, *Cutibacterium acnes* increased colonization, follicular hyperkeratinization, and release of inflammation mediators in the follicle and dermis adjacent. It is a frequent disease that has a chronic course, affecting adolescents and adults, mostly men, but it usually persists in adulthood in about 50% of individuals.[1,2]

The psychological and social impact of acne can lead to depression and anxiety, and its treatment is critical.[2,3]

Different etiopathogenic factors are involved, such as follicular hyperkeratinization, sebaceous hypersecretion, skin microbiome changes, immunological factors, inflammatory process, in addition to other conditions that can influence the skin condition, such as diet and changes in the intestinal microbiome.[4]

Currently, it is considered that the inflammatory process is present in all phases of the pathophysiology of acne, since before the comedone formation.[1]

Cutibacterium acnes

Cutibacterium acnes is a Gram-positive, anaerobic bacterium of the genus *Corynebacterium* and is part of the skin's healthy resident microbiota. The proliferation of this bacterium occurs when the gland overproduces sebum, favoring the appearance of acne. In acne patients, *C. acnes* can reach 120.00 specimens/cm on the skin surface.[2]

The combination of seborrhea and follicular hyperkeratinization produces a favorable environment for *C. acnes* development, which is found in the skin microbiota and is not pathogenic under normal circumstances.[5]

Microbiome

Microbiome is the microbial community that occupies a habitat, composed of billions of bacteria, fungi, and viruses.

The human microbiota is established after birth, dominated by bifidobacteria, and stabilizes between the second and third years of life.

Commensal bacteria have greater importance and are involved in the synthesis of specific vitamins, the development and activation of the immune system, and the inhibition of colonization of certain pathogens.

In short, the intestinal microbiota plays a fundamental role in various metabolic, nutritional, physiological, and immunological processes. On the other hand, microbial communities in the organism can influence the pathogenesis of multiple diseases.[6]

Many conditions related to the microbiome's changes have already been identified, such as obesity, autism, inflammatory bowel disease, atopic dermatitis, and several other diseases, as well as changes in the intestinal microbiota of patients with acne vulgaris. It is assumed that the patient with acne is even more at risk of gastrointestinal discomfort.[7]

Studies of the intestinal microbiome on the organism and its role in the acne's inflammatory process led to the development of a principle called "gut - brain – skin axis". Based on this mechanism, it was postulated that the intestinal microbiome's improvement is shown as a new strategy in the treatment of acne.

However, the microbiome is not limited to the intestine. A review published in 2019, assessing the role of the microbiome in acne, addressed the skin's function as the first line of defense against external agents. It also approaches how, in addition to the skin's physical barrier, there is also a need to protect the skin's microbiome to keep it balanced and capable of combating possible pathogens such as *C. acnes*. The review deepens, including addressing specifically the skin microbiome, considering it as an essential part of human health, as dysbiosis could cause or aggravate skin problems. It is believed that probiotics can modify the pathophysiological factors that contribute to acne.[8]

Probiotics

The World Health Organization (WHO) has been considering probiotics as a more attractive alternative therapy than antibiotics since they do not induce resistance. Probiotics are defined as living microorganisms that, when administered in adequate amounts, can benefit the host's health.

Currently, probiotics are commercialized as nutraceuticals, nutricosmetics, and functional foods, even though Brazil does not recognize this terminology and consider them food supplements. These nomenclatures, however, are widely used both nationally and internationally.[2,7]

Probiotics can balance the intestinal microbiota, restoring normal intestinal permeability. Recently, research has shown that probiotics' use not only offers localized effects in the intestine, such as altering the local pH to create an environment unfavorable to pathogens and favorable to their proliferation but also exerts systemic effects.[2,9]

Studies show the action of probiotics in reducing plasma markers of inflammation and oxidative stress, as well as their action in improving the intestinal barrier's immune function and decreasing the production of pro-inflammatory cytokines (IL) [1,2,6,8] and TNF and stimulation of Toll-like receptors (TLRs).

Regarding its clinical action, effects have been reported in reducing blood pressure, decreasing cholesterol levels, better absorbing certain nutrients, acting, for example, in improving the use of lactose, also acting in relieving the symptoms of intolerance. They also control intestinal infections, as well as stimulate intestinal motility, leading to the consequent relief of constipation and presenting even an anticarcinogenic effect.[2]

There are also reports of improvement in the immune system by stimulating the production of antibodies, increased secretion of gamma-interferon (IFN) in patients with atopic dermatitis and allergy to cow's milk, in addition to the competitive exclusion of the antimicrobial compounds' production.[2]

Although the different actions of probiotics are recognized, their mechanisms of action have not yet been fully elucidated. Various processes are suggested that can act independently or associated, such as competition for adhesion sites, which ends up forming a physical barrier against pathogenic bacteria, compe-

tition with pathogens for nutrients, stimulation of the immune system, production of bacteriocins against pathogens, aid in digestion, absorption and production of nutrients, action on cellular metabolism, reducing the concentration of ammonia in the body, and release of enzymes such as lactase.[2]

Regarding its safety profile, the probiotic to be marketed needs to present a low risk of systemic infection and production of harmful toxins, not offering an excessive stimulus to the immune response and not allowing the transfer of genes between microorganisms.

As they are living cells, they must be used in adequate quantities; the bacterium must also have internationally known identification; exercise clinically proven benefits to the user demonstrated *in vivo* and *in vitro*; survive the attacks of gastric acid and bile salts, ensuring they are alive and active when they reach the site of action; besides having the guarantee of maintaining viability until the moment of consumption in the form of capsule, powder, or when added to dairy products.[2]

We should also highlight that, to guarantee their continuous effect, probiotics must be ingested daily. The required dose varies according to the strain and product and can promote benefits in very low or very high doses, with clinical studies always showing the health benefits.[2]

The National Health Surveillance Agency (ANVISA) determines that the minimum viable quantity for probiotics is between 10^8 and 10^9UFC (Colony Forming Units) in the daily recommendation of the product.[2]

Gut-brain-skin axis

Since 1930 theories on the benefits of probiotics and their action on the gastrointestinal system infer that psychological factors could influence the skin.[10]

Nowadays, it is known that emotional states lead to gastrointestinal dysfunction and changes in bacterial flora, causing local and systemic inflammation. [10]

Studies relate emotional stress to the delay in the average time of intestinal transit, the consequent excessive growth of bacteria and the reduction of species of lactobacilli and bifidobacteria.[11]

Alteration of the intestinal microbiome (dysbiosis) leads to hypochlorhydria and excess bacterial growth, and competition for nutrients leads to the production of toxic metabolites.10

Immune mechanism

Dysbiosis is also involved in the release of inflammatory and neuromodulatory cytokines (such as substance P).

Substance P acts on the organ itself and at a distance, increasing pro-inflammatory mediators (IL-1, IL-6, TN- F- (PPAR –g).

Substance P promotes both proliferation and differentiation of sebaceous glands, leading to the worsening of acne. No less important fact is that substance P can be released under stress, corroborating the theory of the gut-brain-skin axis.

Also, regarding the immune mechanism, we must emphasize that the increase in IGF-1 is also involved in worsening acne conditions.[12, 13,14]

Probiotics in the treatment of acne

Recent studies demonstrate that prebiotics and probiotics can reduce markers of inflammation and oxidative stress.9 Studies have been published demonstrating the effectiveness of using oral probiotics in the clinical improvement of acne.

In addition to improving adherence and tolerability, adverse events are reduced when associated with the use of systemic antibiotics. [15,16]

Of the probiotics, *Lactobacillus acidophilus* is the most studied species in the treatment of acne.[17]

The first study with lactobacilli to treat acne was published in 1961, in which 300 patients used probiotic strains for 30 days. There was an improvement in 80% of the cases, which showed some degree of clinical improvement (with a higher result in the most inflammatory cases).

This research has its relevance, as it was one of the first published studies to infer a possible link between the cutaneous manifestations of acne vulgaris and metabolic processes in the intestinal tract.[2,15,18]

Nowadays, several studies have already shown that the presence of circulating endotoxins derived from intestinal bacteria and changes in intestinal permeability may be common in acne.[19,20] A study conducted with 40 patients undergoing conventional acne treatment divided them into two groups: 50% of the participants used antibiotics alone, and the other half used antibiotics associated with the probiotic. The assessment showed that the supplement group obtained better results and better tolerance to medications than volunteers who used the antibiotic alone[18,21] proving the benefit of the association of probiotics with standard treatment in patients with acne.[2]

An interesting clinical study demonstrated that the consumption of industrialized dairy drinks fermented with Lactobacillus improved the clinical aspects of acne after 12 weeks.[2]

Mechanism of action of probiotics in acne

A possible mechanism of action of probiotics in acne is based on the fact that the loss of bifidobacteria due to bad eating habits (excessive consumption of fat and sugar) leads to an increased intestinal permeability and endotoxins efflux in the circulation (which consequently lead to inflammation, oxidative stress, and insulin resistance). Thus, the administration of probiotics could then decrease systemic access to endotoxins and reduce reactivity to them.[22,23]

A regulatory pathway is linked to the modulation of essential cytokines in developing the disease, such as IL 1-alpha (fundamental for follicular hyperkeratosis - obstruction of the glandular ostium).[24]

We can say that probiotics can regulate the release of inflammatory cytokines in the skin, just as antibiotics can alter the microbiota in places far from the gastrointestinal system.[24,25]

Another factor to consider is that, in acne, the load of lipid peroxidation is high, generating significant demand for antioxidants (qualitative alteration of sebum production), and the ability of oral probiotics to limit systemic oxidative stress could also be considered a therapeutic path (antioxidant effect).[26]

A possible relationship between high glycemic index diets and acne exacerbation has also been investigated. It is evident the relationship of some components of the diet (carbohydrates and high glycemic index) and acne.[2,18]

Systemic probiotics can improve insulin levels, reducing the release of IGF -1, leading to clinical improvement of acne.[2,12,18,27]

In short, we can point out the action of probiotics in acne treatment due to the reduction of local and systemic inflammation, decreased oxidative stress, maintenance of permeability of the intestinal barrier, and reduced release of substance P, regulation of glycemic control, and improved nutrient absorption.

Topical use of probiotics

In 1912, the first report of the use of probiotics directly on the skin (topical use of *Lactobacillus bulgaricus*) was published, which proved to be useful in the treatment of acne and seborrhea.

A study, conducted for only seven days, used probiotic in the form of cream to demonstrate that lactic acid-producing bacteria could increase the production of ceramides, which are recognized for having anti-microbial activity against *C. acnes*, in addition to anti-inflammatory activity. In another clinical study, the application of ceramide promoted a significant reduction of papules and pustules after two months of treatment.[2]

Studies have shown the value of topical therapy with probiotics *Bifidobacterium longum* and *Lactobacillus paracasei* to attenuate the inflammation mediated by substance P in the skin (remembering that substance P is a primary mediator, induced by stress, leading to inflammation and sebum production in acne).[2]

The application of selected probiotic bacteria to the skin can offer a protective effect, similar to a physical barrier, through the competitive inhibition of binding sites to prevent colonization by other pathogenic bacterial strains.[2]

Tyndallized bacteria

It is known that living microorganisms are sensitive to heat and the presence of water and can become a challenge for pharmaceutical forms such as creams. Due to this characteristic, our study sought to use tyndallized bacteria.

Tyndallized bacteria can be defined as microorganisms or non-viable microbial cells, obtained from probiotics. The tyndallization process consists of a fractional sterilization method in which temperatures between 80 °C and 100 °C are applied to the microorganism. Heat-treated probiotics can confer immunomodulatory effects and assist in the inflammatory response. Thus, they and have been used in respiratory and dermatological pathologies.[28]

MATERIALS AND METHODS

This is a clinical, experimental, prospective, randomized.

The study recruited 28 volunteers. The inclusion criteria were: participants of any age group, ethnicity, or gender, presenting with mild or moderate acne (grades I, II, III).

The exclusion criteria were severe acne (grade IV) and/or patient using other medications to treat acne during the study (three months).

METHODS

The volunteers' evaluation was photographic and clinical, performed by two examiners.

In the first evaluation, anamnesis and clinical dermatological examination were performed. The acne was classified as grade I - prevalence of comedones; grade II - presence of papules and pustules; or grade III - presence of cystic lesions. On the same day, the photographic record was performed, and the informed consent form and the complete treatment were provided. The treatment was formulated and handled in a compounding pharmacy (Fórmula e Cia, Manipulação Pharmacy, Campinas, São Paulo, Brazil), including cream containing 30 g, with *Lactobacillus plantarum* GMNL06 in a concentration of 1 billion UFC/g, in a pump bottle, sanitizing lotion composed of saline (Needs®, LBS Laborasa, São Paulo, SP, Brazil) for facial hygiene, and SPF 30 sunscreen in aristoflex gel.

The patient was instructed to use the cream containing *Lactobacillus plantarum* GMNL06, twice a day, in the morning and at night, for 90 days. Patients were also instructed to return every 30 days for clinical evaluation and photographic record, in addition to receiving treatment for the next month.

Each return was recorded on a form if the patient showed correct adherence to treatment, and, in case he was not using the products in the protocoled manner, he was immediately excluded from the study group.

Upon return from the third month of treatment, patients were assessed and classified according to the scale below:

a) Acne worsening (increase in the number of lesions), zero result (when there was no clinical change in the initial condition with post-treatment);
b) Partial improvement (up to 50% decrease in the number of lesions);
c) Great improvement (more than 50% decrease in the number of lesions).

Two researchers clinically evaluated and classified the patients.

RESULTS

Of the 28 selected patients, seven were men, and 21 were women.

The age ranged from 13 to 46 years (average 29.5 years). Eighteen patients did not complete the study, and, most of these voluntary dropouts (12) gave up treatment without giving any reason and did not attend the returns or did not answer our calls. Two dropout volunteers reported worsening of the clinical condition and, therefore, discontinued its use. Four dropout volunteers stated that they were unable to adhere correctly to the treatment. Of these, one volunteer reported liking the result of using the probiotic and was classified as having much improve-

ment since the first month of follow-up (Graph 1). Of the ten patients who completed the three months of protocol treatment, one presented acne worsening; none was classified as zero result; three partially improved; and six were classified as great improvement (Graph 2) (Figure 1).

Of these 10 patients, nine were classified, at the beginning of the protocol, as grade I acne and one as grade II acne.

Adverse events

There were no reports of adverse events such as scaling, itching, burning, or erythema.

DISCUSSION

Lactobacillus plantarum GMNL06 is a probiotic bacterium (sterilized), that is, heat-treated. During heat treatment, bacteriocins are released from cell membranes and perform the "antibiotic-like" action.28 Bacteriocins are proteins with antimicrobial activity that act by inhibiting the growth of *Cutibacterium acnes*.[29,30,31]

Few studies have been conducted with *Lactobacillus plantarum* for acne and with topical use, which denotes the relevance of the present study.

In the theoretical research conducted for the present study, the most relevant study was a clinical trial aimed at treating acne. It was conducted with another lineage of the same genus and species, *Lactobacillus plantarum* GG, also heat-treated, in the form of cream, with 29 women volunteers, aged between 25 and 55 years. The authors considered the effects promising in reducing the erythema caused by acne and in the intensity of the lesions.[32]

Based on our observations and the literature, we can cite as possible mechanisms of action of *Lactobacillus plantarum* GMNL06:

1) Epithelial action:[33]

- Improved barrier function in the epithelial layer;
- Pathogens' competition for the receptor site in epithelial cells.

2) Immunomodulatory action:[34]

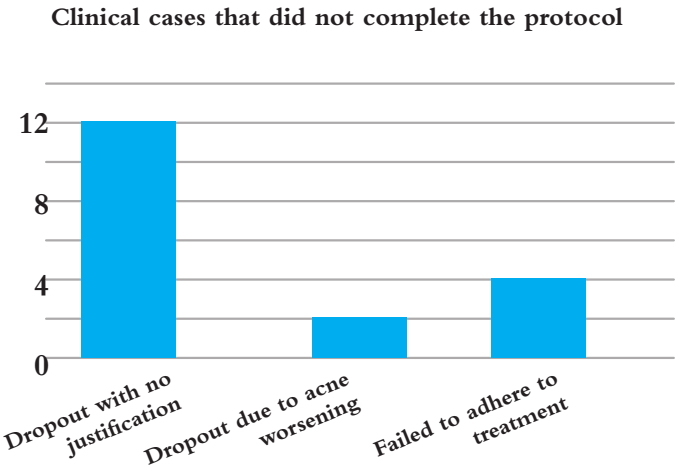
- Prevention of the immune-inflammatory response, by increasing the anti-inflammatory cytokines;
- Stimulation of the immune response;
- Differentiation of B cells, formation of IgA.

3) Increased resistance to pathogens:[35]

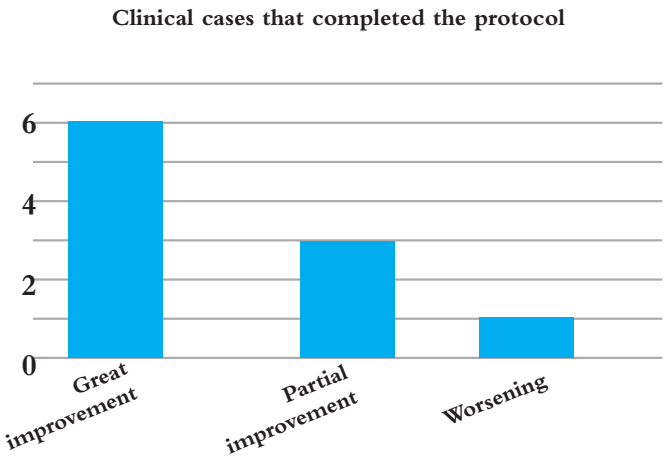
- Inhibition of pathogen adherence by competition;
- External membrane proteins with bactericidal effect.

The interest of this research in using *Lactobacillus plantarum* GMNL06 in the tyndallized form was the possibility of applying it in a compounded formulation for topical use, opening the range of options for professionals in the treatment of acne both as monotherapy and combined with other treatment strategies.

Studies corroborate the fact that tyndallized probiotic bacteria can modulate the growth of pathogenic microorganisms, favoring skin homeostasis.[35] The use of probiotics for their anti-inflammatory action can be considered a therapeutic option in acne treatment.8 In our study, we chose to study the use of topical, probiotic bacterium, topical, in monotherapy, to treat mild or moderate acne.



Graph 1: Reasons for the evasion of study patients using Lactobacillus plantarum GMNL06 treated with compounded cream for the treatment of acne



Graph 2: Classification of the clinical response of patients who completed the treatment of acne with the use of Lactobacillus plantarum GMNL06 treated with compounded cream for three months

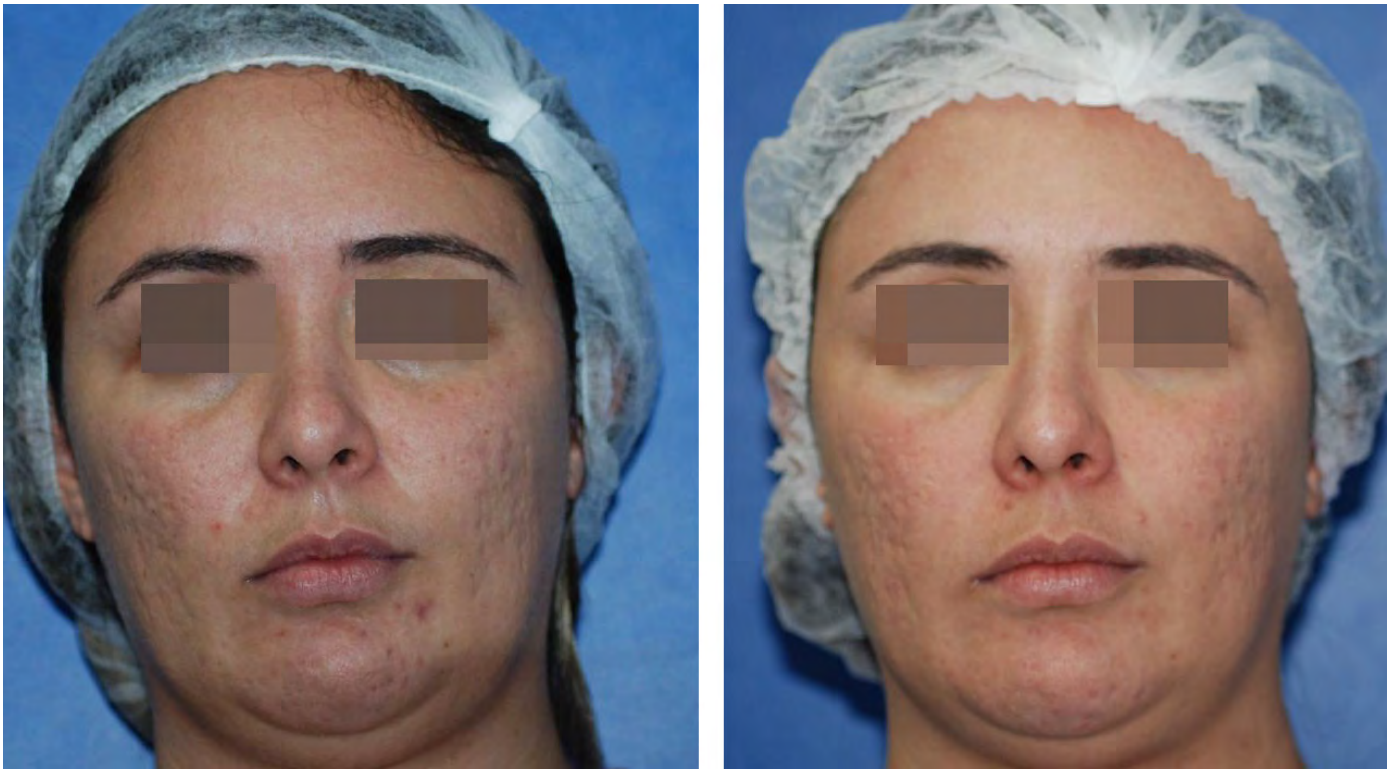


Figure 1: Acne patient before and 90 days after treatment with topical Lactobacillus plantarum

This study's option to use *Lactobacillus plantarum* GMNL06, as monotherapy, apparently showed a slower improvement process in the skin condition, and we assume that this may have caused the abandonment of the protocol by some volunteers, after the first month of treatment. Another hypothesis for the protocol abandonment was that the protocol used establishes the use of the formulation twice a day. This hypothesis, in our analysis, may have contributed to the cases of non-adherence to the proposed protocol. Despite this, we must emphasize that, even within the group of volunteers who gave up treatment because they were not able to follow the protocol correctly, there was a case of clinical improvement considered as a great improvement in the first month of using *Lactobacillus plantarum* GMNL06.

An important fact to be highlighted is that, among the volunteers who managed to follow the protocol by the end of the third month, the majority (60% of the cases) showed improvement classified within the scale established for study as great improvement.

If we combine this result with partial improvement cases, it is possible to state that we obtained a 90% satisfactory result within the proposed protocol. That in the framework of acne for the portion of volunteers that fully adhered to the protocol for the use in monotherapy of *Lactobacillus plantarum* GMNL06, compounded cream, dispensed in a pump bottle, twice daily

In clinical practice, acne is treated with specific sanitizers for oily/acneic skin, association of topical keratolytic and/or bactericidal products and, in cases of more pustular acne, with the introduction of systemic medications. There are also complementary procedures, such as the removal of comedones, chemical peels, microdermabrasions, phototherapy, and others, for three months or more. We emphasize that none of these strategies were used during the proposed protocol so that there was no interference in the results obtained and data collected.

In our evaluation, there are many advantages in the use of probiotic bacteria tyndallized in a topical cream for acne. It did not induce bacterial resistance and did not cause discomfort or skin irritation, according to what we could observe in our study. This feature enables associating it with other products for acne treatment, which may enhance the speed of results. Because *Lactobacillus plantarum* GMNL06 does not produce photosensitization, this strategy used in our protocol presents as an interesting and effective therapeutic option for patients who are overexposed to sunlight or who have sensitive skin to conventional treatments.

CONCLUSION

Based on our data analysis and the results collected in our protocol, we could conclude that the topical use of *Lactobacillus plantarum* GMNL06 in compounded cream proved to be a safe and effective procedure in the treatment of mild and moderate acne, even as monotherapy. It didn't present skin irritations or discomfort; it's not photosensitizing, and it presented satisfactory results in 90% of the tested volunteers.●

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Original Article

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A single blind, randomized clinical trial comparing MMP®, MMP® with 5-FU, and 5-FU intradermal injection for the treatment of idiopathic guttate hypomelanosis: a pilot study

Ensaio clínico cego randomizado comparando MMP®, MMP® com 5-FU e injeção intradérmica de 5-FU para o tratamento da hipomelanose gutata idiopática: um estudo- piloto

DOI: http://www.dx.doi.org/10.5935/scd1984-8773.20201222558

ABSTRACT

Introduction: Idiopathic guttate hypomelanosis (IGH) is a common photoaging manifestation, with no standard treatment and presenting mixed results to interventions. In Brazil, the use of micro-needling associated with 5-fluorouracil (5-FU) has been proposed to treat IGH.
Objective: To compare the use of MMP® (micro-infusion of drugs on the skin) with 5-FU, with MMP® only as micro-needling (with no drugs), and intralesional 5-FU injected with an insulin syringe in the treatment of IGH.
Methods: In a single blind randomized clinical trial, we compared the three treatments: MMP® versus MMP with 5-FU and intralesional 5-FU injection for 180 IGH lesions in the forearm of nine patients.
Results: After two treatment sessions, 5-FU alone was the most effective treatment, with statistical significance, compared with micro-needling alone. MMP+5-FU efficacy was lower than intralesional 5-FU injection and higher than micro-needling alone, although without statistical significance.
Conclusions: The intralesional application of 5-FU was more effective in the treatment of solar leukoderma. The use of a smaller quantity of medication is the great advantage of the MMP + 5-FU technique. Further studies are needed to standardize these techniques.
Keywords: Drug delivery systems; Fluorouracil; Hypopigmentation; Skin aging

RESUMO

Introdução: *A hipomelanose gutata idiopática (IGH) é uma manifestação comum de fotoenvelhecimento, ainda sem tratamento padrão, apresentando resultados variados às intervenções. Atualmente, no Brasil, o uso de microagulhamento associado ao 5-fluorouracil (5-FU) tem sido proposto para o tratamento da IGH.*
Objetivo*: Comparar três tratamentos, quais sejam: o uso do MMP® (microinfusão de medicamentos na pele) com 5-FU, MMP® apenas para microagulhamento, e com o 5-FU intralesional injetado com seringa de insulina no tratamento da IGH.*
Métodos: *Em um ensaio clínico randomizado e cego, comparamos o MMP® ao 5-FU com: microagulhamento isolado e com 5-FU intralesional por punção para o tratamento de 180 lesões de IGH no antebraço de nove pacientes.*
Resultados: *Após duas sessões de tratamento, o 5-FU intralesional foi o tratamento mais efetivo, com significância estatística quando comparado ao uso de microagulhamento. A eficácia da MMP + 5-FU foi inferior a 5-FU injetável e superior ao microagulhamento isoladamente, embora sem significância estatística.*
Conclusões: *A aplicação intralesional do 5-FU foi mais eficaz no tratamento da leucodermia solar. O uso de menor quantidade de medicamentos é a grande vantagem da técnica MMP + 5-FU. São necessários mais estudos para padronizar estas técnicas.*
Palavras-chave: *Envelhecimento da pele; Fluoruracila; Hipopigmentação; Sistemas de liberação de medicamentos*

INTRODUCTION

Idiopathic guttatehypomelanosis (IGH) is a manifestation of photoaging that occurs mainly on the extensor surface of the forearms and pretibial areas, and which still has no standardized treatment and presents varied response to interventions.[1] The use of micro-needlingassociated with 5-fluorouracil(5-FU)has beenproposed for the treatmentofIGH.[2]

5-FUis a pyrimidineanalog used in the treatment of many skin diseases. Intralesional infiltration of this medication and its use in the micro-needled area have been used in the treatmentofvitiligo.[3,4]

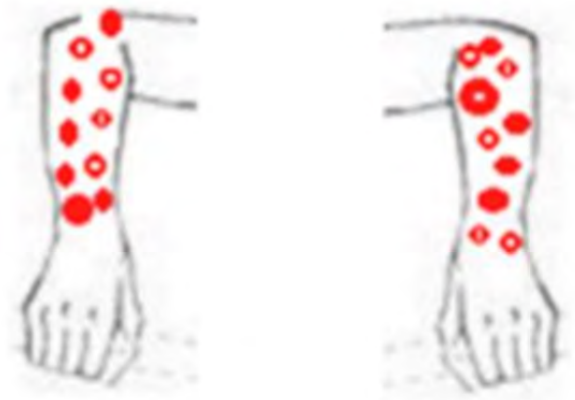
Arbacheetal.described repigmentation of IGHwith administration of 5-FU via a tattooing machine, using the technique called MMP® (micro-infusion of medications in the skin), with exclusive use bydermatologists.[2]

In the search for an effective therapy forIGH, thecurrent study aims to assess the efficacy of MMP with 5-FU compared to MMP without medication and intralesional5-FU with a single puncture in the treatmentofleukodermas on the forearm.

MATERIALS AND METHODS

This single-blind randomized clinical trial compared MMP® with 5-FU to micro-needling (MMP® without drugs) and intralesional 5-FUvia single puncture with an insulin needle for treatmentof180IGHlesions on the forearmin ninepatients. Ten lesions were treated on each forearm, totaling 180 treated lesions (Figure 1).The treatment technique used on each forearmwas selected randomly, each one on six forearms,with a total of 60 lesions.The study was approved by the Institutional Review Board of Hospital do Servidor Público Municipal de São Paulo (CAAE:51923415.1.0000.5442).

Micro-needling 5 was performed with a tattooing machine(Cheyenne,Germany,TRADERM®,SP, Brazil) approved by the Brazilian National Health Regulatory Agency (ANVISA). The cartridge needles used for thisprotocol, model 7-liner-mt, were immersed in 5-FU or used only for micro-needling (Figure 2). Micro-needlingwas performed from the periphery towards the center of the depigmented area(2mm or 20 clicks of the machine) until a mild blood dew appeared, a sign that the dermis had been reached. Maximum dose was 50mg/1ml/forearm per session.



RIGHT FOREARM:1TO 10 LEFT FOREARM:11 TO 20

FIGURE 1: Model for marking lesions

Intradermal injection of 5% 5-FU was 0.1ml in each IGH lesion with BD® syringes mounted with a 0.3ml needle, maximum of 50mg/1ml/forearm per session (Figure 3).

All treatments were performed in twosessions with a 30-day interval. Final evaluation was performed at 120 days.

Improvement was evaluated with images of each lesion (standardized clinical photos), classified by a blinded observer using the repigmentation scale (Figure 4).The results were compared using chi-square test (k proportions) or ANOVA, followed by LSD multiple comparison. Statistical significance was set at 5%.

RESULTS

Mean age was 61years (range: 49 to 70 years), eight patientswere females(89%),two were photo type II, four were photo typeIII, and three were photo type IV.

Of the 180 lesions, sixpresented hyperpigmentationas an adverseeffect and were excluded from the analysis.Of the174 lesions, all presented repigmentation,162(93.1%) with total repigmentation with normochromia, 12 (6.9%) with partial repigmentation. The great majority of the lesions showed total repigmentationwith normochromiafor all the treat-

MMP

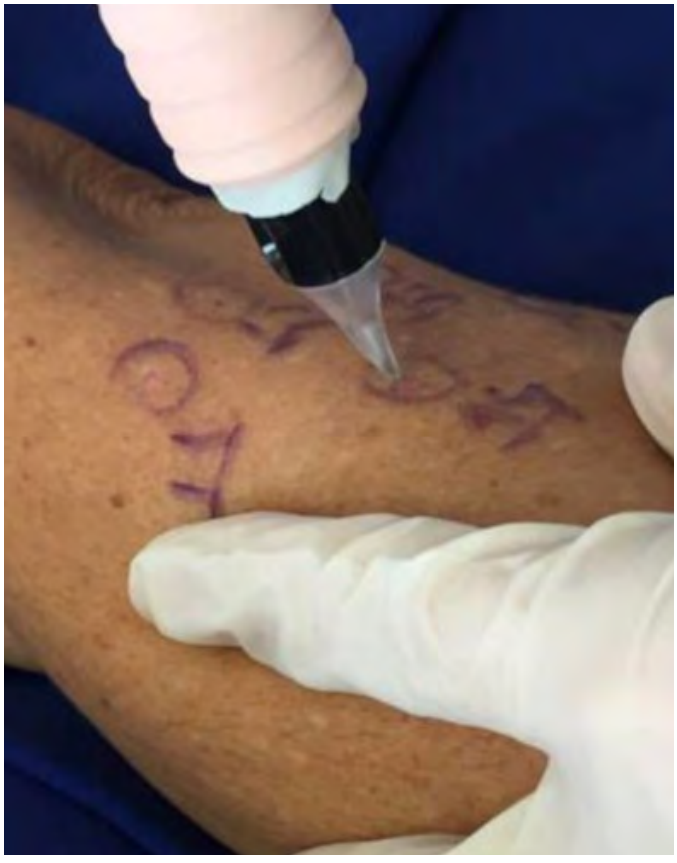


FIGURE 2: MMP technique, using tattooing machine and 7-tipped needle, from periphery to center

ments, with 57/57=100%for5-FU, 50/58=86,2% for MMP, and 55/59=93,2% for MMP+ 5-FU (Figure 5).

Eight forearms were not submitted to a second session, for different reasons, namely: four reached the treatment target(total repigmentationand normochromia), two of whom usingMMP and two MMP+5-FU;three due to erythemain the lesion sites(one used MMPand two MMP+5-FU);and one due to hyperpigmentation of all the lesionsafter the first session with 5-FUalone.

Significant differences were found in the proportions of lesionswith total repigmentationwith normochromiabetween the groups treated with 5-FU andwith MMP (k proportions

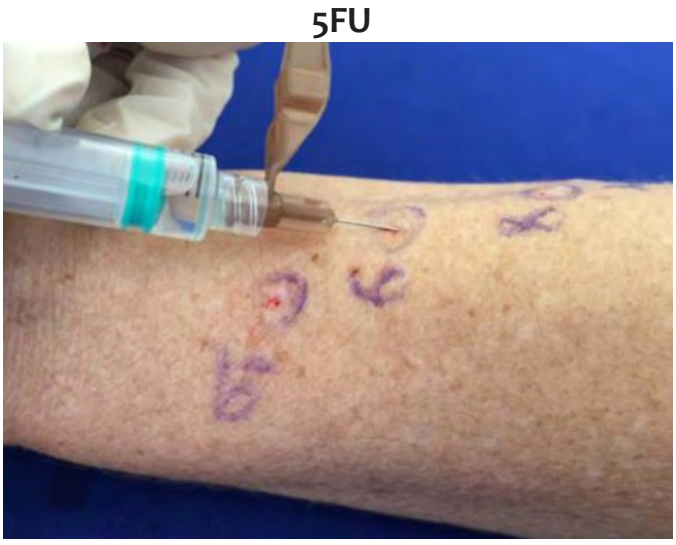


Figure 3: Intradermal application of 5-FU using insulin needle

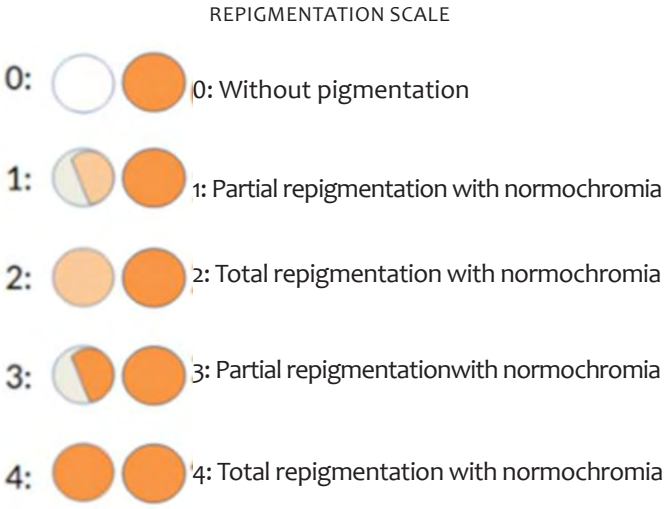


Figure 4: Gradient scale ofrepigmentation

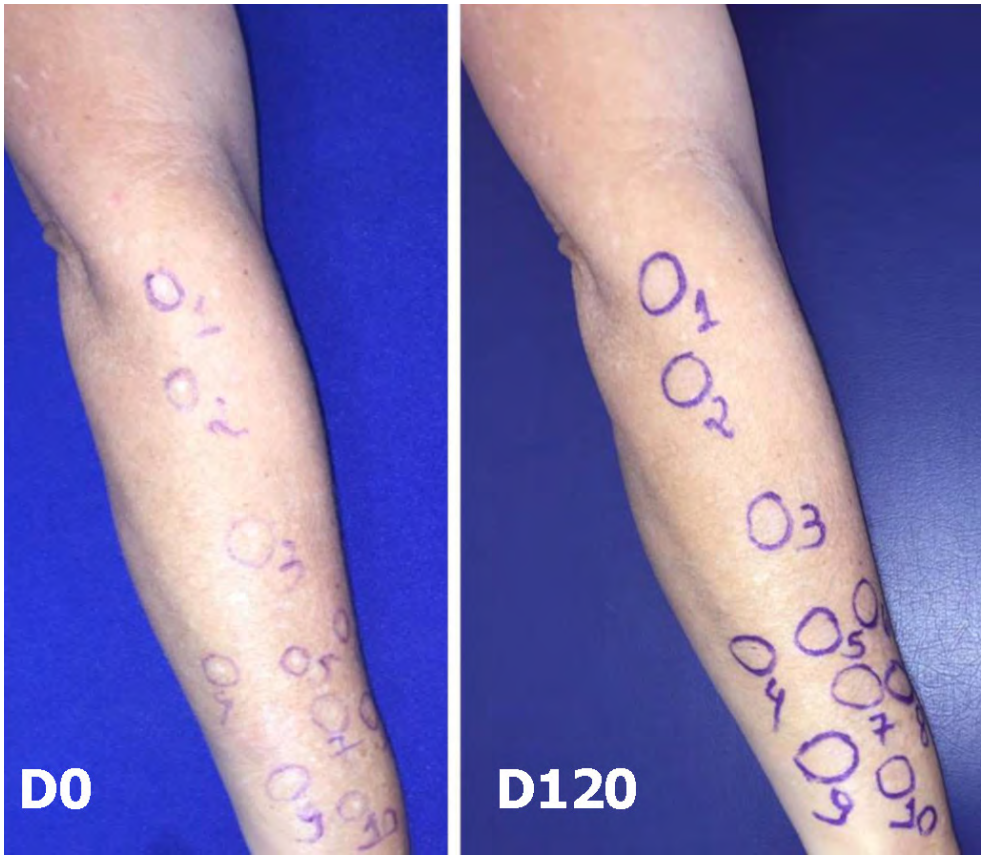


Figure 5: Patient 6 on day 0 and post-treatment(d120)

test;p=0.014).The proportion was lower in lesionstreated with MMP, compared to lesions treated with 5-FU, suggesting greater efficacy with 5-FU injection.

Of the repigmented lesions, 162 (93.1%) presented total repigmentationwith normochromiafor all the treatments, which was the best result of the five possible results in the repigmentationscale (Figure4).

Treatmentwith MMP + 5-FU was the second most effective treatment, although without statistical significance. The lowest efficacy was with micro-needling, which may due to the lack of use of 5-FU;thetreatmentswith MMP+5-FUand5-FU alone showed better clinical and statistical response.

Pain was assessed subjectively by patients, and no statistically significant differences were found between the three treatments. However, pain in the treatmentwith MMP + 5-FU was considered more intense than in the othertreatments.

As for adverse effects such as burning sensation, pruritis, and pain, there were no statistically significant differences between the treatments.

On day 30, one patient presented hyperpigmentation in 10 lesionswith the use of intralesional 5-FU. However, on day 120 all the lesions were normochromic.

At the end of the study, six lesions presentedhyperpigmentation, one of which had been treated with MMP+- 5-FU, two with MMP, and three with 5-FU

DISCUSSION

Abd El-Samad andShaamad, in 2012, were the first to useintralesional 5-FU to treat vitiligo. In60patients, there was greater overall repigmentationin the group in which 5-FUwas injected, compared to controls($p<0.001$).3Attwa, Khashaba, and Ezzat, in 2019, compared to needling and needling followed by topical 5-FU to treat stable localized vitiligo in 27 patients. Micro-needling followed by topical 5-FU showed a better response than micro-needlingalone, with minimal adverse effects.[4]

Arbache S. et al.[2] treated eight patients with IGH lesions, with MMP + 5-FU versus MMP with placebo. Repigmentation of the lesionwith MMP + 5-FU was statistically superior to MMP with placebo (repigmentationwith 5-FU=75.3% versus repigmentationwith placebo 33.8%, $p<0.001$).

In our protocol,all 174 lesions(96.7%)presented repigmentation, and none remained achromic after the procedures, which indicates clinical improvement with all three treatments used. No statistically significant differences were observed between the three techniques.However, in the head-to-head comparison, the proportion was statistically lower (k proportions test; $p=0.014$) for lesions treated with MMP for micro-needling (50/58 = 86.2%) compared to lesions treated with 5-FU(57/57=100%), suggesting better efficacy of treatment with 5-FU.

After two treatment sessions, intralesional 5-FUwas the most effective treatment, with statistical significance, when compared to the use of micro-needling. The efficacy of MMP + 5-FU was inferior to intralesional 5-FUand superior to micro-needling alone, although without statistical significance.The use of a smaller amount of 5-FU (1.175μg/cm² orabout 0.00116ml for each 10 lesions), followed by the technique described by Arbache 2 and the speed and ease of the techniques are the main advantages of MMP + 5-FU compared to injectionwith insulin needle, which used about 50mg (1ml) of medication persession. The adverse effects of 5-FU include pain, pruritis, hyperpigmentation, and burning sensation atthe application site[3,4]Other less frequent reactions include allergic contact dermatitis, pain, tenderness, suppuration, desquamation, and edema.

In our protocol, there were no statistically significant differences between the treatments in relation to pain.

CONCLUSIONS

Intralesional infiltration of 5-FU was the most effective treatmentof localleukoderma.The use of lower amounts of medications and the technique's speed and ease are the main advantages of the MMP + 5-FU technique. More studies are needed on the maintenance of the level of improvement in thelesionswith these three techniques. ●

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Which is the melanoma? Black lesion matters!

Qual é o melanoma? Lesões negras são importantes!

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ABSTRACT

Diagnosing basal cell carcinomas, both clinically and dermoscopically, is part of most dermatologists' daily routine. However, tumors of this lineage, when densely pigmented, can be a challenge for the physician and surgeon. Dermoscopic features typical of melanocytic lesions may be present in these carcinomas, and the similarity with melanoma results in a real dilemma. More in-depth knowledge on this topic can make a difference in the management of these cases.

Keywords: Carcinoma, Basal cell; Dermoscopia; Diagnosis; Melanoma

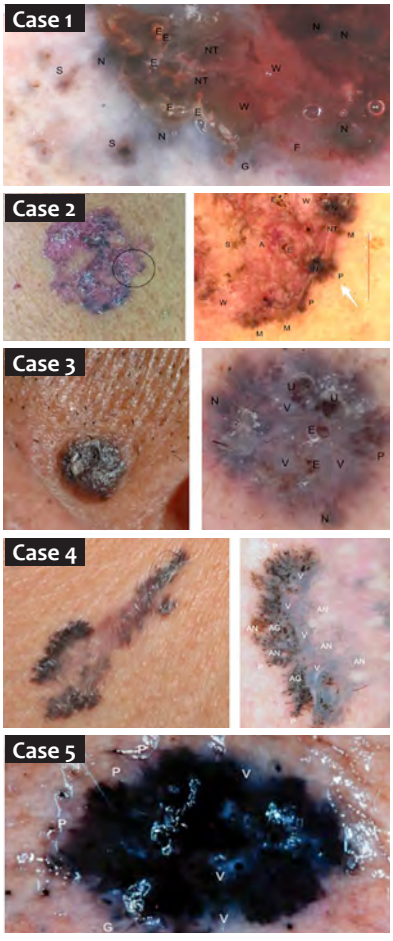
RESUMO

Diagnosticar carcinomas basocelulares por meio da clínica e dermatoscopia faz parte da rotina diária da maioria dos dermatologistas. No entanto, tumores dessa linhagem, quando densamente pigmentados, podem representar um desafio para o médico e cirurgião. Características dermatoscópicas típicas de lesões melanocíticas podem estar presentes nestes carcinomas e a similaridade com o melanoma resultar num verdadeiro dilema. Conhecimentos mais aprofundados sobre este tema podem fazer diferença no manejo destes casos.

Palavras-Chave: *Carcinoma basocelular; Dermoscopia; Diagnóstico; Melanoma*

INTRODUCTION

A relevant success factor for oncologic treatment of pigmented skin lesions is based on precise initial diagnosis. Clinical differentiation between densely pigmented basal cell carcinomas (BCCs) and certain melanomas can be challenging.[1-3] Dermoscopic examination allows identifying different skin neoplasms and greatly assists the clinician in making the proper decision. Different dermoscopic structures for diagnosis of BCC have been described.[1-4] However, the absence of typical BCC characteristics or the presence of characteristic patterns of melanoma can lead to a mistaken diagnosis. This occurs more frequently in cases of densely pigmented BCCs, as demonstrated by Altamura et al.[2] The authors, analyzing 609 BCCs, identified dermoscopic characteristics of melanocytic lesion in 40.6% of these tumors, predominant in those with greater intensity of pigment, and concluded that densely pigmented BCCs were the most difficult type to differentiate from melanoma.[2] Since densely pigmented lesions are more common in individuals with higher photo types, careful analysis of these cases is relevant in tropical and subtropical populations. In this case series, we present five patients with densely pigmented lesions, raising the diagnostic challenge of melanoma hidden in four BCCs.



Imaging Diagnosis

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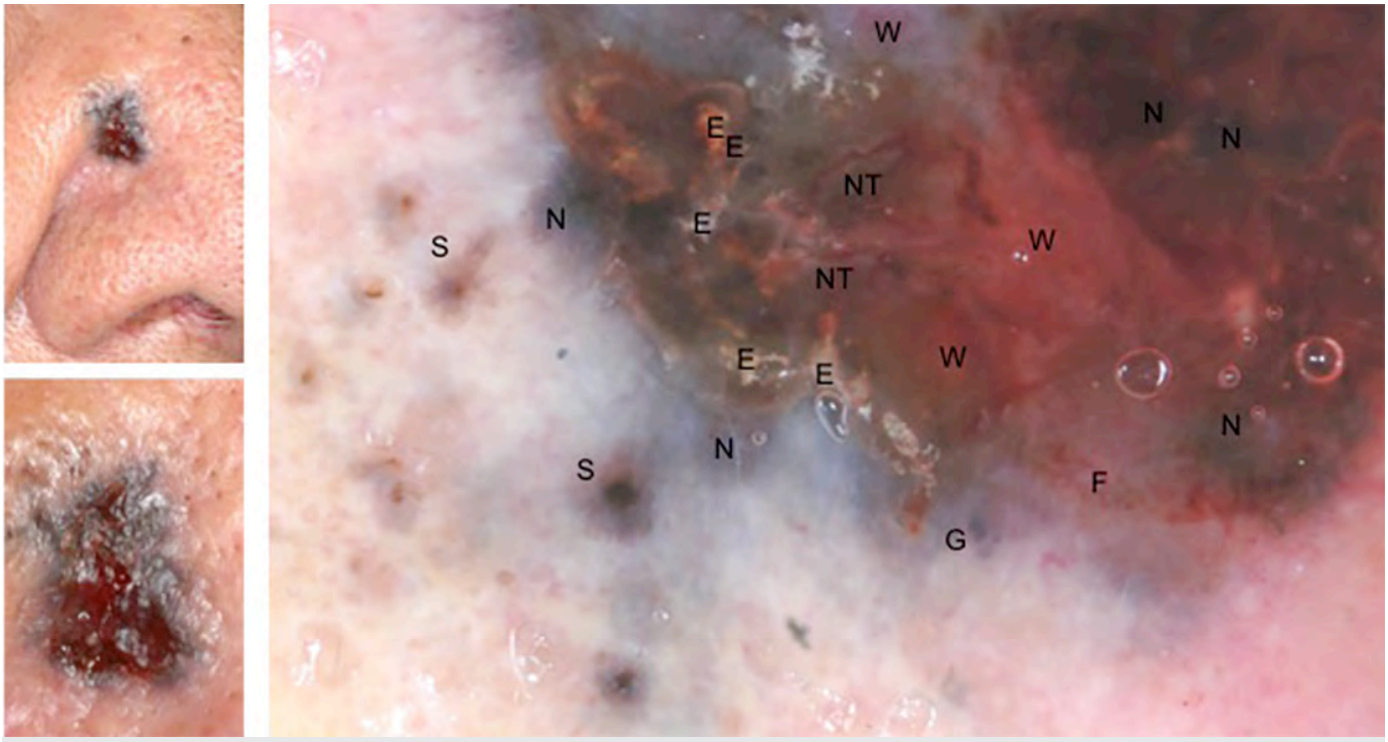
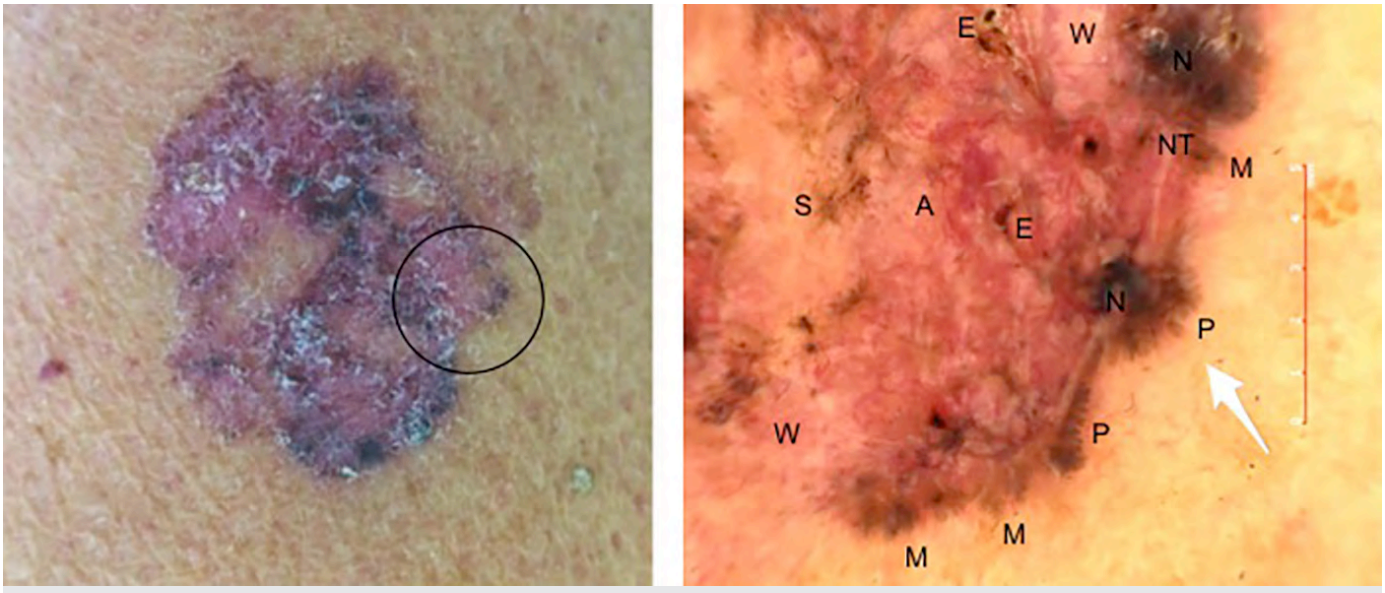
DISCUSSION

This series of five pigmented lesions shows that the differential diagnosis of pigmented BCC or melanoma is not always immediately evident, even with dermoscopy.[1]

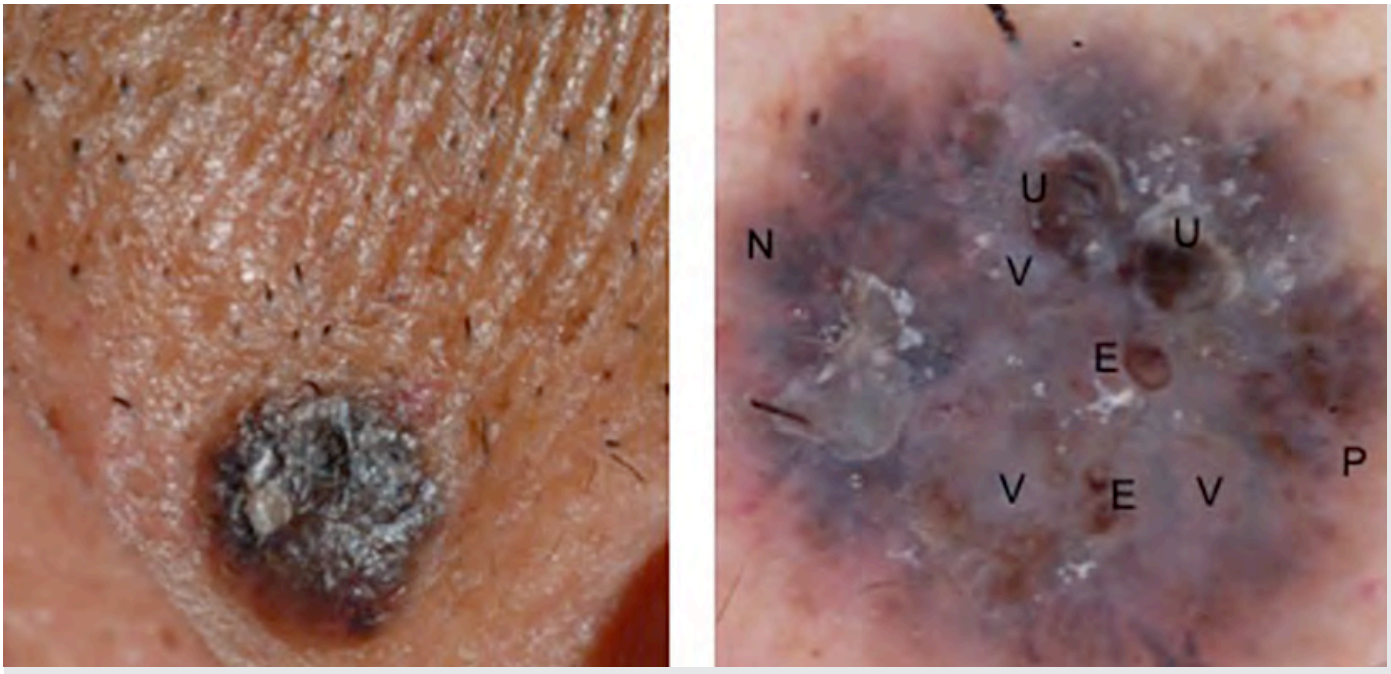
This series includes two cases of BCC (1 and 5) that are reminiscent of nodular melanoma. The dark coloring associated with a bluish veil is typical of melanoma, while the absence of specific characteristics of melanocytic lesions and black color (rule BB negative 5), and presence of spoke wheel and bluish



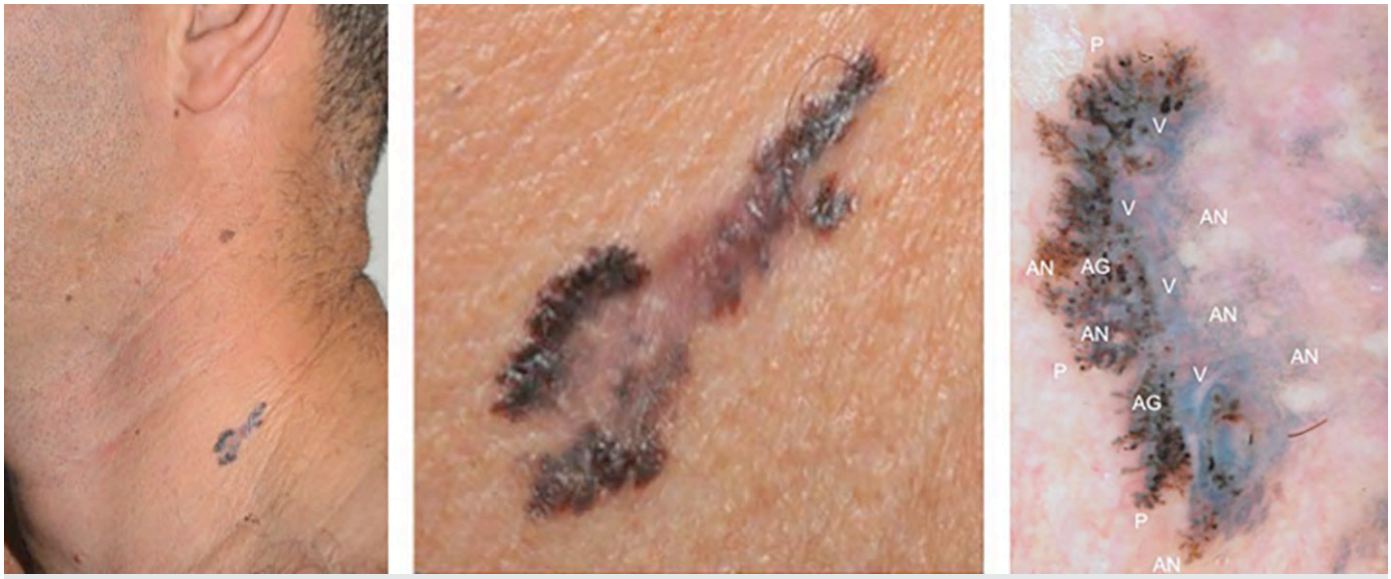
CASE 1 – Densely pigmented basal cell carcinoma: grayish-blue ovoid niches **(N)**, multiple grayish-blue globules **(G)**, areas without shiny reddish-white structure **(W)**, multiple small erosions **(E)**, thin, short telangiectasias **(F)**, spoke wheel areas **(S)**, non-arboriform telangiectasias (NT), absence of pigmented network.



CASE 2 – Pigmented basal cell carcinoma: arboriform vessels **(A)**, radial streaks or pseudopods **(P)**, grayish-blue ovoid niches **(N)**, areas without shiny reddish-white structure **(W)**, spoke wheel areas **(S)**, multiple small erosions **(E)**, non-arboriform telangiectasias **(NT)**, maple leaf areas **(M)**, absence of pigmented area



CASE 3 – Heavily Pigmented Basal Cell Carcinoma: Blue/white veillike structures **(V),** multiple small erosions **(E),** ulceration **(U),** blue-gray ovoid nests **(N),** radial streamingor pseudopods **(P),** no pigmented network.

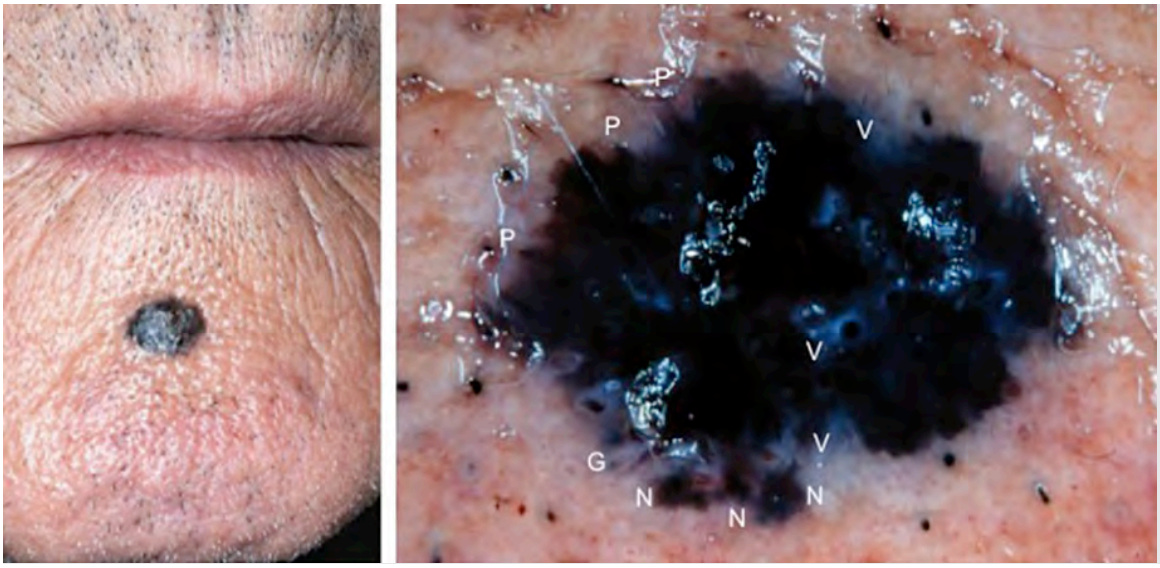


CASE 4 – Extensive superficial in situ melanoma: bluish white veil **(V),** radial streaks or pseudopods **(P),** atypical network **(AN),** atypical globules **(AG).**

ovoid niches, respectively, were suggestive of BCC.

The other three lesions present peripheral structures (similar to radial streaks and pseudopods)[6] at first sight. On more careful analysis, peripheral structures of melanoma (case 4) end in a bulbous projection (drumstick-like) compared to the BCCs (cases 2 and 3), which only present radial linear extensions. Besides, in the context of melanoma, some globules may be confused with bluish ovoid niches due to the blue color, but others clearly suggest melanocytic proliferation due to the dark blackish-brown color, resulting from the upward dissemination of melanocytic niches and clusters of Pagetoid cells.[7]

Differential diagnosis in these cases is obviously not always easy, and patients with high photo type require detailed examination, always with dermoscopy to enhance the differential diagnosis. This difficulty occurs mainly in the differentiation of densely pigmented BCCs.[2] Especially in this subtype, the presence of dermoscopic characteristics suggestive of melanocytic lesion can reach 80%.[2] Patterns including bluish-white veil and



CASE 5 – Densely pigmented basal cell carcinoma, similar bluish-white veil **(V)** Grayish-blue ovoid niches **(N),** grayish-blue globule **(G),** radial streaks or pseudopods **(P),** areas without black colored structure **(B),** absence of pigmented network.

multiple black and blue globules are among the most frequent findings. [2]

Thus, in densely pigmented BCCs, careful recognition of the clinical morphology and dermoscopic aspects can increase the diagnostic accuracy. We also propose that other imaging methods, such as confocal reflectance microscopy, which has proven useful in this context,8 can greatly assist the diagnosis of skin cancer in patients with high photo types. ●

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COVID-19 pandemic: safety recommendations for the dermatologist's return to practice

Pandemia da COVID-19: recomendações de retorno às clínicas dermatológicas

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ABSTRACT

The COVID-19 pandemic represents an unprecedented healthy global threat, leading dermatologist surgeons/aestheticians to interrupt or alter clinical practice and adjust to the necessary precautionary methods. This article aims to prepare dermatologists for the upcoming difficulties and precautions for conducting procedures in the midst of coronavirus pandemics, focusing on recommendations and best practices for reopening aesthetic practice while mitigating risks to practitioners, patients, staff, and the general public.

Keywords: COVID-19; Dermatology; Pandemic; Physicians' office, SARS-CoV-2.

RESUMO

A pandemia da COVID-19 trouxe inúmeros desafios aos profissionais da saúde. O objetivo das recomendações presentes neste artigo é dar diretrizes para promover o cuidado com a saúde de pacientes e equipe médica nas clínicas dermatológicas, minimizando o risco de contágio.

Dado o caráter eletivo dos procedimentos estéticos, cuidado adicional deve ser tomado de modo a proteger a saúde de todos. Por meio de medidas comportamentais e ambientais, é possível manter o funcionamento das clínicas com maior segurança e ajudar os pacientes a sentir-se seguros após um longo período de stress durante o isolamento.

Palavras-chave: *Clínicas, SARS-CoV-2; COVID-19; Dermatologia; Pandemia.*

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INTRODUCTION

The novel coronavirus (SARS-CoV-2) was first identified in Wuhan, China, in December 2019.[1] In March 2020, COVID-19, caused by the novel coronavirus, was officially declared a pandemic by the World Health Organization (WHO), representing an unprecedented global health crisis.[2]

The main transmission route is via respiratory secretions (aerosols or direct contact). Symptoms can appear two to 14 days after exposure, with an incubation period of four to seven days. The symptoms are fever (98%), anosmia (80%), cough (76%), dyspnea (50%), and myalgia or fatigue (44%), but many patients can be asymptomatic and still transmit the infection.[3]

Dermatology practice includes clinical, surgical, and cosmetic care. Assuming that aesthetic procedures are considered non-essential and non-emergency, it is imperative to prepare adequately for safe practice in dermatology.[3,4]

To discuss the safest approach to dermatology practice in this new scenario, a group of Brazilian dermatologists developed a set of safety guidelines for outpatient care based on the guidelines issued by official bodies such as the Brazilian National Health Surveillance Agency (ANVISA) and WHO, as well as scientific publications.[5,6]

Adjustments in clinics and private offices

Since asymptomatic individuals can transmit the virus, preparation of the clinical setting must be done carefully, considering every patient as a possible COVID-19 carrier.

The following measures are essential (Figure 1)[1,5,6,7]

70% alcohol gel: dispensers at the clinic's entrance and in all the rooms, allowing easy hand sanitization.

Social distancing: the clinic or office should be prepared to maintain a minimum distance of 1.5 to 2m between persons. Removing or blocking off seats, marks on the floor, and acrylic barriers are some options for implementing this measure.

Disposable masks: all patients should be instructed to appear for their appointments wearing masks. If a patient comes without a mask, one should be provided at the clinic's entrance and only removed when so requested by the physician.

Sanitization of the environment: staff should be trained in the clinic's correct sanitization and disinfection processes. The clinic should be cleaned at the beginning and end of the day. Shared areas such as restrooms and consultation and procedure rooms should be cleaned before and after use by each patient. Some methods and substances can be used, such as ultraviolet light, 70% alcohol, sodium hypochlorite solution, and commercial solutions containing these substances.

Recommendations for adaptation of clinics and private offices

1. Availability of 70% alcohol gel in all rooms.
2. Spacing of 2 meters between chairs in the waiting room.
3. Disposable masks available in case the patient is not wearing one.
4. Sanitization of the environment, furniture, objects with 70% alcohol or 1% sodium hypochlorite.
5. Remove shared items such as magazines, objects, folders.
6. Beverages and snacks offered in disposable containers.
7. "New" pens for each patient, to be sanitized at the end of the day.
8. Staff rotation. Maintain 2-meter distance between staff members.
9. Wrap credit card machine in cling film wrap and sanitize with 70% alcohol.
10. Whenever possible, keep the clinic ventilated with doors and windows open.
11. Signage on coughing and hand hygiene etiquette.
12. Signage in restrooms on hand hygiene.
13. Valet service: sanitization of all the objects handled, with 70% alcohol.
14. Optional: use of disposable foot coverings and temperature measurement.
15. Training for the entire staff in the safety protocol.

Figure 1: Adaption of clinics and private offices

Removal of shared materials: all material with shared use, such as magazines, newspapers, and pamphlets should be removed from the reception area. Beverages should be served in disposable containers. Pens should be discarded in a recipient for subsequent sanitization, and offered already sanitized.

Decrease the circulation of persons: encouraged by staff rotation, restriction of accompanying persons, and adjustments to appointment scheduling. The authors' suggestion is a minimum 40-minute interval between consultations, which can be longer in case of aesthetic and surgical procedures.

Ventilated and airy rooms: windows and doors should remain open to disperse suspended viral particles. Whenever possible, rotate consultation rooms to facilitate cleaning.

Signage: orientation on coughing etiquette, hand hygiene, and physical distancing.

Disposable foot coverings and temperature measurement: Before patients enter the clinic, their temperature can be taken and they can be offered disposable foot coverings.

Pre-consultation recommendations

It is essential to adopt clear and transparent communication between the clinic and the patient. With resumption of activities during COVID-19, this will facilitate triage of individuals who are fit to appear at the clinic. It will also create an atmosphere of trust, demonstrating the entire staff's concern in maintaining the clinic as safe as possible,[7] according to the flowchart of care in Figure 2.

Telemedicine should be promoted for medical consultations, definition of treatment protocols, and other clarifications.[1,7,8] This will help reduce patient flow, time in the clinic, and risk of infection on route.

If face-to-face consultation is necessary, the patient should answer a questionnaire in advance on risk situations and COVID-19 symptoms, described in Figure 3.[7,8] In case of any symptom, the appointment should be postponed by at least 20 days.

If the individual is fit for a face-to-face consultation, a second contact should be made a day in advance, investigating the appearance of COVID19 symptoms in the patient or family members. If no such symptoms are reported, the person should receive a text message or e-mail with safety instruction, as described in Figure 4.

For patients at high risk for complications of COVID-19, such as the elderly, immunocompromised individuals, and those

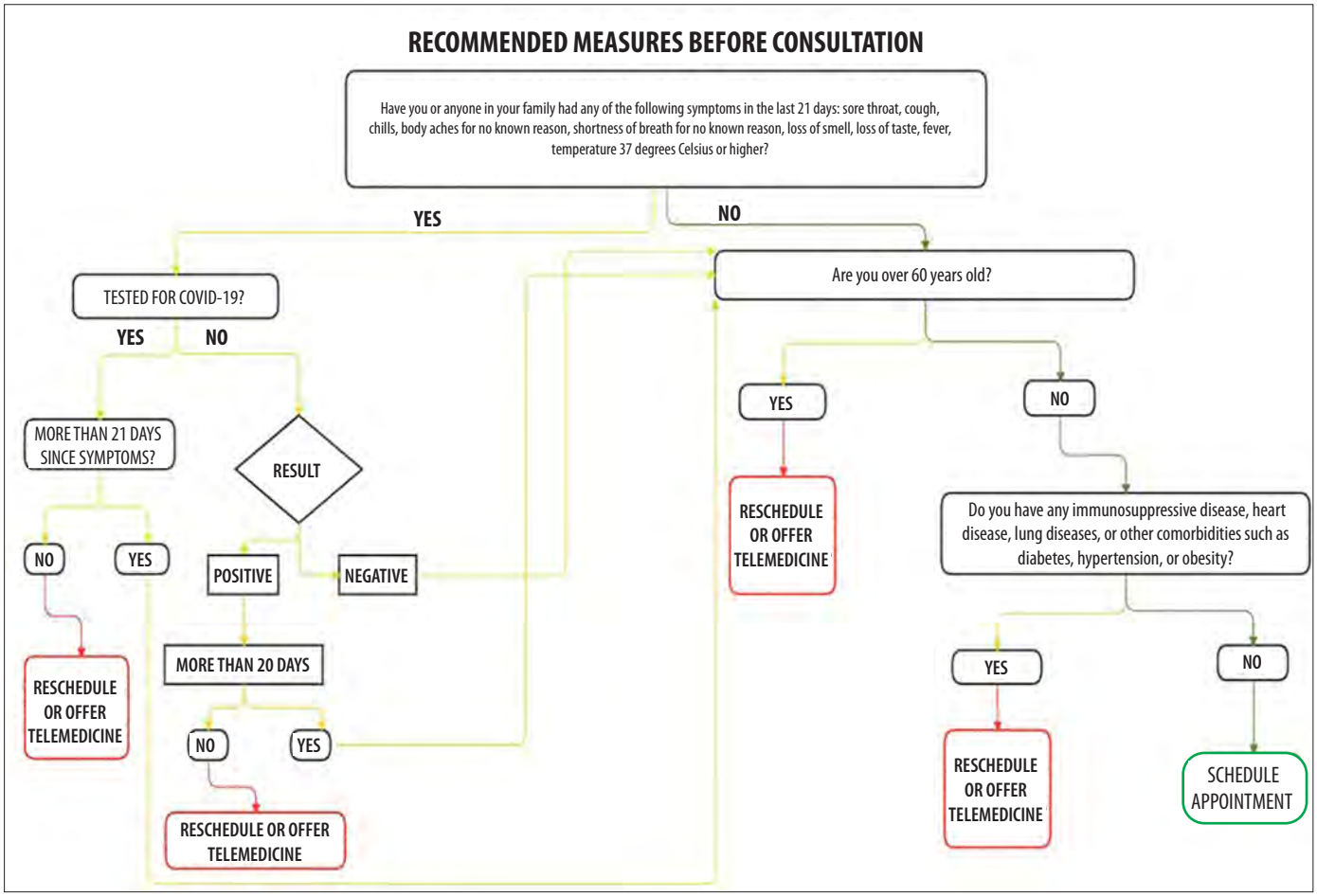

Figure 2: Flowchart of patient care during the COVID-19 pandemic

Patient's Name: Date:
COVID-19 QUESTIONNAIRE

PATIENT'S SYMPTOMS	YES	NO
1. Have you had any of the following symptoms in the last 14 days?		
• Fever	❑	❑
• Cough	❑	❑
• Shortness of breath	❑	❑
• Flu symptoms such as fatigue, nausea, diarrhea, chills, muscle pains, headache, sore throat	❑	❑
• Loss of smell and taste	❑	❑
• Red spots on skin	❑	❑
2. Have you been diagnosed or suspected of having coronavirus?		
• If yes, when?	❑	❑
3. Have you been tested for coronavirus?		
• If yes, when and with which method?	❑	❑
FAMILY MEMBERS AND CLOSE CONTACTS		
1. Has any family member gotten sick or had fever, cough, shortness of breath, or flu symptoms?		
2. Has any family member been diagnosed with COVID-19?		
• If yes, when?	❑	❑
RECENT TRAVEL		
1. Have you traveled recently? Inside Brazil or abroad?		
• If yes, when and where?	❑	❑
2. Has any family member traveled recently?		
• If yes, when and where?	❑	❑

OBSERVATIONS

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Figure 3: Health questionnaire

with cardiac or pulmonary diseases or other comorbidities such as diabetes, hypertension, or obesity, the postponement of non-essential procedures should be considered.[7]

Personal protective equipment

The Brazilian Society of Infectious Diseases recommends wearing a surgical mask while the professional is inside the office, clinic, or hospital, changing the mask regularly. The World Health Organization (WHO) recommends N95 masks. Cloth masks should not be used by health professionals, including physicians and clinical staff, and their use is only allowed for patients (Figure 5).[9]

During the physical examination or procedure, a disposable gown should be worn, changed after each patient. In situations involving proximity to the patient's face, the recommendation is to wear an N95 mask and protective goggles or face shield.[3] Gloves are only necessary during procedures.[3]

Recommendations during patient care

Whenever possible, the care should be performed with the windows open to optimize air circulation. The air conditioner may or may not remain on. While taking the patient history, the physician and patient should both be wearing masks.10

Figure 4: Pre-appointment instructions

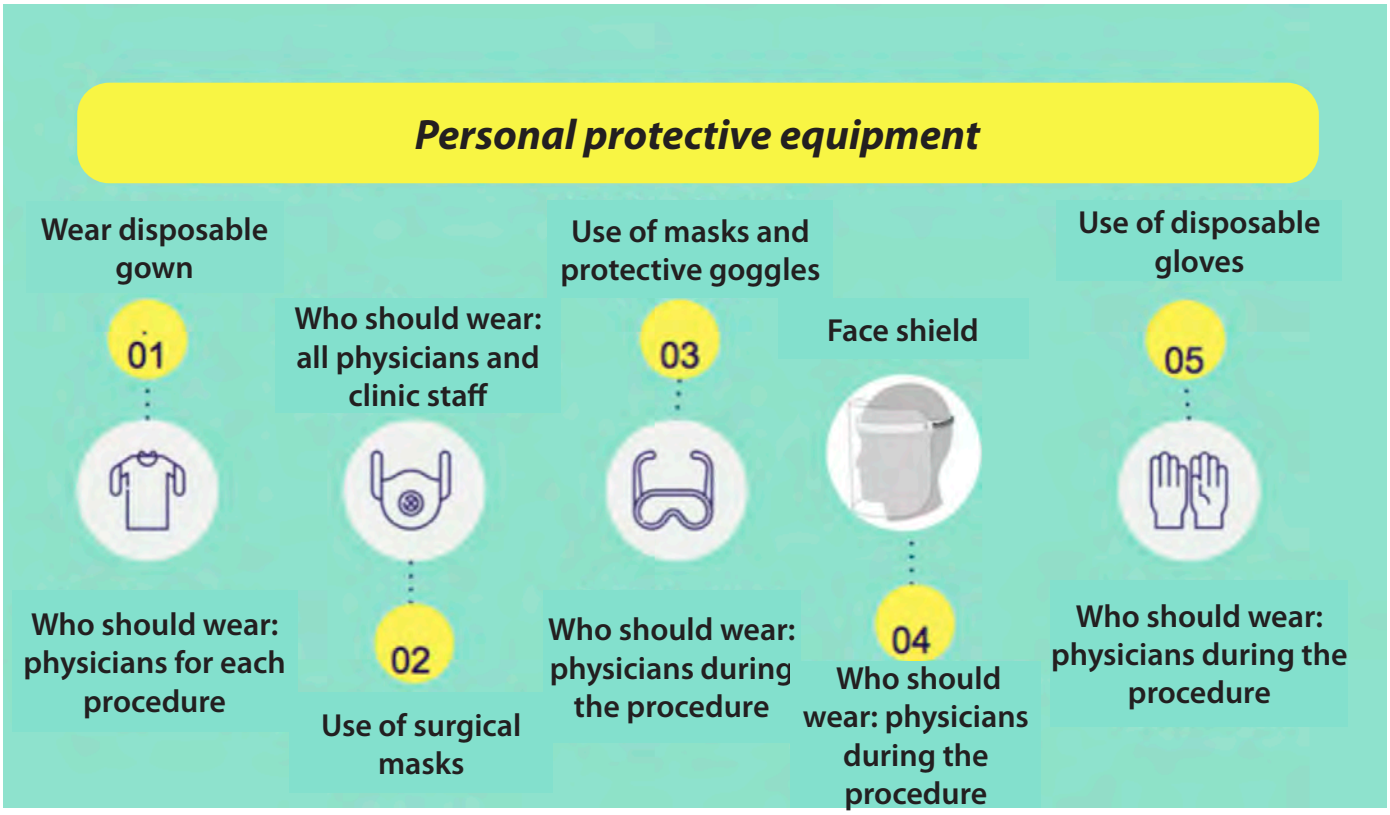

Figure 5: Personal protective equipment

Hand washing/sanitization is recommended before and after contact with the patient, and the face should not be touched with contaminated hands.

Hands should be washed with soap and water or cleaned with 70% alcohol, which are capable of dissolving the lipid membrane of the virus and inactivate it.[3,10,11] If soap and water are used, hands should be washed for approximately one minute. When 70% alcohol gel is used, the hand hygiene should last approximately 20 seconds.

The exam table should be covered with disposable sheets, which should be removed and discarded after use by each patient, always maintaining proper care to avoid self-contamination. All the equipment and instruments that may have been used in direct contact with the patient should be sanitized with 70% alcohol.[3,11]

During physical examination, the patient's mask may be removed to examine the face and oral mucosa.10 Since there is risk of transmission via droplets at this moment, we suggest the use of protective goggles or a face shield, besides an N95 surgical mask, to increase protection.[5,6,10] Figure 6 includes safety recommendations for specific dermatologic procedures.

After each consultation, all the surfaces touched by the patient or accompanying person should be sanitized with 70% alcohol or 1% sodium hypochlorite, including the exam table, chair, scale, sphygmomanometer, thermometer, etc. [3,10,11]

Laboratory tests

COVID-19 tests can be classified as follows:

Test for the virus: RT-PCR/COVID-19.

Antibody or serological tests: for detection of IgM, IgA, IgG, which can be performed by various methods, such as ELISA, chemo fluorescence, and immunofluorescence.

In medical practice, thus far there is no consensus on the testing protocol for COVID-19.[12]

A positive test is highly suggestive of COVID-19, while a negative test does not rule out the disease. Patients and health professionals should assume they have the disease if they have signs or symptoms, even if they test negative.13

Indication for COVID-19 testing should follow figures 7 and 8, while Figure 9 shows the lab tests' interpretation.

PROCEDURE	APPROACH
Anesthesia and analgesia	Apply topical anesthesia in the procedure room itself. Patient keeps mask on while waiting. If ice bags are used, discard or sanitize with 70% alcohol after use.
Photographs	Photos preferably taken in the procedure room itself. Photographer should wear an N95 mask and face shield.
Injectables	Recommended PPE: N95, protective goggles, gown, gloves, face shield. Vials and syringes prepared in advance. Patient should put mask back on immediately after the procedure.
Non-invasive physical procedures (cryolipolysis, radiofrequency)	Patient and professional wearing masks. Sanitize tape measures and equipment/instrument tips according to manufacturer's instructions. Use disposable or sanitized sheets and cushions.
Laser ablation on head and neck region	These are considered non-respiratory procedures that generate aerosol. The use of coolers increases the risk. PPE should include N95 and face shield. After the procedure, the room and equipment should be sanitized. The patient should wear a new mask, since the procedure with epidermal lesion increases the susceptibility to infections.
Other treatments (facial masks, peelings, non-ablative laser, micro-needling)	N95 + face shield. Reduce the number of professionals in the room. Pain control without coolers. New mask for the patient at the end of the procedure.

Figure 6: Safety recommendations for specific dermatologic procedures

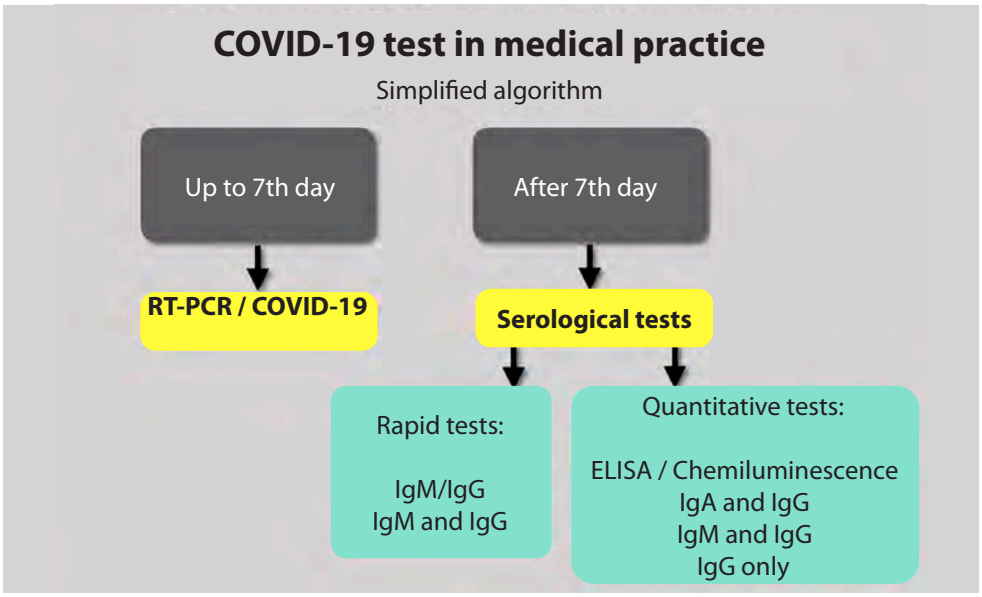

FIGURE 7: Indication for COVID-19 laboratory tests

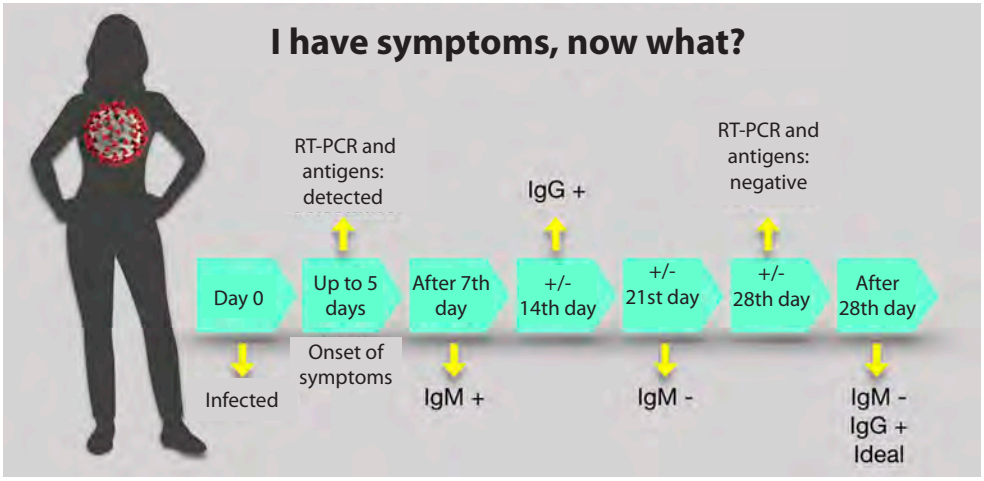

FIGURE 8: Indication for COVID-19 laboratory tests

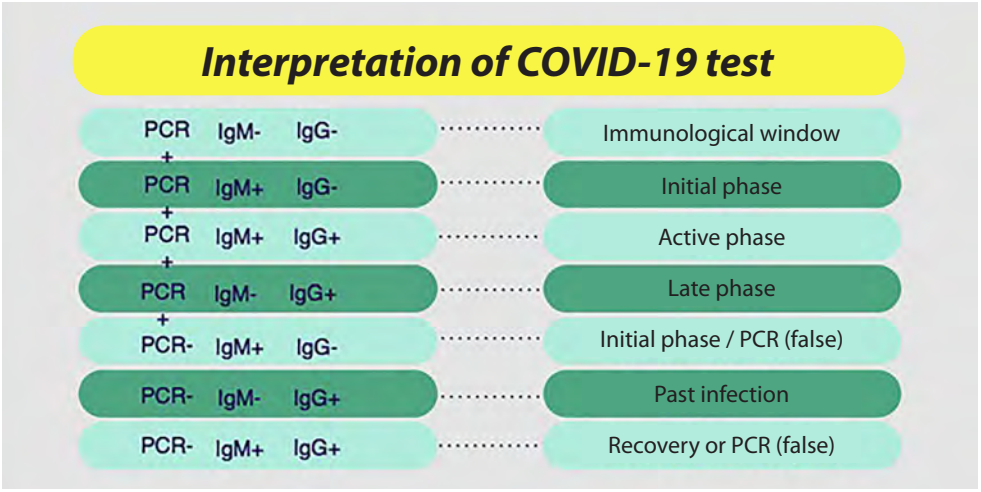

FIGURE 9: Interpretation of COVID-19 laboratory tests

CONCLUSION

The COVID-19 pandemic has raised unimaginable challenges.14-16 Constant discovery of new information means that health professionals face the additional challenge of keeping up-to-date with the best practices.

Adaptations must be made to mitigate risks and guarantee safety for the patient and all professionals involved. ●

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Eyebrow transplant with long hair FUE technique

Transplante de sobrancelha por meio da técnica FUE fio longo

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ABSTRACT

Hair transplant has become one of the most performed cosmetic procedures worldwide, and the follicular unit excision (FUE) method is progressively growing. FUE can be used to treat not only androgenic alopecia, but also eyebrows and beard area. For the eyebrow, follicular unit transplantation (FUT) is considered the gold standard for keeping the hair longer, facilitating the visualization of their direction during the implant. We describe a case of long hair FUE, where this technique was used without shaving the donor area, maintaining the length of the strands, and with no linear scar.

Keywords: Eyebrows; Hair Follicle; Transplantation

RESUMO

O transplante capilar é um procedimento cada vez mais realizado em todo o mundo, sendo que o método FUE (follicular unit excision) cresce progressivamente. O FUE vem sendo utilizado não apenas para a calvície androgenética, mas também para outras áreas, como sobrancelhas e barba. Na região das sobrancelhas, a FUT (follicular unit transplantation) é considerada padrão-ouro por manter os fios longos para visualização da sua direção durante a implantação. Descrevemos um caso de FUE fio longo, sendo que a técnica foi utilizada sem a necessidade de raspagem da área doadora, mantendo a altura dos fios, sem cicatriz linear.

Palavras-Chave: *Cabelo; Sobrancelhas; Transplante*

INTRODUCTION

Hair transplant (HT) is one of the most widely performed cosmetic procedures in the world. The follicular unit excision (FUE) method has been improved and can now be used to treat not only androgenic alopecia, but also other areas with rarified hair, such as the eyebrows and beard.

The gold standard for eyebrow HT is the follicular unit transplantation (FUT) technique.[1] A strip of the scalp is removed, and follicular units (FUs) are separated and dissected under the microscope. The option for FUT is due mainly to the lack of need to shave the hairs, and long hairs can be used. It is extremely important to determine their direction at the moment of implantation. The correct direction of the hairs is one of the essential factors for achieving a natural appearance. FUT is also quicker than FUE. The main disadvantage of FUT is the presence of a linear scar.

FUE has thus been used less in eyebrow HT, due not only to the prolonged surgical time, but also the need to shave the hairs for extraction from the donor area, making it impossible to see the follicles' direction for their correct implantation.[2]

How I do

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The development of devices that allow performing the long hair FUE method has allowed us to extract FUs without shaving the hair. We are thus able to graft long hairs without the need for a linear scar.

CASE REPORT

A patient came to our clinic with a complaint of a scar on his left eyebrow following a fall. He felt aesthetically bothered and asked about the possibility of HT to repair the area.

We opted for the FUE method, because the patient did not want a linear scar on his scalp. He wore his hair short, and a linear scar would be visible. In order for the hairs to have the minimum length to assess their direction, we chose long hair FUE as the best option.

We chose a strip approximately 10cm x 3cm on the left temporal region as the donor area, since it presented long, delicate, and definitive hair (Figure 1). We used the follicular extraction device called Mamba FUE device (Trivellini Tech, Paraguay), with the following parameters: "smart react" (with no need for a pedal; the punch triggers the preprogrammed movement after sensing the pressure difference), and the punch movement for each extraction is divided into 200ms oscillation (at 180 degrees), followed by 400ms of mamba movement (similar to divulsion), followed by 300ms more of oscillation (at 120 degrees). The punch we used was Trivellini Long Hair 0.95mm, developed to extract intact hair grafts without the need for shaving. The device is partially sharp and has grooves that protect the hairs, avoiding their being cut during extraction (Figures 2 and 3). Following local anesthesia, the extracted FUs (total of 86) were separated under the microscope into 44 single-hair FUs and 42 double-hair FUs, maintained in saline solution until the start of implantation. The excess length of each strand was cut with a no. 15 scalpel blade, leaving the strands 1cm long, thereby facilitating both the placement and visualization (Figure 4).

Following conclusion of the extraction and anesthesia of the eyebrow, the FUs were engrafted by the stick-and-place method (each incision followed immediately by placement) with a 21G needle bent int two places to guarantee sharp incisions (Figure 5). The direction of the incisions followed the direction of the hair follicles already at hand. Close attention must be paid not only to the angle and direction of the incisions, but also to the direction and curvature of the implanted hairs, in order to avoid disorderly growth.

The single-hair FUs were placed in the more external areas, and the double-hair FUs in the more internal areas. The patient was advised that since it was a scar area, it would not be possible to perform incisions too close together, or the grafts' viability could be compromised.

After engraftment, the area was cleaned and left without a dressing (Figure 6). The patient was instructed on proper hygiene of the area to avoid traumatic removal of the scabs, and was prescribed 2% topical minoxidil, in addition to Vaseline unguent after the third day.

The transplanted follicles fell out within 30 days, and the new hair began to grow in two months. At six months, the scar

Figure 1: Upper: Intraoperative marking of donor area. Lower: appearance of healing one year after surgery

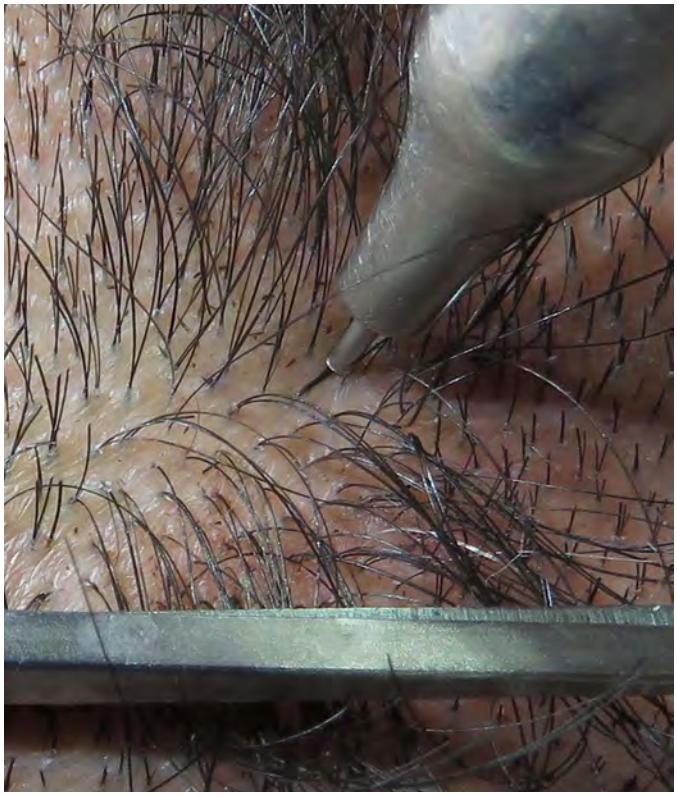

Figure 2: Extraction of grafts with long hair FUE method

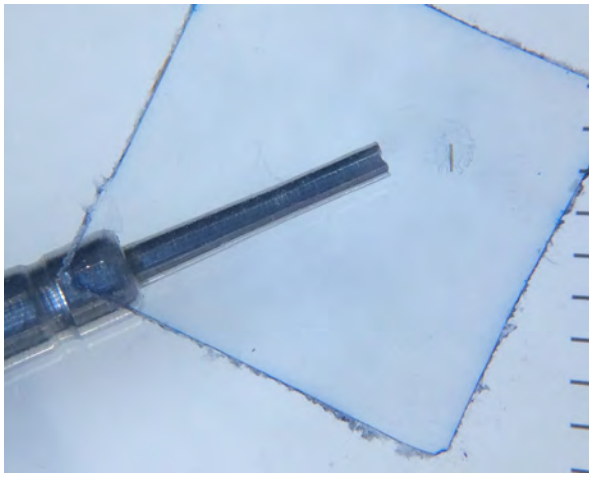

Figure 3: Close-up of 95mm long hair punch. Note the grooves which facilitate extraction of grafts without cutting the hairs

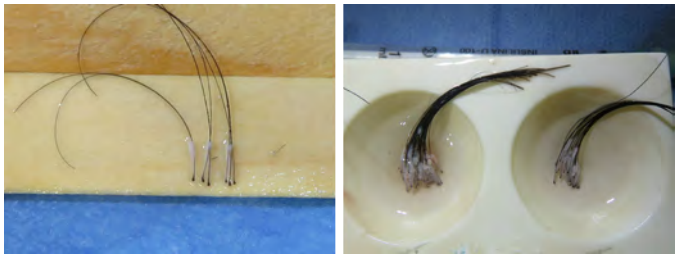

Figure 4: Follicular units following extraction

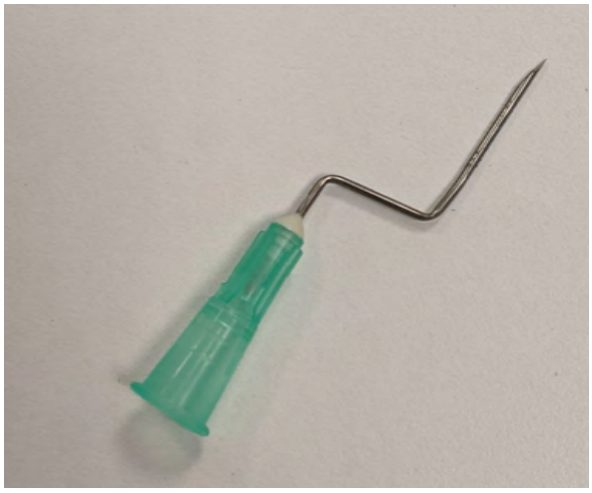

Figure 5: 21 G needle bent in two places to facilitate incision and placement by stick-and-place method at sharp angle

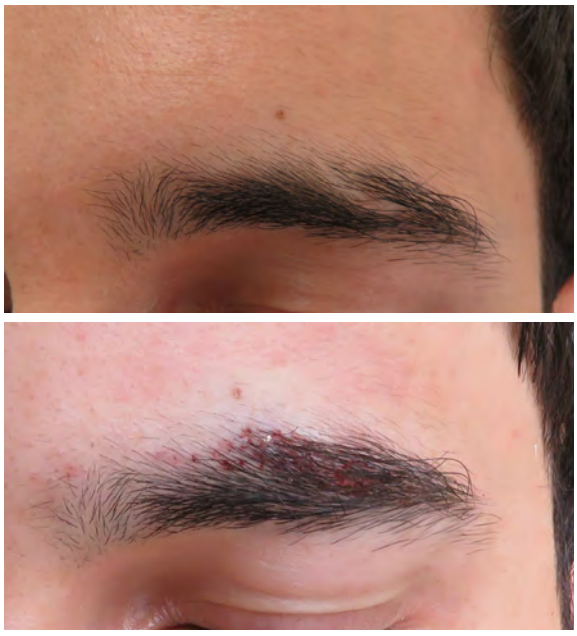

Figure 6: Pre and immediate postop

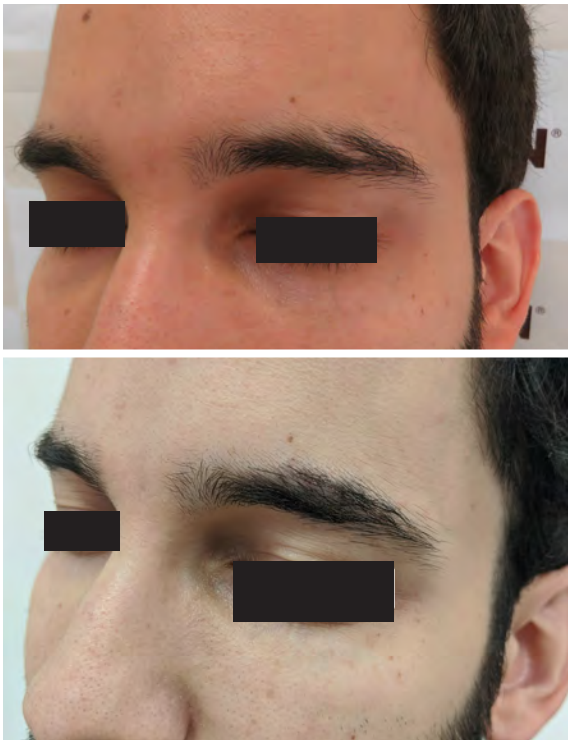

Figure 7: Preop and one year postop

was already covered. The patient was instructed on the need to trim the transplanted hairs routinely, since their anagen growth time is longer than the eyebrow's native hair. Patient returned a year later, satisfied with the outcome, and reported not seeing the punctiform scars in the donor area and not feeling the need for a second procedure to increase the hair density in the eyebrow area (Figure 7).

DISCUSSION

Eyebrow HT is an increasingly popular procedure in our dermatology practice.

The use of single or double-hair FUs, maintaining the follicle's length around 1cm, is essential for a natural-looking result. The single-hair FUs are used for the eyebrow contour to ensure a natural appearance, while the double-hair FUs are used

in the center for greater density.

The importance of maintaining minimal length of the hairs is due to the need for visualization of their angle, essential for ensuring that the hairs are grafted in the right direction.

In the FUT technique, a strip is removed from the donor region of the scalp (usually occipital or temporal), followed by suturing.[3] The strip's thickness and length depend on the amount of FUs needed and the local elasticity, attempting to avoid a wide scar. In the FUE technique, the FUs are removed one by one from a region where there is no risk of miniaturization. Punches are used with diameters less then 1mm. The microincisions heal by second intention, with no need for sutures. The FUE technique classically requires shaving the hair for extraction of the grafts.

Many authors consider FUT the gold standard for eyebrow HT.1 This is because the procedure allows extracting longer hair, and even leaving a linear scar, the latter is usually hidden by the patient's hair. However, recent years have witnessed a demand by patients themselves for the FUE method, influenced by the media and their own desire to avoid the sutures and linear scar.

The new technologies allow us to perform the FUE technique on eyebrows, but leaving hairs long enough to evaluate their direction and angulation.[4] This method, called long hair FUE, uses a specific, partially sharp punch with grooves that protect the hairs, avoiding cutting them during extraction. The main disadvantage is the technical difficulty and operating time, but the hairs are left with a minimal length to evaluate their direction and angulation, essential in eyebrow HT, avoiding the need for a linear scar.

In addition to ruling out inflammatory activity, it is important for the patient to be aware that in cases involving scars, the final density might not be satisfactory due to the impossibility of dense placement (since it was fibrotic scar tissue, with less blood supply). One characteristic of eyebrows is the implantation at sharp angles, strictly following the direction of the preexisting hairs.[4] The patient should be instructed to trim the new hairs, since their growth cycle is longer than that of the original eyebrows. We avoid surgeries in patients with curly hair in the donor area, because the transplanted hair follows the original pattern, which can compromise the natural appearance in such cases.

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Surgical options for pincer nail correction

Opções cirúrgicas para correção de unha em pinça

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ABSTRACT

Pincer nail is an acquired or hereditary nail deformity, which manifests as a transverse hypercurvature of the nail plate, especially in its distal portion, causing compression of the nail bed, which can provoke pain with functional disability, as well as secondary infections. Conservative treatment is associated with high recurrence rates, so surgical reconstruction is generally necessary. Four exemplary clinical cases of different corrective options of the pincer nail are described.

Keywords: Ambulatory surgical procedures; Nail diseases; Nails malformed

RESUMO

A unha em pinça é uma deformidade ungueal, hereditária ou adquirida, que se manifesta como uma hipercurvatura transversal do prato ungueal, sobretudo na sua porção distal, o que provoca uma compressão do leito ungueal, podendo causar dor com incapacidade funcional, assim como infecções secundárias. O tratamento conservador associa-se a uma elevada taxa de recorrência, motivo pelo qual a reconstrução cirúrgica é geralmente necessária. Descrevem-se quatro casos clínicos exemplares de diferentes opções corretivas da unha em pinça.

Palavras-Chave: *Doenças da unha; Cirurgia de ambulatório; Unhas malformadas*

INTRODUÇÃO

Pincer nail is characterized by a transverse over curvature of the nail plate, which causes compression of the nail bed, especially the distal portion, which can cause pain and secondary infection.[1] It is more common in the toes, especially the hallux, but it can also occur in the fingers. The etiology can be hereditary (especially with an autosomal recessive transmission pattern and symmetric involvement of the nails) or acquired (more frequently with an asymmetric topography and secondary to various etiologies, such as tight footwear, osteoarthrosis of the distal interphalangeal joint, psoriasis, subungual exostosis, onychomycosis, tumors of the ungual system, and even some drugs, such as betablockers.[2–4]

Conservative treatment rarely corrects the deformity completely and is associated with a high recurrence rate. Surgery is thus more useful for better long-term control.[5] Various surgical techniques have been described in the literature for correction of this nail deformity.

Case 1: Female patient, 45 years, with pincer nail of the right hallux, underwent corrective surgery with the Mutaf te-

Case Report

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chnique, consisting of avulsion of the nail plate, removal of the osteophyte on the dorsal surface of the phalanx and transverse broadening of the nail bed via modified Z-plasty applied to each of the lateral folds and the distal portion of the nail bed. Incisions performed up to the periosteal plane and posterior transposition of the nail bed flaps allow broadening and flattening of the distal nail bed (Figure 1).

Case 2: Female patient, 84 years, with pincer nail of the right hallux, underwent surgical correction with the Kosaka technique (W or zigzag). In this technique, after avulsion of the nail plate, a W-shaped incision is performed, 5mm below the hyponychium, extending deeply under the nail bed in a supraperiosteal parallel plane. The skin flap containing the nail bed is elevated, stretched in the transverse direction, and the excess skin from the lateral portions of the flap is removed. The dorsal surface of the phalanx is flattened. The flap is then sutured in a zigzag pattern, similar to a classical W-plasty (Figure 2). In addition to the hallux, the technique was also performed on another patient with pincer tail of the second toe, also successfully, showing the technique's versatility (Figure 3).

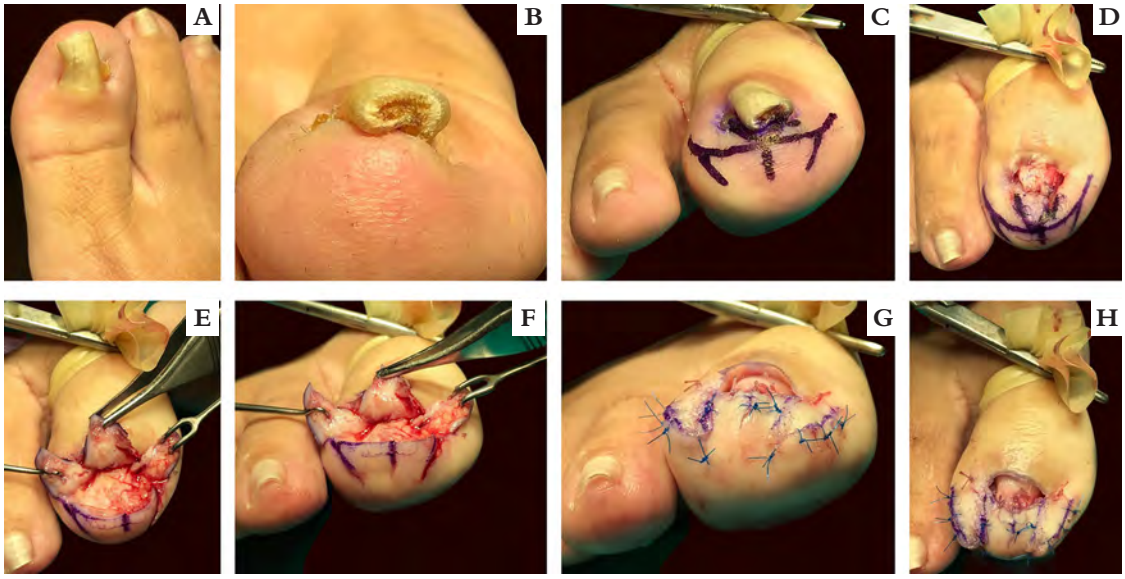

Figure 1: Surgical correction of pincer nail of right hallux **(a, b)** by Mutaf technique; **c)** planning flap, drawing modified Z-plasty on both lateral nail folds and distal portion of nail bed; **d)** Avulsion of nail plate; **e, f)** incisions performed to periosteal plane and then the nail bed flaps transposed, allowing exposure and excision of the subungual exostosis and broadening and flattening of distal nail bed; g, **h)** Closure of incisions with non-resorbable monofilament sutures.

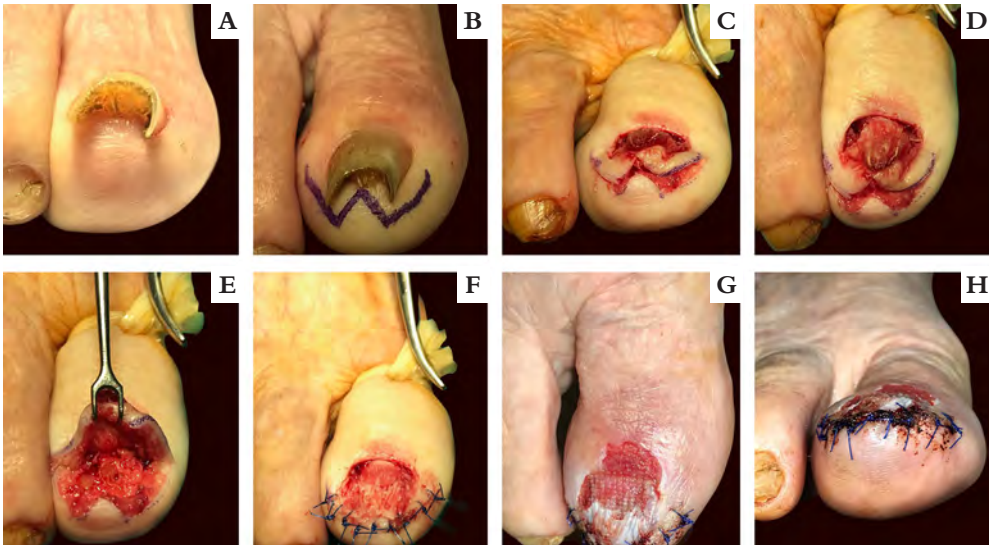

Figure 2: Surgical correction of pincer nail of right hallux **(a)** by Kosaka technique; **b)** planning flap, drawing W-plasty (or zigzag); c**, d)** following nail plate avulsion, W-shaped incision performed 5mm below hyponychium and extended in parallel supraperiosteal plane **; e)** skin flap containing nail bed is elevated, exposing and flattening the dorsal surface of the distal phalanx, stretched transversely, and excess skin from lateral portions of flap is removed; **f)** closure of flap in zigzag pattern with non-resorbable monofilament suture; **g, h)** Result on day 15 postop before removal of sutures

Case 3: Young female, 32 years, with pincer nail of left hallux, underwent Fanti surgical technique (Figure 4), consisting of nail plate avulsion and U-shaped incision around lateral and distal nail folds, plus longitudinal incision along the axis of the nail bed from the proximal to the distal fold. The nail bed is undermined in the supraperiosteal plane, elevating the two flaps to expose the nail bed, allowing removal of the dorsal osteophyte on the distal phalanx. The intervention is finalized by suturing the flaps over the new flattened nail bed.

Case 4: Female patient, 30 years, with pincer nail of the right hallux, causing severe pain and functional disability, treated with modified Zook technique, consisting of removal of the nail plate and flattening of the nail bed via skin grafts (harvested with a scalpel from the ipsilateral inguinal crease) in subcutaneous tunnel created along both lateral edges of the nail bed. Additionally, on one of the lateral folds, since there was a marked over curvature, we opted to combine with a fusiform excision without involving the matrix (modified Zook technique) (Figure 5).

All the procedures were performed under distal digital anesthetic block, and there were no immediate or late complications. Antibiotic prophylaxis was performed with a first-ge-

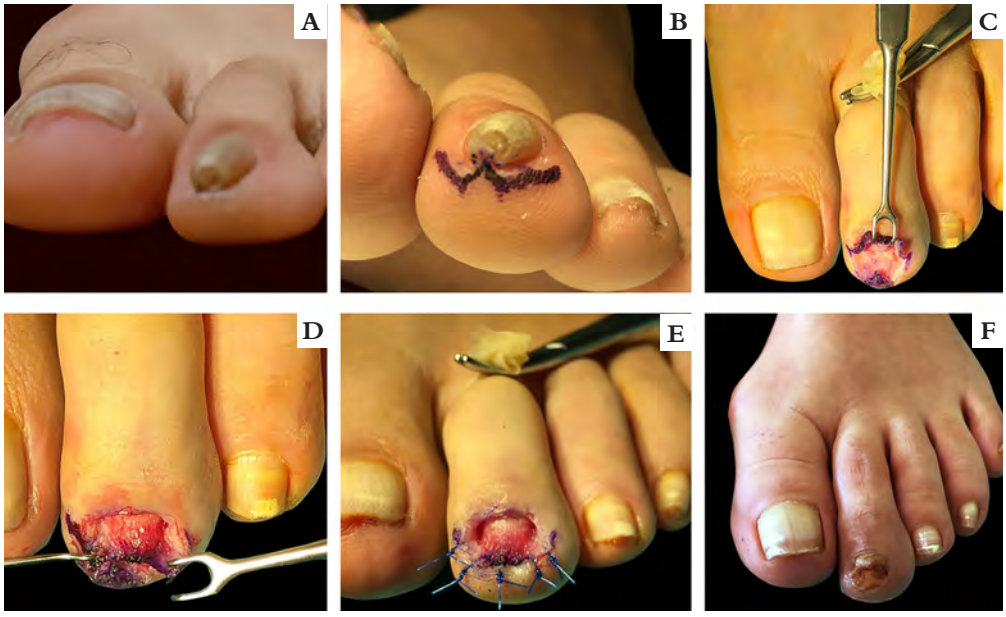

Figure 3: Kosaka technique (in W or zigzag), described in Figure 2, in surgical correction of pincer nail of 2nd left toe, also successful

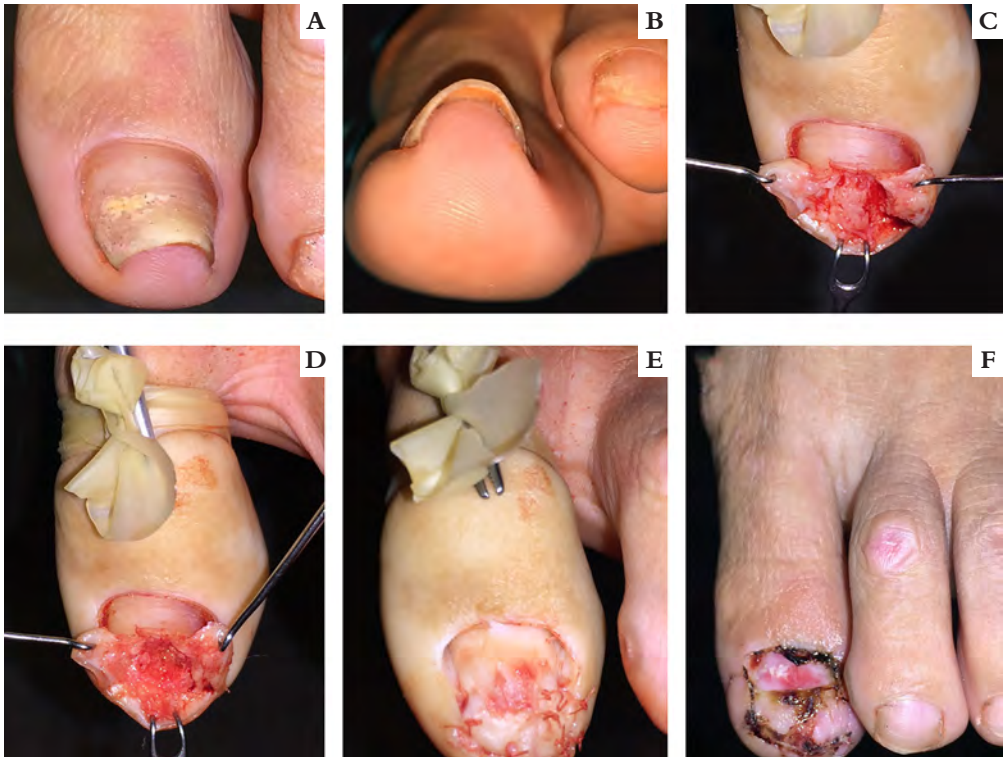

Figure 4: Surgical correction of pincer nail of left hallux **(a, b)** with Fanti technique. In this technique, besides nail plate avulsion, a U-shaped incision is performed around the lateral and distal folds, plus a longitudinal incision along the nail bed axis from the proximal to the distal fold; **c, d)** Undermining nail bed in supra-periosteal plane and elevation of the two flaps that expose the nail bed and allow removal of dorsal osteophyte on distal phalanx; **e)** suturing of flaps over nail bed, now flattened; **f)** postop result on day 15, when sutures were removed

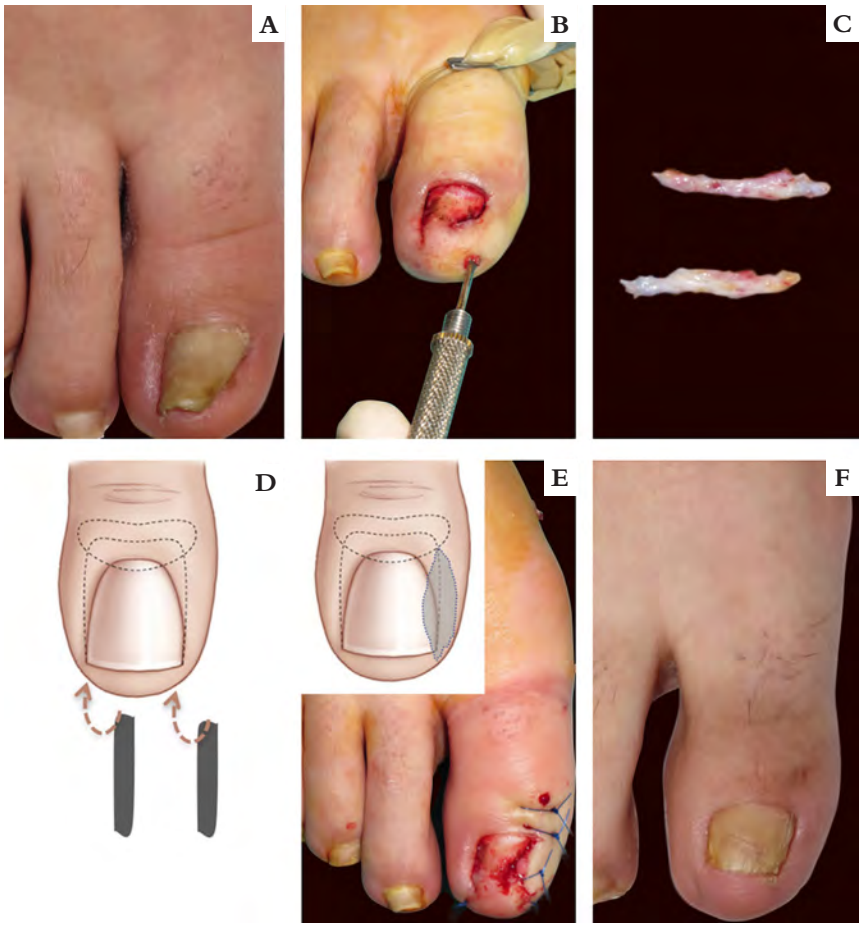

Figure 5: Surgical correction of pincer nail of the right hallux **(a)** with modified Zook technique; **b)** following nail plate avulsion, subcutaneous tunneling performed along lateral edges of the nail bed and harvesting of dermal grafts with scalpel from the ipsilateral inguinal crease **(c); d)** placement of harvested dermal grafts in subcutaneous tunnels, which allowed flattening of nail bed; **e)** additionally, on external lateral fold, due to marked over curvature, we opted to associate fusiform excision without involving the nail matrix (modified Zook technique); **f)** result at one year follow-up

neration cephalosporin in all the cases. Instructions to patients included rest and analgesia on the first days postop. The non--resorbable sutures were removed after seven to 15 days. The cosmetic and functional results were good in all the cases, with effective correction of the nail deformity.

DISCUSSION/CONCLUSION

Although conservative correction of pincer nail may be useful in mild cases, the high rates of treatment failure and relapse mean that surgical correction is the treatment of choice for this deformity, especially in serious cases with marked functional impact associated with inflammation and/or infection. Multiple corrective surgical techniques have been described, which can be classified as those that include destruction of the nail matrix and techniques that preserve it.

The main advantages of the techniques by Mutaf,[6] Kosaka,[7] and Fanti1 are preservation of the nail matrix, exposure and destruction of the subungual osteophyte when it exists, and flattening of the nail bed. Still, the technique's performance involves partial or total avulsion of the nail plate, which increases the complete recovery time. The Zook technique[8] does not require removal of the osteophyte, but it is technically more complex and requires the creation of secondary defects in the donor areas for dermal grafts.

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Case Report

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Squamous cell carcinoma of the lower lip: two cases of bilateral reconstruction with Gilles fan flap associated with zetaplasty

Carcinoma espinocelular do lábio inferior: dois casos de reconstrução bilateral com retalho de Gilles associado à zetaplastia

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ABSTRACT

Introduction: Squamous cell carcinoma (SCC) is the second most frequent malignant tumor of the epidermis. When located in the labial region, it can present a great challenge for the reconstruction, since it's located in the center of the inferior third of the face, causing scars and distortions that negatively affect the quality of life.

Objective and Methods: We report two cases of SCC in the lower lip reconstructed with Gilles fan flap associated with zetaplasty.

Results and Conclusions: In both cases, the result was satisfactory, with tumor resolution, absence of microstomia, preservation of the functionality, and good aesthetic acceptance.

Keywords: Carcinoma Squamous Cell; Case Reports; Lip; Surgical Flaps

RESUMO

Introdução: *O carcinoma espinocelular (CEC) é o segundo tumor maligno mais frequente da epiderme. Quando localizado na região labial, pode representar um grande desafio para a reconstrução, pois se localiza no centro do terço inferior da face, o que faz com que as cicatrizes e distorções labiais afetem negativamente a qualidade de vida de pessoas.*

Objetivos e Métodos*: Relatam-se dois casos de CEC em lábio inferior reconstruídos com retalho de Gilles associado à zetaplastia.*

Resultados e Conclusões*: Em ambos os casos, o resultado foi satisfatório, com resolução do tumor, ausência de microstomia, preservação da funcionalidade e boa aceitação estética.*

Palavras-chave: *Carcinoma de Células Escamosas; Lábio; Retalhos Cirúrgicos; Relatos de Casos*

INTRODUCTION

Squamous cell carcinoma (SCC) is the second most frequent malignant tumor of the epidermis. The tumor originates from atypical proliferation of cells in the squamous layer of the epidermis.[1] It is more frequent in individuals 50 years or older, photo types I and II, and in skin areas with photoaging. Oral SCC in particular is related to smoking and alcohol consumption. Early diagnosis decreases the odds of cervical lymph node metastases, which can occur in 5-20% of cases.[1,2] The lip defects pose a major challenge for reconstruction, since they are located at the center of the lower third of the face, and that the labial scars and deformations negatively affect the patient's' quality of life. Surgeons have studied numerous reconstruction techniques, aimed at good functional and aesthetic results.[3,4]

METHODS

Two patients with diagnosis of SCC of the lower lip were treated:

PATIENT 1: Male patient, 75 years, photo type III, from Londrina, Paraná State, Brazil, a farmer and construction worker, reported a painful lesion on the lower lip that appeared approximately seven months before. There was no report of local trauma or insect bite. The patient was previously healthy, with no history of smoking or alcohol use. Physical examination showed an ulcerated lesion, well-demarcated, with slightly elevated edges, on the lower lip. Palpation revealed infiltration of the tissues adjacent to the lesion (Figures 1a and 1b). Incisional biopsy was performed, revealing moderately differentiated SCC. For staging of the patient, palpation of cervical lymph nodes was negative, and ultrasound of the cervical region did not show enlarged lymph nodes suspected of metastases.

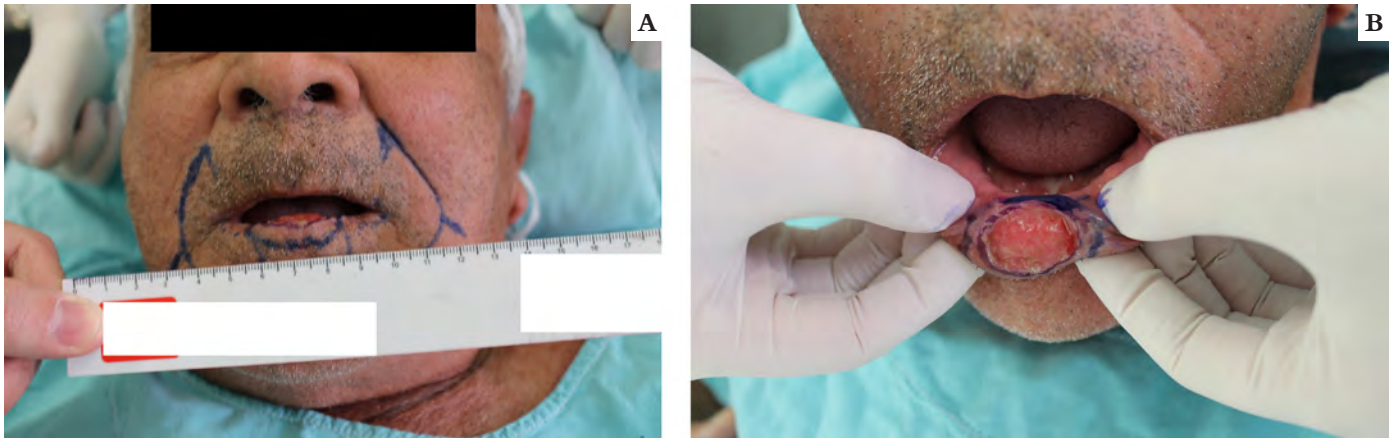

Figure 1: A) Anterior view of lesion; **B)** upper view of lesion

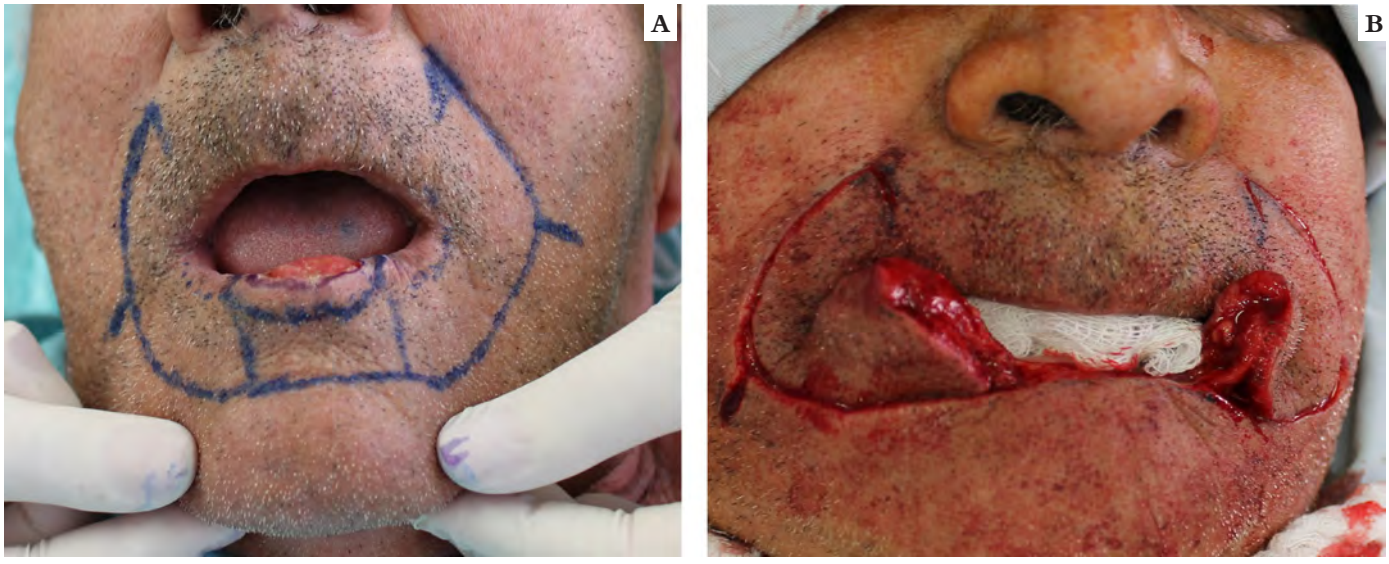

Figure 2: A) Marking of patient's skin; **B)** tumor excision with safety margins (5mm) and Gilles flap with zetaplasty

Following exams, excision of the lesion was performed with 5mm safety margins (Figure 2). Since the defect corresponded to more than 60% of the lower lip, the technique chosen for reconstruction was the Gilles fan flap with bilateral zetaplasty (Figures 2 and 3).

PATIENT 2: Male patient, 79 years, photo type III, from Jataizinho, Paraná State, Brazil, a nurse and administrative assistant in the local government, reported an ulcerated lesion on the lower lip for three months. No report of local trauma, but he suspected having been bitten by an insect. Patient presented a psychiatric disorder and was in follow-up with use of haloperidol, fluoxetine, and clonazepam. He was a former smoker with had a history of alcohol consumption.

Physical examination showed a poorly demarcated ulcerated lesion on the lower lip. Palpation revealed infiltration of the tissues adjacent to the lesion (Figure 5). Biopsy revealed poorly differentiated SCC. Palpation of cervical lymph nodes was negative, as was computerized tomography of the cervical region. Excision of the tumor was performed with 5mm safety margins. Since the defect also corresponded to more than 60% of the lower

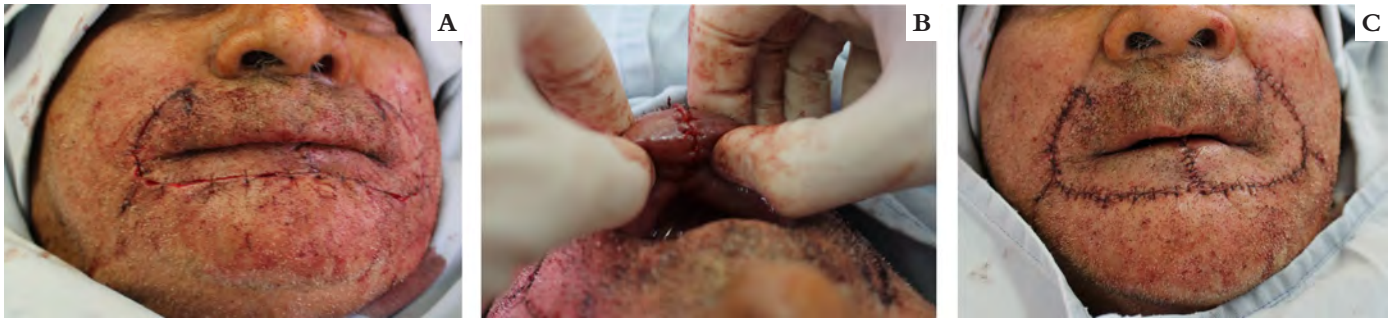

Figure 3: Intraoperative view: **a)** first sutures of flap; **b)** suture of oral mucosa; **c)** immediate postop

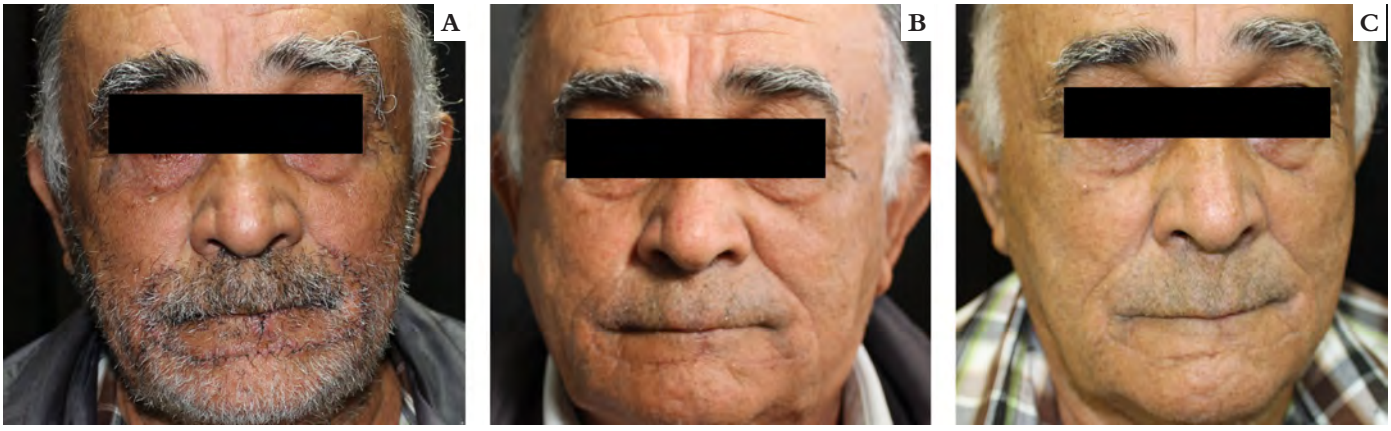

Figure 4: late postop: **a)** 7 days; **b)** 30 days; **c)** 9 months

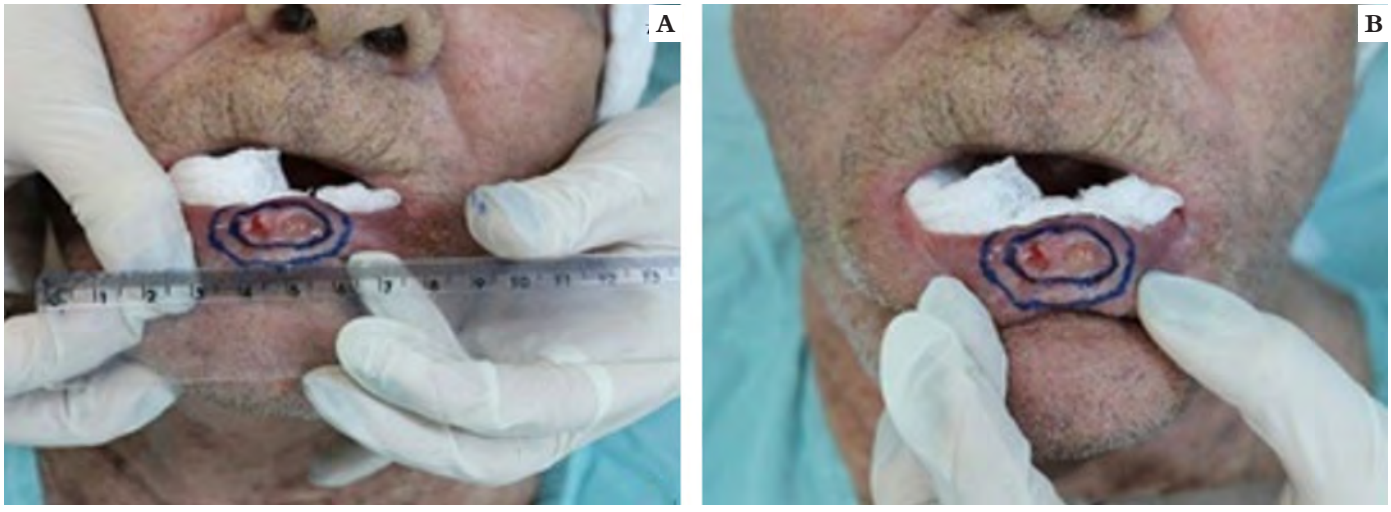

Figure 5: a) anterior view of lesion; **b)** upper view of lesion

lip, the chosen technique was the same as in the previous patient (Figures 6 and 7).

RESULTS

PATIENT 1: Histopathological examination of the surgical specimen showed well-differentiated SCC, without lymph vessel or perineural invasion and with free surgical margins. Patient evolved with good healing and satisfaction, without postoperative complications (Figures 4a, 4b, 4c).

PATIENT 2: Histopathological examination showed moderately differentiated SCC, ulcerated, with infiltration of reticular dermis, moderate lymphocyte infiltrate, without lymph vessel or perineural invasion and free surgical margins. Patient had no postoperative complications and reported good aesthetic satisfaction (Figures 8a, 8b, 8c).

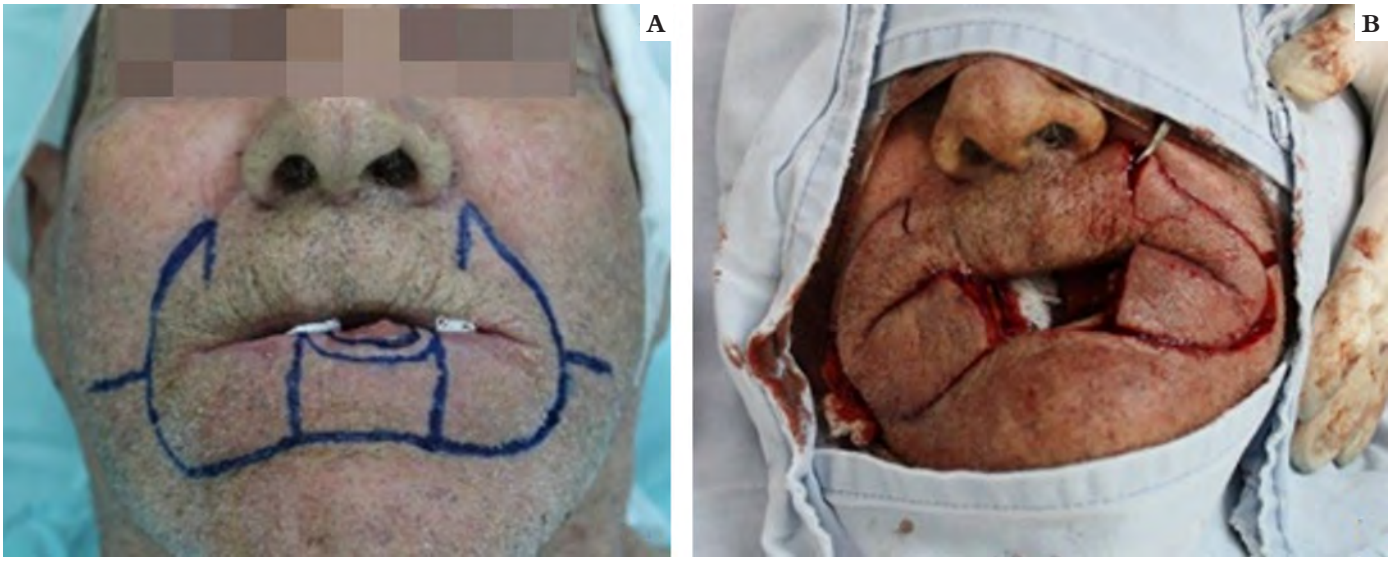

FIGURE 6: A) Marking of patient; **B)** excision of tumor with safety margins (5mm); Gilles flap with zetaplasty

FIGURE 7: Intraoperative view: **A)** flap sutures **B)** suture of oral mucosa; **C)** immediate postop

FIGURE 8: Late postop **A)** 7 days; **B)** 30 days; **C)** 6 months

DISCUSSION

Various techniques for reconstruction of the lower lip have been described in the literature and classified according to the size of the defect: small (up to 30%), medium (30-60%), or large (60% or more). Small defects can be reconstructed with primary closure following excision in V or W. Medium-sized defects can be reconstructed with elliptical excision, edge-to-edge suture, and M-plasty or flaps. However, larger defects need to be reconstructed with more complex techniques, such as Abbé and Estlander flap (repair of the lower lip defect with an upper lip flap), Gilles, or Karapandzic.[2]

The Gilles flap used in these two patients consists of projection of the lower lip commissure and lateral region to cover the defect left by the lesion on the lower lip, representing a full-thickness flap. To prevent microstomia, we associated zetaplasty with the flap.[2]

CONCLUSION

Many studies have indicated a decrease in survival of patients with cervical metastases, since there is a close relationship between tumor size and metastases. This highlights the need for early diagnosis and proper treatment to ensure the patient's cure.

Both cases showed satisfactory late postop results, tumor treatment with free margins, absence of microstomia, preservation of function, and good aesthetic acceptance, providing better quality of life for the patients. ●

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Recommendations to decrease exposure to the SARS-CoV-2 virus

Recomendações para diminuir a exposição ao vírus SARS-COV-2

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During the COVID-19 pandemic, it is vitally important for dermatologists to seek the best ways to treat their patients and at the same time guarantee safety for themselves, their staff, and of course their patients. It is thus essential to know the prevailing guidelines and the protocols for definition of clinical cases, in order to determine whether the care should be performed in person or by telemedicine, or even postponed.

In case of dermatologic surgery, the first step is to determine the nature of the procedure's urgency. However, in situations involving on-site care at the clinic or office, physicians and their staff should follow the guidelines for the appropriate use of personal protective equipment (PPE).

Important care for healthcare workers includes wearing masks and washing hands frequently with soap and water or sanitizing hands with alcohol. Hand sanitizing should be done before and after the procedure on the patient. An excellent tip is to read "My Five Moments for Hand Hygiene", by the World Health Organization (WHO). It is also recommended not to wear nail polish or jewelry below the elbows, such as rings and bracelets. To avoid contamination of the hair, the hair should be kept short or tied up so that it is completely covered by the surgical cap during the procedure. The office should be sanitized frequently due to the possibility of viral transmission by fomites. SARS-COV-2 is easily inactivated by adequate disinfection, that is, cleaning surfaces with sodium hypochlorite or 75% alcohol.

For patients, the current guidelines aim to reduce the risk of exposure, that is, to avoid contact between patients in the waiting room, allowing only one patient to enter at a time

or maintaining a distance of at least one meter between them. Patients should be encouraged to come to the office without accompanying persons and wearing a mask, as well as to wash their hands upon entering and exiting the clinic.

Except for dermatologic urgencies and cases in which a delay in the surgical procedure could increase the morbidity and mortality, patients that have tested positive for COVID-19 or those with symptoms consistent with the infection, such as fever, respiratory symptoms, myalgia, anosmia, chills, and others should have their procedure postponed by at least 14 days after the onset of symptoms. This recommendation also applies to healthcare workers and support staff, considering the unavailability of laboratory tests in some regions, as well as the tests' sensitivity.

The ideal care for patients is that the healthcare professional wears a N95 mask, and when patients present respiratory symptoms, the professional should be wearing a disposable gown and gloves as well as a plastic face shield or the equivalent. The N95 mask should not be worn for more than eight hours consecutively or five days intermittently. Rigorous care should be taken in cases of surgery involving the mouth and/or nose, due to the risk of presence of high viral load in the secretions; in such situations, a smoke evacuation device may be indicated.

Thus, far, blood does not appear to be a potential route for coronavirus transmission, but the use of electric scalpels may create aerosols of viral particles, consistently increasing the risk of contamination. Sterilization of the surgical instruments should comply with the standard techniques already adopted by the Brazilian Society of Dermatologic Surgery.

Finally, since COVID-19 is still a poorly understood disease without a known effective treatment, professional responsibility for patients in the field of dermatology should be based strictly on the technical knowledge of the guidelines for prevention and responsible orientation of patients that come to the office or clinic for dermatologic procedures. ●

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"We are worn out..." - A statement from a doctor working on the front line

"Estamos esfolados..." – Frase de uma médica que atua na linha de frente no combate à pandemia do coronavírus

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The multidisciplinary teams providing frontline care in the health services in the fight against COVID-19, and even those working a little farther back in the community as cleaning, public safety, and healthcare workers, among others, comprise a segment in which personal protective equipment (PPE) is used constantly and for prolonged periods. This use, plus frequent hand hygiene, has led to cases of irritative dermatitis due to breaks in the skin's integrity.

The mask's pressure on the face can lead to the formation of grooves that take days to disappear, excoriations on the skin from constant friction, erythematous areas that evolve to post-inflammatory hyperpigmentation, and palpebral edema adjacent to or underlying the areas under the PPE.

Observations on hands range from macerated appearance and brittle fingernails to effacement of the fingerprints due to severe eczema. Given the severe demands from this new scenario, many of these workers tolerate these problems and suffer (just a little more) in silent resilience, unaware of how to relieve this additional discomfort.

Several skincare measures can be included in the daily work routine to help minimize the signs and symptoms.

a) Skin creams containing retinoic acid or alpha-hydroxy acids, vitamin C, and exfoliators should be suspended temporarily to avoid thinning and drying of the facial skin. These can be replaced with products containing moisturizing and soothing agents, available on the market as serum, lotion, or cream according to each skin type.

b) Washing of the face upon returning home from work should follow the skin hygiene criteria with soaps, since this process is essential for eliminating the virus. Soaps should have a pH

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close to 5.0 during the bath or shower (which should not be too hot), followed by applying skin moisturizer.

c) Hair should be washed with shampoos containing surfactants from the sulphate group in the formula, for example, sodium sulphate lauryl ethyl and sodium sulphate lauryl, since they are more potent. Caution: "no poo" techniques, namely washing the hair without using shampoo (only with water), and "low poo", using shampoos without sulphate, may not be sufficient to completely eliminate the virus.

d) In the post-bath routine, it is extremely important to use body moisturizers to replenish the lipid mantle, with the skin still moist.

e) When the skin on the face and hands has become dry or cracked, use skin moisturizing creams. The best products are those with an oilier feeling, since they will not sting the injured skin.

f) On the face, apply a generous layer on the most affected area in gentle movements with the fingertips until the cream has been completely absorbed. Products aimed at the skin's restoration, containing dexpanthenol, copper, nicotinamide, zinc, and other soothing and regenerating ingredients can be applied immediately over the moisturizer.

g) Draining massages on more intact skin can be recommended, using one of the above-mentioned creams or simple, easily accessible oils (almond, mosqueta rose, coconut). Beside relieving the edema, they help give time for patients to heal themselves, attenuating the feeling of abandonment of their own image and self-esteem.

h) Facial hygiene on the morning after can be done with a "soap-free" or syndets skin cleanser, as long as there was no risk of contamination with the virus at home.

i) Some dressings can be applied to the area supporting the eyeglasses, goggles, and mask, serving as protection or buttress and protecting the skin during their use. Available on the market are self-adhesive hydrogel polyurethane silk film tapes. Micropore tapes may injure the skin more when they are removed.

j) On the hands, moisturizing gloves can be used for about 10-15 minutes a day using the same facial moisturizing cream (oily). In cases of eczema, associate topical corticoid during this procedure or immediately afterwards.

l) During the day, whenever possible, apply milder moisturizers with a drier touch and more rapid absorption. We hope these brief tips will help prevent and treat these skin problems which are so common in the frontline workers fighting the novel coronavirus pandemic. ●

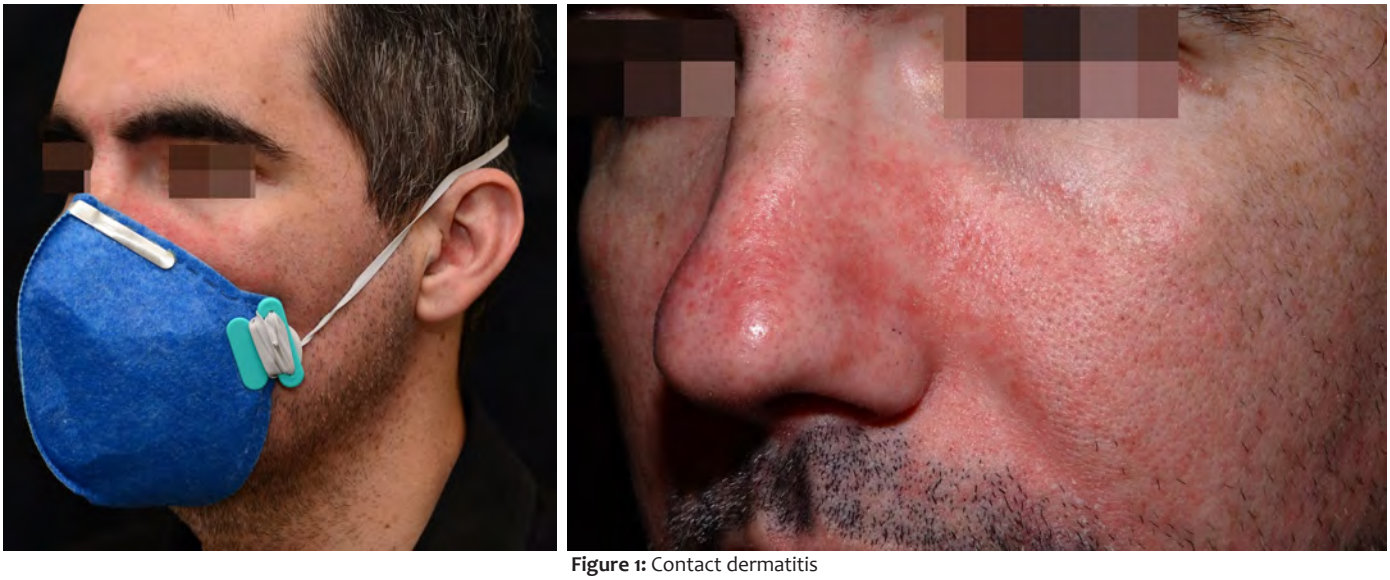

Figure 1: Contact dermatitis

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