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INSTRUÇÕES AOS AUTORES

A Surgical & Cosmetic Dermatology, editada em 2009, constitui publicação médica destinada a difundir conhecimento e experiência nas áreas de Cirurgia Dermatológica e Cosmiatria. É uma publicação trimestral da Sociedade Brasileira de Dermatologia 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 (www.icmje.org). Os manuscritos devem estar de acordo com os padrões editoriais para artigos submetidos a periódicos biomédicos estabelecidos na Convenção de Vancouver (Requisitos Uniformes para Manuscritos Submetidos a Revistas Biomédicas), regras para relatos de ensaios clínicos e revisões sistemáticas (metanálises).

Serão produzidos exemplares impressos da versão em língua portuguesa, com resumos e títulos em inglês. A versão da língua inglesa estará disponível no website da SBD.

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

As pesquisas em seres humanos devem ter a prévia aprovação de um Comitê de Ética em Pesquisa e obedecer aos padrões éticos da Declaração de Helsinki de 1975, revista em 2000.

ORIENTAÇÕES PARA O PREPARO DOS ARTIGOS

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 originais e redigidos no idioma de origem do autor (português, espanhol ou inglês): a equipe editorial providenciará as versões necessárias.

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, titulações máximas, instituições aos quais estão vinculados e local de realização do trabalho. Um deles deve ser designado como autor correspondente, com endereço completo, números de telefone comercial e fax e endereço de e-mail.

5- Os autores devem informar se houve conflitos de interesse e suporte financeiro.

6- As palavras-chave devem ser citadas em português e em inglês (Keywords), totalizando 3 a 10 por idioma, devendo ser incluídas em todos os tipos de artigos. Estas palavras deverão estar contidas no DeCS (Descritores em Ciências da Saúde) e/ou 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- Abreviaturas e acrônimos devem ser limitados aos de uso geral, não devendo constar no título ou no resumo.

9- 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.

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

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12- Após a sequência de itens para cada tipo de trabalho podem se acrescentados agradecimentos, antes das referências bibliográficas.

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13B. Capítulo de livro:

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14- Ilustrações (imagens, 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 curtas, porém suficientes para a compreensão ainda que o artigo não seja totalmente lido.

15- As imagens deverão ter resolução mínima de 300 DPI, largura mínima de 1.200 pixels com altura proporcional, e serem gravadas nos formatos JPG ou TIF. Podem ser colocadas setas ou linhas para localizar as áreas de interesse. As legendas das imagens histológicas devem especificar a coloração e o aumento.

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.

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

1- ARTIGO ORIGINAL

É o relato de uma pesquisa investigativa original clínico-cosmiátrica ou relacionada a procedimentos na área de Dermatologia. Exemplos: estudos experimentais, estudos clínicos, comparações e descrições de técnicas ou de métodos de avaliação, estudos de áreas afins (ex: estudos farmacêuticos em cosmiatria).

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.

O texto deverá conter até 4000 palavras, 10 ilustrações e 35 referências e seguir o formato IMRDC (Introdução e objetivo, Métodos, Resultados, Discussão, Conclusão)

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"). Esses 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 pesquisas futuras.

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

2- ARTIGOS DE REVISÃO

Poderão ser abordados temas cirúrgicos ou de cosmiatria, procedimentos, algoritmos , compilações, 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 (http://cochrane.bireme.br)

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Publicação de cunho educacional, abordando profunda e completamente grandes temas de Cirurgia Dermatológica, Cosmiatria ou Laser. Deve conter resumo não estruturado de até 100 palavras. Limite: texto até 4000 palavras, 10 ilustrações e 40 referências. Para evitar duplicações, os autores devem comunicar o tema aos editores antes de escrever o artigo.

Os autores são solicitados a definir objetivos educativos para o artigo que transmitam o que o participante deve ter absorvido após completar a atividade de EMC (ex: identificar uma condição, conhecer seus tratamentos, selecionar a melhor técnica). O entendimento destes objetivos devem ser mensurados por meio de 10 perguntas com respostas em 5 alternativas, cujo gabarito deve também ser enviado.

4 - RELATO DE CASO

Descrição de casos ou serie de casos de particular interesse nas áreas de Cirurgia Dermatológica, Oncologia Cutânea, Cosmiatria, Tratamento de dermatoses inestéticas, 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 10 referências.

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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 10 referências.

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Artigos originais, breves, abordando resultados preliminares de novos achados de interesse para a Cirurgia Dermatológica, Cosmiatria ou Oncologia cutânea entre outros. Texto com formatação livre. Resumo não estruturado de até 100 palavras. Limite: texto até 1200 palavras, 8 ilustrações e 10 referências.

7- DERMATOSCOPIA APLICADA

Uma a seis imagens dermatoscópicas aplicadas à cirurgia dermatológica e cosmiatria, acompanhadas de curta descrição. Resumo não estruturado de até 100 palavras, texto até 800 palavras, 5 ilustrações e 5 referências.

8- CARTAS

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

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Editorial

Surgical & Cosmetic Dermatology's editorial goal continues to be disseminating the findings of Brazil's dermatologic surgery and cosmetic dermatology specialities, as can be seen from the content of the current issue.

Such is the frequency and importance of some disorders that they constantly call for new studies. The recurrence of acne following treatment with isotretinoin and the quality of life in melasma were described in original investigation articles. Likewise, hypomelanosis – which for a long time had no clear etiopathogeny or recommended treatment – can now be treated with minocycline, as suggested by a double-blind randomized study.

Comparing the cutaneous responses to solar exposure of Caucasian and Asian women was the subject of an interesting study. In turn, an analysis of 493 cases revealed that 308 nm Excimer laser-based treatment of vitiligo is very promising.

A new mineral water from Serra do Japí, in the countryside of São Paulo State, Brazil, was the object of a comprehensive and well-conducted study that demonstrated important properties of human skin.

Among procedures that are considered minimally invasive, cutaneous filling techniques deserve great emphasis not only for the frequency with which they are now carried out, but also for the undesirable effects that may result. In this issue, there are two studies that focus on the safety of those techniques: the evaluation of radiological images produced by calcium hydroxyapatite and the use of delicate cannulas instead of needles to fill the lip area.

Two articles focused on surgeries in the upper lip. One reported on reconstruction after the removal of a large basal cell carcinoma, while the other described rejuvenating this area by the simultaneous exeresis of subnasal skin and dermabrasion.

CME and revision articles emphasized a complete and up-to-date understanding of micrographic surgery and palpebral hyperpigmentation, respectively. Successful treatments, such as the exeresis of large keloids in the earlobe combined with bleomycin injections, and the case report of a large scalp ulceration by a surgeon in the city of Luanda, Angola, were described.

In addition, the reader will find a report about treating earlobe clefts with trichloroacetic acid, which confirms the versatility of this caustic agent, and a study suggesting that dermatoscopy is a considerably effective technique for use in pregnant women with melanocytic lesions.

Good reading for all!

Dra. Bogdana Victoria Kadunc
Editor-in-Chief of Surgical & Cosmetic Dermatology

Original Article

Acne recurrence after treatment with oral isotretinoin: 5-year follow-up

Recidiva de acne após tratamento com isotretinoína oral: seguimento de cinco anos

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ABSTRACT

Introduction: Isotretinoin was initially used to treat severe inflammatory acne and is now widely recognized as an effective therapy for acne vulgaris. Many factors are associated with the recurrence of this condition, which ranges from 5.6-65.4%. There is much controversy regarding the importance and contribution of each factor.

Objectives: To determine the recurrence rate in patients who underwent full treatment with oral isotretinoin (dose between 120 and 150 mg/kg) and risk factors.

Methods: Retrospective study of data from 276 patients treated with isotretinoin. The analysis was carried out after a minimum of 30 months after the end of the treatment. Recurrence was defined as the appearance of new active lesions that required retreatment.

Results: While the recurrence rate in patients who underwent the full dose was 25.53%, it reached 81.03% in those who received an incomplete dose. The other studied factors presented no statistical significance.

Conclusion: Oral isotretinoin therapy is effective in producing a significant and long-term reduction of acne. Nevertheless, it is important to note that recurrence can occur, especially when recommended doses are not reached.

Keywords: acne vulgaris; isotretinoin; recurrence.

RESUMO

Introdução: *A isotretinoína foi inicialmente utilizada no tratamento da acne inflamatória grave, sendo atualmente bem reconhecida como tratamento de sucesso para acne vulgar. Muitos são os fatores associados com a recorrência da doença, que varia entre 5,6% e 65,4%. Há muita controvérsia sobre a importância e a contribuição de cada um desses fatores.* ***Objetivos:*** *Determinar a taxa de recidiva dos pacientes que receberam tratamento completo com isotretinoína oral (dose entre 120 e 150mg/kg) e fatores associados ao risco.*

Métodos: *Estudo retrospectivo a partir de dados de 276 pacientes tratados com isotretinoína. Após período mínimo de 30 meses a contar do término do tratamento realizou-se a análise. Considerou-se recidiva o surgimento de lesões ativas que necessitassem de retratamento.*

Resultados: *Houve 25,53% de recidiva nos pacientes que fizeram dose completa, e 81,03% nos que receberam dose incompleta. Os demais fatores estudados não demonstraram significância estatística.*

Conclusão: *A isotretinoína oral é tratamento efetivo em produzir redução significativa e de longa duração da acne. No entanto, deve ser reforçado o fato de que recidivas ocorrem com frequência significativa principalmente quando não se atingem as doses preconizadas.*

Palavras-chave: *acne vulgar; isotretinoína; recidiva.*

INTRODUCTION

Acne, one of the most prevalent dermatologic disorders [1], can affect patients' quality of life and cause relevant psychosocial impacts. Isotretinoin (13-cis-retinoic acid) was first used to treat serious inflammatory acne in Europe in 1976 and in the US in 1982. Its use transformed the therapeutics of serious and resistant acne, and it is now widely recognized as an effective treatment for acne vulgaris [2,4].

This retinoid is known to have many action mechanisms through connections to specific receptors. It reduces the size of the sebaceous glands and inhibits their activity and lipidic production; modulates epithelium proliferation and differentiation; decreases the proliferation of *Proprionibacterium acnes* in the hair follicles; and has other immunological and anti-inflammatory effects [4,6].

It is considered to be the most effective treatment for acne due to its capacity to induce complete and prolonged remission in all degrees of severity of the condition; recommended daily doses range between 0.5 and 2.0 mg/kg, with a total recommended dose between 120 and 150 mg/kg [7,8]. Nevertheless, notwithstanding fully completed treatments, recurrence is frequently seen in the literature and in daily practice. The condition reappears in 5.6% to 65.4% of cases; [2] this great variation relates to diverse factors and their interaction such as; daily average dose, cumulative dose, treatment duration, variations in patient characteristics (e.g., gender, age, degree and location). There is much controversy over the importance and contribution of each factor in the rates of recurrence [9].

METHODS

A retrospective study was conducted to determine the recurrence rate and potential risk factors linked to recurrence in patients who completed a treatment regimen of oral isotretinoin (accumulated dose of 120-150 mg/kg) in a public health service in Brazil (Instituto Lauro de Souza Lima/Bauru, SP, Brazil). The medical records of patients (n = 1,167) diagnosed with and treated for acne from 01/01/2005 to 31/12/2006 in a general dermatology outpatient clinic were analyzed. During that period, 276 patients used free isotretinoin supplied by the Brazilian Health Ministry s exceptional medications program. This study was carried out in compliance with the ethical rules of the Declaration of Helsinki.

More than half (n = 188) of the patients completed the treatment regimen, while 58 abandoned the treatment after at least 3 months of use. Patients were excluded from the analysis if they used the medication for less than 3 months or if they could not be contacted after the follow-up period.

Data was available on gender, age, severity, location, total dose of isotretinoin, and treatment duration. A treatment was considered to be complete at accumulated doses between 120 and 150 mg/kg. After a minimum of 30 months after the end of treatment, patients answered a telephone questionnaire about whether or not the acne reappeared and about their use of maintenance treatments and oral contraceptives during that period. Recurrence was defined as the emergence of active lesions that, in the patient's opinion, needed treatment.

The Chi-square Test and Fisher s Exact Test (5% significance level) were used in the statistical comparison between different factors and the recurrence event.

RESULTS

Of a total of 188 who completed the treatment, 145 (77.12%) were male and 43 were female (22.87%). The average of age at the beginning of the treatment was 18.1 (17.4 for men and 20.2 for women).

Regarding acne severity, 22 patients (11.7%) were diagnosed as Grade 2 (with papules and pustules), 146 (77.65%) as Grade 3 (with nodules and cysts) and 20 (10.63%) as Grade 4 (conglobata). Regarding location, 29 patients (15.42%) had lesions only on the face and 159 on the face and trunk (84.57%). No patients presented lesions only on the trunk. When studying the correlation between location and recurrence, we found that those with acne only on the face had a 13.79% rate of recurrence, while those with lesions on the face and back had a rate of recurrence of 27. 67% (Table 1).

The average duration of isotretinoin use was 8.6 months (range 4-15 months). Treatments lasting 4-8 months presented a 23.16% recurrence rate, while treatments lasting longer than 8 months had a recurrence rate of 27.96% (Table 2).

Of the 58 women who used isotretinoin, only 43 completed the treatment regimen and were included in the analysis. Of these, 17 continued using oral contraceptives after the end of the treatment. In this group, the recurrence rate was 29.41%, while among those that didn't use oral contraceptives after treatment the recurrence rate was 15.38% (Table 3).No use

Only 26 patients (13.82%) used topical treatments during the observation period. Of these, 11 presented recurrence (42.31%), while of the 162 who did not use such treatments, 37 experienced a reappearance of lesions (22.8%) (Table 4).

Among female and male patients, there were 9 (20.93%) and 39 (26.89%) cases of recurrence, respectively. After the

Table 1: Acne location X recurrence

	Recurrence	%	No recurrence	%	Total	%
Face	4	13,79	25	86,21	29	100
Face and back	44	27,67	115	72,33	159	100
Total	48	25,53	140	74,47	188	100

Table 2: Treatment duration X recurrence

	Recurrence	%	No recurrence	%	Total	%
4 to 8 months	22	23,26	73	76,84	95	100
More than 8 months	26	27,96	67	72,04	93	100
total	48	25,53	140	74,47	188	100

Table 3: Contraceptive use X recurrence

	Recurrence	%	No recurrence	%	Total	%
Use	5	29,41	12	70,59	17	100
No use	4	15,38	22	84,62	26	100
Total	9	20,93	34	79,07	43	100

Table 4: Use of topical treatments X recurrence

	Recurrence	%	No recurrence	%	Total	%
Use	11	42,31	15	57,69	26	100
No use	37	22,84	125	77,16	162	100
Total	48	25,53	140	74,47	188	100

Table 5: Recurrence with complete dose X recurrence with incomplete dose

	Recurrence	%	No recurrence	%	Total	%
Complete dose	48	25,53	140	74,47	188	100
Incomplete dose	47	81,03	11	18,97	58	100
Total	95	38,62	151	61,38	246	100

analysis of these variables regarding the presence of recurrence, none showed statistical significance.

On the other hand, when comparing the use of complete and incomplete doses of isotretinoin, there was a statistically significant difference regarding recurrence. Recurrence was verified in 48 patients (25.53%) who received a complete dose. Of the 58 patients who did not use a complete dose but used the medication for more than 3 months, 47 (81.03%) presented recurrence (Table 5).

DISCUSSION

During more than 30 years of isotretinoin use, many authors have found great variability in recurrence rates. That is due to differences in criteria for including patients in studies, in the definition of recurrence, in daily doses and, in particular, in the cumulative dose and in the duration of the follow-up period. Rates varying from 23.2% to 65.3% [10,12] illustrate this difficulty. In the present study, the recurrence rate after a complete treatment regimen was 25.53%.

Consistent with findings in the literature, the recurrence rate found in the present study for patients who had a total dose less than 120 mg/kg was 81.03%. This finding demonstrates that reaching the minimum recommended dose is the main factor linked to a long-term maintenance of the treatment effects.

The present study did not succeed in demonstrating significant correlations of individual factors (such as gender, age at the beginning of the treatment, acne severity and location of lesions) with the total risk of recurrence. There is no consensus in the literature regarding the location of the lesions; some authors have found more frequent recurrence in patients who presented lesions only on the face, while others found more frequent recurrence in patients with lesions on the back. Additionally, some authors found greater recurrence in women older than 25, while others found this trend in younger men [3]. Such findings can be due to differences in the studied populations.

It is inferred that the number of men who used isotretinoin in the study period was much greater than that of women due to the drug's teratogenic risks and the fact that many women can present significant improvement by using oral contraceptives. In addition, the average age at the beginning of treatment was 17.4 for men and 20.2 for women. This difference might be explained by the fact that the women tried other medications for longer due to the teratogenic risks.

Although the rate of recurrence was slightly greater in patients who took longer to reach the full dose, when they did so this fact was not statistically significant. Therefore, there seems to be no difference between reaching the full dose in a shorter period with higher daily doses and implementing gradual increases of the daily dose until the full dose is reached.

Contrary to the authors' expectations, the use of oral contraceptives following a completed treatment regimen did not reduce recurrence rates. Even when analyzing all female participants (both incomplete and full doses), there was no statistically significant difference regarding the use of oral contraceptives. This might be explained by the small size of the sample of women studied.

The high recurrence rate verified in patients who used topical medications after their treatment was complete (42.31%) compared to participants who did not use such substances (22.84%) suggests the existence of a bias, given that patients who begin to present new lesions are more likely to use topical medications. Furthermore, the number of topical medication users was very small. Even so, the variable for using topical medications after a successful outcome did not significantly affect the rate of recurrence.

CONCLUSION

Oral isotretinoin is an effective treatment that produces a relevant and long-lasting reduction of acne. Nevertheless, it is important to note that the condition frequently recurs, especially when recommended doses are not reached. ●

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Phototype comparison between caucasian and asian skin types

Comparação do fototipo entre caucasianos e orientais

Original Article

ABSTRACT

Introduction: Evaluating the response of various skin types to ultraviolet radiation exposure is very important in dermatology. The Fitzpatrick system is the most frequently used classification technique. It is straightforward and practical, assesses photodamage and skin cancer risks, and helps in defining light-based treatments. Nevertheless, there seem to be limitations to its use in non-Caucasians.

Objective: To compare the subjective phototype evaluation method to the Fitzpatrick classification in Caucasian and Asian (East and Southeast Asian, in particular) skin types.

Methods: Caucasian and Asian women (n = 42) were classified using 3 evaluation methods (clinical, Fitzpatrick and Modified Fitzpatrick). The data were collected through questionnaires and analyzed using non-parametric methods. A 5% significance level was adopted.

Results: There were no statistically significant differences within each group between the clinical evaluation, Fitzpatrick classification and the Modified Fitzpatrick classification (Caucasian cr2 = 0.375, p = 0.93 and Asians cr2 = 3.5, p = 0.182).

Conclusion: The three methods evaluate phototypes equally, yet studies with larger population samples are still necessary.

Keywords: skin; skin pigmentation; photobiology.

RESUMO

Introdução: *A avaliação da resposta cutânea à exposição à radiação ultravioleta tem grande importância na prática dermatológica. De uma variedade de métodos, a classificação dos fototipos de pele de Fitzpatrick é a mais utilizada. Simples e prática, permite avaliar o risco de fotodano e câncer de pele, além de auxiliar na definição dos tratamentos com luz. Apesar disso, parece haver considerações em relação aos não caucasianos.*

Objetivo: *Comparar a avaliação subjetiva do fototipo com a classificação de Fitzpatrick em pacientes caucasianas e orientais.*

Métodos: *Quarenta e duas mulheres caucasianas e orientais foram classificadas de acordo com três métodos de avaliação (clínico, Fitzpatrick e Fitzpatrick modificado). Os dados foram coletados através de questionário e analisados por métodos não paramétricos.*

Resultados: *Na comparação entre a avaliação médica, e as classificações de Fitzpatrick e Fitzpatrick modificada não houve diferença estatisticamente significativa dentro de cada grupo.*

Conclusões: *Com base nesses resultados, pode-se concluir que os três métodos são equivalentes na avaliação do fototipo. Estudos com amostra populacional maior ainda serão necessários.*

Palavras-chave: *pele; pigmentação da pele; fotobiologia.*

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INTRODUCTION

Many patients of Asian descent seek dermatological care. Knowledge about the skin type, anatomy, physiology and unique aspects of Asian ethnicities allows for better decision making and treatment planning for these patients.

The Fitzpatrick classification is widely used to determine a patient's skin type. While Asian patients are usually considered to be phototypes IV and V, that classification has been questioned by some authors.[1,2] Therefore this study compares the subjective assessment of phototypes using the Fitzpatrick classification in Caucasian and Asian patients.

Table 1 - Fitzpatrick phototype scale

Phototype	Characteristics	Sensitivity to the sun
I – White	Always burns, never tans	Very sensitive
II – White	Easily burns, tans poorly	Sensitive
III – Light brown	Burns moderately, tans moderately	Normal
IV – Moderate brown	Burns somewhat, tans easily	Normal
V – Dark brown	Rarely burns, tans considerably	Somewhat sensitive
VI – Black	Never burns, totally pigmented	Insensitive

METHODS

This study consisted of a transversal analysis carried out through data collection and interviews. All methodological criteria complied with the current terms and rules for research in human beings – Resolution 196/96 of the Brazilian National Health Council and the most recent version of the Declaration of Helsinki. The study was also approved by the Research in Human Beings Ethics Committee of the hospital where it was carried out.

Caucasian women were recruited at the dermatology outpatient clinic of the hospital where the study took place, and Asian women (of Japanese, Chinese or Korean descent) were randomly recruited at an Asian community event in Curitiba (SP, Brazil). All study participants were classified using three assessment methods (clinical, Fitzpatrick classification and Modified Fitzpatrick classification).

All participants answered a questionnaire about maternal descent, paternal descent, their personal features (eye color, natural hair color, color of the skin in areas without exposure to the sun, presence of freckles in exposed areas, skin sensitivity to the sun and degree of tan grade). A dermatologist physician from the study hospital and a medical scholar evaluated patients' phototypes using the subjective classification method. The phototypes were also classified according to the Fitzpatrick (Table 1) and Modified Fitzpatrick (Table 2) classifications based on the data supplied in the questionnaires, which were answered without the researchers' involvement.

The data collected from the questionnaires were input into an Excel spreadsheet and analyzed using the Friedman test. A 5% significance level was adopted.

Table 2 - Modified Fitzpatrick phototype scale

PHOTOTYPE SUM OF THE POINTS FROM THE TABLE BELOW	I 0-7	II 8-16	III 17-25	IV 26-30	V or VI >30
Points	**0**	**1**	**2**	**3**	**4**
Eye color	Light blue or gray	Blue or green	Amber, light chestnut brown	Dark chestnut brown	Dark brown
Natural hair color	Red, reddish	Blond	Dark blond, chestnut brown	Light brown, dark brown	Black
Skin color (areas without exposure to the sun)	Reddish	Very pale	Pale, beige	Light brown	Dark brown
Prolonged exposure to the sun	Redness, painful blisters and desquamation	Blisters followed by desquamation	Burns, sometimes desquamates	Sometimes burns intensively	Never burns
Tanning degree	None or almost none	Light tan	Reasonably tan	Tans very easily	Darkens quickly
Tan after several hours of exposure to the sun	Never	Rarely	Sometimes	Usually	Always
Sensitivity of the face to the sun	Very sensitive	Sensitive	Normal	Very resistant	Never had problems
Last exposure (sun, tanning equipment or tanning creams)	More than 3 months ago	From 2 to 3 months ago	From 1 to 2 months ago	Less than 1 month ago	Less than 2 weeks ago
Frequency of exposure to the sun in the treated area	Never	Rarely	Sometimes	Usually	Always

RESULTS

Female patients (n = 48, 18 Asian and 30 non-Asian) were analyzed. Of the Asian patients, 15 had both maternal and paternal Japanese ancestry, and three had paternal Japanese ancestry only. The average age was 29 (range 22-38). In the non-Asian group, patients' ancestry varied between French, German, Italian, Brazilian native Indians, Polish and Portuguese, with an average age of 36 (range 22-63).

There was no significant statistical difference within each group between the medical evaluation and the Fitzpatrick and Modified Fitzpatrick classifications when analyzed using the Friedman test. Caucasian cr 2 = 0.375, p = 0.93 (Table 3 and Figure 1) and Asian cr 2 = 3.5, p = 0.182 (Table 4 and Figure 2).

DISCUSSION

Few studies on the dermatological implications of ethnic differences have been published in the indexed literature. Most published papers compare Caucasian and black populations. Although Asians constitute a huge portion of the world's population, studies about Asian individuals are rare except in medical journals published in Asia.

Since Brazil has one of the largest Asian-descended populations in the world, there is a significant number of medical consultations with that population. Moreover, with migration and intermarriage, it is increasingly common to find traces of several races in the same individual. For that reason – not only in dermatology but also in other medical specialties – a broad understanding of each ethnic group's unique aspects is important to improve patient treatment.

Evaluating the skin's response to ultraviolet radiation exposure is very important in dermatology, especially in photodermatosis, phototherapy, photoaging, photocarcinogenesis and photoprotection. It is also very useful when planning procedures such as surgery, laser therapy, peelings and dermabrasion.

Table 3 - Classification of Caucasian prototypes

Classification	Phototype evaluation		Fitzpatrick		Modified Fitspatriick	
	#	%	#	%	#	%
II	11	36,7	10	33,3	9	30
III	12	40	15	50	13	43,3
IV	6	20	5	16,7	8	26,7
V	1	3,3	0	0	0	0
Total	**30**	**100**	**30**	**100**	**30**	**100**

Table 4 - Classification of Asian phototypes

Classification	Phototype evaluation		Fitzpatrick		Modified Fitzpatrick	
	#	%	#	%	#	%
I	0	0	0	0	1	5,56
II	5	27,8	0	0	3	16,7
III	8	44,4	9	50	4	22,2
IV	4	22,2	7	38,9	6	33,3
V	1	5,6	2	11,1	4	22,22
Total	**18**	**100**	**18**	**100**	**18**	**100**

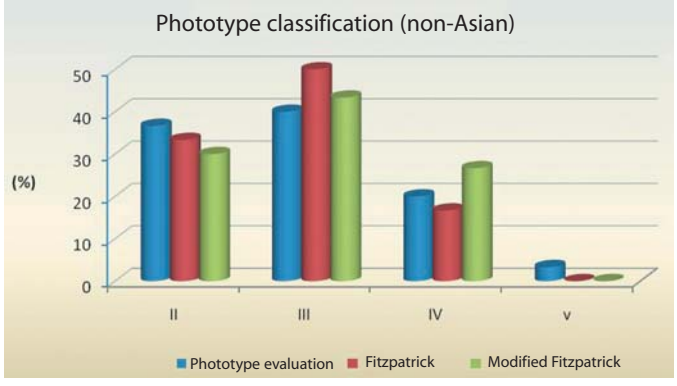

Figure 1 - Distribution of phototype proportions among Caucasians

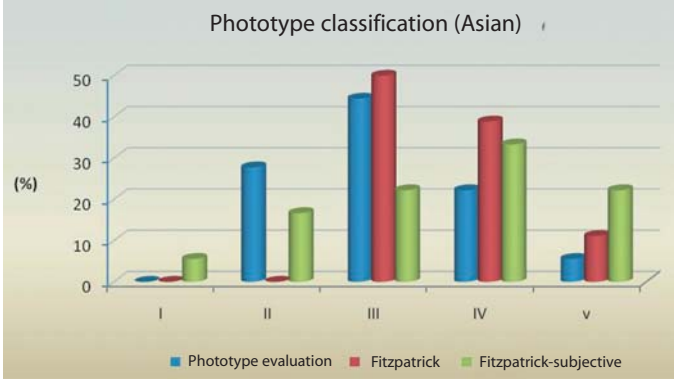

Figure 2 - Distribution of phototype proportions among Asians

Classifying the skin by phototype is the most frequently used method because it is simple, straightforward and practical.

The classification of skin phototypes developed by Fitzpatrick in 1975 assesses the skin's sensitivity to ultraviolet radiation, in the context of an individual's tendency to burn or tan. It is a subjective evaluation based on answers to patient-administered questionnaires. Classifying the skin into six types allows an assessment of the risks of photodamage and skin cancer, and helps plan phototherapy treatments by estimating the correct UV dose to minimize erythema and define the parameters of light-based treatments.[2-4]

The phototype category might not be the most effective evaluation of photosensitivity; this can be better estimated by determining the minimum dose of UV radiation that causes erythema, according to Wee and colleagues [2], who also suggest that genetics and environmental influence can affect that determination. Studies by Satoh and Kawada showed different responses from Japanese and Caucasian skin to ultraviolet radiation, and proposed the Japanese Skin Type assessment method.[1,4,5] Other authors demonstrated that UVB radiation is more erythemogenic than melanogenic in mongoloids.[6]

Although no statistical difference was observed among the three methods, the phototypes of Asian patients ranged from II to V, according to the assessment method used in this study. It was also verified that the physician's subjective evaluation can diverge from the questionnaires on the skin's reaction to sun exposure. In the Caucasian population, the medical evaluations correlated more closely with the other methods.

CONCLUSION

In light of these results, a more detailed individual analysis should be made of Asian skin characteristics and reaction to ultraviolet exposure, when in preparation for aesthetic procedures and phototherapy. More studies and a larger sample population are necessary to more broadly confirm those results. ●

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Original Article

Biochemical and toxicological assessment of a Brazilian mineral water and its effects on the skin

Avaliação bioquímica e toxicológica de uma água mineral brasileira e seus efeitos cutâneos em uso tópico

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ABSTRACT

Introduction: The French cosmetics industry sells spring mineral waters that are advertised as having biological benefits.

Objective: This study analyzes, in vitro and in vivo, a Brazilian mineral water's oligominerals composition, as well as its physical and chemical characteristics and biological effects.

Methods: Tests to evaluate physical chemical properties, cytotoxicity (viable cells) and irritability (het-cam test) were conducted. In vitro studies were performed to evaluate its capacity to induce the genic expression and immunohistochemical detection of filaggrin and aquaporin 3, nf-kb activity and fibroblast proliferation compared to Milli Q water.

Results: This water was found to be non-cytotoxic and non-irritating. In addition, it presented a high content of strontium (0.61 mg/ml). The expression of filaggrin and its immunohistochemical tests were relevant. The aquaporin 3 increased 1.8 times and nf-kb decreased its activity by 47%. It was also capable of stimulating fibroblast proliferation.

Conclusion: The initial evaluation of the mineral water from Serra do Japi (SP, Brazil) indicates that it has the potential to be an adjuvant treatment in dermatology, since the results suggest it moisturizes the skin barrier, stimulates the proliferation of fibroblasts, and repairs and inhibits inflammatory reactions. Clinical studies should be done in order to reassure the in vitro results achieved on the present study.

Keywords: mineral waters; Brazil; cosmetics.

RESUMO

Introdução: *A indústria de cosméticos francesa comercializa águas minerais como tendo benefícios biológicos.*

Objetivo: *O presente estudo analisa, in vitro e in vivo, a composição oligomineral, assim como as características físico-químicas e efeitos biológicos de uma água mineral brasileira.*

Métodos: *Foram conduzidos testes para avaliar as propriedades químicas, a citotoxidade (células viáveis) e a irritabilidade (teste het-cam). Estudos in vitro foram realizados para avaliar a capacidade de indução de expressão gênica e de detecção imunohistogênica de filagrina e aquaporina 3, de atividade de nf-kb e de proliferação de fibroblastos, em relação à água Milli Q.*

Resultados: *A água estudada apresentou um alto índice de estrôncio (0,61 mg/ml). A expressão da filagrina e respectivos testes munohistoquímicos foram relevantes. A aquaporina 3 aumentou 1,8 vezes e a atividade do nf-kb decresceu 47%. A água em questão também foi capaz de estimular a proliferação de fibroblastos.*

Conclusão: *A avaliação dessa água mineral originária da Serra do Japi (SP, Brasil), indica a existência de potencial para figurar como tratamento adjuvante em dermatologia, pois os resultados sugerem que ha hidratação da barreira cutânea, estimulo`a proliferação de fibroblastos, além da reparação e inibição de reações inflamatórias. Estudos clínicos adicionais devem ser realizados para que tais resultados sejam confirmados.*

Palavras-chave: *águas minerais; Brasil; cosméticos.*

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INTRODUCTION

A number of studies published in the literature have shown that spring mineral or thermal water have different physiochemical properties that can affect their clinical application in dermatology. With plenty of hydrographic basins and mineral water springs, Brazil offers a sizeable opportunity to leverage its natural resources; the waters should be analyzed and possible dermatologic applications should be explored. This study describes the characteristics and biological effects of a Brazilian mineral water and clinical studies about its application on the skin. The mineral water in question originates from pluvial waters infiltrated in the underground Alvorada spring, which is located in an estate owned by Mineração Joana Leite Ltda. (a bottled water company), in the Serra do Japí ridge in Jundiaí (SP), Brazil. Serra do Japí is a geological landmark, with hundreds of squared kilometers covered by upland type Atlantic Forest, comprising one of the largest areas of plant and animal life biodiversity in São Paulo State. Its rocks are extremely hard and are among the region's oldest (dating back more than 570 million years); they are located more than approximately 4,000 feet above sea level and were covered by glaciers in the distant past. The region has a tropical climate, with annual average temperatures of 18-20°C, and around 1,300 ml of rainfall each year.

OBJECTIVE

To study the composition, safety features, in vitro efficacy and physiochemical and biological characteristics and effects of Alvorada spring mineral water.

METHODS

Physiochemical features, cytotoxicity and ocular irritability

Alvorada spring mineral water's physiochemical features, cytotoxicity (viable cells) and ocular irritability (HET-CAM) were analyzed. The cytotoxicity test was carried out in cell cultures (fibroblasts BALB/c 3T3, clone A31). The method was based on the reduction of cellular growth and a count of viable cells, which indicates the cytotoxicity level. The irritability test (HET-CAM) was carried out with a positive control (1% SDS solution), a negative control (saline solution) and a sample of water without minerals (Milli-Q water).

Stimulation of filaggrin and aquaporin 3 genic expression

Additional studies to assess the genic expression of filaggrin and aquaporin 3 were carried out using the Real-Time PCR test. Human keratinocytes (Cascade Biologics, USA) were cultivated, and after six hours of contact with the studied water, the total RNA was extracted using the Trireagent® Solution (Applied Biosystems) and quantified using the Quant-iTTM RNA Assay Kit (Invitrogen); the reading was taken with the Quibit® Fluorometer (Invitrogen). The tests were conducted in a StepOnePlus (Applied Byosystems) device. The trials of genic expression of filaggrin were carried out using the trial system TaqMan® Gene Expression Assays (Applied Byosystems); in the analysis of the genic expression of aquaporin 3, the kit EXPRESS One-Step SYBR® GreenERTM (Invitrogen) was used. In both evaluations, the relative amount of mRNA was calculated as described by Pfaffl[1] and Gregory and Edith.[2] To evaluate the stimulation of the genic expression of filaggrin, the immunohistochemical analysis in fluorescence microscope (Leica DM 1000) of ex vivo skin fragments collected after plastic surgery was conducted. The antibodies used in that analysis were: anti-filaggrin primary antibody (Santa Cruz, sc-AKH1) and Alexa Flour 488 goat anti-mouse secondary antibody (Invitrogen, A11001).

Decrease in the activity of the nuclear transcription factor (NF-κβ)

Nuclear transcription factor kappa B (NF-κβ) activity was evaluated using a culture of human keratinocytes. The cells underwent UVA/UVB radiation and were kept in contact with the product for a further 24 hours. NF-κβ activity was gauged using a kit marketed by Cayman Chemical, USA.

Stimulation of fibroblast proliferation

In order to evaluate the stimulation of cellular growth, fixation and lysis were carried out, followed by a reading of the absorbance at 260 nm. The plating was carried out in DMEM media, diluted in demineralized water (Milli-Q control), and, comparatively, in a media diluted with Alvorada spring mineral water.

RESULTS

Physiochemical features

Alvorada spring mineral water is characterized by the presence of 15 macro and micro minerals. The Serra do Japí's mineral water emerges at 21°C, with a 5.9 pH and no microbiologic contamination, from a spring located 3,200 feet above sea level. The water's physiochemical characteristics and composition are shown in Table 1.

Cytotoxicity and ocular irritability (HET-CAM)

The Alvorada spring mineral water did not present cytotoxic activity or irritant potential in the HET-CAM test.

Stimulation of genic expression of filaggrin

The Alvorada spring mineral water's incubation in human keratinocytes culture significantly increased the relative expression of filaggrin (mRNA) in the 12.5 and 6.25% (v/v) concentrations (by 1.75 and 2.87 times, respectively), as can be verified in Graph 1. The results demonstrate a 1.5 increase in the genic expression of filaggrin (m-RNA) compared to the control group. The increased production of filaggrin was also demonstrated using the immunohistochemical technique (Figure 1). The cuts were incubated with anti-filaggrin antibodies (in green) and DNA marker (in blue). The analyses were carried out using a fluorescence microscope.

Table 1 - Alvorada spring mineral water's physicochemichal characteristics	
Alvorada spring mineral water	
Temperature (ºC)	21
pH	5,9
Dry residue at 180°C (mg/L)	42,27
Bicarbonates (mg/L)	27,79
SO_2^{-4} (sulphates) (mg/L)	0,1
Cl- (chlorides) (mg/L)	0,12
NO_3 (nitrates) (mg/L)	1,7
F- (fluorides) (mg/L)	0,08
Ca^{2+} (calcium) (mg/L)	2,87
Mg^{2+} magnesium) (mg/L)	1,94
K^+ (potasium)(mg/L)	1,89
Na^+ (sodium) (mg/L)	3,18
Sr^{2+} (strontium) (mg/L)	0,61
Ba (barium) (ug/L)	0,71
Radioactivity at the source (matches)	2,28

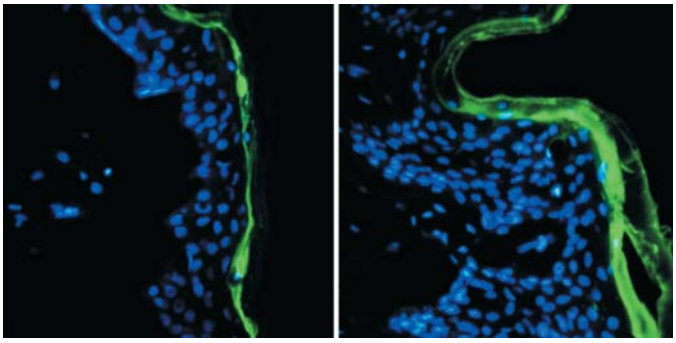
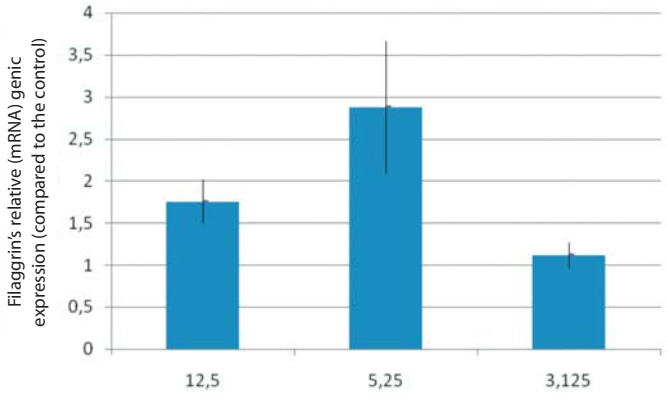
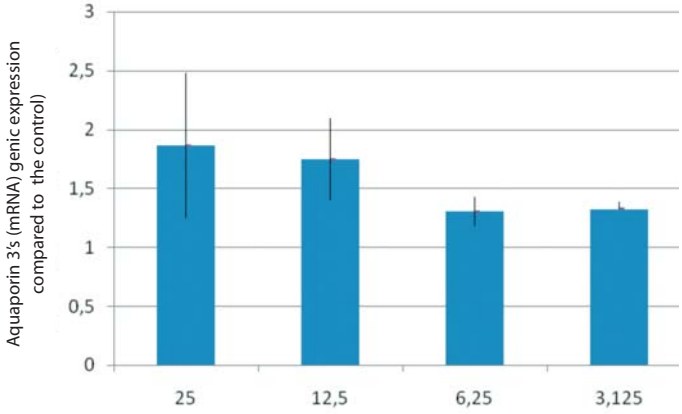


Figure I - Anti-filaggrin immunofluorescence (green) and contracoloration with DAPI (blue; DNA marker). Ex vivo human skin fragments with 5Vm histological cuts incubated with culture media (control) (a) and with Alvorada spring mineral water (b) (40x magnification)



Graph 1 - Filaggrin's (mRNA) relative genic expression compared to the control group in different Alvorada spring mineral water concentrations



Graph 2 - Relative expression of mRNA for aquaporin 3 in human keratinocytes culture incubated with Alvorada spring mineral water compared to the control group (demineralized water)

Stimulation of genic expression of aquaporin 3

The results shown in Graph 2 demonstrate that Alvorada spring mineral water significantly increased the relative expression of aquaporin 3 in the 25% and 12.5% concentrations, by 1.8 and 1.7 times, respectively.

Decrease in activity of the nuclear transcription factor (NF-$\kappa\beta$)

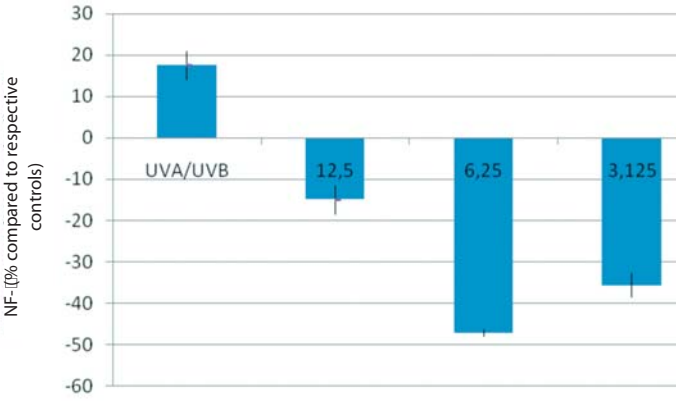
Scientific tests with keratinocytes cultivated in vitro showed that Alvorada spring mineral water reduced the amount of NF-$\kappa\beta$ produced by those cells, especially after exposure to the sun (Graph 3).

Stimulation of fibroblast proliferation

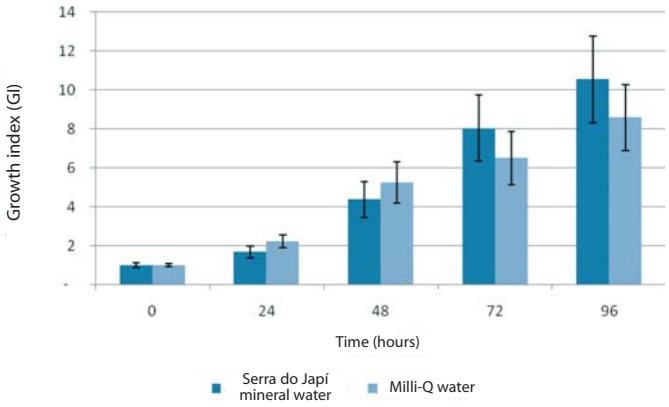
The results verified that Alvorada spring mineral water stimulated fibroblast growth; there was a statistically significant difference compared to Milli-Q water, which is usually used in cell culture growth. The results are shown in Graph 4.

DISCUSSION

The physiochemical characteristics observed show that Alvorada spring water can be classified as a mineral water, but not a thermal water, given that its emerges from the spring at 21°C – almost at room temperature. By definition, thermal water is a mineral water that emerges from its source at a minimum of 4°C above room temperature. The verified pH value (5.9) is very close to that of the skin, indicating an excellent physiological compatibility in cutaneous conditions. The low content of dry residue (42.27 mg /L), corresponding to that of a mild water – meaning a smaller concentration of mineral salts – suggests a good acceptability in conditions that involve a compromised cutaneous barrier. Regarding its chemical composition, it is important to note the high concentration of strontium and calcium; the *in vitro* tests demonstrate anti-inflammatory action. *In vitro* tests have indicated that the other minerals present in Alvorada spring mineral water are appropriate for use in inflammatory dermatologic conditions.



Graph 3 - Alvorada spring mineral water's effect on NF-κB activity in cultures of keratinocytes that were exposed to UVA/UVB radiation



Graph 4 - Growth index of fibroblasts for 96h, in culture media with Milli-Q water (light blue) and Alvorada spring mineral water (dark blue)

Cytotoxicity and irritability (HET-CAM) tests demonstrated in vitro cutaneous and ocular safety of the Alvorada mineral water.

The genic expression tests and immunohistochemical analysis for filaggrin analyzed the mineral water's action in recovering the cutaneous barrier. The cutaneous barrier's integrity and the maintenance of the skin's hydric balance cannot only be evaluated by the presence of specific substances; the complexity of the balance among its other elements also needs to be considered.[3] Part of that complex balance is controlled by the epidermal cornified cell envelope (ECE), which is a lipoprotein layer that substitutes the corneocytes' plasma membrane, which consists of a complex combination of interconnected proteins covalently associated to a layer with lipidic characteristics, attached to the extracellular surface of the protein layer.[4] Many components of the ECE, such as the pro-filaggrin, filaggrin, involucrin, loricrin, and many keratin subtypes, have been identified.[5] The epidermal protein pro-filaggrin, synthesized at a late stage during the epidermal differentiation, plays a crucial role in the generation and preservation of the flexibility and hydration of the stratum corneum (SC).[4,6] In the transition from the granular layer to the SC, pro-filaggrin (highly phosphorylized) is converted into filaggrin by a specific proteolysis and dephosphorylation process. [5] The resulting filaggrin monomers combine with the intermediate keratin filaments, which are responsible for their cohesion.[7,8] In the SC, the filaggrin – a cationic protein that assists in the aggregation and subsequent disulfide cross-links among keratin filaments – is liberated from the interactions with keratin and totally degraded into its amino acid components, such as pyrrolidone carboxylic acid (PCA) and urocanic acid.[4,8,9] Those amino acids constitute around 50% of the natural moisturizing factors (NMF)s and are kept inside mature corneocytes in the SC. NMFs are crucial for maintaining the epidermal barrier's hydration, and are found in reduced numbers in dry or very dry skin – an effect that is intensified by the aging process and seasonal changes. In conditions that involve reduced pro-filaggrin (as in atopic dermatitis) or absent pro-filaggrin (e.g., vulgar ichthyosis), the SC's quality becomes compromised due to the deficiency of NMF and the resulting loss of transepidermal water. [10,11] The filaggrin increase that was detected by those tests can be clinically significant in the adjuvating treatment of many dermatologic disorders.

The increase in cutaneous hydration can be demonstrated by a further test that evaluates the genic expression of aquaporin 3. Aquaporins are channels present in the plasma membranes of the cells that are responsible for the transportation of water and small solute molecules, especially glycerol, which are essential for maintaining the cellular hydroelectrolytic balance of all living organisms. Aquaporins are largely distributed in cellular membranes and are part of a broader class of proteins known as integral proteins (major intrinsic protein, or MIP). Among several aquaporins, AQP3 is located in the epidermis and has a greater intensity in the basal cells' and adjacent intermediate cells' plasma membranes.[12] As epidermis cells differentiate continuously, the presence of AQP3 gradually decreases until it disappears completely in the keratinized layer of the skin (SC). AQP3 is also present in structures associated with the epidermis, for example hair follicles and capillary glands, and acts as a specialized mechanism to counterbalance the excessive loss of water.[13] Other studies reveal the capacity of aquaporin channels to carry water. In epidermal cells, the permeability to water is inhibited by mercurial agents and acidic pHs, which confirms that the transportation of water is in fact made by those channels. [14] In that context, it was demonstrated that the reduction of water permeability was accompanied by changes in the permeability to glycerol, proving that AQP3 has an important role in the hydration of the epidermis. [15] Keratinocytes, melanocytes, fibroblasts, endothelial cells and adipocytes are equally involved in a dynamic interaction capable of detecting a variety of disturbances in the cutaneous environment and swiftly transmitting appropriate signals that warn and recruit elements of the immunological system.[16,17] Once stimulated, those cells are capable of enabling and liberating several factors that promote the expression of a great number of receptors that are significantly

involved in the eicosanoids' immunoregulation and biosynthesis.[18,19]

NF-$\kappa\beta$ is a protein complex that regulates immunological responses and is involved in the cellular response to stimuli such as stress and ultraviolet radiation. NF-$\kappa\beta$ was analyzed due to its importance in a number of dermatologic disorders. NF-$\kappa\beta$ is known to play a crucial role in the activation processes of genes that encode the synthesis of proinflammatory cytokines, adhesion molecules, chemokines, eicosanoids and nitric oxide, triggering a series of physiological processes that culminate in the degradation of tissue.[20,21] It is important to note that NF-$\kappa\beta$ is one of the main transcription factors involved in the signs and symptoms observed in the skin after acute exposure to UV radiation. [20] In that context, products containing active substances with anti-inflammatory and calmative properties can prevent tissular damage and photoaging caused by sun exposure.

The last in vitro test carried out analyzed the fibroblast proliferation stimulated by Alvorada spring mineral water. Cells reproduce by replicating their contents and dividing themselves in two: this cellular division cycle is the fundamental way in which all living beings reproduce themselves. In multicellular species, many cellular division cycles are required, and cellular division is necessary to substitute damaged or functionally deficient cells, or those that are lost through programmed cellular death (apoptosis). An adult human being needs to produce millions of new cells every second to maintain this balance. If the cellular division process is damaged, for instance by an ionizing radiation dose, an individual would die in a few days. [22] The cellular growth index shows how long a cell takes to duplicate (or the duration of the period of cellular replication). The fibroblast proliferation observed in the study test might have happened due to the presence of the ions necessary for cellular growth – for instance, calcium ions.

All in vitro tests seem to corroborate the hypothesis that the mineral water from Serra do Japí induces s biological effects in the skin due to its physiochemical characteristics. The presence of strontium in its composition makes it different from other waters available on the market. Hahn [23] demonstrated that strontium salts can be used prior to some treatments or even combined with an irritant substance, in order to inhibit sensorial irritation and irritative dermatitis. Zhai and colleagues tested a combination of 20% strontium nitrate and 70% glycolic acid, which also demonstrated that strontium could suppress the chemically induced irritation sensation.[24] This evidence suggests that the studied water has moisturizing properties that help rebuild the cutaneous barrier, and anti-inflammatory effects through the reduction of NF-kß activity. The role of the strontium also suggests that this composition can reduce skin irritation. It is worth noting that the latter is involved in the physiopathogeny of a number of dermatologic disorders. All in vitro effects proven in this study should be tested in controlled clinical trials.

CONCLUSION

This study is an initial assessment of Alvorada spring mineral water, which has shown promising results including reducing inflammation, reconstructing the cutaneous barrier and restoring the skin's hydration. Its in vitro effects must be further proven in clinical trials. Since Brazil boasts one of the greatest varieties of mineral water springs, there are considerable potential research opportunities relating to the different biological effects of various Brazilian mineral waters. Examining all of the physiochemical and biological characteristics of Alvorada mineral water is very important in order to understand its clinical and dermatologic applicability. ●

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Radiological evaluation of Calcium Hydroxyapatite-based cutaneous fillers

Avaliação radiológica de implantes cutâneos com Hidroxiapatita de Cálcio

Original Article

ABSTRACT

Introduction: Calcium hydroxyapatite is a radiopaque material that was traditionally used to provide radiologic contrast. It has recently been approved for use in cutaneous filling.

Objectives: To define the radiologic characteristics of Calcium hydroxyapatite and its potential to compromise radiologic evaluations.

Methods: Twelve patients received Calcium hydroxyapatite filler in the malar eminence and had radiography of the face (frontal, lateral, mentum-nasal-plaque (Waters), and Hirtz axial incidence technique) 1-8 weeks after the procedure. The X-rays were examined by two radiologists – one of whom was unaware of the filling procedure.

Results: The Hirtz axial incidence technique demonstrated amorphous radiopaque images in the suprazygomatic soft tissues in all cases, in both evaluations. Radiesse® was not detected using the other techniques, and did not illustrate the filler's position and symmetry. The evaluation of subjacent osseous structures was not compromised by the material's presence.

Discussion: Calcium hydroxyapatite can be identified in facial radiography when evaluated using a method that avoids overlapping with adjacent osseous structures. Although it does not impair the osseous evaluation, it is recommended that the radiologist or dentist is notified of the material's presence.

Conclusion: Cutaneous fillings containing Calcium hydroxyapatite can be identified, although not precisely located, using conventional X-ray.

Keywords: face, durapatite, X-rays.

RESUMO

Introdução: *A hidroxiapatita de cálcio é material radiopaco, usado como contraste radiológico décadas antes de seu emprego na dermatologia. Recentemente teve seu uso cosmético aprovado para preenchimento cutâneo, esperando-se que, quando aplicado em tecidos moles da face, possa ser identificado no raio X convencional.*

Objetivos: *Definir as características radiológicas da hidroxiapatita de cálcio usada em preenchimentos e seu potencial de comprometer avaliações radiológicas.*

Método: *12 pacientes realizaram preenchimento com hidroxiapatita de cálcio na eminência malar. Foram submetidas à radiografia de face nas incidências frontal, perfil, mento-naso-placa (Waters) e axial de Hirtz, no intervalo de uma a oito semanas após o preenchimento. Esses exames foram avaliados por dois radiologistas; um deles desconhecia o antecedente do preenchimento.*

Resultados: *A incidência axial de Hirtz evidenciou em todos os casos imagens radiopacas amorfas em partes moles suprazigomáticas, nas duas avaliações. O Radiesse® não foi detectado nas demais incidências. Não se mostrou útil como método para avaliar posição e simetria do preenchedor. Sua presença não prejudicou a avaliação das estruturas ósseas subjacentes.*

Discussão: *A hidroxiapatita de cálcio usada em preenchimentos cutâneos pode ser identificada em radiografias de face quando avaliada em incidência que evite sobreposição com as estruturas ósseas adjacentes. Apesar de não prejudicar a avaliação óssea, recomenda-se comunicar previamente sua presença ao radiologista ou dentista, já que seu reconhecimento inadvertido pode gerar dúvidas diagnósticas e investigações desnecessárias.*

Conclusão: *O preenchedor cutâneo composto por hidroxiapatita de cálcio pode ser reconhecido no raio X convencional, porém sem determinação precisa de posição e simetria. Sua presença não interferiu na avaliação das estruturas ósseas da face.*

Palavras-chave: *face, durapatita, raio X*

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Conflicts of interests: none
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INTRODUCTION

Cutaneous fillers have been increasingly used during the last decade as a versatile and safe non-surgical alternative for the correction of contours and volumetric augmentation with multiple aesthetic applications.[1] Radiesse® is a cutaneous filler compounded by microspheres of calcium hydroxyapatite (CaHA) dispersed in a carrier gel. CaHA is known to have radiopaque properties, and has been used as a radiological contrast for two decades. [2]

Some reports and case series demonstrate that conventional x-ray can occasionally clearly show CaHA that has been applied in facial soft tissue for aesthetic purposes – especially when large volumes are used, for example in the treatment of HIV-related lipodystrophia. [3] CaHA is also identifiable in computerized tomography (CT), magnetic resonance imaging (MRI) and in positron emission tomography (PET/CT), when the 2-fluoro 2-dioxi-D-glucose (FDG) is detected in the area that received that filler. [4]

This study evaluates the radiological repercussions of using a small volume of CaHA in the restoration of the malar volume for facial rejuvenation.

OBJECTIVE

To evaluate the radiological characteristics of CaHA when applied in small volumes to the soft tissue of the face for aesthetic reasons, the interference capacity of CaHA in conventional x-ray evaluations, and the use of x-ray to evaluate the presence and position of the filler.

METHOD

This observational, qualitative prospective study was approved by the Ethics Committee of the Hospital de Clínicas da Universidade Federal do Paraná (PR), Brazil. Female patients (n = 12) aged 41-73, received 0.05 ml CaHA (Radiesse®,Merz-Biolab, São Paulo, Brazil,) in the deep dermis and subcutaneous region of the malar eminence for correcting age-related hypotrophy (Figure 1). The patients underwent facial radiography using frontal, lateral, mentum-nasal-plaque (Waters), and Hirtz axial (Figure 2) incidence techniques, with two penetration intensities. The study complied with good clinical practice rules and the patients signed a term of free and informed consent.

Examinations were carried out in intervals of one to eight weeks after the filling procedure. The radiographies were evaluated at different time points by two radiologists – one of whom was unaware that the filling procedure had been carried out.

RESULTS

The Hortz's axial incidence technique demonstrated amorphous radiopaque images projected in the soft parts of each paramedian region of the face, in suprazygomatic position, in sites corresponding to the Radiesse® injection points (Figures 3 and 4). This finding was present in all 12 images when the evaluation was carried out under strong light. The filler was seen more clearly in radiographies with smaller penetration of the x-ray. Similar results were obtained in the evaluation conducted by the radiologist who was unaware of the filler's presence, who supplied a descriptive report of the finding without suggesting its etiology. Radiesse® was not detected in the lateral, frontal or Waters incidence x-rays.

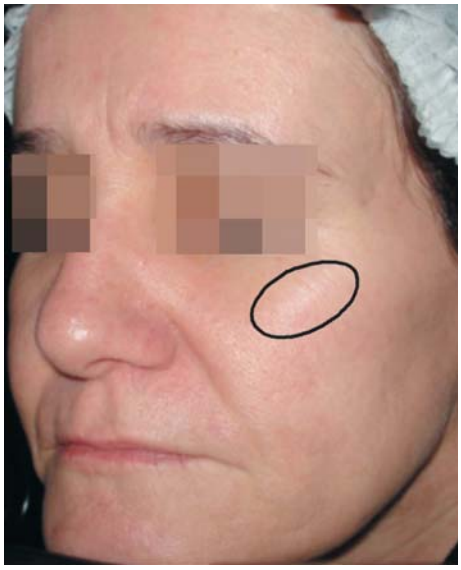

Figure 1: Lateral malar region above the zygomatic arch; the site that received CaHA filling is indicated

Figure 2: Technique for obtaining the Hirtz's axial incidence

DISCUSSION

According to the literature, CT is more sensitive to Radiesse®, while x-rays only present positive results when large volumes are used. [3] However, this study suggests that when the correct incidence is used, Radiesse® can be detected by x-ray even in small volumes. In order to choose the best incidence, the physician must know the studied region's anatomy, the available incidence options and how the relevant images are obtained. For that, the physician can rely on the opinion of a radiologist. CaHA is visible in x-rays with a higher density than that of soft tissue, but lower than that of the cortical and medullar bone [5] (Figures 3 and 4). Therefore it is not usually visible when its image overlaps that of a bone, as happened in the lateral, frontal and Waters (or chin-nasal-plaque) images.

The Hirtz incidence involves the patient lying on their back, with their head in maximum extension and the rays beaming perpendicularly on his/her face in the inferior to supe-

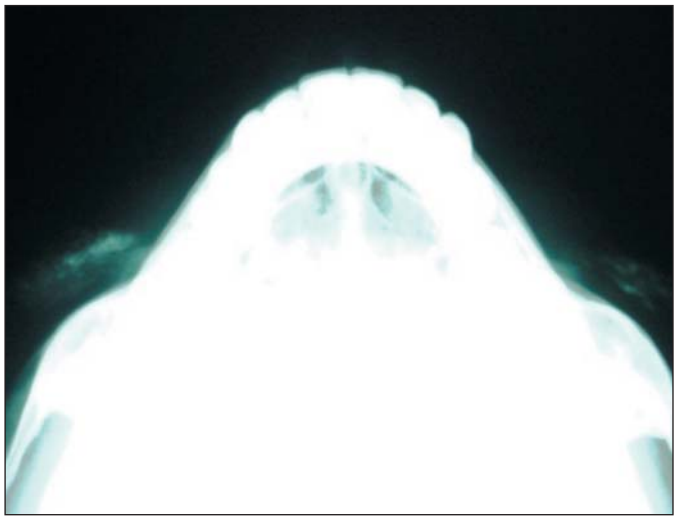

Figure 3: Radiological image with Hirtz's axial incidence: CaHA appears as a radiopaque image in a region of soft tissue above the zygomatic arch

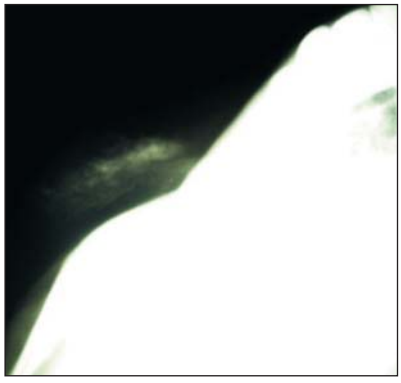

Figure 4: Detail of the radiological image of the zygomatic arch region: CaHA has intermediate radiopacity between those of the bone and the soft tissue

rior direction (Figure 2). In this position, the malar region's soft tissue can be analyzed without osseous superposition. In practice, this position is used for diagnosing fractures in the zygomatic arch. The absence of an overlap between the zygomatic bone and the filler makes it unlikely that the latter would obstruct the diagnosis of a fracture. Carruthers and colleagues also assert that the presence of CaHA does not compromise the evaluation of adjacent structures; in addition, the bilateral symmetrical position helps distinguish them from pathological findings that would not otherwise show those features.[3]

It was not possible to evaluate the filler's 's position and symmetry in this study. That would have been possible if the filler was identified in orthogonal incidences, allowing the analysis of its relationship with adjacent structures in two dimensions and the inference of its height and depth. For that purpose, CT would be more suitable. CaHA radiopacity might help verify the type of filler used, information that is not always reliably obtained in the patient history yet is necessary when planning new procedures in the region or treating complications. A histopathologic evaluation is often necessary if there is a complication. X-rays – a cost-effective, accessible and non-invasive type of examination – can assist in that investigation, given that radiopacity is a feature that distinguishes fillers containing CaHA from others.

When CaHA is detected in soft tissue, it needs to be distinguished from other entities such as dystrophic or heterotopic calcifications, multiple milliary osteoma cutis, myositis ossificans and foreign bodies.[4,6] Patients who receive fillers with CaHA should be aware that they need to warn their physician or dentist before an x-ray of the treated site in order to avoid diagnostic suspicions that could lead to unnecessary additional examinations.

CONCLUSION

When a cutaneous filler containing CaHA microspheres (Radiesse®) is applied in the malar region, it can be recognized in conventional x-ray examinations when Hirtz's axial incidence technique is used. Nevertheless, this technique was proven to be ineffective in determining the position and symmetry of the filler. Its presence does not impede the diagnosis of osseous fractures in the face – the original purpose of that incidence type – given that the filler image does not superpose that of the zygomatic bone. ●

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Original Article

Avaliação da melhoria na qualidade de vida de portadoras de melasma após uso de combinação botânica à base de Bellis perennis, *Glycyrrhiza glabra e Phyllanthus emblica* comparado ao da hidroquinona, medido pelo MELASQoL

Evaluation of quality of life improvement in melasma patients, measured by the MELASQoL following the use of a botanical combination based on Bellis perennis, Glycyrrhiza glabra e Phyllanthus emblica.

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ABSTRACT

Introduction: Melasma is a common hypermelanosis that mainly affects women and has a negative impact on the quality of life. It is a chronic and recurrent condition, and a number of treatments have already been proposed.

Objective: Assessment of quality of life for women with melasma before and after treatment with botanical extracts and hydroquinone.

Methods: A clinical, phase IV, randomized, blinded study was conducted at a clinical research institute. Women (n = 56) aged 18-60, with phototypes I-IV, were randomized into two groups (epidermal or mixed melasma). The Melasma Quality of Life Scale was used to compare the patients' quality of life before and after the use of Bellis perennis, Glycyrrhiza glabra and Phyllanthus emblica botanical extracts twice a day (Group A), or 2% hydroquinone used at night (Group B). The Melasma Area and Severity Index was used to assess the treatments' efficacy.

Results: Appearance, frustration, embarrassment and feeling less attractive were the Melasma Quality of Life Scale variables that had the greatest negative impact on quality of life at the beginning of the study. After 60 days of treatment, there was improvement in all MELASQoL aspects, with no statistical differences between the two groups.

Conclusion: The improvement in melasma patients' self esteem provided by the use of the botanical extracts matched that of 2% hydroquinone.

Keywords: *melasma; quality of life; phyllanthus emblica.*

RESUMO

Introdução: *Melasma é hipermelanose comum que afeta principalmente mulheres e gera impacto negativo na qualidade de vida. É doença crônica, recorrente, e diversos tratamentos já foram propostos.*

Objetivo: *Avaliação da qualidade de vida de mulheres com melasma antes e após o tratamento,com extratos vegetais ou hidroquinona.*

Métodos: *Trata-se de estudo clínico, fase IV, comparativo, prospectivo, randomizado, monocego, monocêntrico, realizado em instituto de pesquisa clínica. Foram randomizadas em dois grupos 56 mulheres, com melasma epidérmico ou misto, entre 18 e 60 anos, fototipos I a IV. Utilizou-se o MELASQoL como instrumento para avaliar a qualidade de vida dos pacientes com melasma, antes e após o uso da associação dos extratos botânicos de Bellis perennis, Glycyrrhiza glabra e Phyllanthus emblica, aplicada duas vezes ao dia (grupo A), em comparação com o da hidroquinona 2% aplicada à noite (grupo B). O MASI foi o padrão de eficácia clínica utilizado.*

Resultados: *Das variáveis do MELASQoL, aparência, frustração, constrangimento e sentir-se menos atraente apresentaram maior impacto negativo na qualidade de vida no início do estudo. Após 60 dias de uso do produto houve melhora em todos os aspectos do MELASQoL, em ambos os grupos, sem diferenças estatísticas entre eles.*

Conclusão: *O uso da associação dos extratos botânicos de Bellis perennis, Glycyrrhiza glabra e Phyllanthus emblica melhora a autoestima dos pacientes com melasma tanto quanto o da hidroquinona 2%.*

Palavras-chave: *melasma; qualidade de vida; phyllanthus emblica.*

INTRODUCTION

Melasma is a common hypermelanosis characterized by hyperchromic brownish macules. It occurs mainly in the face but can also affect the arms; however, it is not found in the mucus membranes.[1-10] It can occur in three forms on the face: centrofacial (the most frequent pattern, affecting the malar, forehead, supralabial, nasal and chin regions); malar (the second most frequent pattern, affecting the zygomatic regions); and mandibular (affects the masseterian and infrabuccal regions).[2,3,10]

The term *melasma* derives from the Greek *melas*, which means "black."[2,3] It usually occurs in women of childbearing age that have intermediate phototypes (chestnut brown to red skins), of Hispanic or Asian origins, who live in tropical regions. It presents a higher frequency among those of Latin descent, and rarely occurs in men.[1-3,5,6,8,11] Melasma's prevalence is not yet precisely known.[2]

Although its etiopathogeny is not fully understood, [1,2,4] many of the disorder's contributing factors have been identified: solar radiation, genetic predisposition, pregnancy, estrogen and progestogen, endocrinologic disorders, cosmetics and phototoxic drugs.[1-5,8-14] Using Wood light, it is possible to classify melasma as epidermal, dermal, mixed or indeterminate.[3] Epidermal melasma is the most common type, and responds better to treatment. Wood's light intensifies the pigmentation, which is located in the epidermis. The dermal type of melasma is not intensified when illuminated with Wood's light, while in the mixed type, some areas are intensified and others are not. That examination becomes less effective in intensely dark skin types, and results in the melasma being classified as indetermined.[3,10] Dermal melasma is more resistant to treatment, due to its dependence on the elimination of melanin by the macrophages.[3] Melasma can also be classified as transient or persistent. When the hormonal stimulus is interrupted for one year and the melasma disappears, it can be classified as transient. Otherwise it is classified as persistent; solar radiation is one frequent causal factor.[3]

Melasma is a chronic and recurring disorder,[2,6-8,15] and there are several topical depigmenting agents that can be used in its treatment.[16] In addition, there are therapeutic options, such as microdermabrasion, chemical peels, intense pulsed light and lasers.1 The use of photoprotection against the sun is essential in its treatment.[2,17] Sunscreens containing physical blockers such as titanium dioxide and zinc oxide offer greater protection, and are therefore preferable to chemical protectors.[12] Hydroquinone, the most frequently used depigmenting drug,[5,9,17] inhibits tyrosinase and reduces the conversion of dopa to melanin. In addition, hydroquinone might inhibit DNA and RNA synthesis and destruct melanocytes and melanosomes.[3,18] The combination of hydroquinone with tretinoin and corticosteroid – as in the Kligman formula – increases its efficacy. [5,8] Side effects include irritation, erythema, colloid milium, ochronosis, post-inflammatory hyperpigmentation, irritant and allergic contact dermatitis, nail dyschromia, and confetti-type depigmentation, among others.[3,5,17] Such undesirable effects, in addition to the need for effective treatments, stimulate a great demand for new whitening products.

Emblica, liquorice and belides botanical extracts have whitening properties. Emblica has antioxidant effects and increases collagen production.[19] Liquorice inhibits tyrosinase (an enzyme that is integral in the formation of melanin) and has anti-inflammatory properties.[3,20] Belides play a role in the process of melanin formation.[18] If combined, these extracts can be an alternative treatment for melasma.[18]

Since melasma occurs mainly in the face and is very visible, it is an inconvenience for the patient. As a result, it negatively affects their quality of life and psychological and emotional well-being, and frequently leads the patient to seek the help of a dermatologist.[2,5,8,21,22] Facial lesions generate dissatisfaction, low self esteem, deprivation of social interactions and lower professional or academic productivity.[2,7]

This situation encouraged the development of a standardized and validated questionnaire to evaluate patients' quality of life. The Melasma Quality of Life Scale (MELASQoL) is a instrument that meets that need, comprising the three domains that are most intensely affected by melasma: social life, recreation/leisure and emotional well-being. [1,2,7,22,23]

The use of that questionnaire in countries where English is not the official language requires appropriate translation and cultural adjustments. It was translated into Brazilian Portuguese in 2006 (MELASQoL-BP), in compliance with the World Health Organization's rules.[6-8]

This study evaluated the quality of life of women with melasma before and after treatment with products containing vegetable extracts or hydroquinone.

METHODS

This was a phase IV, comparative, prospective, randomized, single-blind (only the investigator did not know the name of the product being analyzed), monocentric clinical study. It was approved by the Ethics Committee for Research in Human Beings.

Women (n = 56) aged 18-60, with phototypes I to IV, with epidermal or mixed melasma were selected. All participants signed a term of free and informed consent and agreed to take part in the study and to have their photographs published for scientific ends. All underwent a 60-day washout period with the isolated use of SPF 35 sunscreen, reapplied every two hours. The exclusion criteria were: pregnancy or breastfeeding; presence of active dermatoses in the area to be treated; previous adverse reaction to the formulas' agents; use of products containing vitamin C, azelaic acid, kojic acid, phytic acid, glycolic acid, anti-inflammatory and retinoid derivatives in the 30-day period preceding the washout.

The study participants were randomized to receive either a cream consisting of emblica depigmenting complex, liquorice and belides 7% (Clariderm Clear®, Laboratórios Stiefel Ltda., Guarulhos, SP, Brazil) twice a day (Group A) or 2% hydroquinone cream (Clariderm® cream, Laboratórios Stiefel Ltda., Guarulhos, SP, Brazil) during the night (Group B). The ins-

tructions received by the participants were the same as the recommended by the manufacturer for both products.. Both groups used the product for 60 consecutive days, together with sunscreen (SpectraBAN T® SPF 35, Laboratórios Stiefel Ltda., Guarulhos, SP, Brazil).

Five (twice monthly) follow-up visits took place during the course of the study; the product was distributed to the volunteer at the first visit. A physician conducted the clinical evaluations at the follow-up visits and assessed each patient's melasma as: worsened, stable, improved or improved considerably. In addition, photographs of the face were taken in the frontal, right and left positions at the beginning, halfway through and at the end of treatment, using a digital imaging device (Visia®, Canfield Imaging System, Fairfield, USA).

The MELASQoL was administered at each visit to evaluate patients' quality of life. The questionnaire has 10 questions on diverse aspects (skin appearance, frustration, embarrassment, depression, relationship with other people, desire to be with other people, feeling attractive, feeling less important and changes in one's sense of freedom), as demonstrated in Table 1. The final MELASQoL score can range between 7 and 70; higher values indicate worse quality of life.

RESULTS

Of the 56 volunteers, 50 (Group A: 23; Group B: 26) completed the study. Six were excluded for personal reasons. A 0.05% significance level and a 95% confidence interval were established. Since the Anderson-Darling test showed that the studied variables did not have a standard normal distribution, the non-parametric Friedman and Wilcoxon tests, in addition to the McNemar test of equality of paired proportions, were used.

In general, most MELASQoL questionnaire aspects presented significant improvement after 15 days of treatment, for both groups. Group A showed significant improvement in frustration (26.5% in 30 days of product use, p-value = 0.014), and significant improvement in the sensation of freedom (46.6% in 45 days, p-value = 0.006). Group B presented significant improvement in demonstration of affection (42% in 30 days of use, p-value = 0.002), improvement in feeling less important (34.6% in 30 days, p-value = 0.011), and improvement in the sensation of freedom (41.7% in 45 days, p-value = 0.016) (Figures 1 and 2). At the end of the study there was an average improvement of 63.64% in Group A, and 60.77% in Group B, including all parameters evaluated by MELASQoL, with no statistically significant between-group differences.

Chart 1: Quality of life questionnaire for melasma patients (MELASQoL)

Regarding your melasma condition, how have you been feeling during the last week, before this consultation?	Not annoyed at all	Not annoyed most of the time	Not annoyed sometimes	Indifferent	Annoyed sometimes	Annoyed most of the time	Annoyed all of the time
1. Your skin's appearance	1	2	3	4	5	6	7
2. Frustration due to your skin's condition	1	2	3	4	5	6	7
3. Embarrassment due to your skin's condition	1	2	3	4	5	6	7
4. Feeling depressed due to your skin's condition	1	2	3	4	5	6	7
5. Effects on relationships with other people due to your skin's condition (e.g., interaction with family, friends, personal relationships, etc)	1	2	3	4	5	6	7
6. Effects on your desire to be with other people due to your skin's condition	1	2	3	4	5	6	7
7. Your skin's condition hampers your expression of affection	1	2	3	4	5	6	7
8. The macules on your skin make you feel unattractive to others	1	2	3	4	5	6	7
9. The macules on your skin make you feel less important or productive	1	2	3	4	5	6	7
10. The macules on your skin affect your sensation of freedom	1	2	3	4	5	6	7

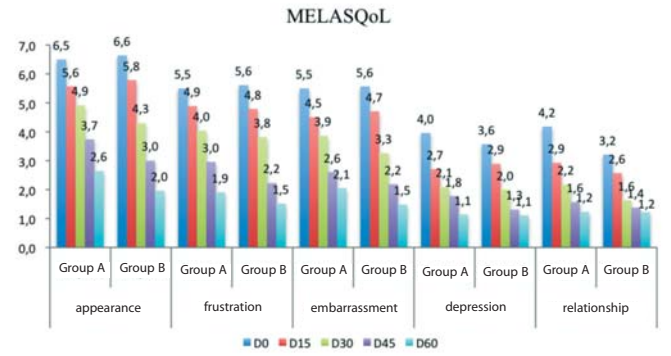

Figure 1: Appearance, frustration, embarrassment, depression and relationship items as evaluated by MELASQoL-BP

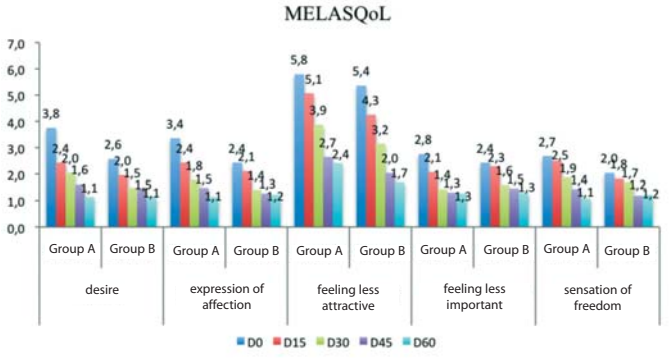

Figure 2: Desire, expression of affection, feeling less attractive, feeling less important and sensation of freedom items as evaluated by MELASQoL-BP

DISCUSSION

Melasma has been continuously studied, given that many factors are present in its etiopathogeny. Solar radiation is one of the most important factors contributing to its development and exacerbation.[3]

After repeated exposure to ultraviolet radiation, an increase in the number of melanosomes and active melanocytes takes place.[2] Melanosomes are organelles present within melanocytes, where the synthesis and storage of melanin occurs.[2] Tyrosine is the amino acid on which the enzyme tyrosinase acts, resulting in the formation of melanin.[2] Melanocytes have dendritic prolongations through which melanosomes are injected into the keratinocytes, and are distributed in the cytoplasm above the cell's nucleus.[2]

Melasma occurs more frequently among individuals with a family history of the condition, and among people of Hispanic and Asian descent .[2,3] In turn, the estrogen's action mechanism is likely due to the presence of estrogen receptors in melanocytes, which stimulate melanin production.[3] The expression of α-MHS (melanocortin) and MC1-R (melanocortin receptor) in melanocytes involved in the melasma's physiopathogeny[2] is increased by the hormone β-estradiol.[2]

Melasma is a common dermatosis. Studies show that affected patients feel annoyed and less attractive, and use cosmetics to cover the macules. Social and leisure activities are hampered due to the skin's appearance. [8,21] Patients believe that people focus on their skin rather than on what they are saying.[21]

Thus melasma greatly affects patients' quality of life.[5] The MELASQoL questionnaire is increasingly used to evaluate that impact.[6,8] It is important that that tool be adapted to the analyzed population's culture and language. The Brazilian version of MELASQoL has been validated, allowing the cultural identity to be preserved when using it in clinical and research activities.[8]

A number of studies have used the MELASQoL. In 2006, Cestari and colleagues conducted a study validating the MELASQoL-BP in a treatment with a fixed dose of a triple combination containing 4% hydroquinone, 0.05% tretinoin and 0.01% fluocinolone acetonide. The average pre-treatment MELASQoL score was 44.4 (standard deviation, SD, ±14.9); after treatment, the average score dropped to 24.3 (SD 15.5), a statistically significant improvement ($p < 0.001$). For the item "annoyed most of the time" or "annoyed all of the time," there was a special focus on the factors "appearance of the skin before and after treatment" (decreasing from 69.8% to 10.1%), "frustration" (from 59.7% to 12.2%), "embarrassment" (from 56% to 9.3%) and "impact on relationships with other people" (from 35.3% to 5.8%).[8]

A 2008 study by Scherdin and others described that after eight weeks of treatment, MELASQoL decreased to 19.4 from 28.3 ($p < 0.001$), with the greatest improvement in the items "appearance of the skin" and "frustration and depression due to the skin's condition."[5] In 2008, Freitag published a sectional study evaluating the impact of melasma in the quality of life of 84 Brazilian women. The average MELASQoL-BP was 37.5 (SD ±15.2); the most affected aspects were related to the patients' emotional well-being (appearance, frustration, embarrassment and not feeling attractive).[6]

In line with the studies mentioned above, the MELASQoL items that presented the worst scores at the beginning of the present study were appearance, frustration, embarrassment and feeling less attractive. While both groups presented improvement in the present study, there were no statistically significant differences between the groups.

Hydroquinone is a phenolic agent structurally similar to the melanin precursors that, in addition to acting in the degradation of melanosomes, act upon melanocytes, possibly causing their necrosis. [3] After using hydroquinone for five to seven weeks, it is possible to note a considerable depigmentation. That treatment should last at least three months.[3] Hydroquinone is a primary irritant agent and can cause erythema and desquamation before the depigmentation takes place; those effects are proportional to the concentration employed.[24]

The botanical extract *belides*, extracted from *Bellis perennis* flowers, inhibits endothelin-1 and decreases the production of eumelanin in order to reduce the linking of α-MHS to its receptors. Regarding the melanin already that has already been produced, *belides* has a whitening effect when reducing the transfer of melanosomes from the melanocytes to the cells of the epider-

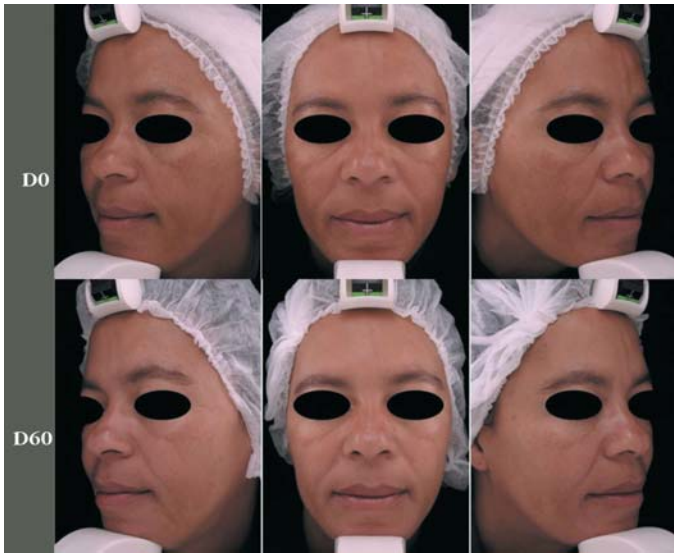

Figure 3: Group A volunteer before (Day 0) and after (Day 60) treatment

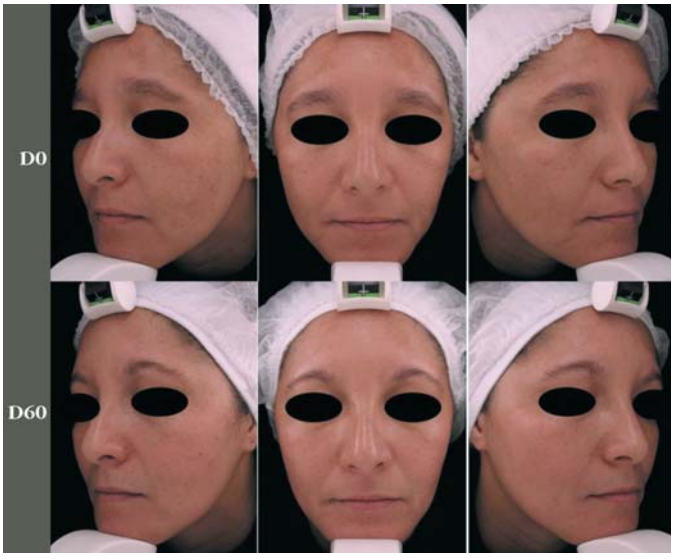

Figure 4: Group B volunteer before (Day 0) and after (Day 60) treatment

mis.[18] Liquorice, in turn, is extracted from the liquorice plant, named *Glycyrhiza glabr*a.[3] Its glabridin component inhibits tyrosinase without altering the synthesis of DNA. [3,20,25] Saponins and flavonoids are the active principles with the greatest anti-inflammatory properties. Liquiritin, also present in *Glycyrhiza glabr*a, has a melanin dispersing action, which results in depigmentation.[18] Liquiritin's efficacy suggests it can be an alternative to hydroquinone.[26] An additional extract is *emblica*, an active principle extracted from the *Phyllanthus emblica* fruit; its antioxidant mechanism moderately inhibits peroxidase and strongly inhibits the reaction of iron with peroxide. It also leads to the whitening of the skin when inhibiting tyrosinase.[18,19]

The depigmenting clinical benefits of botanical extracts *Bellis perennis*, *Glycyrrhiza glabra* and *Phyllanthus emblica*, compared to 2% hydroquinone, in patients with melasma were demonstrated in this study. [18] We found significant – and statistically similar – clinical improvement for both groups (Figures 1 and 2) (Graphs 1 and 2). Such improvement was detected by using the Melasma Area Severity Index (MASI) for a period of 60 days after the beginning of treatment. 18 The MASI scale (from 0 to 48) average score for the group that used botanical extracts was 10.9 (before treatment) and 5.7 (after treatment), meaning an improvement of 47.2%. For the hydroquinone group, MASI scores dropped from 10.2 to 4.4 after treatment (improvement of 57.3%). There was no statistically significant difference between the groups (p-value > 0.05).18 Average MASI scores range from 10-13 in most published studies.[6]

CONCLUSION

From those data, it is possible to note the importance of appreciating the quality of life of melasma patients and not treating that condition as only an aesthetic problem. Many patients forego treatment since melasma is a clinically benign disorder, although their psychological and emotional well-being is affected. The physician must weigh the benefits that the treatment will provide for the patient's life, as well as choose the best therapeutic option in each case. Therefore, the search for effective alternative treatments to hydroquinone must be considered and incentivized. In addition to providing depigmenting potential in the treatment of melasma, the use of botanical extracts of *Bellis perennis*, *Glycyrrhiza glabra* and *Phyllanthus emblica* improves the quality of life of patients with that dermatosis. ●

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Treating vitiligo with Excimer laser: a retrospective study

Excimer Laser no tratamento do vitiligo em 123 pacientes: estudo retrospectivo

Original Article

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ABSTRACT

Introduction: Vitiligo is cosmetically disfiguring and can cause significant psychological morbidity. Most therapies require protracted treatments and can lead to disappointing results. More recently, 308 nm Excimer laser has proven to be effective in treating vitiligo.
Objective: To analyze the effectiveness and patient satisfaction of 308 nm Excimer treatment for vitiligo patches in a variety of locations on the body.
Methods: Patients with generalized or localized vitiligo (n = 123, 321 lesions), were studied. The patients were treated at a private practice between 2007 and 2010. Two independent examiners analyzed the response to the therapy by comparing clinical and photographic records before and after treatment.
Results: More than half (n = 77) of the patients presented repigmentation greater than 60%, 26 presented 40-59%, and 20% had levels less than 39%. Facial lesions responded better to treatment than those in other body parts. Elbows, hands and feet were the less sensitive areas. In general, the patients were satisfied with the treatment.
Conclusion: The use of Excimer laser for treating vitiligo was effective and safe, producing satisfactory cosmetic results and improving patients' self esteem.
Keywords: vitiligo; lasers, excimer; phototherapy.

RESUMO

Introdução: *O vitiligo é cosmeticamente desfigurante e pode causar significativa morbidade psicológica. A maioria das terapêuticas requer tratamento longo e pode levar a resultados decepcionantes. Recentemente, o Excimer laser-308nm revelou ser efetivo no tratamento de vitiligo.*
Objetivo: *Neste estudo retrospectivo foram analisadas a eficácia e satisfação dos pacientes que usaram Excimer laser-308nm no tratamento de manchas de vitiligo em diferentes regiões anatômicas.*
Métodos: *Participaram 123 pacientes com vitiligo generalizado ou localizado, apresentando 321 lesões. Os pacientes foram tratados em clínica privada de 2007 a 2010. A análise da resposta ao tratamento foi feita por comparação de registros clínicos e fotográficos obtidos antes e após o tratamento, por dois examinadores independentes.*
Resultados: *Setenta e sete dos 123 pacientes apresentaram repigmentação superior a 60%; 26 entre 40 e 59%; e 20% tiveram repigmentação inferior a 39%. Lesões na face responderam melhor ao tratamento do que as localizadas em outras regiões corporais. As áreas menos sensíveis foram cotovelos, mãos e pés. De forma geral, os pacientes ficaram satisfeitos com o tratamento.*
Conclusões: *O uso do Excimer laser para tratamento do vitiligo foi eficaz, seguro e levou a resultados cosmeticamente satisfatórios com melhora da autoestima dos pacientes.*
Palavras-chave: *vitiligo; lasers de excimer; fototerapia.*

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INTRODUCTION

Vitiligo is an acquired chronic leucoderma that is clinically characterized by single or multiple hypopigmented macules, which are often symmetrical and clearly delimited, with a localized, segmented or widespread distribution.[1-2] It affects 1-2% of the population, with no apparent correlation to age, gender or ethnicity.[3-4] All areas of the body's surface can be affected, however the face, neck, axillae, back of the hands, fingers, the inguinal region, the anterior and lateral regions of the legs and malleolar regions are most commonly affected.[5]

The pathogenesis of vitiligo is still unknown.6 Autoimmune, cytotoxic and neural mechanisms have been investigated, however the exact physiopathology of the mechanism that causes the destruction of melanocytes is not clearly understood.7 There are descriptions in the literature of associations with other autoimmune diseases such as thyroid disorders, Addison's disease, *Diabetes mellitus*, *Alopecia areata*, and pernicious anemia.[8-9-10]

Vitiligo's natural course is variable, however most of the time it progresses slowly. In 10-20% of cases spontaneous repigmentation, which is rarely complete, takes place. Vitiligo lesions are asymptomatic, but can be disfiguring, above all on darker skin, and entail significant psychological morbidity and negative effects on quality of life.[1-5]

Several therapeutic approaches have been described for vitiligo, however they require long treatment courses and often lead to disappointing results.[11] The most common therapeutic options include corticosteroids; topical immunomodulators; topical and systemic psoralens that can be associated with sun radiation or artificial UVA (PUVA) and broadband and narrowband ultraviolet B radiation (UVB)-based phototherapy; and excimer or monochromatic light. Surgical options include autologous mini-grafts with punch, suction blister epidermal grafts, and epidermal cell transplants.[9]

A meta-analysis carried out in 1998 showed that the use of class 3 and 4 corticoids resulted in greater than 75% repigmentation in 56% of patients with segmental vitiligo, and in 55% of those with widespread vitiligo. Other studies have shown that class 3 corticoids constitute the most effective and safe treatment for segmental vitiligo.[12] The introduction of topical immunomodulators meant the possibility of a more appropriate treatment for several cutaneous disorders, including vitiligo. Many studies demonstrated an efficacy similar to that of topical corticosteroids, however without their adverse effects, such as atrophy.[13-14]

Phototherapy aims to promote the activation and migration of melanocytes located in hair follicles to the depigmented basal layer of the skin, and to induce the apoptosis of cytotoxic T cells, which are responsible for the destruction of the melanocytes.[7] Repigmentation success rates of 50-60% have been observed after months or years of PUVA treatment,15 in addition to many adverse effects, such as phototoxicity reactions, nausea, vomiting, cataracts and the risk of developing several skin cancers, such as epidermoid carcinoma and melanoma.[8]

Studies have demonstrated that narrowband UVB-based (NBUVB) phototherapy is as effective as topical PUVA, nevertheless producing fewer adverse effects in addition to a smaller accumulated UVB dose. However, both modalities require regular phototherapy sessions (several times per week), and treatment takes up to a year to reach the appropriate therapeutic response.[11] Although the treatments described above can produce good results, a quicker, straightforward and effective therapy was thought to be necessary.

More recently, the 308 nm Excimer laser has proven to be effective in the treatment of localized vitiligo.[16] Evidence suggests that laser therapy can trigger follicular repigmentation after a few weeks of treatment and produce cosmetically satisfactory results. Comparative studies have shown that Excimer laser presents biological and clinical effects that are similar – and often superior – to those of NBUVB phototherapy.[8]

Phototherapy devices, such as Excimer laser, allow high intensity radiation to be applied only to the affected skin, protecting the healthy skin from UV damage. This selectivity limits the hyperpigmentation of the skin adjacent to the lesion, a side effect that is commonly observed with other types of phototherapy. Furthermore, the Excimer laser equipment has an articulated arm that makes it easier to reach difficult areas such as skin folds and mucous membranes.[17]

Studies have shown that lesions in UV-sensitive areas (face, neck, back, trunk and arms) respond better to Excimer laser treatment than those located in UV-resistant areas (knees, elbows, wrists, hands, ankles and feet).[18-19] All UV-sensitive areas present similar results when treated with laser therapy, while among UV-resistant areas, knees, elbows and wrists respond significantly better than hands, ankles and feet.[18]

This study investigated the efficacy – degree of repigmentation and patient satisfaction – of Excimer laser treatment of vitiligo lesions in different parts of the body.

METHODS

Studied population

The study population comprised patients treated at a private practice located in the city of São José do Rio Preto, State of São Paulo, Brazil, between 2007 and 2010. This retrospective study was presented and approved by the Faculdade de Medicina de São José do Rio Preto research ethics committee. Patients (n = 123, 47 men and 76 women) between 4 and 76 years old (average age 32) were included in the study. Study participants presented lesions in different parts of the body (face, trunk, arms, elbows, back of the hands/fingers, legs, genitalia, knees and soles of the feet).

Before starting the therapy, the patients were clinically assessed to determine the type of vitiligo and the sites of the lesions. Patients with less than 30% of the surface area of the body affected were included. Patients who had been treated with topical or systemic immunosuppressants or had undergone phototherapy in the previous six months were excluded. Patients who were pregnant or had a history of skin cancer or photosensitivity were also excluded.

Source of Light, Application and Dosage

The treatment of the vitiligo lesions was carried out with collimated Excimer laser radiation, which beams 308 nm wavelength monochromatic light, generated by xenon-chloride gasses (Xtrac, Photomedex, Carlsbad, CA, USA). The laser beam was transmitted using an articulated arm with a spot diameter of 4-30 mm. The UV radiation was conveyed by a flexible fiber optics cable, and was transmitted to the hand piece that beamed it in a circular shape with an area of 1-10 cm^2. The laser used energy pulses of 3 mJ/cm^2, with a 30 ns duration and frequency below 200 Hz. The sessions were carried out twice a week, with at least 72 hours between sessions.

All patients were exposed to the radiation through progressively increasing energy levels according to the skin's degree of tolerance to the irradiation, aiming at reaching or exceeding a 60% rate of repigmentation. The initial irradiation doses were determined by skin type. The average initial dose used was 100 mJ, with subsequent increments determined as follows: (i) a 100 mJ/cm^2 increment if no erythema occurred after the initial treatment and (ii) a 50 mJ/cm^2 increment if erythema occurred but lasted less than 24 hours. The initial dosage was maintained if the erythema lasted 24 hours or longer. In cases of serious erythema, pain, burning sensation or presence of blisters, the treatment was suspended until the situation was resolved, and the dose was reduced to the last well-tolerated level.

The irradiation dose for each treatment ranged from 100-2,800 mJ/cm^2, with a minimum of 8 and a maximum of 110 sessions (average of 23 sessions). During the treatment, the patients' eyes were covered with UV protection glasses.

Response to the Treatment and Degree of Satisfaction

The variables representing the clinical examination, as well as the photographic records and the patients' satisfaction with the treatment, all registered in the medical records, provided the data for this study. The analysis of the treatment response was carried out by comparing clinical and photographic records obtained by two independent evaluators, before and after treatment. That process yielded a rate, which was evaluated quantitatively according to the percentage of repigmentation achieved in the treated area and scored by each examiner according to the following classification: 1 = 0% (poor), 2 = 1-19% (very bad), 3 = 20-39% (bad), 4 = 40-59% (average), 5 = 60-79% (good), 6 = 80-99% (very good) and 7 = 100% (excellent). Patients who presented no repigmentation were defined as non-responsive.

The degree of erythema and patient satisfaction were assessed qualitatively. Erythema was classified according to the following scale: 1 = absent, 2 = mild, 3 = moderate and 4 = serious. Patient satisfaction was assessed using a 3-point scale: 1 = bad, 2 = good or 3 = excellent.

RESULTS

In order to evaluate the therapeutic effects of the Excimer laser, all 123 patients' vitiligo patches were considered. Ninety-four patients (59 women, average age 33, range 4-76 years old) presented the generalized type of vitiligo while 29 patients (17 women, average age 26, range 4-62 years old) presented the localized type of vitiligo. Seventy-seven patients (62.60%) presented lesions with more than 60% repigmentation (Figure 1). The average number of sessions needed to achieve this target was 23. Among these patients, 25 (20.33%) presented total repigmentation of their macules after an average of 20 sessions (Figure 2).

Twenty-six patients (21.14%) presented repigmentation of 40-59%, with an average of 23 sessions. Thirteen patients (10.57%) presented repigmentation of 20-39% and 7 (5.69%) presented a repigmentation rate below 19%. Lesions on the face responded better to the treatment than those located on other parts of the body. Eighty-nine of the 105 patients (84.76%) with achromic patches on the face presented repigmentation rates above 60%. Ten of the individuals with facial lesions (9.52%) presented repigmentation rates of 40-59%. Only 6 (5.71%) patients presented rates below 39%.

This study showed that although patches located on the arms responded well to the treatment, those located on the face had a better response. Ten of the 20 patients (50%) with lesions on the arms presented repigmentation above 60%. Four of the 20 patients (20%) presented a repigmentation rate of 40-59%. Lesions on the trunk showed a favorable response, however not as much as those on the face and arms. Eighteen of 38 patients (47.37%) with patches on the trunk presented repigmentation

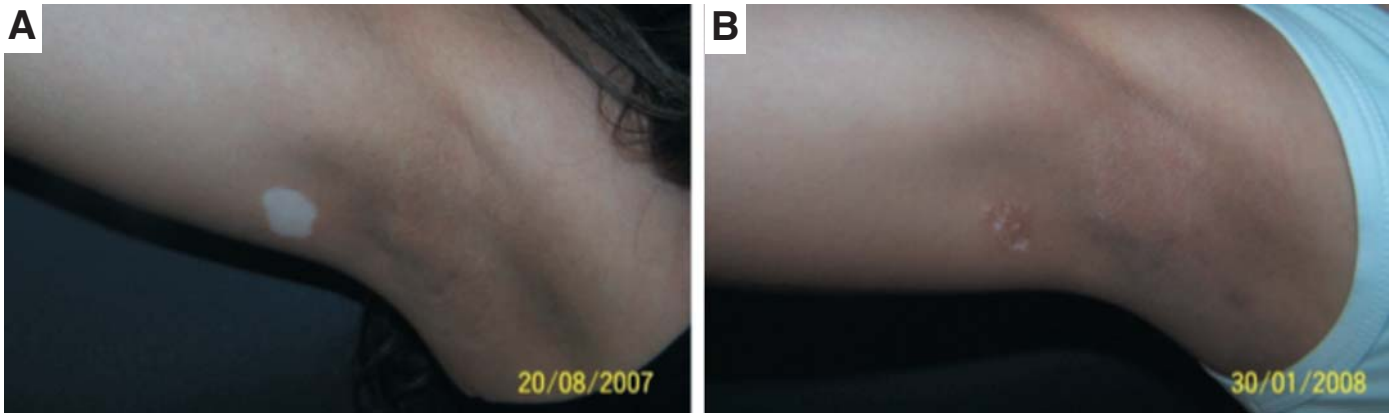


Figure 1 - Repigmentation of vitiligo lesion in 5 months

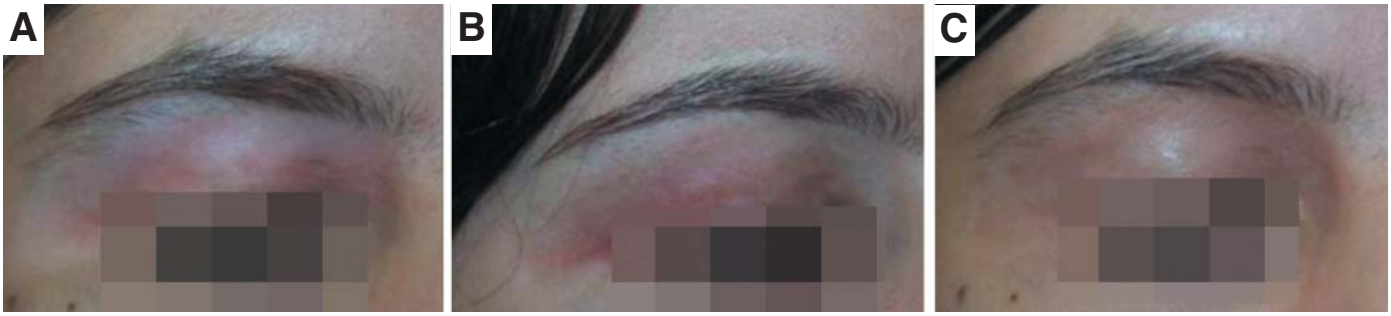


Figure 2 - Repigmentation of vitiligo lesion after 20 sessions

above 60%; 8 in 38 (21.05%) repigmented from 40-59%. Results at levels above 60% were obtained in 9 of the 22 lesions (40.91%) located on the genitalia, in 5 of the 11 lesions (45.45%) located in the legs and in 7 of the 18 lesions (38.89%) located on the knees. Lesions located on the extremities and elbows were less responsive to treatment.

Of the 32 patients with hypochromic patches on the feet, 12 (37.5%) presented repigmentation of 20-39% and 1 (3.13%) did not repigment. Of the 62 patients with lesions on the hands, 17 (27.42%) also presented repigmentation rates of 20-39% and 7 (11.29%) did not repigment. Four of the 13 patients (30.76%) with patches on the elbows presented repigmentation rates of 20-39%, while 4 presented repigmentation rates of 40-50%. Of the patients with lesions on the hands, 24 (38.71%) presented repigmentation greater than 60%; 11 with lesions on the feet (34.38%) and 5 with lesions on the elbows (38.46%) also presented rates greater than 60% (Table 1, Graphs 1 and 2).

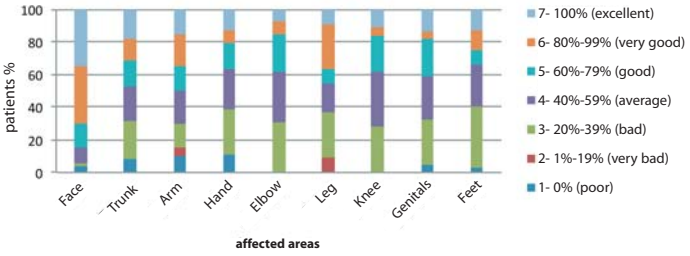
According to the Fitzpatrick classification, the study patients had phototypes between II and IV. Of the 77 patients who experienced repigmentation greater than 60%, 13 (16.88%) were phototype II, 37 (48.05%) were phototype III and 27 (35.06%) were phototype IV. The majority of the 26 patients who presented repigmentation rates of 40-59% were phototypes III (53.85%) and IV (38.46%) (Graph 3).

The treatment presented minimal side effects, including mild (2 events in 17 of the 123 patients) and moderate (1 event in 4 patients) erythema. Serious side effects were not observed (Graph 4).

Table 1 - Number of lesions and rates of repigmentation

Affected areas	Repigmentation scale*							
	1	2	3	4	5	6	7	Total
Face	4	0	2	10	15	37	37	105
Trunk	3	0	9	8	6	5	7	38
Arm	2	1	3	4	3	4	3	20
Hand	7	0	17	15	10	5	8	62
Elbow	0	0	4	4	3	1	1	13
Leg	0	1	3	2	1	3	1	11
Knee	0	0	5	6	4	1	2	18
Genital	1	0	6	6	5	1	3	22
Feet	1	0	12	8	3	4	4	32

*1 = 0% (poor), 2 = 1-19% (very bad), 3 = 20-39% (bad), 4 = 40-59% (average), 5 = 60-79% (good), 6 = 80-99% (very good) and 7 = 100% (excellent)



Graph 1 - Comparison of the repigmentation rates (%) of affected areas

At the end of the treatment, all patients were asked about the results of the therapy. Given a choice between excellent, good and bad, 88 patients (71.54%) classified the treatment as excellent, 29 (23.58%) as good and only 6 (4.88%) as bad (Graph 5).

DISCUSSION

Most currently available therapies for treating vitiligo are not very effective or present significant adverse effects. Among non-surgical repigmentation methods, narrowband UV presented good results, followed by broadband UV, class 3 and 4 topical corticoids, and psoralen combined with long-wave UV radiation [17-19].

Gastrointestinal side effects (nausea and vomiting) and phototoxicity are expected with the use of psoralen and long-wave UV radiation. In turn, skin atrophy, striae and telangiectasias are common adverse events in the prolonged use of corticoids. Narrowband UVB radiation has fewer side effects, however good results are only obtained with long-term treatmenst.[15]

The use of 308 nm Excimer laser – recently established for treating vitiligo – presented great efficacy, given that improvements were observed after only 10 sessions and repigmentation rates increased as the treatment progressed. Considering that in other UV treatment modalities initial repigmentation can rarely be expected to take place before the tenth week, the results obtained with the Excimer laser represent an advance in the treatment of vitiligo.[17-19]

The present study confirmed that the 308 nm monochromatic UVB radiation generated by the Excimer laser is effective in repigmenting patches of localized and generalized vitiligo in different areas of the body. Greater than 60% repigmentation rates were observed in 62.60% of the patients, with an average of 23 sessions or 11.5 weeks. Of those patients, 32.47% pre-

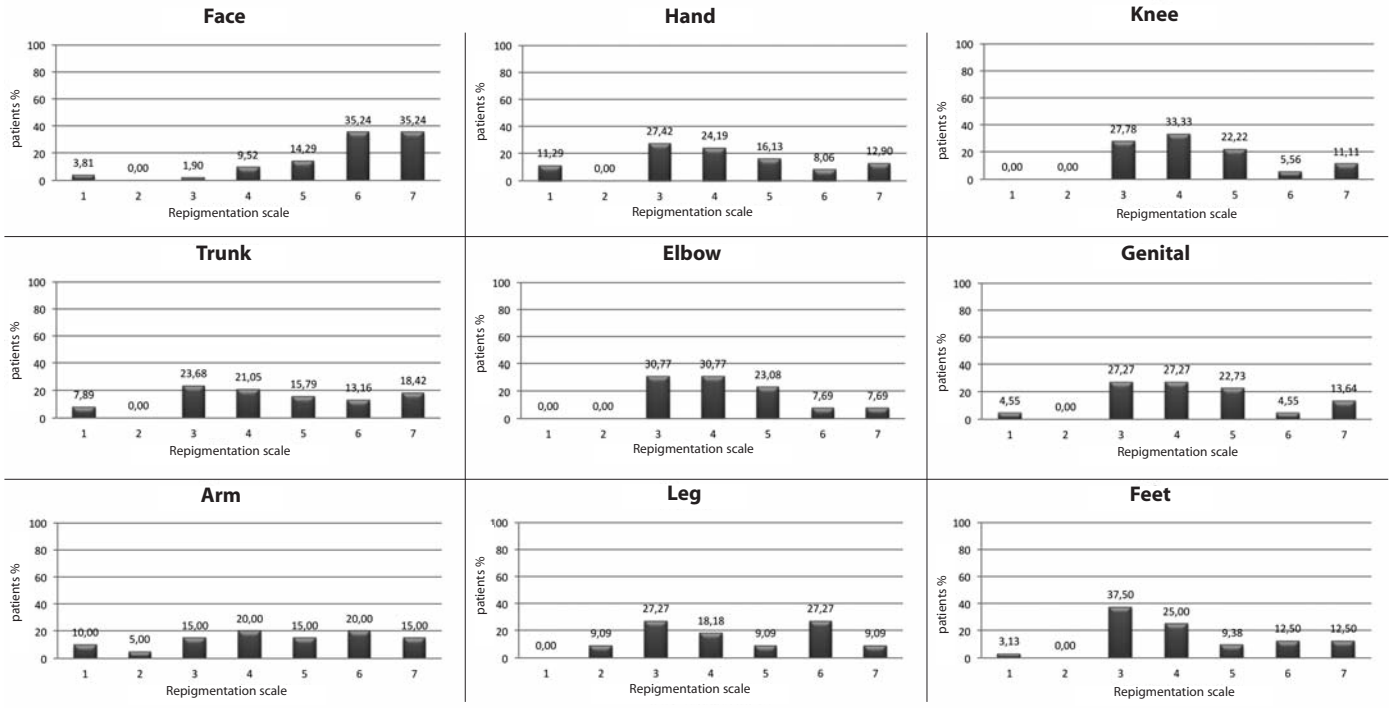


Gráfico 2 - Repigmentation rates (%) by affected area

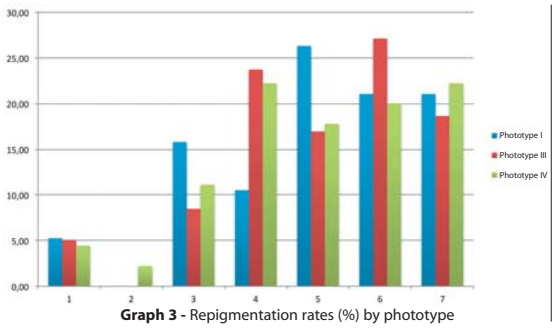
[repigmentation Scale: 1 = 0% (poor), 2 = 1-19% (very bad), 3 = 20-39% (bad), 4 = 40-59% (average), 5 = 60-79% (good), 6 = 80-99% (very good) and 7 = 100% (excellent)]

sented 100% repigmentation of their lesions after an average of 20 sessions. Among patients with total repigmentation, 11 were exposed to 10 or fewer sessions, meaning that a cure was achieved in less than 5 weeks.

In 1997, Westerhof and colleagues20 observed that 67% of vitiligo patients obtained some degree of repigmentation after 4 months of treatment with 311 nm UVB. Those results corroborate previous studies, which show that Excimer laser treatment can lead to faster and more effective repigmentation than that obtained with 311 nm UVB.[8-19]

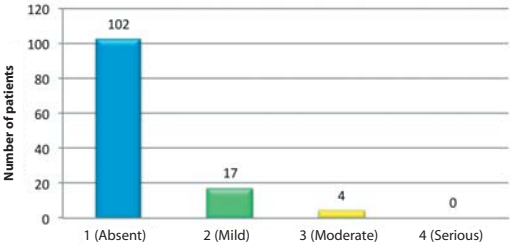
The Fitzpatrick phototype evaluation plays a key role in the patient's response to the treatment. Individuals with III-IV skin types were more tolerant to the irradiation doses and presented fewer adverse effects (such as burns and blisters) than those with fairer skin (type II). Greater repigmentation rates (above 60%) were achieved in phototype III and IV patients (83.12%). In the present study, the use of the Excimer laser was found to be well tolerated and caused minimal side effects, evidence of this new technique's safety level. In addition, this treatment modality can be considered less harmful than combined psoralen and long-wave UV radiation therapy or conventional UVB phototherapy regarding the aging affects on the skin and carcinogenesis. This is because healthy skin is not damaged by the laser.[15]

Although a number of studies show that the location of the lesions seems to play a crucial role in the clinical response to treatment, the main reason for this fact remains unclear. In body sites where the skin is thicker, such as elbows and knees, the

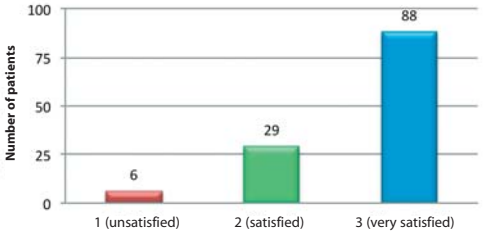


Graph 3 - Repigmentation rates (%) by phototype

[repigmentation Scale: 1 = 0% (poor), 2 = 1-19% (very bad), 3 = 20-39% (bad), 4 = 40-59% (average), 5 = 60-79% (good), 6 = 80-99% (very good) and 7 = 100% (excellent)]



Graph 4 - Side effects in patients who received treatment with Excimer laser according to degree of erythema [1 (absent), 2 (mild), 3 (moderate) and 4 (serious)]



Graph 5 - Satisfaction degree of patients who received treatment with Excimer laser [1 (unsatisfied), 2 (satisfied), 3 (very satisfied)]

response is limited. The present research indicated that lesions on the face, trunk, arms, legs and genitalia (UV sensitive areas) presented a better response to treatment with Excimer laser than those located on the elbows, back of the hands, knees and soles of the feet (UV resistant areas). Nevertheless, repigmentation rates in the extremities were greater than those found in other recent studies.

Hofer and contributors (2006) 19 observed that lesions on the back of the hands and soles of the feet reached a repigmentation rate of less than 10%, on average, during the 10-week treatment interval. Al-Otaibi and others (2009) 8 did not find improvement greater than 25% in nine patients with lesions on their feet and observed that only 1 of the 11 patients with patches on their hands presented a repigmentation rate greater than 75%. This study demonstrated repigmentation greater than 60% in 24 patients with lesions on the hands (38.71%) and in 11 patients with lesions on the feet (34.38%). In 12.90% and 12.50% of patients with macules on the hands and feet, respectively, total repigmentation was observed.

The present study verified a direct correlation between a lack of treatment success and patient dissatisfaction in only 6 cases (4.88%). In general, patients were satisfied with the Excimer laser treatment. This finding is important in the case of vitiligo, because this condition can cause emotional alterations and compromise self-esteem and social relationships.[10] The results of this study confirm that Excimer laser-based phototherapy is an important tool in the treatment of vitiligo.

CONCLUSION

In this study Excimer laser-generated 308 nm UVB radiation was found to be a promising option to treat vitiligo. Its use in vitiligo treatment was effective and safe, and produced a faster response than other modalities described in the literature.

The location of vitiligo patches on the body seems to have an important effect on treatment success. Lesions on the face presented the best results, while those on the elbows, hands and feet were less responsive. Nevertheless, the degree of repigmentation on the extremities (feet and hands) was greater than those found in other recent studies.

The tolerance to the treatment was helpful. Minimal side effects, such as erythema and rare blisters, appeared mainly in phototype II patients. The degree of satisfaction with Excimer laser treatment was significant. The rapid repigmentation after the start of the treatment led to cosmetically satisfactory results, with an improvement in the patients' quality of life and self-esteem. Based on the fact that it is difficult to treat – and that although it does not cause functional incapacity, it has a significant psychological/social/cultural impact – patient satisfaction is considerably relevant in the case of vitiligo. ●

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Original Article

Randomized, double-blind study of minocycline vs. placebo in the treatment of progressive macular hypomelanosis

Estudo duplo-cego randomizado e comparativo entre minociclina e placebo no tratamento da hipomelanose macular progressiva

ABSTRACT

Introduction: Progressive macular hypomelanosis is a common skin hypopigmentation found in all ethnicities, yet it is seldom diagnosed. It affects young adults, especially women, and is often mistaken with pityriasis alba and pityriasis versicolor. It is characterized by symmetric, well-defined, non-desquamative nummular hypopigmented macules in body areas with a greater concentration of sebaceous glands (trunk, thorax, abdomen and lumbar regions). Its etiology is poorly understood, and there is no effective treatment. A red fluorescence has recently been discovered in the lesion, suggesting the presence of porphyrin, produced by Propionibacterium acnes.

Objective: To compare the efficacy of 100 mg/day minocycline vs. placebo in the treatment of progressive macular hypomelanosis.

Methods: Patients over 18 (n = 20), who had suffered from the condition for more than 3 months (without treatment in the previous 3 months), who did not have an allergy to tetracycline, were randomized to receive minocycline or placebo. Wood's Lamp examinations and clinical evaluations (with descriptions and classifications using a color scale), and standardized picture records were conducted at baseline and 30 and 90 days after treatment.

Results: Eighteen patients completed the study. The group treated with minocycline presented a statistically significant improvement ($p < 0.05$) compared to the control group.

Conclusion: 100 mg/day minocycline for 30 days was effective in treating progressive macular hypomelanosis, meaning that Propionibacterium acnes probably has a role in the condition's pathogeny.

Keywords: minocycline; hypopigmentation; placebo effect; treatment.

RESUMO

Introdução: *A hipomelanose macular progressiva (HMP) é hipopigmentação comum da pele, porém pouco diagnosticada. Ocorre em todas as raças e tem sido encontrada no mundo todo. Atinge adultos jovens, especialmente mulheres, sendo muitas vezes confundida com pitiríase alba e pitiríase versicolor. Caracteriza-se por máculas hipopigmentadas numulares, não descamativas, bem definidas e simétricas, em áreas corporais de maior concentração de glândulas sebáceas (tronco, tórax, abdome e região lombar). Não há tratamento efetivo, e sua etiologia é pouco conhecida, mas recentemente foi descoberta fluorescência vermelha nas lesões, o que sugere a presença de porfirina, produzida pelo Propionibacterium acnes.*

Objetivo: *Avaliar a eficácia clínica do uso da minociclina 100mg/dia no tratamento da hipomelanose macular progressiva, comparado com grupo placebo.*

Métodos: *Foram incluídos 20 pacientes maiores de 18 anos, com tempo de doença superior a três meses, sem alergias a derivados de tetraciclinas, sem tratamento prévio pelo menos nos últimos três meses, e houve a randomização aleatória em dois grupos (10 pacientes no grupo placebo e 10 no grupo da minociclina). As seguintes avaliações foram realizadas (pré-tratamento, 30 e 90 dias após o término do tratamento): lâmpada de Wood, exame clínico com descrição das lesões além da classificação na escala de cor e fotografias padronizadas.*

Resultados: *Dos 20 pacientes incluídos, 18 completaram o estudo. Destes, o grupo que tomou minociclina teve melhora estatisticamente significante ($p< 0,05$) em comparação ao grupo-controle.*

Conclusão: *Minociclina 100mg/dia por 30 dias foi eficaz isoladamente no tratamento da HMP, relacionando o provável papel do Propionibacterium acnes na patogenia da doença.*

Palavras-chave: *minociclina; hipopigmentação; efeito placebo; tratamento.*

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INTRODUCTION

Progressive macular hypomelanosis is a common skin hypopigmentation that occurs in all ethnic groups and is found all over the world. It affects young adults, especially women, and is often mistaken with pityriasis alba and pityriasis versicolor.[1,2] Only one study has described an increase in incidence among men.[3]

Progressive macular hypomelanosis is characterized by well-defined and symmetrical hypopigmented nummular macules in body areas that have a greater concentration of sebaceous glands [2,4,5] (trunk, thorax, abdomen, lumbar region and proximal region of upper limbs); there is no systemic manifestation. Lesions are not preceded by inflammation, and get progressively worse. It occurs most commonly on the back (90%), followed by the abdomen (85%), buttocks (35%), thorax (15%) and upper extremities (5%).

Progressive macular hypomelanosis is an important dermatologic problem that stigmatizes the people that suffer from it, affects their daily activities, and elicits undesirable questions about the lesions.

Guilet and colleagues [6,7] found that the condition's progression phase lasts approximately one year, while its regression phase is most likely to last between two and five years. However, other authors believe that spontaneous regression does not occur and that hypomelanosis can remain stable for many years or progress slowly and gradually.[1,3]

Its etiology is still unknown. Dutch researchers 8 have observed follicular red fluorescence of the lesions under Wood's light, suggesting a possible correlation with the *Propionibacterium acnes* (*P acnes*) bacterium, which produces porphyrin. That type of fluorescence is not observed in patients with pityriasis alba or pityriasis versicolor. Westerhof and others [1] concluded that there must be a correlation between the presence of *P acnes* and the hypopigmented macules; they postulated that the bacterium produces the whitening factor that causes hypopigmentation.

Histopathologic findings are usually unspecific, however a common characteristic is a smaller amount of melanin in the lesion[9] and an absence of spongiosis. Using biopsies and electronic microscopy, Relyvelt and colleagues [4] compared the normal and affected skin of eight patients with a clinical diagnosis of progressive macular hypomelanosis and concluded that there was a decrease in melanin production and in the distribution of melanosomes. In other studies, Relyveld [4,5] and Westerhof 1 have found a high density of gram-positive bacteria compatible with *P acnes* through Gram staining

The proposed treatments described in the literature include phototherapy (Psoralen + ultraviolet A (PUVA), ultraviolet A (UVA) or narrowband ultraviolet B (NBUVB)), topical 5% benzoyl peroxide combined with 1% clindamycin, and oral minocycline. There is also a report of using oral doxycycline. One study compared benzoyl peroxide and clindamycin on one side of the body and fluticasone on the other, with UV exposure on both sides; the side treated with antimicrobials showed steady improvement.[5] In a case report, Perman and others [10] treated patients with doxycycline and UV radiation, and improvements lasted for six months. Duarte and colleagues [2] described improvement in both PUVA and NBUVB, however the lesions returned in 72% of their patients.

In a recent publication on approaches to acne treatment, the American Academy of Dermatology [11] asserted that "doxycycline and minocycline are more effective than tetracycline, with evidence that minocycline is superior to doxycycline in reducing the *Propionibacterium acnes* population."

A prospective, open, uncontrolled study demonstrated repigmentation in all patients after the use of 100 mg/day minocycline for three months, without the combined exposure to the sun. Eleven patients were followed up, and the clinical improvement was found to persist at least 11 months after the end of treatment.[12]

In the literature describing therapeutic success, it was not possible to find controlled, randomized double-blind studies. Most studies combine this treatment with exposure to UV radiation.

OBJECTIVE

To compare the clinical efficacy of 100 mg/day minocycline vs. placebo, without sun exposure, in the treatment of progressive macular hypomelanosis.

METHODS

This was a double-blind, randomized, placebo-controlled study of 20 progressive macular hypomelanosis patients of the Dermatology outpatient clinic of the Hospital Servidor Público Municipal de São Paulo, (SP) Brazil. Study participants were randomized to receive 100 mg/day minocycline or placebo for 30 days. All were instructed on the study's details and procedures and signed a term of informed consent and authorization for photographs to be taken. The study protocol was submitted to and approved by the Clinical Research Ethics Committee of the Hospital Servidor Público Municipal de São Paulo (n. 189/2010).

The diagnosis was based on the clinical appearance of the skin lesions, which were assessed by two dermatologist physicians who verified the presence of follicular red fluorescence under Wood's light and negative direct fungal examination.

The study included patients aged 18-60 years who had been inflicted with the disorder for more than three months and who had not taken topical, systemic, antibiotic or antifungal medication in the 3 months preceding the study. Pregnant or breastfeeding women, and patients with a hypersensitivity to tetracyclines, were excluded.

Twenty patients of both genders (17% men, 83% women) aged 18-60 (average 24 years), who had lesions for 8-240 months (average 54 months) on their back/abdomen (61%) or back (39%) were randomized.

The pre-treatment assessment involved a clinical examination that included a description of the lesions and standardized photographs, a direct fungal examination and assessment under Wood's light (long-wave UVA light beamed through Wood's fil-

ter, which only allows 320-400 nm wavelength radiation to pass through).[13,14]

In order to obtain a less subjective evaluation of clinical improvement, the hue of the normal and adjacent altered skin were compared using a numerical skin color scale (1 = lightest, 20 = darkest, see Figure 1). A decrease in the numerical difference between the affected skin of the macule and the normal skin (i.e., a lower contrast between the skin colors) signified clinical improvement. The photographs, taken with a Sony DSC-W170 digital camera, each used the same focal distance and lighting.

The patients were followed up 30 and 90 days after treatment. The clinical and Wood's light examinations, the classification with the numerical skin color scale, and photographs were repeated in the follow-up consultations, and possible adverse effects and intercurrences were assessed. Clinical improvement was defined as a decrease in the lesion's red fluorescence under Wood's light and an increase in the color scale score, with an emphasis on a decrease in the difference between the hues of the lesion and the normal skin. A smaller difference between the scores of the normal and affected skin indicated less color discrepancy, with the macule's color more closely matching that of the normal skin.

Fisher's and Student's t-tests were used in the statistical analysis to calculate relative risk. Statistical significance was defined as $p < 0.05$.

RESULTS

Of the 20 volunteers selected, 18 completed the study (nine in each group). Two participants dropped out due to travel and relocation. Between-group comparisons of gender, age, duration and lesion site, evaluations with Wood's light and difference in color between normal and affected skin before, 30 and 90 days after treatment is shown in table 1. There were no statistically significant differences in gender, age, site or duration of lesions between the placebo and medicated groups (Table 2).

Regarding clinical improvement, the statistical analysis indicated that there was a significant difference ($p = 0.0285$) and relative risk of 3.5. In the control group, 78% of patients did not improve, while 78% of patients in the medicated group presented clinical improvement, as shown in Table 2. Clinical improvement was quantified according to the numerical skin color scale's gradient (0: absence of improvement in the macule's color; 1: darkening of the macule's color by one hue; 2: darkening of the macule's color by two hues, and 3: darkening of the macule's color by three hues). As shown in Table 3, 22% of patients in the medicated group did not demonstrate clinical improvement; 34% presented a one-point improvement in the color scale, 22% improved by two points, and 22% improved by three points, with a more significant and evident improvement in the last group (Figure 2). In the placebo group, only 22% of patients demonstrated a two-point improvement.

All nine patients (100%) of the placebo group continued to demonstrate red fluorescence under Wood light. Six patients (67%) in the medicated group stopped displaying red fluorescence after treatment, and three (33%) remained unchanged.

None of the patients in the placebo group presented any side effects, while five medicated patients (56%) presented mild side effects (nausea, vomiting, improvement of acne), and four (44%) did not present any symptoms linked to the use of minocycline.

DISCUSSION

The term progressive macular hypomelanosis was used for the first time by Guillet and colleagues to describe lesions in young women in Southern India and in the population of Caribbean immigrants in France.6 Other descriptions of this condition are "*Cutis trunci Variata*,"[15] "*Creole dyschromia,*" [7] "*Idiopathic multiple large-blemish hypomelanosis* "[16] and "*Extensive pityriasis alba*."[17]

While its prevalence is unknown, it is believed to be very common, but is seldom diagnosed because it is often confused with other pathologies that present a similar clinical picture. For that reason, direct fungal examination was carried out in the lesions, and a negative result was found in all study patients.

In this study, lesions were located on the abdomen and back, with an average duration of 54 months, and there was predominance in women (83% of cases) and a higher incidence among young adults, all of which coincides with the data described in the literature. Although this pathology's predominance in women has been described in many studies, this finding might be partly explained by the fact that women seek dermatological care more frequently. Although it has been described as rarely affecting patients older than 30,1 three study patients fell into that age group (36, 43 and 46 years old).

Progressive macular hypomelanosis' etiology is uncertain. Among the explanations of its origins are genodermatoses 1,8 and, more recently, a correlation with *P acnes*. The link with *P acnes* is based on the observation of follicular red fluorescence under Wood's light and a positive culture of *P acnes* in the lesions, as demonstrated by Westerhoff and others. 1 In a recently published case report, Neynaber and colleagues found no evi-

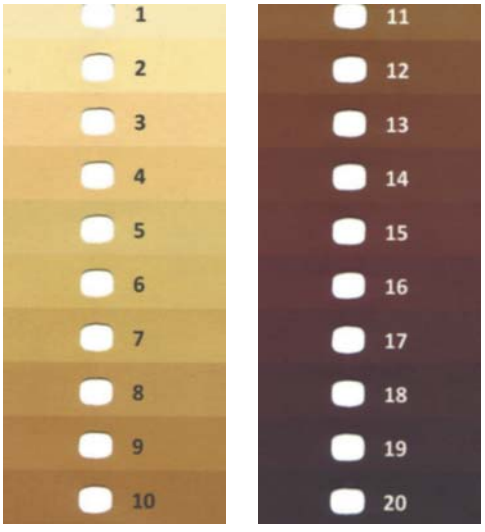


Figure 1 – Skin color level classification scale

Table 1- Study population features

Patient's number	Gender	Age	Lesion site	Duration (months)	Wood light before treatment	Wood light 30 days after treatment	Wood light 90 days after treatment	Skin color level before treatment	Skin color level 30 days after treatment	Skin color level 90 days after treatment	Clinical improvement	Medication
6	Female	18	Abdomen/back	12	+	+	+	7	7	7	No	Minocycline
18	Female	18	Abdomen/back	8	+	+	+	4	4	4	No	Minocycline
2	Female	43	Abdomen/back	240	+	+	-	7	7	6	Yes	Minocycline
5	Female	18	Abdomen/back	24	+	+	-	7	7	6	Yes	Minocycline
7	Female	18	Back	48	+	+	+	6	5	5	Yes	Minocycline
9	Female	21	Abdomen/back	24	+	+	-	5	5	2	Yes	Minocycline
10	Female	18	Back	36	+	-	-	5	4	3	Yes	Minocycline
14	Female	18	Abdomen/back	36	+	-	-	4	2	1	Yes	Minocycline
15	Female	18	Back	36	+	-	-	7	6	5	Yes	Minocycline
1	Female	30	Abdomen/back	96	+	+	+	6	6	6	No	Placebo
8	Female	21	Back	96	+	+	+	7	7	7	No	PlaceboFemale x
11	Female	26	Back	24	+	+	+	9	9	9	No	Placebo
12	Female	18	Back	48	+	+	+	15	15	15	No	Placebo
16	Female	18	Abdomen/back	24	+	+	+	11	11	11	No	Placebo
4	Male	36	Abdomen/back	48	+	+	+	5	5	5	No	Placebo
13	Male	20	Abdomen/back	48	+	+	+	7	7	7	No	Placebo
3	Female	19	Back	12	+	+	+	11	10	9	Yes	Placebo
17	Male	46	Abdomen/back	120	+	+	+	8	7	6	Yes	Placebo

Note: The figures in the skin color level columns before, 30 days after and 90 days after treatment refer to the difference between the color levels of the affected and normal skin. A decrease in that difference corresponds to a clinical improvement, meaning a less intense contrast between the colors of the affected and normal skin

dence of *P acnes* using Wood's light or in the histopathologic analysis, which used a special stain for bacteria.[18]

In the present study, all patients who were clinically diagnosed before treatment presented positive red fluorescence under Wood's light, a result that was sustained after treatment in all patients in the placebo group (Table 4).

There is no consensus on a widely recognized and effective treatment option. Kwah and others [19] evaluated the effectiveness of NBUVB as a monotherapy, which demonstrated satisfactory yet short-lived results. Duarte and colleagues [2] found similar satisfactory results with PUVA and NBUVB; there was no statistically significant difference between the two methods. However, 72% of the patients experienced a recurrence of the lesions.

Based on Westerhoff and others' hypothesis [1] about the inhibitory role of *P acnes* in melanogenesis, some authors have used antibiotics to treat progressive macular hypomelanosis. One study obtained satisfactory results with the topical combination of 5% benzoyl peroxide gel and 1% clindamycin, [5] while another also obtained a satisfactory outcome in one case using topical benzoyl peroxide and erythromycin [20]. A third case successfully used a combination of doxycycline and sun exposure. [10] An earlier pilot study (prospective, open, non-controlled) conducted by the authors found that 100 mg/day minocycline for three months stimulated repigmentation in all patients even without exposure to the sun. No recurrences were observed in the 11 months of post-treatment follow-up.[12]

In therapeutic successes reported in the literature, no other randomized, placebo-controlled, double-blind studies that did not involve solar exposure were found. The present research yielded improvement in seven out of nine individuals who used the medication, which matches the satisfactory results of minocycline described by Almeida and colleagues [12]. Yet repigmentation occurred in only two cases in the placebo group.

Despite descriptions of rare cases of hypersensitivity to minocycline,[21] induction of lupus-like, autoimmune hepatitis, hyperpigmentation and vasculitis, [22,23] the only effects reported in this study were nausea and vomiting in three patients and improvement of acne in two (56% of patients in the medicated group). Although the causes of these effects are not fully understood, hypotheses have been proposed that suggest a reduction in the production of free radicals, inhibition of phospholipase a^2, and changes in the expression of the tumorous necrosis factor and alpha interferon are involved.[24-26] The improvement in acne can be even considered as an advantage provided by the medication that increases patient satisfaction.

Of the nine participants in the minocycline group, two (22%) did not respond. This outcome might be explained by the duration of the treatment (30 days), which is considerably less than the three months described by Almeida and col-

Table 2 - Comparison of variables between placebo and minocycline groups (gender, lesion site and duration, age, clinical improvement and side effects)

Characteristics		Drug				Total (n=18)		Relative risk	p- value	Test
		Minocycline (n=9)		Placebo (n=9)						
		Number of patients	%	Number of patients	%	Number of patients	%			
Gender	Male	0	0%	3	33%	3	17%	–	0,2059	Fisher's exact
	Female	9	100%	6	67%	15	83%			
Lesion site	Abdome/ Back	6	67%	5	56%	11	61%	1,27	1000	Fisher's exact
	Back	3	33%	4	44%	7	39%			
Clinical improvement	Yes	7	78%	2	22%	9	50%	3,5 sig	0.0283	Fisher's exact
	No	2	22%	7	78%	9	50%			
Age (years)	Average	21		26		24		–	0,2670	Student-t
	CI 95%	14,76 to 27,47		18,54 to 33,46		19,03 to 28,08				
Duration (months)	Average	52		57		54		–	0,8336	Student-t
	CI 95%	-3,63 to 106,74		28,25 to 86,427822		26,72 to 82,17				
Side effects	No	4	44%	9	100%	13	72%	–	0.0147	Fisher's exact
	Yes	5	56%	0	0%	5	28%		sig	

Table 3: Medicated group's clinical improvement quantification using the skin color level scale

Result	Minocycline (n = 9)		Placebo (n = 9)	
	Number of patients	%	Number of patients	%
0	2	22	7	78
1	3	33	0	0
2	2	22	2	22
3	2	22	0	0
Total	**9**	**100**	**9**	**100**

Table 4: Medicated group's Wood light fluorescence evaluation before and 90 days after treatment

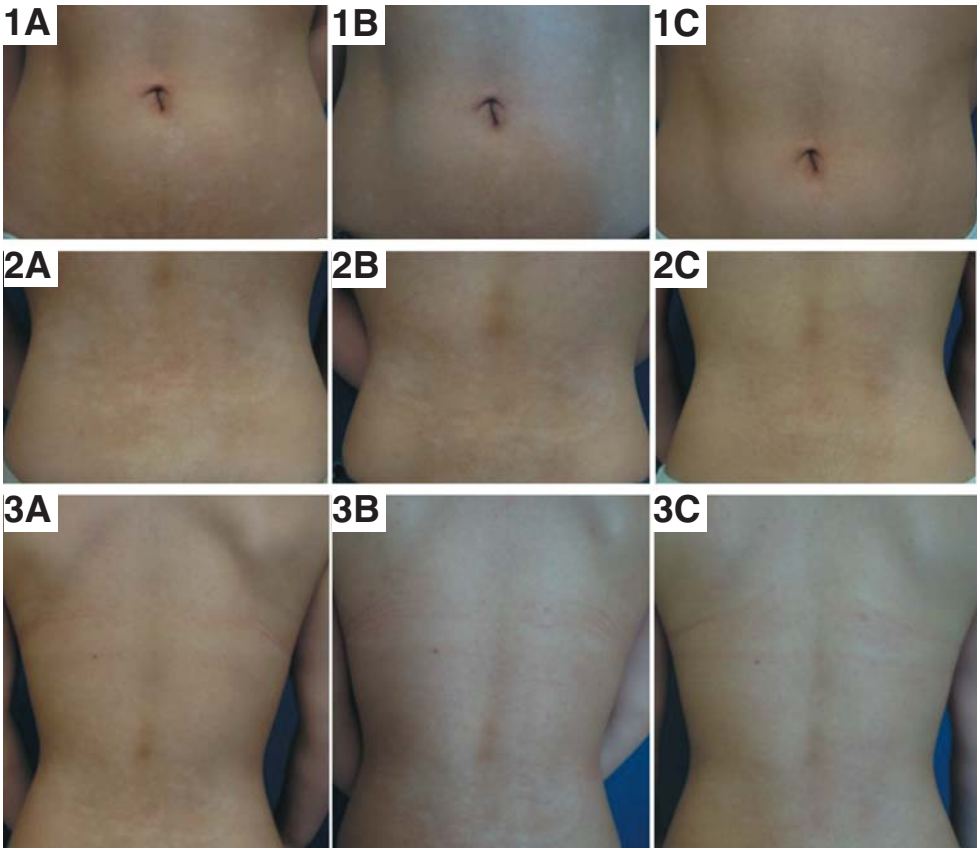
Fluorescence under Wood light	Pre-treatment		90 days after treatment	
	Number of patients	%	Number of patients	%
+ 9	100	3	33	
–	0	0	6	67
Total	**9**	**100**	**9**	**100**

leagues' study [12] that demonstrated 100% repigmentation in all treated cases.

The statistically significant difference between the cases treated with placebo and minocycline demonstrates that the latter – a recognizably effective agent against *P acnes* even when not combined with UV exposure – is an effective therapeutic option in treating progressive macular hypomelanosis. Studies with a larger sample and a longer follow-up period are necessary to confirm these results and assess their long-term permanence.

CONCLUSION

The use of 100 mg/day minocycline for 30 days was effective in treating progressive macular hypomelanosis, even without solar exposure. ●



Figures 2: Clinical improvement in the minocycline group:
1A, 2A and 3A: Before treatment;
1B, 2B and 3B: 30 days after treatment;
1C, 2C and 3C: 90 days after treatment

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Mohs micrographic surgery

Cirurgia micrográfica de Mohs

ABSTRACT

Mohs Micrographic Surgery is regarded as a very useful technique for the excision of difficult to handle skin cancers. The procedure is divided into clearly defined steps: tumor evaluation and marking, tumor exeresis, tissue preparation and mapping, histologic processing and analysis, and closing of the surgical wound. The histologic analysis of all surgical margins leads to higher cure rates and tissue conservation, which make the procedure safer and more reliable.

Keywords: skin neoplasms; Mohs surgery; frozen sections.

RESUMO

A técnica cirúrgica micrográfica de Mohs é modalidade muito útil para excisão de cânceres de pele de difícil manejo. Desde que corretamente realizada, oferece vantagens sobre os outros métodos de tratamento para malignidades cutâneas. O procedimento é dividido em etapas bem definidas: avaliação e marcação da lesão, exérese, preparação e mapeamento da peça cirúrgica, processamento e análise histológica e fechamento da ferida cirúrgica. A avaliação histológica de todas as margens cirúrgicas leva a maiores taxas de cura e maior conservação tecidual, conferindo ao procedimento segurança e confiabilidade.

Palavras-chave: *neoplasias cutâneas; cirurgia de Mohs; seções congeladas.*

INTRODUCTION

Mohs Micrographic Surgery (MMS) is considered to be the most reliable conservative method for treating cutaneous malignancies. It is a surgical procedure carried out in progressive stages; sections are made observing meticulously mapped margins until the tumor is completely removed. In addition to boasting higher cure rates than other treatment types, MMS helps preserve the maximum amount of healthy tissue [1].

The MMS technique has continuously evolved since it was first described and is currently the treatment of choice for tumors located in critical areas, sites that have previously undergone radiotherapy, large or recurring tumors, and tumors with aggressive histological characteristics In 1941, Frédéric Mohs described a new surgical technique for the phased removal of skin cancers through *in situ* fixation of cutaneous tissue [2]. After fixing the tumor, Mohs excised the cancer and cut the excised piece into tangential sections that included as much of the epidermis as the underlying tissue. These cuts were carried out with enough depth to allow microscopic analysis of the margins.

Continuing Medical Education

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Several types of procedures, such as curettage and electrodissection (CE), cryotherapy, photodynamic therapy, radiotherapy, conventional surgery and MMS, have been used to treat skin cancers. Cryotherapy, CE and radiotherapy are destructive procedures based on visual and clinical assessments of the extent of the tumor; there is only a limited ability to check the free margins when using these methods. With 3-6 mm safety margins, conventional exeresis is used in the majority of skin cancers [3]. Although conventional exeresis is systematically followed by histological analysis of the surgical margins [4], these assessments are limited compared to those of MMS, in which all peripheral and deep margins are analyzed (Figure 1).

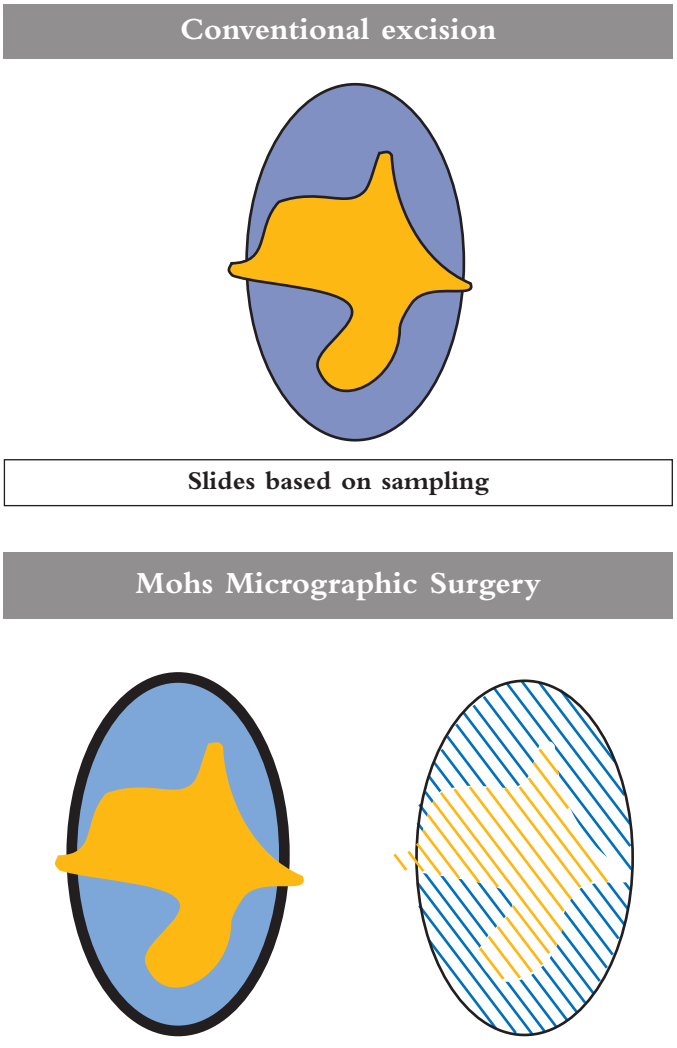

Figure 1 - Comparison of histological analysis carried out through conventional surgery and Mohs Micrographic Surgery (MMS). Note that in the conventional excision, the cut of the tissue is made by sampling, which can lead to flaws in the analysis of tumor-free margins. Conversely, given that all peripheral and deep margins are analyzed in MMS, the entire extent of the tumor is analyzed

Although conventional treatments yield high cure rates for small and well-delimited skin cancers in general, MMS yields higher cure rates for both primary and recurrent tumors [5,6]. The 5-year recurrence rates for primary and recurrent basal cell carcinomas treated conventionally are 10% and 17%, respectively. When treated with MMS, those rates fall to 1% and 6% [6].

Besides presenting considerably higher cure rates than conventional surgery, MMS allows greater preservation of healthy tissue around the lesion. In order to obtain cure rates similar to those achieved with MMS, conventional surgery frequently needs much more extensive margins. For instance, the cure rate for conventional excisions of basal cell carcinomas with less than 10 mm with 3-mm margins is 85%. A 4-mm margin would increase the cure rate to 95%7. For large sclerosing or recurrent basal cell carcinomas, sections with 13-15 mm margins are necessary in order to obtain a 99% cure rate [8].

A biopsy to confirm a skin cancer diagnosis is usually carried out before MMS is recommended. The indications for MMS are well established, especially for non-melanoma skin cancers (Table 1). The role of MMS in the treatment of other tumors such as melanoma and Merkel Cell Carcinomas is more controversial; its indication depends on the dermatologist's preference and comfort.

TECHNIQUE

The MMS technique includes the examination and marking of the area to be excised, the removal and mapping of the surgical piece, and the histological processing and microscopic examination (Figure 2). The procedure is repeated until there are no traces of tumor in the surgical margins. Once the tumor is completely removed, the surgical wound is closed.

When examining the patient, the clinical margins of the

Table 1. Main indications for MMS

Tumors > 2 cm in diameter
Recurrent tumors
Tumors that have not been completely excised
Tumors located in areas with a high risk of local recurrence (e.g., central areas of the face, periocular, periorbital and periauricular areas)
Tumors located in areas where tissue preservation and high cure rates are important
Tumors with poorly defined clinical margins
Tumors with aggressive histological subtypes (e.g., micronodular, infiltrative, squamous or sclerodermiform basal cell carcinomas or poorly differentiated squamous cell carcinomas) or that have evidence of perineural infiltration
Tumors on irradiated areas or scars

tumor are initially delimited using a surgical marking pen. The tumor's location is then confirmed by the patient with the help of a mirror. Once confirmed, local anesthesia, usually with lidocaine and epinephrine, is applied. Curettage can be used before the excision to remove any excess tumorous tissue and check for any subclinical expansion of the tumor [9,10]. Nonetheless, curettage should not be considered as a necessary step, since it does not always benefit the procedure.

A study analyzing the effectiveness of curettage before MMS in non-melanoma skin cancers concluded that, although it is useful for removing excess friable tumorous mass before MMS, it does not completely delimit the extent of the tumor [11]. In addition, pre-operative curettage might not reduce the number of MMS phases. When treating a patient with MMS, one should take into account the fact that 24% of non-melanoma skin cancers are completely removed when histologically examined [12]. For those tumors, aggressive curettage can cause more damage to the surrounding tissue without necessarily increasing the accuracy of the procedure.

Once the clinical delimitation of the tumor is defined, with or without using curettage, the surgical marking is carried out 2 mm outside the previous marking to indicate the scalpel's point of incision.

In classic MMS, the scalpel blade forms a 45° angle with the skin during the excision of the tumor's margins. This allows the epidermis, dermis and deep tissues to be cut in a straight line by the cryostat, allowing the examination of a single plane [13]. The excision of peripheral margins at 90° is a variant of the original technique. In that variant, the surgical piece is divided into peripheral and deep margins, with a separate analysis of each 14 (Figure 2).

The processing of the excised tissue efore the microscopic examination includes marking it with dye, leveling, freezing, cutting and staining. Once the tumor is excised, the removed tissue is divided into fragments to allow its inclusion underneath a coverslip.. The fragments must be mapped and color-coded with tissue dye to produce a map of the tissue in order to orient the surgeon while he or she analyzes the tissue under the microscope. A study carried out in the USA 15 showed that most Mohs surgeons use hand-drawn maps of excised tissue. This is a straightforward, cheap and fast method, which allows the surgeon greater flexibility to illustrate the size and format of the tumorous tissue and the surgical defect. However, hand drawings are not as accurate when analyzing the skin in recurrent cases. Digital pictures allow more precise representations of the excised tissue and surgical defect, and provide better dimensions and information for the follow-up. Digital pictures are currently used by a minority of Mohs surgeons (less than 2%), a number that will certainly rise with the increasing use of digital pictures and electronic medical records.

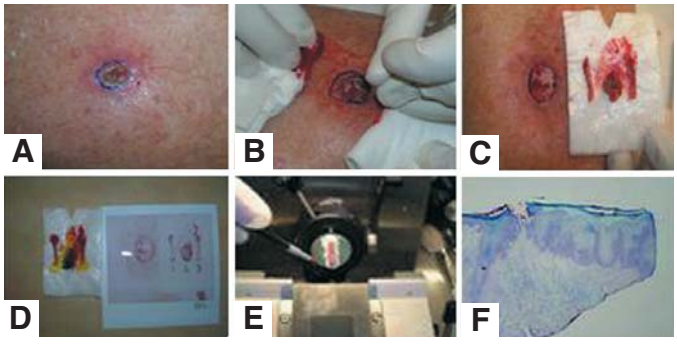

Figure 2 - Stages of the preparation of excised tissue, according to a variant of the Mohs technique (incision at 90°). **(A)** Clinical marking of the lesion. **(B)** Exeresis with 2-mm margins. **(C)** Fragmentation of the removed tissue. **(D)** Mapping of the lesion. Note that each stain color of the excised tissue to the left corresponds to a different marking in the picture to the right. **(E)** Cutting of the tissue using a cryostat. **(F)** Slide showing the red marking of one of the fragment's extremities.

The excised tissue must be level on the microscope slide in order to cut the combined epidermis and dermis in a single plane. Although in most cases the tissue is leveled spontaneously or by using light mechanical pressure, it is sometimes necessary to relax the tissue by making cuts on its surface – a particularly useful technique for thick tissue.

The tissue is then sectioned, and the slides are prepared for histological analysis. Hematoxylin-eosin is the most commonly used stain in MMS, and can be used for all cutaneous neoplasias. Toluidine blue is a particularly useful alternative stain for basal cell carcinomas, since it clearly demarcates the islands of tumorous cells by staining the surrounding mucopolysaccharides pink.

Dermis and epidermis sections are usually 5-6 mm thick, while those of adipose tissue normally measure 15-25 μm [16]. Exceptionally thick sections are difficult to analyze and can lead to misinterpretation. Conversely, details in the cells are more clearly defined in thinner sections.

Oblique sections of adnexal structures can be mistaken with basal cell carcinomas. However, serial cuts help distinguish the two.

Laboratory technicians play a key role in the process and should always position the tissue so that the correct section is made in the epidermis' surface. Mohs surgeons must know how to flatten, freeze, cut and stain the tissue in order to communicate efficiently with laboratory technicians in case the quality of damaged tissues needs to be discussed.

One of the biggest advantages of MMS for the dermatologic surgeon is that it maximizes the preservation of normal tissue. The surgeon must analyze the microscope slides to determine whether the margins are affected. If the tumor has been completely excised, the surgical defect can be reconstructed. If tumorous cells are present in the tissue sample, their corresponding location is marked on the map. If the lateral margin is compromised, an additional 1-2 mm of tissue is removed. If the tumor is present in the deep margin, an incision along the base of the surgical wound is made in order to remove a thin slice of its bottom. These steps are repeated until the margins are found to be tumor free; reconstruction follows.

MMS does not require prophylactic antibiotic therapy afterwards. This type of treatment is restricted to specific cases and is not linked to the MMS surgical technique [17].

FINAL CONSIDERATIONS

The MMS technique was developed to allow the complete histological control of the margins of excised cutaneous tumors. In spite of significant variations in the techniques used by different Mohs surgeons, these techniques share several common points, including: (1) the complete histological control of both peripheral and deep margins, (2) tissue preservation due to the use of narrow margins, (3) clinical-pathological correlation and surgical/histopathologic assessments that are carried out by the same physician. Since its introduction, techniques used in MMS have evolved continuously. In spite of some technical differences, the accuracy and meticulousness applied in each step of the procedure lead to consistently high, replicable cure rates. When carried out by properly trained professionals, MMS is a safe and reliable method that is increasingly used in dermatologist physicians' daily practice. ●

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Questions for continuing medical education (CME)

1. About Mohs Micrographic Surgery (MMS), it is correct to state that:

a) it is the method of choice for the treatment of cutaneous tumors.
b) prophylaxis with antibiotics is suitable when the surgical time exceeds 1 hour.
c) it is not suitable for superficial basal cell carcinomas (BCCs).
d) it presents cure rates similar to those of conventional surgery, yet with greater tissular preservation.
e) none of the above

2. There is consensus on the indication of MMS in the following cases, except for:

a) Nodular BCC located 1 mm from the palpebral border.
b) Merkel cell carcinoma.
c) Squamous cell carcinoma (SCC) on scars.
d) Recurrent micronodular BCC on the nasal wing.
e) Poorly differentiated pre-auricular SCCs measuring 1.5 cm.

3. Regarding curettage carried out before the removal of the tumor, it is possible to state that:

a) it can be useful for reducing the friable tumorous mass.
b) it is a reliable method of delimitating tumors.
c) it is always indicated in BCC cases.
d) it reduces the number of MMS phases.
e) it is more suitable in cases of poorly defined margins.

4. The distance between the clinical tumorous margin and the initial surgical margin must be:

a) 1 mm.
b) 2 mm.
c) 3 mm.
d) it depends on the tumor's histology.
e) it depends on the tumor's location.

5. The excised tissue is leveled on the slide in order to:

a) better visualize the cutaneous annexes.
b) facilitate serial cuts.
c) allow the dermis and epidermis to be cut in a single plane.
d) reduce the cut's thickness.
e) none of the above

6. The most frequently used staining in MMS is hematoxylin-eosin. An alternative is toluidine blue. The type of tumor in which it is particularly useful and its characteristic color are, respectively:

a) BCC – pink stroma
b) BCC – blue tumorous cells
c) SCC – pink tumorous cells
d) SCC – blue stroma
e) SCC – blue tumorous cells

7. The cure rates for treating recurring BCC with conventional surgery and MMS are, respectively:

a) 17% and 10%.
b) 17% and 6%.
c) 17% and 1%.
d) 10% and 6%.
e) 10% and 1%.

8. When analyzing a slide, if it is unclear whether the tissue presents an adnexal structure or BCC, the physician should:

a) request extra cuts of that slide.
b) use a different stain.
c) carry out immunohistochemistry.
d) assume it is a tumor and increase the margins.
e) none of the above

9. If the lateral margin is compromised, the physician should:

a) increase the peripheral margins by 1-2 mm.
b) repeat the procedure carried out in the first phase.
c) increase the compromised border with greater margins (3-4 mm) in order to shorten the length of the procedure.
d) increase the compromised border with a 1-2 mm margin.
e) none of the above

10. Antibiotic prophylaxis is indicated:

a) in all MMS cases.
b) never in MMS cases.
c) it depends on the technique used.
d) in the same situations as conventional surgery.
e) none of the above

Key

Complications in laser dermatologic surgery. Part II: Fractional and non-fractional ablative lasers, and fractional non-ablative lasers. 2011;3(2):135-53

1 e, 2 d, 3 d, 4 c, 5 b, 6 b, 7 c, 8 d, 9 b, 10 d

Answers must be sent directly using the website www.surgicalcosmetic.org.br
The deadline for submitting answers will be provided by e-mail with a direct link for accessing the journal

Periorbital hyperchromia

Hiperpigmentação periorbital

Review Article

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ABSTRACT

Periorbital hyperchromia (dark eye circles) is a recurrent complaint in dermatologic consultations, as it interferes with patients' self esteem. The eyes are central in the communication process, and dark eye circles are very noticeable and make the face look tired; thus they have a considerable impact on patients' quality of life. Although many treatment options are available, publications on periorbital hyperpigmentation are scarce, and the vast majority lack a sound scientific basis to prove their efficacy and duration. This article analyzes the palpebral region's anatomy and periorbital hyperchromia's epidemiology, etiopathogeny, and treatments recommended in the literature.

Keywords: hyperpigmentation; eyelids; skin pigmentation; products for eye areas.

RESUMO

A hipercromia cutânea periorbital ou "olheira" é queixa comum nos consultórios de dermatologia por interferir na autoestima dos pacientes. Os olhos são o centro das atenções na comunicação, e a "olheira" dificilmente passa despercebida, proporcionando à face aspecto de cansaço, causando importante impacto na qualidade de vida. Há poucas publicações na literatura sobre hiperpigmentação periorbital e, embora as opções de tratamento sejam muito vastas, a maioria carece de embasamento científico que comprove sua eficácia e duração. Este artigo aborda a anatomia da região palpebral, a epidemiologia, a etiopatogenia e os tratamentos propostos na literatura para a hipercromia periorbital.

Palavras-chave: *hiperpigmentação; pálpebras; pigmentação da pele; produtos para áreas dos olhos.*

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INTRODUCTION

Although periorbital hyperpigmentation (also called peripalpebral hyperpigmentation, dark eyelids, dark eye circles, dark circles, or simply under-eye circles) is a mere color difference between the palpebral skin and the remaining facial skin, it makes people look tired or older, which negatively affects their quality of life.[1,-4]

It has a higher prevalence in individuals with darker skin, hair and eyes, and affects age groups and genders equally. Nevertheless, there are a higher number of complaints from women, especially senior women. There are few studies about the etiology of this condition, however dark eye circles with a vascular component are known to present a dominant autosomal family inheritance pattern.[2,3]

Periorbital hyperpigmentation seems to have multifactorial causes that involve intrinsic factors (determined by the individual's genetics), and extrinsic factors (sun exposure, smoking,

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alcoholism and sleep deprivation, for instance). However, the presence of melanic pigment and hemosiderotic pigment in the affected sites is a distinctive feature in its etiopathogeny.[2-4]

Melanic hyperpigmentation is more frequent in brunet adults, as a consequence of excessive and cumulative exposure to the sun, which increases the production of melanin, reduces the skin's thickness and increases the dilatation of blood vessels.[2,4,5]

Intense vascularization is mainly found in people belonging to certain ethnic groups such as Arabs, Turks, Hindus, inhabitants of the Iberian Peninsula and their respective descendants. In these ethnicities, its manifestation tends to take place earlier, often during childhood. In those individuals there is no change in the color of the skin; the eyelid appears darkened because the dilated vessels are visible due to the transparency of the skin. [2] In those cases, therefore, the problem is often aggravated when the lower eyelid's vessels are more dilated (e.g., from fatigue, insomnia, oral breathing, crying), causing dermal blood extravasation. The liberation of ferric ions takes place locally, entailing the formation of free radicals that stimulate the melanocytes, which generates melanic pigmentation. [2, 4-6]

Other causes noted as being responsible for the appearance of dark eye circles are post-inflammatory hyperpigmentation secondary to atopic and contact dermatitis, sleep deprivation, oral breathing, alcoholism, smoking, use of certain medications (contraceptives, chemotherapy, antipsychotic and some types of eye drops), the presence of palpebral sagging (due to aging) and of disorders that develop with hydric retention and palpebral edema (thyroid disorders, nephropathies, cardiopathies and pneumopathies) – all of which worsen the unattractive appearance of dark eye circles.[2-4,7]

Various treatments have been proposed for periorbital hyperchromia, however there are few studies on their long-term efficacy. The main types of treatment are: topical application of depigmenting products, chemical peelings, dermabrasion, cryosurgery, fillings with hyaluronic acid, intense pulsed light, CO2, argon, ruby and excimer lasers. [2-4, 6, 8-12]

PALPEBRAL ANATOMY

The eyelids are tegumentary pleats that participate in facial expression and aesthetics, however their main function is to protect the eyeballs through sensorial filtration actions carried out by the palpebral cilia, and the Meibomian and lachrymal glands' secretions. In this manner, the cornea remains hydrated and the closing movements of the eyes function as a barrier to external traumas and prevent the cornea from drying out.[13-17]

The upper eyelid reaches upwards to the eyebrow, which separates it from the forehead. The lower eyelid extends downwards up to the lower border of the orbit, and is delimited by the genian region.[15]

The palpebral fissure, which measures 9-10 mm in adults, is determined by the interaction of the muscles that open and close the eyelids. To open the eyelid, the palpebral elevator muscle is assisted by two other accessory muscles (Muller's and frontalis muscles).[18] The aging process decreases the palpebral fissure's vertical opening, due to the progressive lowering of the upper eyelid, [14] which is caused by a decrease in the upper eyelid lifter muscle's aponeurosis action.[15] The skin becomes more flaccid, less elastic and has a greater propensity to wrinkle 16. The orbicular and tarsal muscles, the orbital septum and the conjunctival mucous membrane also go through transformations in the elderly. In addition, gravity and facial expressions influence the mechanical deformation of those structures. [17]

A cohort study with 320 patients (aged 10-89) evaluated participants' eyelids frontally and laterally and found that there is a correlation between a decrease in the palpebral fissure and an increase in the age of patients. [19]

PALPEBRAL REGION'S SKIN AND SUBCUTANEOUS TISSUE

Palpebral skin is the thinnest in the human body (< 1 mm). Its epidermis is constituted of stratified epithelium, which is very thin (0.4 mm) compared to that of the palmoplantar region (the thickness of which is approximately 1.6 mm).[13]

The nasal portion of the palpebral skin has thinner hair and more sebaceous glands (i.e., it is softer and oilier) than its temporal portion. The transition between the eyelids' thin skin and the remaining facial skin is clinically observable.[13]

The palpebral dermis is composed of loose conjunctive tissue, and is extremely thin in that region. It is absent in the pre-tarsal skin, in the medial and lateral ligaments of the eyelid, where the skin adheres to the underlying fibrous tissue. The thinness of the skin, combined with the lack of fatty tissue, gives that region its characteristic translucency. As a result, the accumulation of melanin and/or vessel dilatation in that region can be easily seen, through transparency, as bilateral homogeneous hyperpigmentation.[2,4,5,13]

PALPEBRAL REGION'S VENOUS AND LYMPH VASCULARIZATION

The eyelids' arterial irrigation comes through many vessels: the supratrochlear, supraorbital, lachrymal and dorsum of the nose arteries (all originating in the facial artery); the angular artery (originating in the facial artery); the transverse artery (originating in the facial artery); the transverse facial artery (originating in the superficial temporal artery) and the branches of the superficial temporal artery itself 20 (Figure 1).

Venous drainage (following an external pattern) takes place through the veins associated with these arteries and (following an internal pattern) penetrates the orbit through connections with ophthalmic veins 20 (Figure 2).

Lymphatic drainage takes place mainly through the parotid lymph nodes; some of the drainage from the medial angle of the eye to the lymph vessels is associated with the angular and facial arteries, towards the submandibular lymph nodes.[20]

COLOR OF THE SKIN IN THE PALPEBRAL REGION

The palpebral skin's color results from the combination of several factors, some of genetic-racial origin (such as the amount of melanin pigment), others of individual or regional and even gender l origins, such as the thickness of the several components and the blood volume in their vessels.[2,4,5,21]

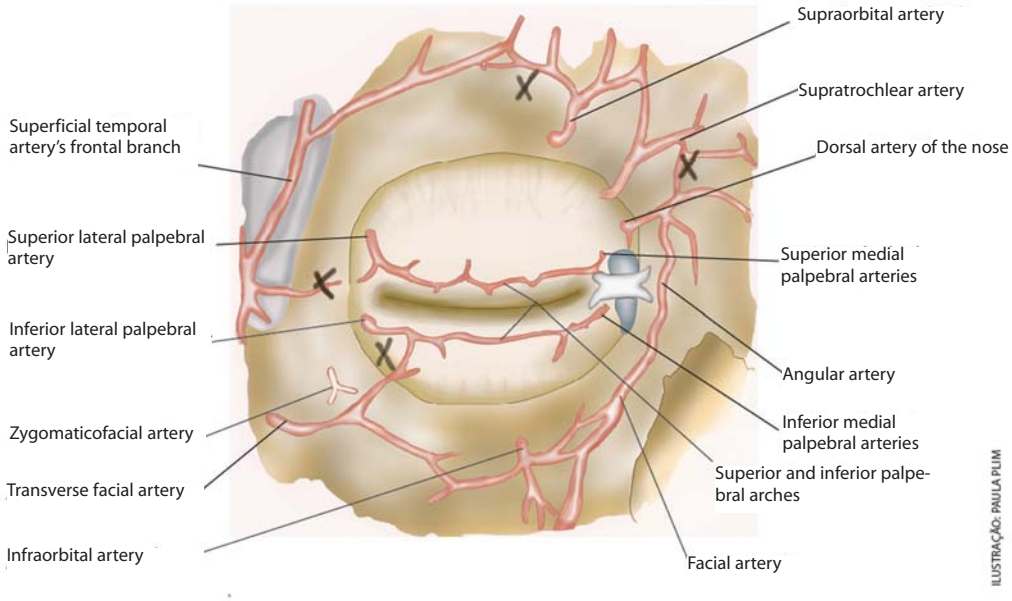

Figure 1 - Eyelids' arterial irrigation

DARK EYE CIRCLES' ETIOPATHOGENY

There are two types of dark eye circles: those of predominantly vascular etiology and those of predominantly melanic etiology. The majority, however, have mixed origins and are caused by the combination of the pigments melanin and hemosiderin.[2-4]

Dark circles with a predominantly vascular etiology present a pattern of dominant autosomal family inheritance. [2-4] They usually appear earlier, during childhood or adolescence, and are more common in Arab, Turkish, Hindu and Iberian ethnic groups.[2] Diagnosing the type of dark eye circles is carried out by tractioning the lower eyelid in order to better visualize the transparency of the vessels under the skin 2 (Figure 3).

Dark eye circles of predominantly melanic etiology occur more frequently in patients with higher phototypes (Figure 4), but can affect patients with lower phototypes – usually older patients who have had excessive and cumulative sun exposure.[2,22-24]

The physiological cutaneous aging process that leads to palpebral flaccidity and sagging worsens the dark circles' appearance. In addition, excessive exposure to the sun, which causes an increase in pigmentation, a decrease in the thickness of the skin and local vasodilatation, can be a significant etiologic factor for dark eye circles.[2,7,14-16,25]

Due to the vasoconstricting effects of nicotine, smoking causes a pale appearance of the skin in general, increasing the contrast with under-eye circles; alcoholism and sleep deprivation cause vasodilatation and an increase in palpebral blood flow; oral breathing causes edema in the nasal and paranasal mucous membrane, obstructing the palpebral veins' drainage and leading to blood stasis and dark circles.[2,25]

The use of hormonal replacement therapy and contraceptives, and menstruation and pregnancy worsen under-eye circles due to the hormonal stimulus of melanin production.[2,3,22,25]

The use of vasodilating drugs and eye drops based on similar analogous prostaglandins for the treatment of glaucoma causes, in addition to palpebral hyperpigmentation, the reabsorption of orbital fat.[3,26]

A deficiency in vitamin K, vital in the blood coagulation process, can cause small hemorrhages and cause dark circles.[2,3,25]

EPIDEMIOLOGY

No epidemiological studies carried out in patients with periorbital hyperpigmentation were found in the researched literature.

It is believed that dark eye circles and palpebral affections are more frequent in women and in individuals with darker skin, hair and eyes,regardless of their etiology. It affects all age groups, however it is more evident in older people.[2-4] After menopause, cutaneous collagen synthesis decreases 2.1% per year, and as the hypodermis becomes thinner, the skin's aesthetic condition worsens. The aging process also causes structural changes in the skin due to gravity and physiological alterations in the skin, which can be more intense when combined with actinic damage. When acting in an area that is low in collagen or subcutaneous tissue, or in areas with little muscular sustentation, gravity causes the skin to move downwards, becoming stretched and thinner, making the palpebral vessels more visible. [2,6,14,16,25]

Ohshima and colleagues studied palpebral skin and noticed that it is significantly less dense in patients with dark eye circles, which allows a clearer visualization of vessels and pigmentation due to the transparency of this area.[7]

TOPICAL TREATMENTS

Periorbital hyperpigmentation is a common complaint in dermatology practices. However, it is rarely studied. Since it does not have a clearly defined etiopathogeny, there is no consensus regarding its treatment.

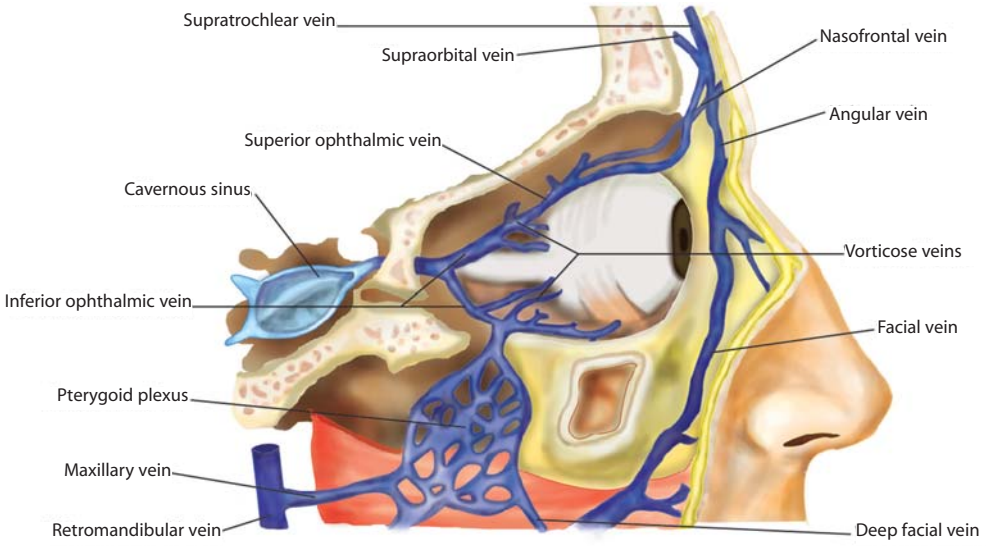

Figure 2 - Eyelids' venous drainage

Most topical treatments consist of the application of depigmenting products (vitamins C, E and K1; azelaic, phytic and kojic acids; arbutin; biosome C; magnesium ascorbyl phosphate; thioglycolic acid; hydroquinone; haloxyl). Nevertheless, there are few studies analyzing or comparing the efficacy of those medications or correlating the results with patients' epidemiological characteristics.[2-4,25]

An open, monocentric, non-paired clinical and non-randomized pilot study was recently published that demonstrated the efficacy and safety of treating infraorbicular pigmentation with 10% acid thioglycolic gel peeling. The study included 10 volunteers, aged 24-50, who underwent five sessions of peeling with 10% acid thioglycolic gel at 15-day intervals. The average clinical satisfaction rated by patients was 7.8; that of the applicator physician was 7.6; and that of the evaluator blunt physician was 6.8, with no statistically significant difference between them ($p = 0.065$).[3] Thioglycolic acid, a depigmenter with an unpleasant scent, is suitable for hyperchromias with a predominantly vascular component, due to its capacity to absorb the hemoglobin's iron oxide, alleviating the dark eye circles.[3,27]

Ascorbic acid is a depigmenting agent that is less chemically stable in topical formulations. In addition to its whitening effect, it can also increase collagen synthesis, improving the skin's thickness, and in turn attenuate dark eye circles. Preference should be given to magnesium ascorbyl phosphate, a vitamin C derivative that is more stable and acts by inhibiting melanogenesis. [28] Ohshima and others conducted a clinical study to evaluate vitamin C's efficacy in treating dark eye circles. Volunteers ($n = 14$) with lower eyelid hyperpigmentation were evaluated for six months, using a solution containing 10% sodium ascorbate on one side of the face and ascorbic acid glucoside on the other. The melanin and erythema indices, thickness and the inferior papillae dermis' echogenicity were evaluated bilaterally during the course of the study. The change in the erythema index was significantly smaller on the side treated with sodium ascorbate compared to the side treated with the vehicle. The dermal thickness was greater on the side treated with sodium ascorbate compared to the other side, but the difference was not statistically significant. No significant differences were observed between the sides treated with ascorbic acid glucoside and those treated with the vehicle regarding the erythema index, echogenicity or dermal thickness. The authors concluded that sodium ascorbate can improve dark eye circles by increasing the lower eyelids' thickness and reducing the dark staining caused by the congestion of blood circulation.[29]

A study combining 2% phytonadione, 0.1% retinol, 0.1% vitamin C and 0.1% vitamin E in a gel, applied twice a day for eight weeks in 57 patients' lower eyelids, demonstrated that 27 (47%) presented reduced pigmentation; the procedure was considered by the authors to be very or moderately effective in the reduction of dark eye circles.[6]

Hydroquinone is a topical depigmenting agent that acts immediately by inhibiting the tyrosinase's activity. Secondarily, and more slowly, it induces structural modifications in the membranes of the organelles of the melanocytes, accelerating the degradation of the melanosomes.[7,14] A combined study conducted with 18 patients who used 5% hydroquinone gel and 0.1% retinoic acid for six weeks, followed by the application of q-switched Ruby laser with the purpose of reducing epidermal and dermal pigmentation, respectively, showed excellent results that were confirmed by the patients' satisfaction level (considered excellent by 83.3%) and by the skin biopsies carried out before and after treatment (which demonstrated a decrease in dermal pigmentation in all patients).[14] There are several cosmeceuticals containing hydroquinone in the market, however none of them was specifically formulated for the treatment of the eye area. The safety and efficacy of using those creams to treat hyperpigmentation in conditions other than melasma have not

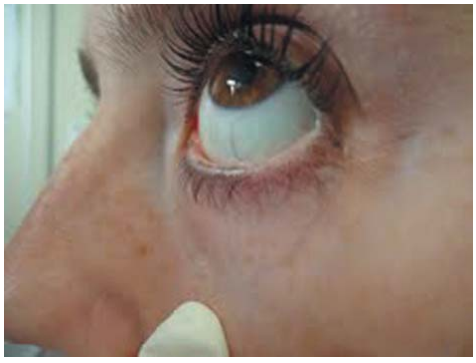

Figure 3 - Periorbital hyperpigmentation of vascular pattern. Visualization of the vascularization under the skin when tractioning the inferior eyelid

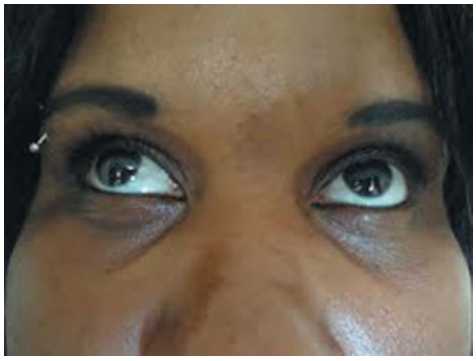

Figure 4 - Predominantly melanic periorbital hyperpigmentation in phototype VI patient

yet been studied.[30-32]

Haloxyl is an anti-dark eye circles active substance that was shown to be effective in a study carried out in 22 patients who applied a gel containing 2% haloxidyl around one eye for 56 days. Participants were later evaluated by analyzing images using specialized software that gauged the shade of the dark circles. Haloxidyl is composed of chrysin, N-hydroxysuccinimide and matrikines – peptides liberated by extracellular matrix macromolecules' proteolysis. That medication's components seem to act synergically in the reduction of dark eye circles. Matrikines stimulate the synthesis of the extracellular matrix's components, reinforcing the palpebral tonus, while the chrysin and the N-hydroxysuccinimide act as bilirubin and iron chelators, respectively, reducing local pigmentation.[33]

Phytomenadione (phytokine) is synthetic vitamin K, which performs the same functions as natural vitamin K. It participates in the coagulation factors II, VII, IX and X synthesis, and acts as an essential cofactor in the post-transductional carboxylation of the precursors of the above mentioned coagulation factors. Vitamin K1 (0.5-2%) has been used topically to treat actinic purpura and traumatic purpura resulting from surgeries, and has been proven to help reduce the amount of extravascular blood and ecchymosis. As a result of its antihemorrhagic action, its use was also tested in the reduction of dark eye circles, however it was scientifically confirmed to cause allergic reactions, increased sensitivity and contact dermatitis at the site of application. It was subsequently forbidden by ANVISA (Brazilian General Agency of Cosmetics and Sanitary Surveillance), which prohibited the use of vitamin K in cosmetics.[34,35]

LASER AND INTENSE PULSED LIGHT TREATMENTS

The use of intense pulsed light is recommended in the treatment of vascular dark eye circles due to its capacity to stimulate collagen synthesis and improve the skin's texture and color by selectively stimulating the temperature at the desired depth, without heating up the skin's surface.[12]

Intense pulsed light is more suitable for treating poikiloderma of Civatte, rosacea vascular lesions and solar melanoses, but can present good results in infraorbital hyperpigmentation after one to three sessions.[12]

West and Alster observed the whitening of the infraorbital skin after nine weeks of treatment with intense pulsed light, however the melanin spectrometry did not correlate with the results. Cymbalista described the clinical whitening of the lower eyelid's skin, and the maintenance of the results, without recurrence, after one year of treatment with intense pulsed light.[8]

Manuskiatti and others demonstrated that the combination of several laser types (CO2, Q-switched Alexandrite, Er:YAG and pulsed dye lasers) in a single session presented 75-100% positive results, with no reported complications.[9]

The combination of epidermal ablation with the CO2 and Q-switched Alexandrite lasers presents better results than the use of the same lasers individually to treat dark eye circles. If the pigment is mainly originating in the epidermis, CO2 removes it more efficiently, reaching a depth closer to the dermis, where Q-switched Alexandrite complements the therapy. The effects begin to appear six to eight weeks after the treatment. [9] The isolated use of CO2 laser can also demonstrate good results, as in a study by West and Alster, carried out in a group of 12 patients, with a 50% improvement after nine weeks of treatment.[10]

The 694 nm q-switched Rubi laser has also demonstrated good results in the treatment of periorbital hyperpigmentation; Lowe and others [36] had 88.9% satisfactory responses in 17 patients and Watanabe and colleagues [37] had excellent results in two patients and good results in two of their other five patients.

Erbium laser can also be a good option for dark eye circles. With a 2,940 nm wavelength and water as its chromophore, it is recommended for some conditions in which there are constraints for the use of CO2 laser. Erbium-YAG laser has weaker thermal and greater ablative effects; it can eliminate pigment without stimulating the formation of new pigment. Nonetheless, as its effects are superficial, deeper ablations (at the papillary dermis depth or deeper) cause bleeding. Whitening substances must be used for two or three months before the procedure to allow some reduction in pigmentation. The postoperative use of whitening substances and sunscreen is essential. Results have been definitive over three years of observation, without the long-term need to use whitening substances.[38]

TREATMENTS WITH FILLERS

Another treatment recommended for dark eye circles is filling the nasojugal fold with hyaluronic acid. This substance is an essential component of the cellular matrix found in all tissues; it can retain water, to provide hydration and turgor to the

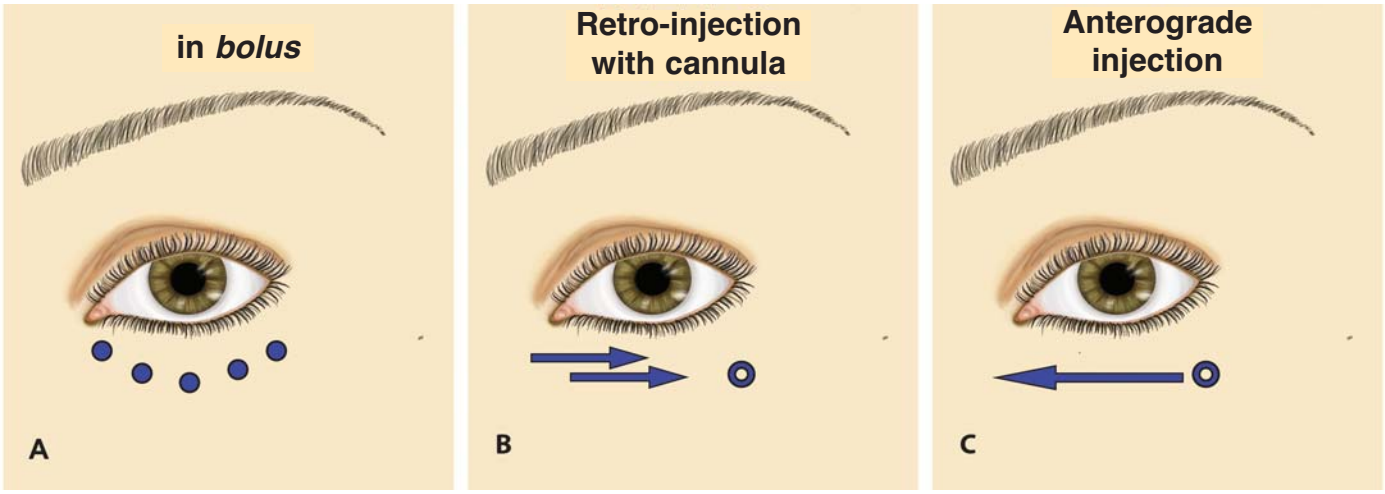

Figure 5 - Palpebral filling application techniques: **A)** in bolus, **B)** retro-injection with cannula and **C)** Anteroinjection with cannula

skin. It is a polysaccharide with a gelatinous consistency, formed by several interlinked units of disaccharide containing glucuronic acid and N-acetyl glycosaminoglycan. It can be extracted from tissues or biosynthesized by bacteria through fermentation.[12]

When tractioning the malar region of some patients, a depression below the lower eyelid, medially towards the lachrymal duct, can be noticed. That is the area indicated for injecting hyaluronic acid. Better results are obtained in young patients, who have less skin and adipose tissue in that area. Based on experience and obtained results, it is suggested that the area is whitened with pulsed light sessions and the use of topical depigmenters at home in monthly intervals before the filling procedure. There are several application techniques. The main three are: in *bolus*; retro-injection with cannula and anterograde injection[39 - 45] (Figure 5).

1. In *bolus* technique (deep puncture): the area of application is marked in advance with small circles. The needle is then introduced at a 90° angle. When the deep supraperiosteal plane is reached, the needle must be retracted by 1 mm in order to avoid intravascular injection. Next, the product is injected in *bolus* in the site. The procedure is repeated in all marked circles. In order to avoid compromising the ocular lubrication, fillings are not carried out close to the lachrymal duct. Massage is recommended at the end of the procedure, in order to allow adequate modelling.[39,44]

2. Retro-injection with cannula technique: the filling region is marked with the shape of an ellipse and with a circle at the site of the anesthetic button. Next, an incision is made with a 27G needle , through which the 25x0.8 cannula (connected to the syringe containing the filling material) is introduced. A slight traction is applied in order for the supraperiosteal plane to be reached. The syringe is brought close to the entry orifice in order to inject the filler. If necessary, the procedure is repeated. The cannula is removed and the area is massaged.[39]

3. Anterograde injection technique (more common in Europe): the needle is introduced until it reaches the supraperiosteal plane, injecting the product at the same time.[40,42,45] It is believed that, since it is viscouselastic, as the product is injected it displaces important structures, avoiding intravascular injection.[46,47] It is important to apply a gentle massage after the procedure.

Goldberg and others described a technique in which several hyaluronic acid retro-injections are made in a fan-like shape in the infraorbicular plane, slightly above the periosteum (around 20-50 per side).[41] Kane[39] prefers the application of crossed retro-injections in two planes (deep and infraorbicular dermis, in a sandwich-like manner). Those two techniques have a greater likelihood of side effects, such as popular or string hypercorrections, ecchymoses, local hyper or hypopigmentation, ischemia due to intravascular injection, etc.[39-45]

Autologous fat transplants can also be a good alternative for dark eye circles; the increase in the subcutaneous fat vascularization and skin transparency in the periorbital region can be involved in its physiopathogeny.[46] A study by Pinski and colleagues (1992) [47] demonstrates good results for this procedure, which seems to be safe, however there is a controversy regarding the duration of the results.[48,49]

CONCLUSION

Although dark eye circles are a constant complaint in dermatology practices, they do not yet have a clearly defined etiology or therapeutic method. Further studies on its etiology and epidemiology should be carried out, so that treatment alternatives can be developed for patients. ●

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Case Report

Surgical treatment of scalp ulcers

Abordagem cirúrgica de úlcera do couro cabeludo

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ABSTRACT

The scalp has a key role in maintaining the integrity of the osseous structure that protects the central nervous system. Its restoration, especially keeping the aesthetic appearance and shape following lesions, is challenging. The present study describes the case of a child with extensive slough and bone exposure in the scalp following a necrotising cellulitis-type infection, which was treated with debridement, microperforation of the calvaria, and application of a gauze bandage with vaseline. Granulation tissue formed after 10 days. A partial skin graft was later carried out with satisfactory results.

Keywords: bacterial infections; scalp; reconstruction.

RESUMO

O couro cabeludo tem fundamental importância para a manutenção da integridade do arcabouço ósseo que protege o sistema nervoso central. Sua restauração mantendo forma e aspecto estético após lesões é um desafio. O presente trabalho descreve o caso de uma criança com grande área de esfacelo e exposição óssea no couro cabeludo, após infecção do tipo celulite necrotizante, tratada com desbridamento, microperfurações da calota craniana e curativo com gaze vaselinada. Houve formação de tecido de granulação em 10 dias. Posteriormente realizou-se enxerto de pele parcial com resultado satisfatório.

Palavras-chave: *infecções bacterianas; couro cabeludo; reconstrução.*

INTRODUCTION

The outer protective covering structure of the brain is constituted of different and clearly distinct anatomical structures that can be classified as either soft parts (the scalp and its respective layers) or osseous tissue (calvaria). The soft parts are subclassified into five different anatomical layers: skin, subcutaneous layer, galea, soft areolar tissue and pericranium. [1] Scalp ulcerations can be classified as either partial or total according to their thickness and anatomical compromising.

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This study was carried out at the Hospital Josina Machel, in Luanda, Angola through an agreement of international technical cooperation with the Universidade Estadual de Campinas (Unicamp)– Campinas (SP), Brazil

Conflicts of interests: none
Financial support: None

The clinical history of scalp lesions can be acute or delayed. In full-thickness scalp lesions (i.e., the lesion goes through all scalp layers to expose the calvaria), the osseous structure should be covered with vascularized tissue and the affected site should be properly closed in order to avoid areas of alopecia. In addition to furunculoid or cavitary myiasis, abscesses and necrotizing cellulite (as seen in the present case), other causes of scalp ulcers are traumatic injuries such as dog bites, burns, and neoplasias.[2]

CASE REPORT

A 17-month old patient was admitted to the emergency room of the Hospital Josina Machel (Luanda, Angola) with a neglected furuncle in the frontal region. Treatment had been attempted at home. The boil developed necrotic tissue and full-thickness ulcerated lesions on the scalp (Figure 1). The lesion measured 15 cm and 8 cm at its largest and smallest diameters, respectively, with irregular borders and purulent secretion. The external surface of the calvaria was visible The debridement and cleansing with 0.9% saline solution were carried out, and a dressing with 1% silver sulfadiazine was applied and left in place for two days. The patient was then referred to the surgical center, where microperforations of the external osseous surface of the calvaria were carried out (Figure2) and a dressing with petrolatum was applied and removed on the seventh day. On the tenth day, after the lesion was 95% granulated (Figure 3), a partial skin graft was carried out (Figure 4), resulting in the satisfactory integration of the graft (Figure 5).

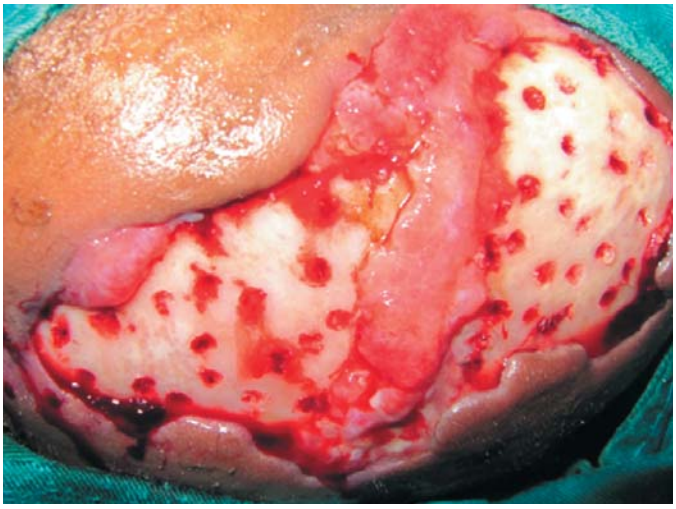

Figure 2- Microperforation of the external osseous surface at the surgical center, two days after the lesion's debridement

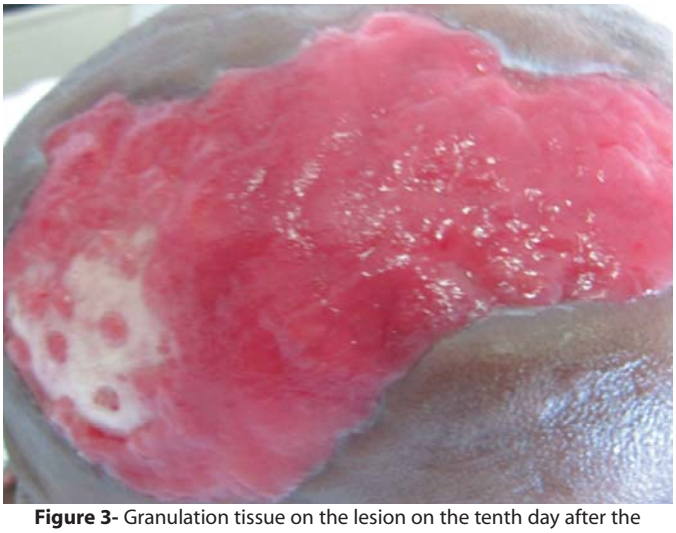

Figure 3- Granulation tissue on the lesion on the tenth day after the microperforations were carried out

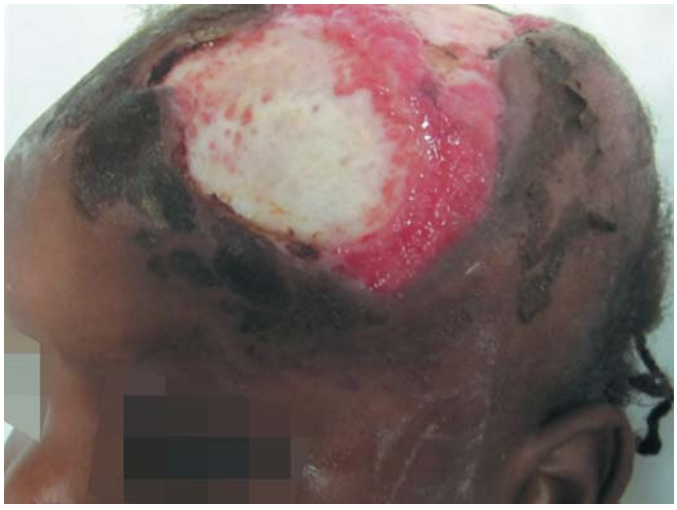

Figure 1- Areas of ischemia on the external surface of the frontal and left parietal bones; the periosteum was destroyed by the infectious origin scalp lesion

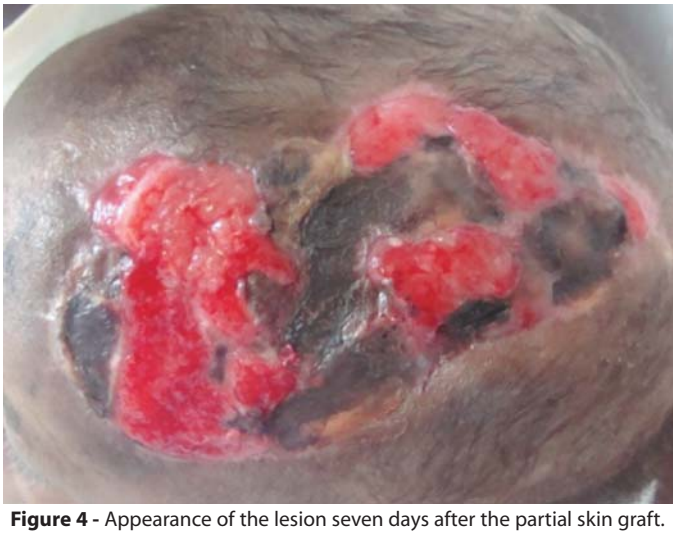

Figure 4 - Appearance of the lesion seven days after the partial skin graft. Some areas still lack total integration of the graft

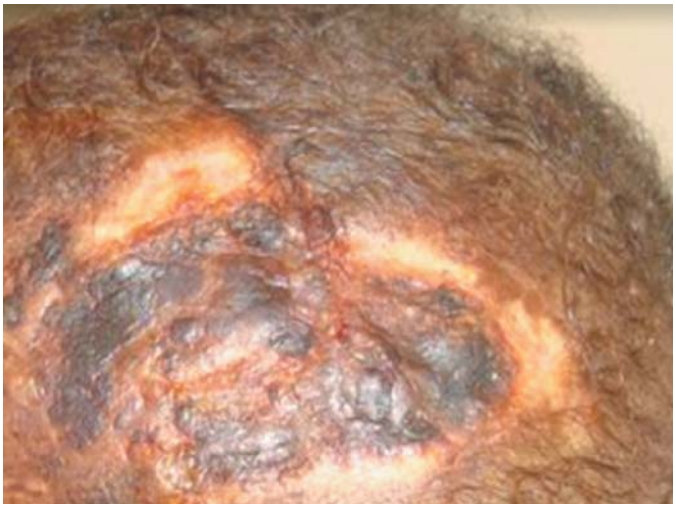

Figure 5 - Appearance of the lesion 30 days after the partial skin graft was carried out

DISCUSSION

In extensive lesions of the scalp, when there is a loss of pericranium [1] and infection, or when the patient is debilitated, the technique of creating multiple perforations in the external surface of the calvaria is the most suitable. This is especially true in children, since their diploë contains a large amount of richly vascularized spongy osseous tissue, which allows the formation of granulation tissue in a few days, on which a thin skin graft can be applied. [3]

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Case Report

Upper lip basal cell carcinoma: surgical treatment and reconstruction with transposition flap

Carcinoma basocelular no lábio superior: tratamento cirúrgico e reconstrução com retalho de transposição

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ABSTRACT

Basal cell carcinoma is the most common human malignant tumor, and is most frequently located on the face. The excision of lesions greater than 2 cm from the upper lip requires a complex and difficult reconstruction. The authors describe the case of a 74-year-old female patient who had a nodular basal cell carcinoma of approximately 2 cm on the upper lip, which crossed the vermillion border. The lesion was excised and the reconstruction carried out using a nasolabial transposition flap with an inferior base. Histologic analysis showed there was a complete resection, with a satisfactory aesthetic result after one year.

Keywords: carcinoma, basal cell; lip; reconstructive surgical procedures.

RESUMO

O carcinoma basocelular é o tumor maligno mais frequente do ser humano, sendo a face, a sua localização mais comum. A excisão de lesões iguais ou maiores do que 2 cm no lábio superior, requer reconstrução complexa e difícil. Relata-se o caso de uma paciente do sexo feminino, de 74 anos, portadora de carcinoma basocelular nodular, de ± 2 cm de diâmetro, localizado na metade esquerda do lábio superior e invadindo parte do vermelhão. A lesão foi excisada e a reconstrução feita com retalho de transposição naso-labial, com base inferior. O histopatológico mostrou ressecção completa e o resultado estético após 1 ano mostrou-se satisfatório.

Palavras-chave: *carcinoma basocelular, lábio, procedimentos cirúrgicos reconstrutivos.*

INTRODUCTION

Basal cell carcinomas (BCCs) are the most common malignant tumor in humans, occurring most frequently in the face. They have unique clinical and histological features, grow slowly and have several clinical and histopathologic variants. They rarely result in metastases and the causes of its occurring in mucous membranes are unclear. Most BCCs appear without an apparent cause, however there are several predisponent factors, such as fair skin and prolonged exposure to the sun. It is estimated that 40% of patients who develop one lesion will have one or more BCC within the following 10 years.[1,2]

BCCs appear in several different shapes; the nodular shape is one of the most prevalent. In general nodular BCCs begin as a red or skin-colored pearly papule. They grow slowly and develop telangiectasia on the surface. As they grow, the central portion frequently becomes ulcerated, developing into the nodule-ulcerative form. Sometimes they develop without ulcerating, as was observed in the present case.

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This study was carried out at the Dermatology Clinic of the Hospital Getúlio Vargas (UFPI) – Teresina (PI), Brazil

Conflicts of interests: none
Financial support: none

CASE REPORT

A 74-year-old patient originally from Teresina, state of Piaui, Brazil, was referred to the dermatologic clinic of Hospital Getúlio Vargas – UFPI, in Teresina. The patient presented with a tumoration in the upper lip, which had been slowly developing for several years. A pearly and apparently solid tumorous lesion with a hyperchromic base and approximately a 2-cm diameter was observed in the left half of the upper lip. The tumoration partially crossed into the vermilion area (Figures 1 and 2). Significant hirsutism could also be observed. The histopathologic examination of the punch biopsy indicated the presence of a solid-pattern BCC (Figure 3). The lesion was excised with 5-mm safety margins, and a naso-labial crease transposition flap was used in the reconstruction with an inferior pedicle (Figures 4 and 5) from the apex of the nasal crease. There were no complications in the immediate post-operative period. The patient presented very satisfactory aesthetic results (Figures 6 and 7) and no signs of recurrence during the 18-month follow-up period.

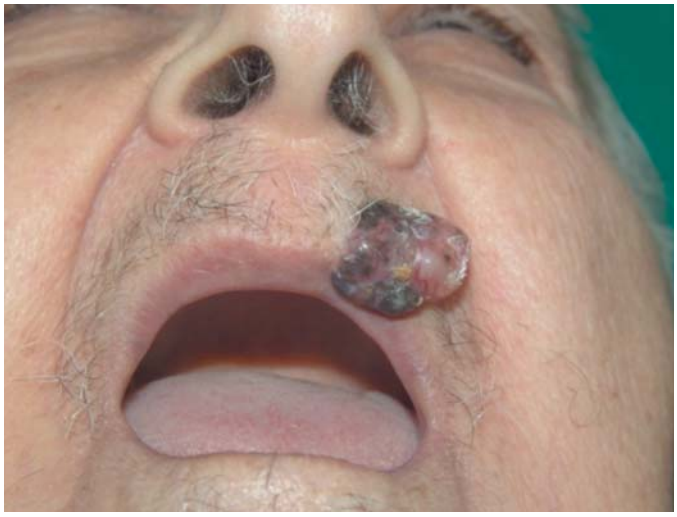

Figure 2 – Tumor affecting the vermilion

DISCUSSION

According to data from the Instituto Nacional do Câncer – INCA (Brazilian National Institute of Cancer), BCCs account for roughly 25% of all cancer cases and 70% of the cutaneous cancers reported in Brazil.[3] In spite of their high prevalence, these tumors are unlikely to metastasize and are usually curable with a single surgical treatment.[1] When they are located in the upper lip, the reconstruction requires increased care to preserve the functional and aesthetic aspects of this sensitive area.[2] Particularly important are the positioning of the lip's border with the vermilion, maintaining the original position of the philtrum, and the maintenance of the bilateral symmetry and height of the nasolabial creases. Among the several excision and reconstruction techniques that can be used to meet those objectives, a nasolabial flap [4-7] is the best option, especially in elderly patients who frequently have excess skin in that area.[4] Due to

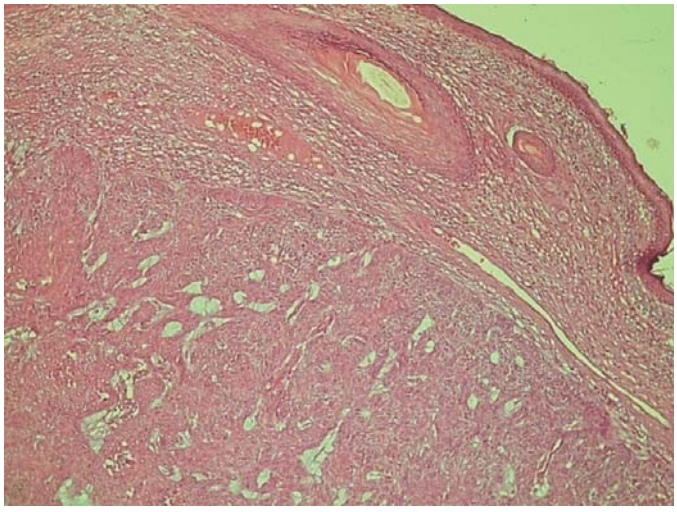

Figure 3 – Histopathologic analysis of the tumor biopsy

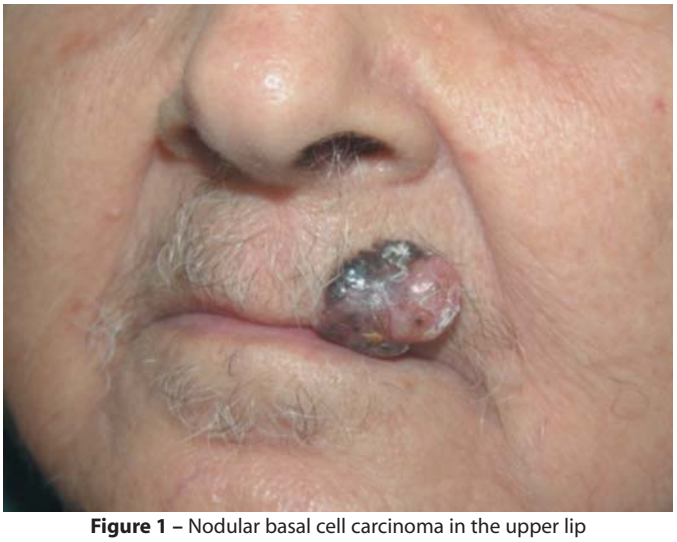

Figure 1 – Nodular basal cell carcinoma in the upper lip

Figure 4 – Immediate post-operative period

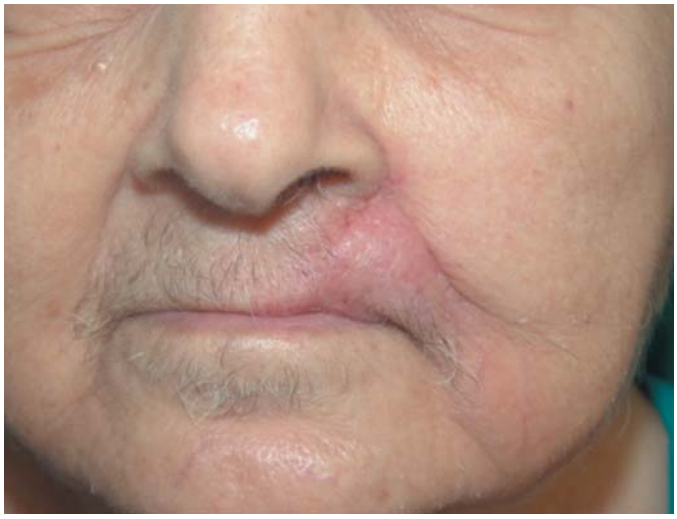

Figure 5 – 30 days after procedure

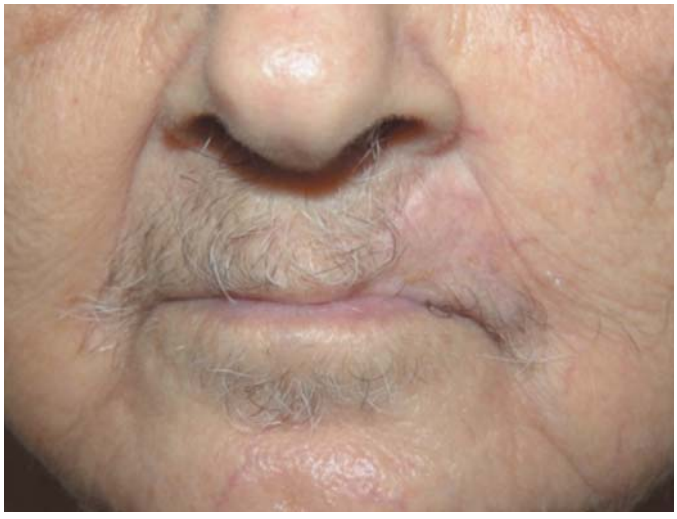

Figure 6 – 11 months after procedure

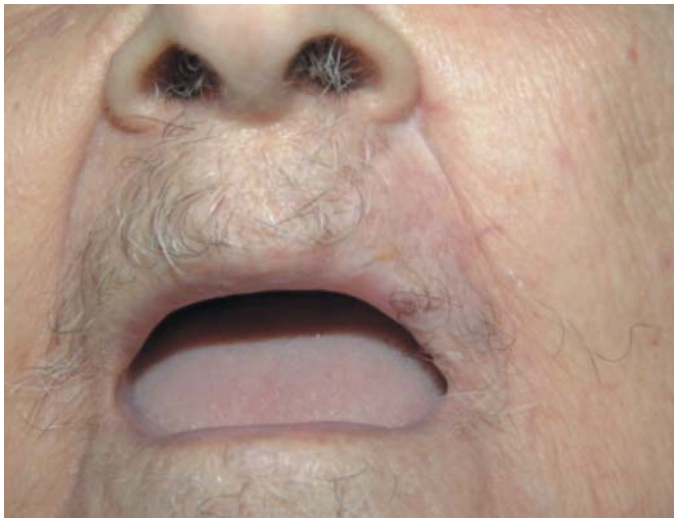

Figure 7 – 11 months after procedure

the dimensions of the area to be rebuilt in this case, the flap was extended up to the nasal crease, where the suture was positioned in order to hide the scar. An additional important detail was that the excision had to be extended and the undermining of the lip line towards the right half of the lip had to be carried out in order to facilitate the closure in the flap's extremity to prevent high tension in the suture line, which could lead to the necrosis of the flap's tip.

In the present case, in addition to the difficulty imposed by the location in the upper lip, the tumor had a large diameter (± 2 cm) and had partially invaded the vermilion. Thus the incision had to extend into the lip's mucus membrane due to the safety margin. The reconstruction with a nasolabial flap was chosen due to the availability of donor skin and the donor area's similarity and proximity to the receiving area. The procedure involved the complete removal of the tumor with a good aesthetic result. The patient has been periodically followed up, with no signs of recurrence as of the last consultation in July 2011. ●

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Case Report

Artigo 12

Bleomycin in refractory giant keloids: a new treatment alternative

Bleomicina para queloide rebelde e gigante – nova opção de tratamento

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ABSTRACT

Keloids were first described several centuries ago, however their handling and treatment are still often inadequate. A number of treatments are available, such as intralesional corticotherapy and compressive therapy. The case of a 24-year-old female patient with a 5-year history of keloids in the ear lobules, with recurrence after treatment, is reported. She experienced a full regression of the lesions (for 2 years) after surgical reduction followed by intralesional bleomycin injections. Bleomycin is emerging as a therapeutic option with few side effects and lasting results for keloids that are unresponsive to conventional treatments.

Keywords: bleomycin; cicatrix, hypertrophic; keloid.

RESUMO

Queloide é afecção descrita há alguns séculos, porém ainda hoje seu manejo e terapia apresentam resultados muitas vezes insuficientes. Há, atualmente, diversos tratamentos, como corticoterapia intralesional e terapia compressiva, entre outras. Relata-se o caso de paciente com histórico de queloides nos lóbulos das orelhas há cinco anos, com evolução recidivante após as terapêuticas empregadas. Utilizando injeções intralesionais de bleomicina após redução cirúrgica, houve regressão completa das lesões por dois anos. A bleomicina tem-se tornado opção terapêutica para queloides refratários aos tratamentos convencionais com poucos efeitos colaterais e resposta duradoura.

Palavras-chave: *bleomicina; cicatriz hipertrófica; queloide.*

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Financial support: none

INTRODUCTION

Cutaneous healing is a complex process that results in the formation of new tissue that repairs the skin. Normal healing in healthy individuals usually results in a scar with a good aesthetic appearance and maintenance of functional properties. [1] Any interference in the healing process can lead to the formation of poor quality, wide and pigmented scarring. Among cicatricial affections, hypertrophic scars and keloids stand out. They are caused by a hyperproliferation of fibroblasts, which results in the accumulation of extracellular matrix and, more importantly, in the excessive production of collagen.[1-3] Keloids are elevated, shiny, itchy or painful lesions located in the dermis. They are differentiated from a hypertrophic scar by their location (beyond the limits of the original wound, encroaching onto the normal adjacent skin), continuous growth over time, absence of spontaneous regression, recurrence after excision, and personal or family history.[4] This paper describes the case of a patient with giant lesions that were resistant to conventional treatments such as intralesional injections of corticosteroids and radiotherapy.

CASE REPORT

A 24-year-old white female patient presented, for 5 years, extensive keloids in the right (R) and left (L) earlobes, as well as the right jawline. (Figures 1, 2 and 3). The keloids originated from earring holes. The lesions were unattractive, presented ulcerations and a strong smell, and caused great discomfort to the patient.

The patient had already undergone three previous treatments. The first two involved the exeresis of the lesions followed by infiltration of corticosteroid at monthly intervals. The third treatment also consisted of exeresis of the lesions, followed by 5 subsequent radiotherapy sessions and the use of compression garments. The lesions worsened; their dimensions increased approximately three fold.

The proposed treatment comprised the surgical reduction of the keloids combined with bleomycin injections. For the surgical reduction, different techniques were employed, on each side (R and L). In the R earlobe and jawline keloids, incisions within the keloids' margins, and exeresis of the tumorous mass were carried out, followed by suture. In the L ear lesion, the procedure consisted of a sub-total tangential excision (shaving) of the keloid, which healed by secondary intention.

Ten bleomycin (15 u diluted in 5 ml of 0.9% saline solution) injection sessions were carried out, with an average of 0.04 ml per session, with six infiltrations in monthly intervals, two in quarterly intervals, and the last two in six-month intervals. The treatment started in January 2007 and ended in January 2009.

There was an excellent response, with outstanding aesthetic results (Figures 4, 5 and 6). Nevertheless, in the keloid in which the exeresis and suture were carried out, the scar became slightly infiltrated, while in the one in which the shaving tech-

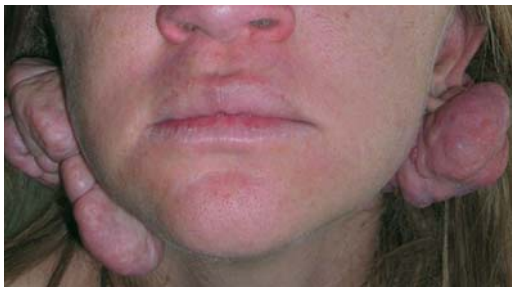

Figure 1 - Keloids before treatment

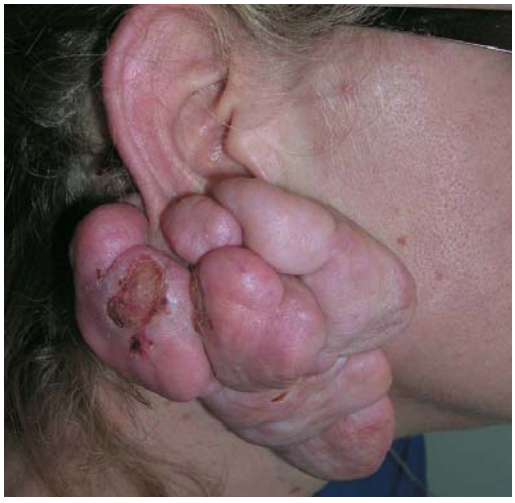

Figure 2 - R keloid profile

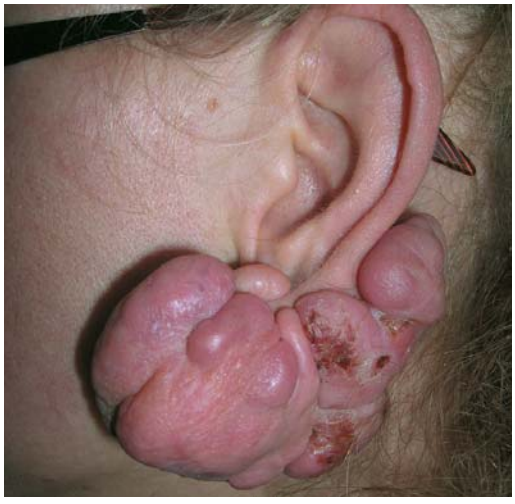

Figure 3 - L keloid profile

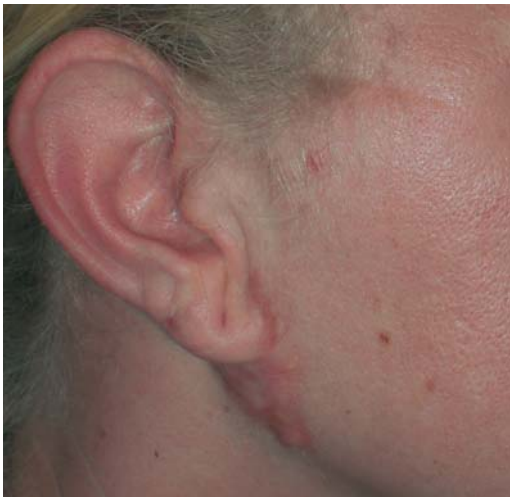

Figure 4 - Close view after exeresis and bleomycin

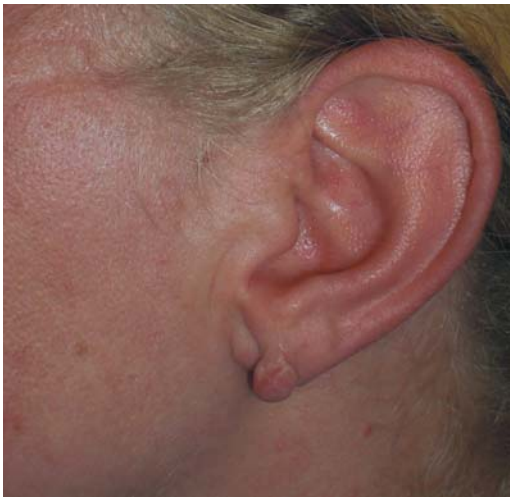

Figure 5 - L side after shaving and bleomycin

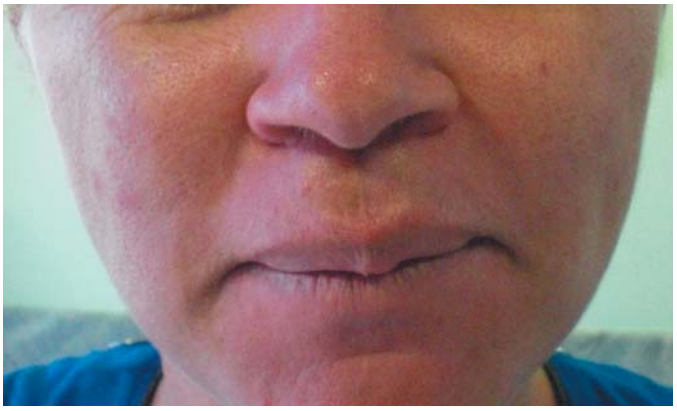

Figure 6 - Final outcome

nique was used, the scar softened and became less noticeable, suggesting that this technique would be ideal for reducing keloids. The patient was followed up for 30 months; the scars remained stable and presented no signs of recurrence.

DISCUSSION

Bleomycin is a widely used substance in oncology. It is a mixture of cytotoxic polypeptides with antibacterial, antiviral and antitumoral properties. It was isolated from a soil fungus, *Streptomyces verticillus*, in the beginning of the 1960s.[3] While its action mechanism in the skin remains unclear, there is evidence that it increases the local tumor necrosis factor (TNF).[2] The side effects are minimal, with hyperpigmentation and atrophy described in some patients.[1,4] Due to the high selectivity for epithelial cells, there are reports of using intralesional bleomycin to treat certain skin disorders, such as warts, Kaposi's sarcoma, leukoplakia, hemangiomas and lymphangiomas. [1,5] The results were satisfactory and promising for all these lesions; however, due to the limited number of patients studied, the method cannot be considered to be a routine treatment until new elements corroborate these findings. The literature has presented good results for using bleomycin to treat keloids, suggesting it is an interesting option among the existing alternatives. Nevertheless, more extensive and precisely controlled studies are necessary to confirm this fact. ●

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Case Report

Upper lip lifting associated with mechanical dermabrasion

Lifting de lábio superior associado à dermabrasão mecânica

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ABSTRACT

The aging process causes significant changes to the face. There is an increasing demand for aesthetic facial procedures such as blepharoplasty, rhytidectomy, and the use of filling substances and botulinum toxin, among others. The subnasal region receives comparatively less attention. This report aims to demonstrate the use of upper lip lifting combined with dermabrasion as an option to obtain greater facial harmony. In addition, it emphasizes the possibility of its use in association with other surgical procedures.

Keywords: lip; rhytidoplasty; skin aging; dermabrasion.

RESUMO

O envelhecimento traz profundas modificações na face. Existe demanda crescente de procedimentos para tratamento estético facial. São exemplos as blefaroplatias, ritidoplastias, uso de substâncias preenchedoras e de toxina botulínica, entre outros. Infelizmente a região subnasal não recebe comparativamente igual atenção. Este relato tem por objetivo demonstrar o uso do lifting do lábio superior associado a dermabrasão como alternativa para se obter maior harmonia facial. Além disso, cabe reforçar a possibilidade de sua realização associada à de outros procedimentos cirúrgicos.

Palavras-chave: *lábio; ritidoplastia; envelhecimento da pele; dermabrasão.*

INTRODUCTION

Facial aging is a complex process. Alterations take place in the osseous plane, in the distribution of fatty tissue in the muscular fibers and in the skin.[1] These changes caused by aging – which take place all over the face – also cause important modifications to the subnasal portion of the upper lip.

With the aging process, intensified by the effects of gravity, a thinning of the upper lip and the widening of its cutaneous portion (i.e., an increase in the distance between the base of the nose and the mucocutaneous transition line of the lip) is observed. Additional changes are the effacement of the filter, the inversion of the vermilion, the loss of the incisors visualization and the flattening of the vermilion.[2,3] Simultaneously, perioral wrinkles appear.

In 1971, Cardosa and Sperli described a surgical technique for approaching and treating this problem. Around ten years later, Rozner and Isaacs described the first series of cases.[2] Austin and colleagues worked on approximately 1,200 lip lifting cases and reported about 28 years of experience.[4] The present case

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report describes a surgical approach that can be used to improve the subnasal and upper lip region. This procedure can be used isolated or combined with others such as rhytidoplasty.

METHODS

The patient was a 56-year-old woman, Fitzpatrick phototype II, with no history of smoking. She used phenobarbital for treating epilepsy (her last epileptic crisis was 15 years earlier), and was a class II anesthetic risk – NYHA (New York Heart Association). She presented no other comorbidities in her pre-operative clinical examination.

The patient sought care wanting to improve her facial aesthetic appearance. During the pre-operative assessment, surgery was selected for the middle and lower thirds of the face and to correct lower eyelid fat pseudo-herniations.

The patient also presented an increased distance between the columellar base and the mucocutaneous transition line in the upper lip, a flattening of the upper lip combined with a decrease in the visible vermilion area, and the presence of perioral wrinkles (Figure 1).

Description of the Technique

Under general anesthesia, the patient initially underwent inferior blepharoplasty with the removal of the fat pseudo-herniations. Classic rhytidoplasty was subsequently initiated, following the previously applied surgical markings. As is routinely carried out in the care service in question during this type of surgical procedure, SMAS (Superficial Muscular Aponeurotic System) treatment with the vectorial traction of the SMAS flap, followed by its attachment in the mastoid region and the cutaneous vectorial traction for treatment of the superficial plane, were executed.

The final surgical procedure – this case report's main subject – comprised the lifting of the upper lip combined with mechanical dermabrasion. The lift was approached using a marking at the base of the nose. This marking extended from one base of the nasal wing to the other through a curve that touched the middle of the columellar base (Figure 2).

After the excision of the marked area, the subcutaneous undermining of the inferior surgical border towards the vermilion of the upper lip was carried out in order to allow the traction of the detached tissue (Figure 3). The closure was meticulously executed using a 6-0 mononylon suture , observing the subcutaneous and subcuticular planes (Figure 4). Simultaneously, a motor dermabrasion with a diamond fraise was carried out along the entire upper lip (Figure 5).

Only a thin gauze layer was kept on the exfoliated site, which came off naturally as the epithelization took place. No topical medication was applied to the exfoliated area, however anti-herpetic prophylaxis was used.

The patient returned for evaluations two and seven days after, and the stitches were removed 10 days after the procedure. One week before the 90-day post-operative evaluation, the patient received botulinum toxin to treat dynamic wrinkles in the upper third of the face.

RESULTS

10 days after the procedure, the exfoliated skin was com-

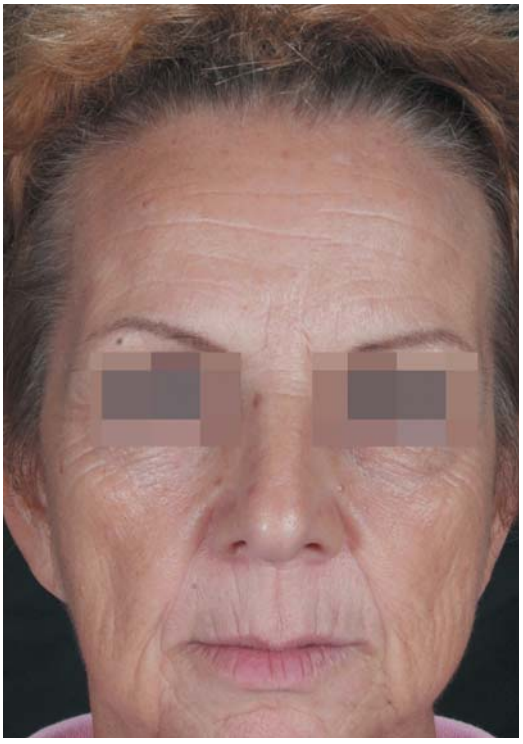

Figure 1 - Pre-operative assessment

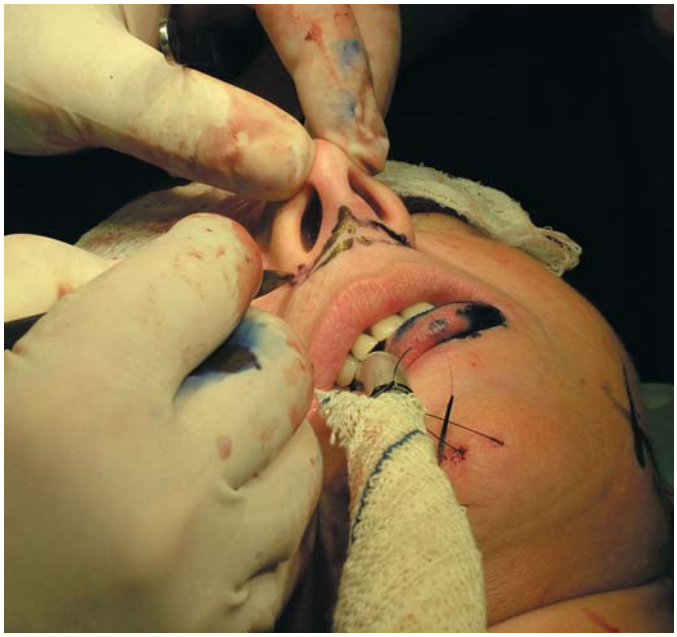

Figure 2 - Surgical marking of the area to be excised ("gull–wing lip lift technique")

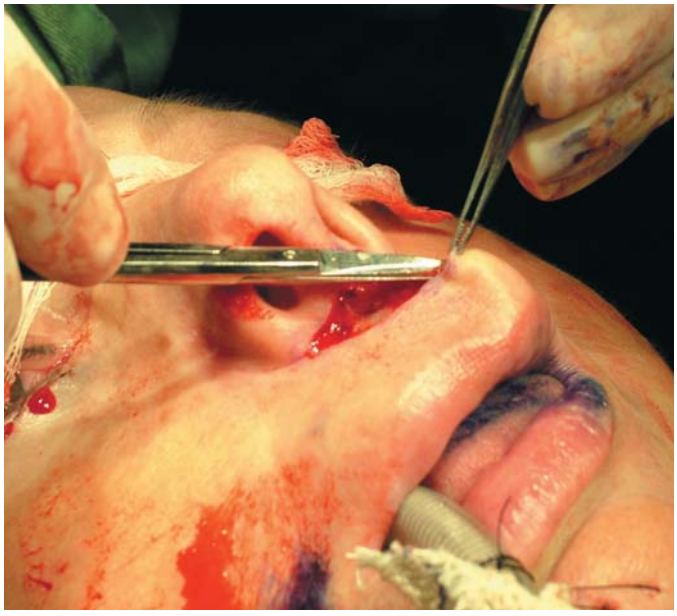

Figure 3 - Subcutaneous detachment of the inferior border of the excised area

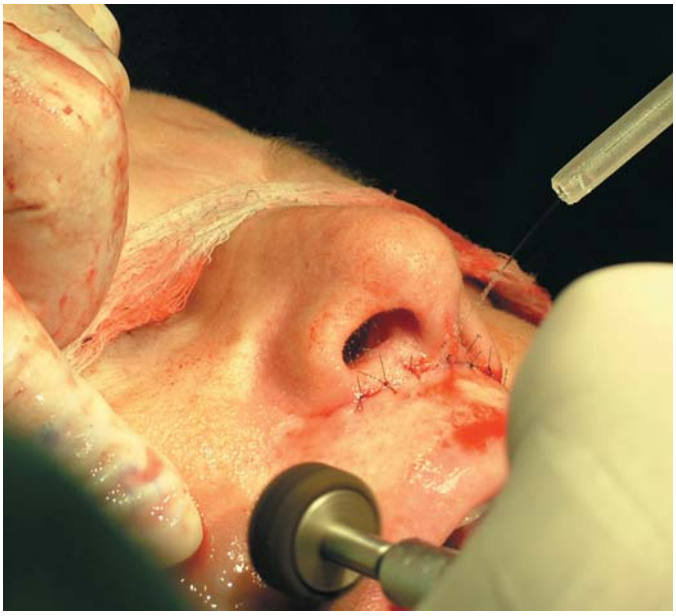

Figure 5 - Upper lip dermabrasion

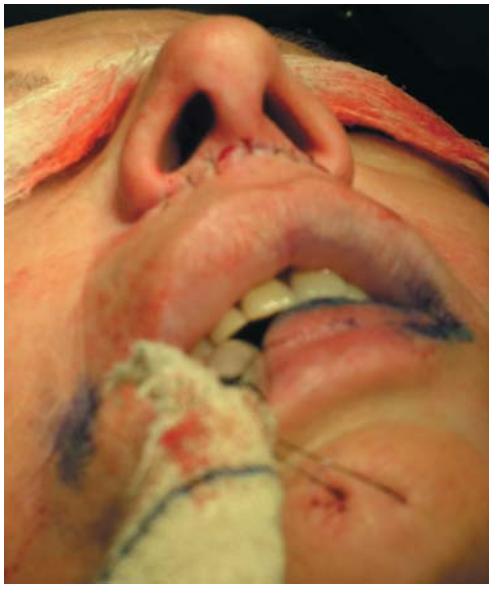

Figure 4 - Closure in two planes (subcutaneous and subcuticular)

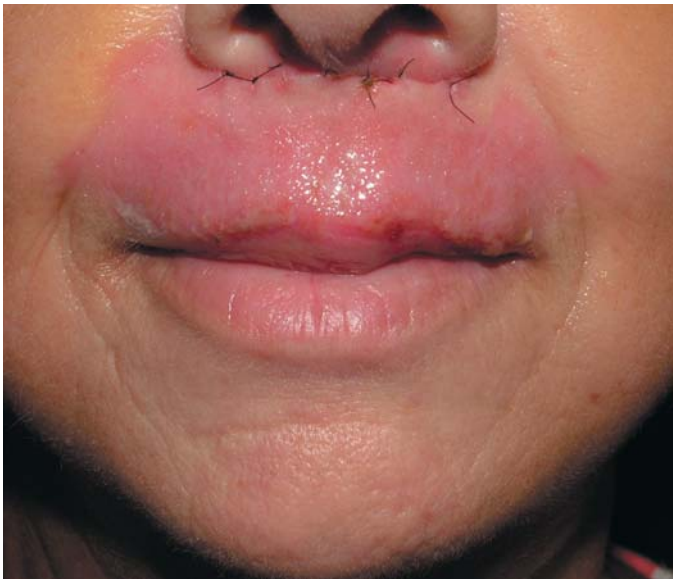

Figure 6 - 10 days after the procedure

pletely epithelialized, with the presence of erythema (Figure 6). The suture at the base of the nose was visible (Figure 6).

The patient demonstrated significant facial aesthetic improvement during the 90 days after surgery. The resolution of the facial ptosis and the definition of the cervical-mandibular angle were achieved through conventional rhytidoplasty combined with SMASectomy followed by the SMAS plicature. There were also satisfactory alterations in the infrapalpebral regions as a result of the inferior blepharoplasty.

The combination of the procedures carried out provided facial harmony and improved the subnasal area and upper lip (Figure 7). There was a reduction in the distance between the nasal base and the upper lip's mucocutaneous transition line, a reduction in perioral wrinkles and greater exposure of the vermilion of the upper lip.

There was also an improvement of the upper third of the face following the application of botulinum toxin (Figure 7).

DISCUSSION

Knowledge of the proportions between the anatomical structures of the face is the key in aesthetic planning. Figure 8 shows the vertical proportions of the face. The aging process, as well as racial differences, [5] cause variations in these proportions.

In planning upper lip lifting surgery, it is important to

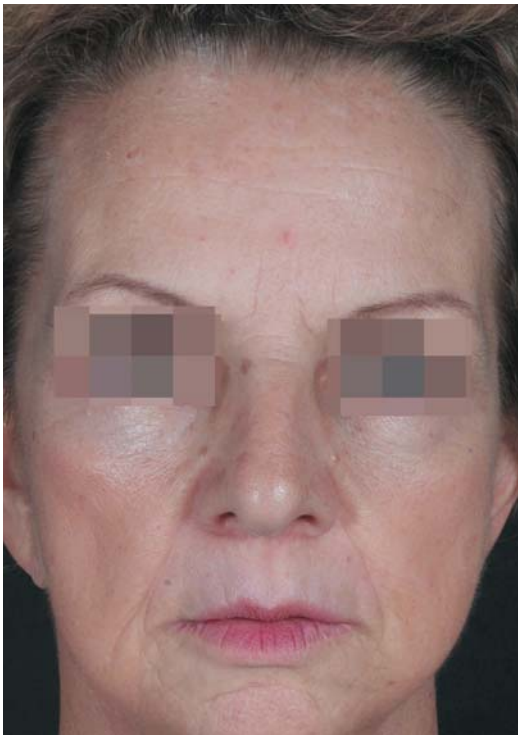

Figure 7 - 90 days after the procedure

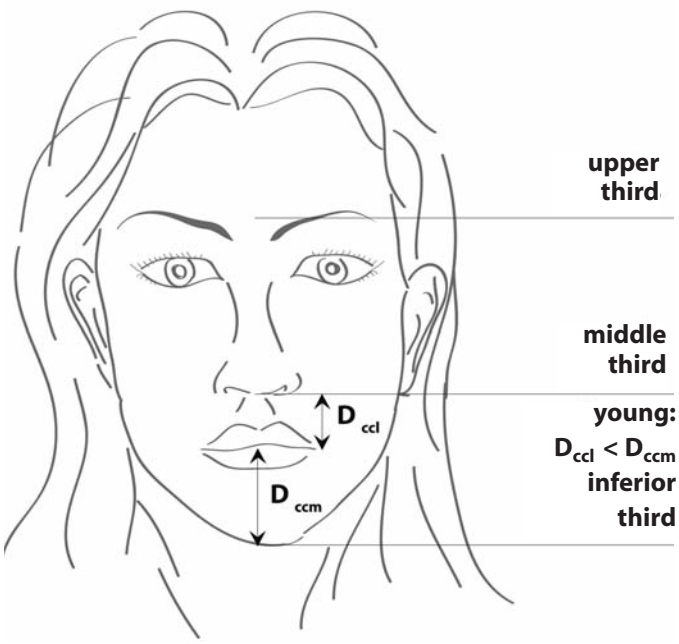

Figure 8 - Face proportions and vertical references for the surgical planning

observe the vertical distance between the nasal base and the horizontal line that connects the labial commissures (D_{ccl}). Figure 8 shows that in young Caucasians, this distance is shorter than the vertical distance between the line that connects the labial commissures and the bottom of the chin (D_{clm}).[5]

In the present case, the alteration caused by the aging process in this proportion, and the later improvement resulting from surgery, are evident. There was eversion and greater exposure of the vermilion, a clear improvement in the perioral wrinkles and a reduction in the horizontal flattening of the upper lip. These are surgical objectives described by Waldman, and were achieved by carrying out the upper lip lift.[2] Mechanical dermabrasion, implemented during the same surgery, aimed to improve the skin's surface.[1,6] When the procedure is carried out very deeply, crossing the limit between the papillary and the reticular dermis, the risk of definitive dyschromias and undesired scars is greater.[1,6]

Waldman and Austin and colleagues affirm that the base of the nose heals satisfactorily and that the procedure is very well tolerated in a wide range of patient conditions.[2,4] Surgical variations are possible. Excisions can be carried out in the vermilion's transition line and in the subnasal region.[3,7] The choice of technique depends on the surgeon's experience and on anatomical planning.

CONCLUSION

This study demonstrated the good surgical result of combined upper lip lift and dermabrasion. These procedures can be carried out separately or combined with other techniques. ●

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Minimally invasive technique for repairing complete earlobe cleft

Técnica minimamente invasiva para correção de lóbulo de orelha totalmente fendido

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ABSTRACT

In an effort to avoid some common undesirable consequences of surgical techniques for repairing earlobe clefts, such as notch formation and cosmetic deformities, the authors describe a minimally invasive technique for repairing a complete earlobe cleft. A single simple suture was followed by 90% trichloroacetic acid applications to transform a complete earlobe cleft into an incomplete cleft. Due to its ease of execution, low cost and good functional results, this technique is a good option for repairing complete earlobe clefts.

Keywords: ear; ear deformities, acquired; cosmetic techniques.

RESUMO

Devido a algumas limitações nas técnicas cirúrgicas de correção de lóbulo de orelha fendido, como cicatrizes inestéticas e recidivas, os autores descrevem técnica corretiva minimamente invasiva com base em ponto único de sutura simples, seguido de aplicação de ácido tricloroacético a 90%. Devido à facilidade técnica do procedimento, baixo custo e ótimos resultados, a técnica descrita deve ser considerada opção terapêutica para a correção de lóbulos de orelha totalmente fendidos.

Palavras-chave: *orelha; deformidades adquiridas da orelha; técnicas cosméticas.*

INTRODUCTION

Due to the cultural habit of wearing earrings, the earlobe is very sensitive to ruptures. Earrings are often too heavy for such a delicate structure, which does not have the cartilaginous support that is present in other parts of the ear.

The repair of split earlobes is a frequent demand in the daily practice of dermatologists and plastic surgeons. The several surgical techniques described in the literature for repairing fully split earlobes have limitations, such as recurrences, the formation of unattractive scars, keloids and undesirable angulations in the earlobe's contour.[1-3]

This case report describes a straightforward correction technique based on the application of 90% trichloroacetic acid in the cleft, followed by a single simple suture in the distal end. The advantages of this technique suggest it is a good option for repairing this type of clefts.

METHODS

A 49-year-old female patient (Patient A), Fitzpatrick phototype II (Figure 1) and a 33-year-old female patient (Patient B), Fitzpatrick phototype IV (Figure 2) presented complete clefts in the earlobe of their right ears. Neither had undergone any type of surgical treatment to repair the defect.

After local asepsis and anesthetic infiltration of the lobule with 2% lidocaine without epinephrine, 90% trichloroacetic acid was applied directly onto the two edges of the cleft with a wooden stick until the frosting effect was obtained; there was no need to neutralize the acid. The two edges of the cleft were then brought together with a single simple suture in the distal tip of the cleft with 5-0 non-absorbable monofilament suture. Finally, the cleft was closed with micropored tape, which was kept in place for 4 days.

The patients were instructed to return to the practice each week for six weeks for the application of 90% trichloroacetic acid with a wooden stick inside the cleft. The suture was removed only after the cleft was completely repaired. In both patients, the clefts' edges were completely closed after the fifth application. The sixth and final session of acid application prevented the edges from inverting and corrected the shape of the tip of the earlobe – which was observed after the fifth application (Figure 3).

The patients were followed up monthly for 10 months. Local transient erythema was observed in both cases. Keloids or unattractive scars were not observed after the end of treatment. The patients were allowed to have the treated earlobes pierced again after the third month of follow-up; the new hole was made beside the scar (Figures 4 and 5).

DISCUSSION

Many of the surgical techniques described in the literature preserve the original hole, however this does not happen in the

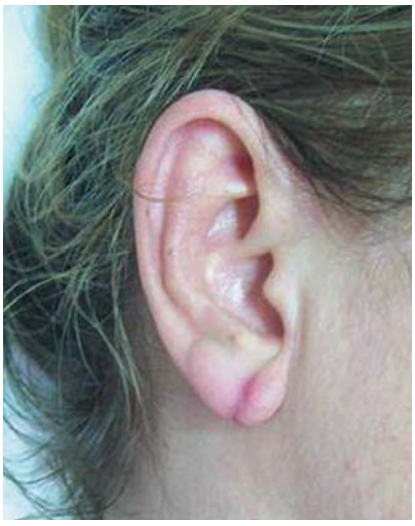

Figure 3 - Patient A: Complete coaptation of the edges of the cleft after the fifth 90% trichloroacetic acid application. Local erythema and tendency of the edges to invert are observed

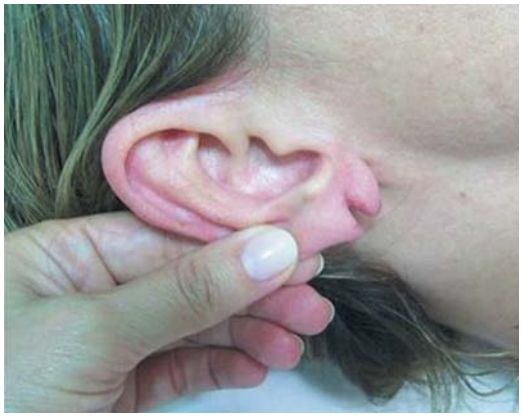

Figure 1 - Patient A: Pre-treatment appearance of split earlobe

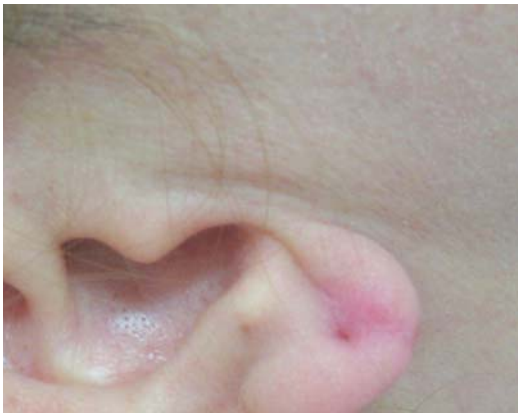

Figure 4 - Patient A: Final appearance of the treated earlobe after the 10 month follow-up

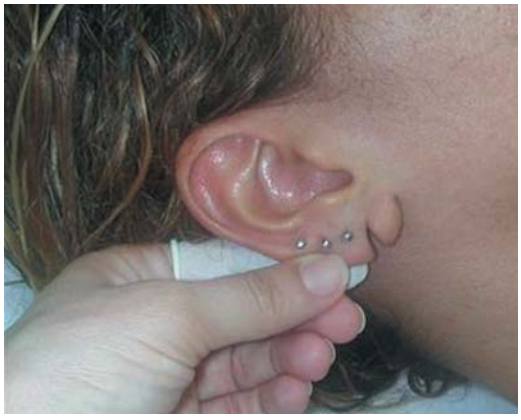

Figure 2 - Patient B: Pre-treatment appearance of torn earlobe

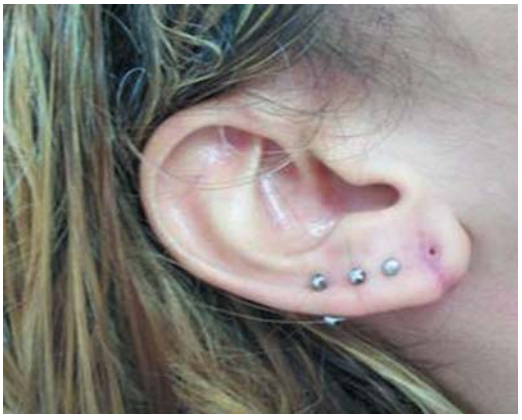

Figure 5 - Patient B: Final appearance of the treated earlobe 3 months after the end of treatment

technique described in the present study, which lets the patient decide whether to repierce the earlobe.[4,5]

De Mendonça et al. proposed a non-surgical technique for repairing incomplete earlobe clefts also using 90% trichloroacetic acid inside the cleft. The closure of the cleft is based on the cicatricial adhesion of the tissue caused by the acid's action.[6]

This study describes a technique that turns a fully split earlobe into an incomplete split earlobe through a single suture in the distal tip of the cleft, with serial applications of trichloroacetic acid that follow the same cicatricial adhesion principle.

A tendency for the edges of the cleft to invert can be observed, yet this is easily corrected with a further application of acid in the site and the molding of the coapted cleft.

The authors consider this technique to be a good treatment option for earlobes' complete clefts since it is technically simple and cost effective, and yields good aesthetic and functional results. ●

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Lip filling with microcannulas

Preenchimento labial com microcânulas

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ABSTRACT

This paper describes a lip filling technique that administers hyaluronic acid using microcannulas. This technique considerably reduces the number of punctures compared to the conventional method, which uses needles. In addition, the microcannula's blunt tip reduces the risks of intravascular injection of the substance and of disrupting key structures such as vessels and nerves. The results obtained by the authors confirm the less frequent occurrence of adverse effects and a high degree of physician and patient satisfaction.

Keywords: hialuronic acid; lip; rejuvenation.

RESUMO

Trata-se da descrição de técnica de preenchimento labial com ácido hialurônico utilizando microcânulas, que diminui muito o número de pertuitos necessários ao método convencional com agulhas e reduz a possibilidade de injeção intravascular do produto, além de restringir o risco de ruptura de estruturas nobres, como vasos e nervos, devido à ponta romba. Os resultados encontrados confirmam a menor ocorrência de efeitos indesejáveis e alto grau de satisfação de médicos e pacientes.

Palavras-chave: *ácido hialurônico; lábio; rejuvenescimento.*

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INTRODUCTION

Despite their wide use in other medical specialties, such as ophthalmology, there are few reports on the use of microcannulas to inject filling material in dermatology[1,2] Aging causes the lips to become narrower and lose their volume and contour, however hyaluronic acid injections help re-establish those characteristics.[3,4]

METHODS

Patients with aesthetic complaints about their lips (such as deficiency in contour definition, volume and projection) were included in the study. Patients with a history of allergy to the filler product, those with collagen disorders and pregnant women were excluded. The treatments were carried out at a private practice between October 2010 and May 2011.

APPLICATION TECHNIQUE

If the needles and cannulas used has a small gauge , there is no need for an anesthetic point to introduce the microcannula into the skin. Punctures are made in the skin 25 mm from the apex of the cupid's bow on the upper lip with a 26G ½ needle, as shown in Figure 1. After inserting the 30G calibre 25-mm long microcannula (Magic Needles®, Needle Concept, Paris, France), the practitioner will feel a resistance caused by the dermis' fibrotic fibers. Continuing the injection past that point indicates that the subdermic plane, where the filling should be placed, has been reached. We used 24-mg/ml hyaluronic acid with added lidocaine (Juvéderm Ultra®, Allergan inc, Irvine,

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Conflicts of interests: The author is a consultant and speaker at Allergan Cosmetics
Financial support: None

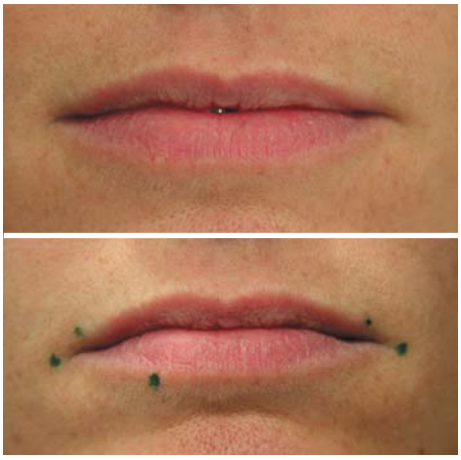

Figure 1 - Lips before and after the green dots mark the introduction of the 30G x 25 mm microcannula

Figure 3 - Implementation of the technique for lip projection: the 30G x 25 mm microcannula is moved through the same puncture towards the labial mucous membrane and the product is applied *in bolus* or through retro-injection; the tip of the microcannula can be seen as a moderated relief shown in the treated lip

California, USA) for the implant.

This technique uses only one micropuncture for the introduction of the microcannula, allowing the treatment of three different features of the lips with different results: contour definition, projection and increase in lip volume.

To improve the upper lip's contour, the microcannula is introduced between the skin and the vermilion of the lip. Next, the linear retro-injection of the product is carried out starting from the apex of the cupid's bow (on the side being treated) towards the corner of the mouth (Figure 2).

To improve the projection of the lips, the microcannula, which is still in the subdermic plane, is moved towards the lip's mucus membrane. The product is then retro-injected or injected all at once (Figure 3).

To increase the lips' volume, the microcannula is directed towards the oral mucus membrane and inject the product all at once (Figure 4).

To treat the lower lip's contour, a 26G ½ needle enters 10 mm from each corner of the mouth and the same technique used for the upper lip is carried out. For treating the shape of the middle of the lower lip, a micropuncture is made 25 mm from the first orifice, and the hyaluronic acid is retro-injected (Figure 5).

When the objective is to treat the corners of the mouth, the filling of the contour of the lower lip is carried out by retro-injection with a microcannula so as to form the 25-mm base of an inverted triangle. Next, three vertical support pillars are formed by retro-injecting hyaluronic acid from the same entry micropuncture, located 7 mm from the horizontal base, with a 30G needle, as shown in Figure 6.

Using the same micropuncture made in the corner of the lip, it is possible to treat perioral wrinkles by directing the 30G microcannula upwards to those wrinkles to carry out the retro-injection (Figure 7).

RESULTS

Patients aged 18-71 (n = 55, 47 women and 8 men) were treated. The patients reported a high degree of satisfaction (Figure 8). We observed minimal edema and erythema compared to conventional procedures that use needles when reshaping the lips. Mild edema, without erythema, was noticed in the treatment of the lip and oral mucus membrane areas. There was no bleeding and, consequently, no ecchymose. No edema or erythema was observed in the treated lips in the six hours following the procedure.

Figure 2 - Left: 30G x 25 mm microcannula; Right: demonstration of the technique to improve the contour of the lip: the microcannula is introduced into the micropuncture made with a 26G ½ needle and the product is retro-injected linearly from the apex of the cupid's bow to the corner of the mough; the microcannula's tip can be seen in the apex of the cupid's bow

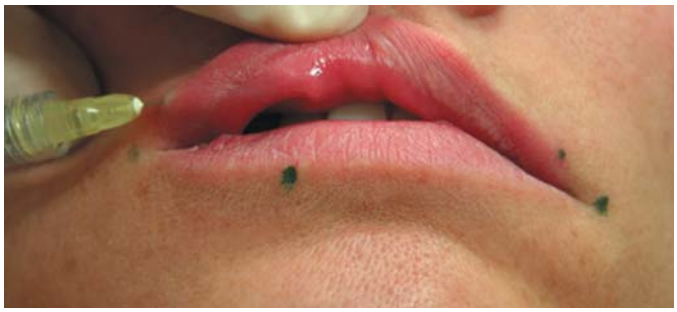

Figure 4 - Implementation of the technique for increasing the lips' volume: the 30G x 25 mm microcannula is moved through the puncture towards the oral mucous membrane and the product is applied *in bolus;* the tip of the microcannula can be seen inside the treated lip

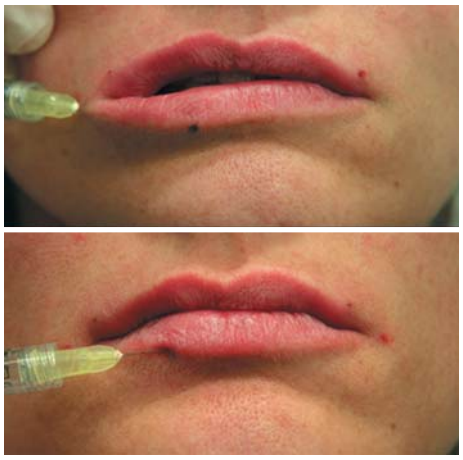

Figure 5 - Above: Implementation of the technique to improve the commissure and lateral labial contours through the same puncture in the lower lip; Below: Implementation of the technique to improve the shape of the center of the lower lip

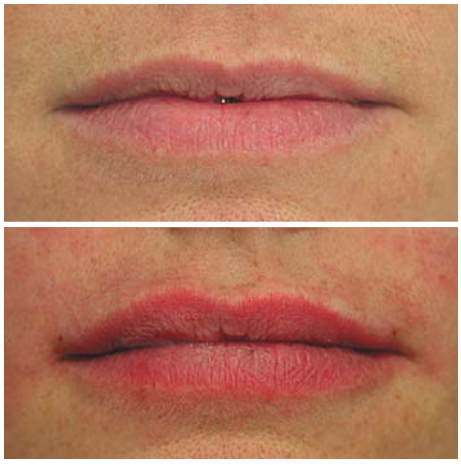

Figure 6 - Above: The technique's method for treating the corner of the mouth with a needle is seen on the left: a horizontal line, 1 cm laterally from the corner, is made by retro-injecting up to 1 cm medially; Below: the needle is introduced below the horizontal pillar and three vertical lines are retro-injected starting from the same micropuncture, forming an inverted triangle to the right of the corner of the mouth

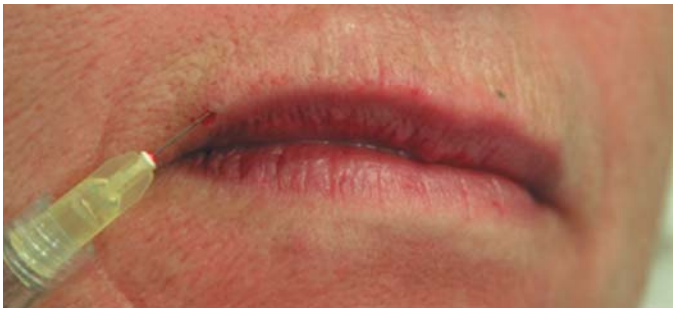

Figure 7 - The 30G x 25 mm microcannula treating perioral wrinkles in the upper lip; its tip can be seen in the supralabial region

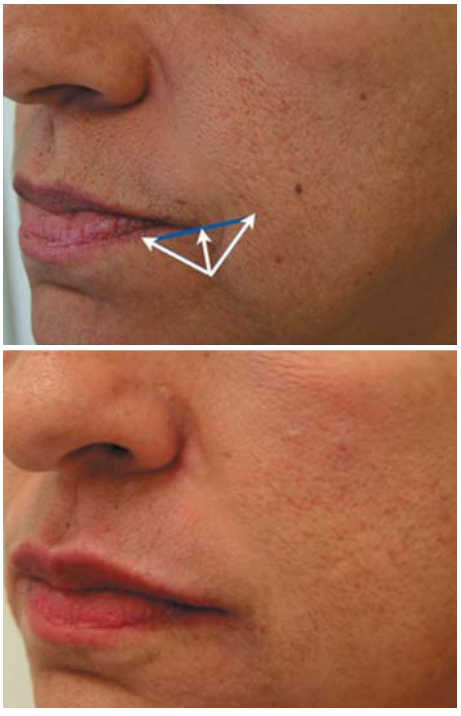

Figure 8 - Above: lips before treatment; Below: the lips, newly filled with hyaluronic acid through a 30G x 25 mm microcannula; the contour was corrected and the projection was increased in the upper lip; the contour was corrected and the projection and volume were increased in the lower lip

DISCUSSION

The lips are centrally located in the lower third of the face and are capable of expressing emotion, sensuality and vitality.[3] In this technique to treat the lips, the author's classification, which divides the lips into three different anatomical areas, was employed. A different result will be obtained in each of those areas after the filling:

- Lip contour: it is enhanced when the product is retro-injected linearly from the central to the lateral area of the lips.
- Lip mucous membrane: the projection of the lips is obtained when this area is injected.
- Oral mucous membrane: when filling that region using the *bolus* technique, the volume of the lips is increased because the local dental arch pushes the filled area to the front.[4]

The skin of the lips can be described as thick and juxtaposed to the muscular layer, with its thin and delicate red zone comprised of transition epithelium between the skin and the mucous membrane. The lateral region of the lips' subcutaneous layer affects the adhesion of the skin and mucus membrane to the muscles.[5]

The superior and inferior labial arteries (branches of the facial artery) are responsible for irrigating the lips. Facial arteries are extremely tortuous; needle-based or intravascular injection techniques frequently perforate them, producing a greater risk of hematomas and ecchymoses.[6] Injections with sharp and short (7 mm) needles require several punctures for the fillings to be carried out,[7] which causes a higher release of histamine and increases the risk of edema, erythema and hematomas, in addition to causing more pain.

Microcannulas are very safe due to their flexibility and blunt tip, which does not hurt vessels or nerves, and is more comfortable for patients. Although the procedure is not completely without complications, the use of microcannulas avoids the lesion of important structures and accidents that can be caused by intravenous injection, considerably decreasing the amount of bruising. [8]

CONCLUSION

If procedures are carried out carefully and delicately, it is safe to work in deep, subdermic planes with microcannulas, which reduce the risks to the patient. ●

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Dermatoscopy in pregnancy

Dermatoscopia na gestação

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ABSTRACT

Cutaneous melanoma's prognoses depend primarily on the tumor's thickness; early detection of melanomas is extremely important to increase a patient's chances of survival. The use of dermatoscopy can be up to 90% accurate. Changes in pigmented lesions may occur during pregnancy, however the challenge lies in knowing whether such changes are benign or whether they indicate a melanoma. Dermatoscopy is an important diagnostic tool that increases the accuracy of detection and diagnosis of the margins of melanomas in their earliest stages, which consequently improves patients' prognosis and survival rates.
Keywords: pregnancy; melanoma; dermoscopy.

RESUMO

O prognóstico do melanoma cutâneo depende principalmente da sua espessura, sendo a detecção precoce de melanomas iniciais extremamente importante para a maior sobrevida dos pacientes. Com a utilização do exame dermatoscópico, pode-se alcançar acurácia de aproximadamente 90%. Alterações em lesões pigmentadas durante a gestação podem ocorrer, porém a dificuldade é saber se são benignas ou se correspondem a melanoma. O recurso diagnóstico da dermatoscopia permite aumentar a margem de acerto no diagnóstico e na detecção do melanoma nos estádios mais iniciais, melhorando o prognóstico e consequentemente a sobrevida do paciente.
Palavras-chave: *gravidez; melanoma; dermoscopia.*

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INTRODUCTION

Cutaneous melanoma's prognosis mainly depends on its thickness, and early detection of initial melanomas is extremely important for the patient's long-term survival. When carried out by dermatologists using the naked eye, the diagnostic accuracy of cutaneous melanoma is estimated at 75-80%. It can be even lower when carried out by general practitioners and resident physicians. However, the diagnosis of cutaneous tumors can be up to 90% accurate when physicians use dermatoscopic examinations, [1-3] a non-invasive method.

Dermatoscopic structures and colors, and their distribution, can help differentiate between melanocytic and non-melanocytic lesions and between malignant and benign tumors.[3]

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CASE REPORT

This case describes a 30-year-old white female patient originally from Sao Paulo, state of Sao Paulo, Brazil. Her family history includes a father with esophageal cancer and a mother and paternal aunt with breast cancer. The patient was referred to Hospital AC Camargo by another care service after reporting a lesion in the upper right arm, which was removed in January 2010. The pathological examination of the excised tissue revealed an extensive superficial melanoma of radial growth, with a 0.3 mm Melanoma Breslow Score, a 0/10 mitotic index high-power fields (HPF,) 0 /mm², minor peritumoral lymphocitary infiltration, and the presence of a pre-existing nevus and free margins. An increase of the margins was then recommended; the pathological exam the following month displayed cicatricial dermal fibrosis with foreign body type gigantocellular reaction and a lack of residual neoplasia.

Digital dermatoscopy was conducted on February 22, 2010 (Figure 1), with the inclusion of 208 lesions; an exeresis was not recommended. According to the hospital's follow-up protocol, another digital dermatoscopy was carried out on March 31, 2010 (Figure 2), again without an indication for exeresis. The patient then did not show up for the six-month follow-up visit, as instructed. During the one-year period after the March 2010 visit, the patient became pregnant and had an abortion, only undergoing a new digital dermatoscopy on March 25, 2011. One of the lesions in the abdomen presented significant growth, suggesting melanoma (Figures 3). The anatomical pathological report dated June 1, 2011 is as follows:

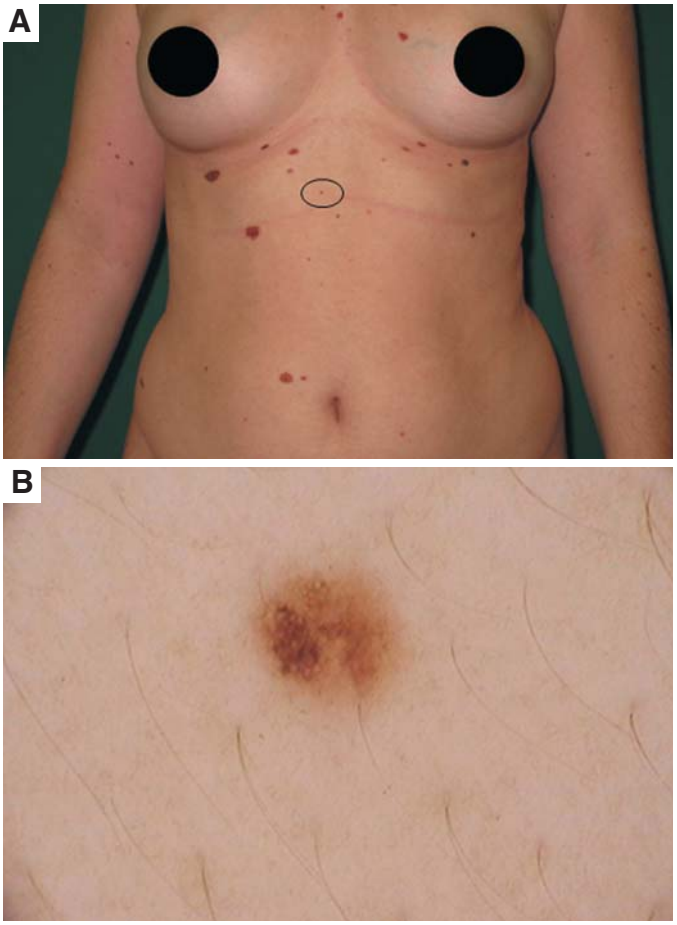

Figure 1 - Total corporal mapping and digital dermatoscopy carried out on February 22, 2010; **A -** Macroscopic photograph; **B -** Dermatoscopy of the lesion followed up

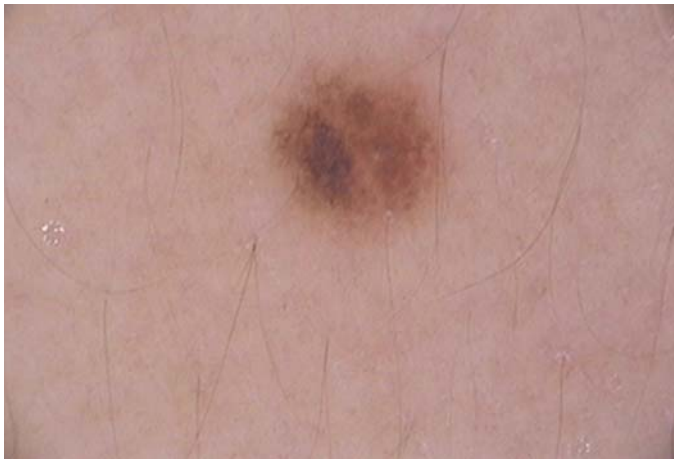

Figure 2 - Dermatoscopy of the lesion followed up, carried out on March 31, 2010

Invasive malignant melanoma.
Type: superficial extensive.
Growth phase: radial.
Ulceration: Not detected.
Clark's level: II.
Infiltration depth (Breslow): 0.33 mm.
Mitotic index: 0/10 HPF 0/mm².
Peritumoral inflammatory infiltrate: intense.
Intratumoral inflammatory infiltrate: not detected.
Regression areas: not detected.
Vascular invasion: not detected.
Lymphatic invasion: not detected.
Perineural invasion: not detected.
Microscopic satellitosis: not detected.
Pre-existent nevus: not detected.
Surgical margins of resection: not compromising.

DISCUSSION

Melanoma is one of the most commonly diagnosed tumors during pregnancy, after breast and cervical cancers. While the occurrence of malignant tumors in pregnant women is approximately one in 1,000, around 8% of all tumors detected during pregnancy are melanomas.[4,5] Modifications in pigmented lesions are known to take place during pregnancy, however it is difficult to differentiate between benign alterations and melanomas. For that reason, diagnostic dermatoscopy was used in order to increase the diagnostic accuracy and the probability of detecting

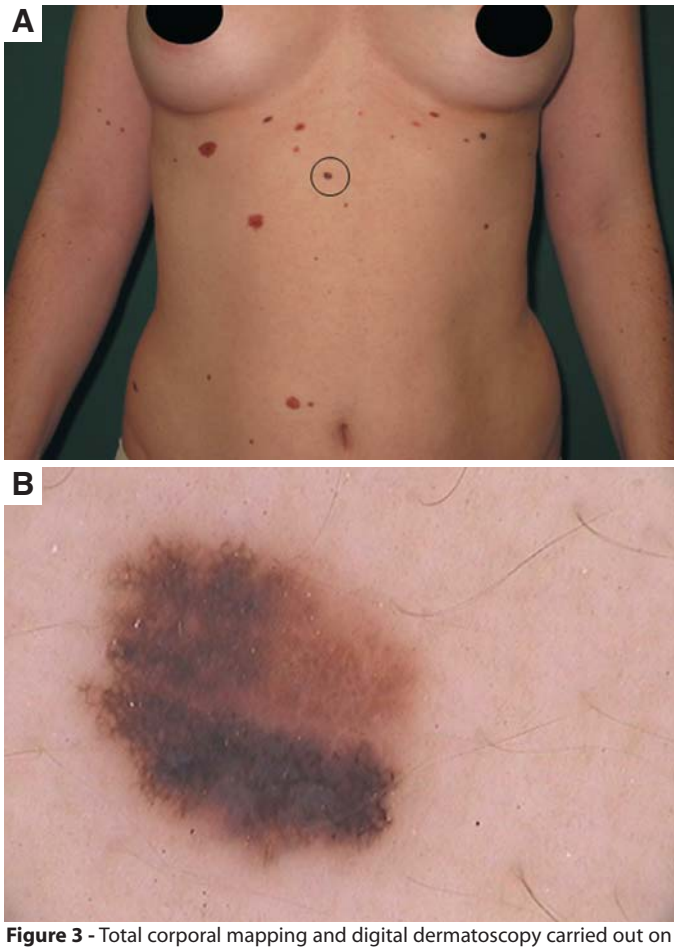

Figure 3 - Total corporal mapping and digital dermatoscopy carried out on March 25, 2011; **A -** Macroscopic photograph; **B -** Dermatoscopy of the lesion followed up

melanomas in the earliest stages, consequently improving the prognosis and the patients' chance of survival.[1]

According to Menzies and colleagues, some initial melanomas might not present features that distinguish them from benign lesions. In those cases, a dermatoscopic follow-up is crucial for early detection.[1]

At the time of writing, the study patient was under a clinical and dermatoscopic follow-up program at the outpatient clinic of the Núcleo de Câncer de Pele e Dermatologia (Skin Cancer and Dermatology Center) of Hospital AC Camargo. ●

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