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Sumário / *Table of contents*

Laser assisted tattoo removal: a literature review

Remoção de tatuagens com laser: revisão de literatura

ABSTRACT

Tattooing has existed in humankind's culture since the onset of civilization. Tattoo removal attempts are also very ancient. The following current methods are reported for the removal of tattoos: dermabrasion, surgical excision, and laser procedures. The most commonly used lasers for tattoo removal are: QS-Nd:YAG (1,064 and 532nm), QS-Ruby (694nm) and QS-Alexandrite (755nm). The present review is aimed at studying the action mechanism of lasers for tattoo removal and the correct indication for each type of pigment, in addition to describing complications and the best manner of preventing them.

Keywords: *lasers; laser therapy; tattooing.*

RESUMO

A tatuagem está presente na cultura do homem desde o começo da civilização. Tentativas de remoção de tatuagens também são muito antigas. São relatados para remoção de tatuagens os seguintes procedimentos: dermoabrasão, retirada cirúrgica e procedimentos com lasers. Os lasers mais utilizados para remoção de tatuagens são: QS- Nd:YAG (1064 e 532nm), QS Rubi (694nm) e QS Alexandrite (755nm). Nossa revisão visa ao estudo do mecanismo de ação dos lasers na remoção de tatuagens e sua indicação correta para cada tipo de pigmento, além da descrição das complicações e a melhor forma de as prevenir.

Palavras-chave: lasers; terapia a laser; tatuagem.

INTRODUCTION

Tattoos have been present in the culture of mankind since the beginning of civilization. They are permanent signs on the body that have different meanings: amulets, symbols of status, declarations of love, statements of religious beliefs, adornments, and even sometimes a form of punishment. The first described reports of tattoos date from 2,000 BC, and were found in Egyptian mummies. In 1991 a mummy from the ice age (around 5,200 years old) was found, which had several tattoos on its body. One development during the history of tattoo artistry was the introduction of different colored pigments, allowing more complex tattoos. Attempts to remove tattoos are also very old.

Continuing Medical Education

Authors:
Carla Gregório Barbosa de Oliveira[1]
Simão Cohen[2]
Valter Alves[3]

[1] Voluntary Physician at the Laser Ambulatory of the Faculdade de Medicina do ABC (FMABC)—Santo André (SP), Brazil

[2] Head of the Laser Ambulatory, FMABC—Santo André (SP)

[3] Third-year Dermatology Resident Physician, FMABC—Santo André (SP)

Correspondence:
Dr. Carla Gregório
Av. Príncipe de Gales, 821
Cep: 09060-650 - Santo André—SP, Brazil
E-mail: dermatologia@fmabc.br

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Types of tattoos

Tattoos can be divided into five categories: professional, amateur, cosmetic, medical, and traumatic. The professional type is performed using professional devices that contain vibratory needles, and pigments of various colors. The granules of pigment are deposited superficially in the dermis. Amateur tattoos are performed with needles or improvised devices and pen ink, charcoal, and soot are usually used as pigments. The use of cosmetic tattoos has increased in recent times, especially in eyebrows, eyelids (eyeliner), lip (contour), reconstruction of breast areola tissue and of other scars. Mostly brown, black, pink, and red pigments are used in those cases.

Traumatic tattoos occur when pigment is deposited in the skin through abrasion or resulting from the force of an explosion. The materials (asphalt, gunpowder, etc.) remain housed in the dermis after the trauma, lending a black or bluish hue to the skin, depending on the depth at which they settle.

Medical tattoos are used, for example, in radiotherapy protocols. [2]

Tattoo removal techniques

The oldest tattoo removal techniques date back to 543 BC, having been developed by the Greeks, who performed abrasion followed by the application of salts and chemicals.[3] Dermabrasion has also been widely used. The principle of this technique is based on the local destruction of the skin and the consequent removal of the tattoo's pigment. The use of trichloroacetic acid in high concentrations has also been described. These two techniques do not always lead to complete removal of the tattoo and have a high risk of skin depigmentation and unaesthetic scars. [4]

Surgical removal of tattoos can also be performed. Nevertheless, linear scars may result from the procedure, and often tattoos are too large or in difficult to access sites. 5 Surgical removals can be indicated for patients who have allergic reactions to the pigments of tattoos. In such cases, removal attempts using laser can cause hypersensitivity reactions and even anaphylactic shock. Another therapeutic option described in this situation is the CO_2 laser.

The first report of laser based tattoo removal using QS Nd:YAG laser was published in 1965 by Goldman et al.[5,6] However, the lack of a thorough understanding of the physics of this laser type, combined with unpredictable clinical results,led it to fall into disuse at that time.

At the end of the 1970's and in the beginning of the 1980's, the most widely used lasers for tattoo removal were the carbon dioxide (CO_2) and argon types. 6 Given that these lasers have water as the chromophore and that they are not selective, the problem of inconsistent clinical outcomes, with the possibility of the formation of unaesthetic scars and hypopigmentation arose again. [7,8] The argon laser emits blue or green light and has a wavelength of 488 or 514nm.

Early in the 1980's there was great progress following the publication of the theory of selective photothermolysis by Anderson and Parrish.[9] In this manner, selective Q-switched lasers (QS) would only destroy specific targets, with minimal damage to the underlying tissue. The theory previously proposed by Goldman was put into practice, inaugurating the use of QS Ruby laser for removing tattoos.[10]

Devices with pulses in the magnitude of milliseconds, such as those employing intense pulsed light, should not be used for tattoo removal, for they heat the granules of the pigment, allowing that heat to spread to adjacent tissue, causing damage. Attempts at removing tattoos with these devices usually results in scarring and does not completely remove the pigment. For best results Q-switched lasers must be used.

Q-Switched Laser

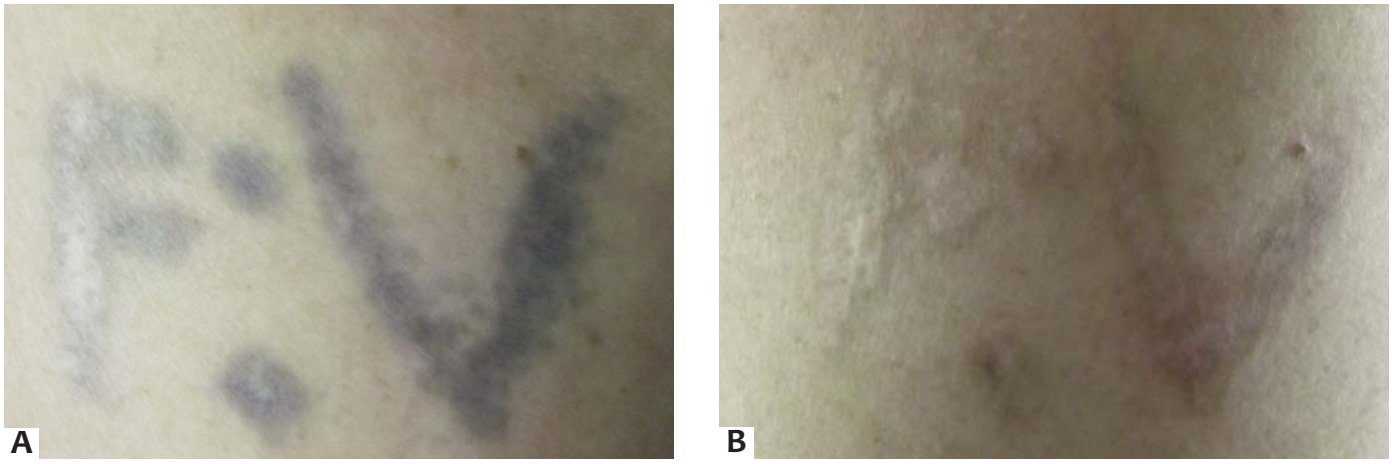
The way that Q-switched lasers operate in tattoo removal is not completely understood. In a study of tattoos treated with the use of QS lasers (with evaluation through electron microscopy) the destruction of pigment contained in the cells, with the fragmentation of target-pigments, can be observed. That pigment is then phagocytised, and an inflammatory response is responsible for transporting those cells into the lymphatic tissue. QS Ruby laser was the first QS laser to become commercially available, followed next by the QS Nd:YAG and QS Alexandrite lasers. These three lasers are still currently used—and it is important to note that each has a different wavelength. In order to select the correct laser to be used, the following criteria must be considered: the patient's skin phototype, laser pulse duration, spot size, and fluence.[2]

QS Ruby lasers have a wavelength of 694nm, emit red light, and are better absorbed by the black and dark blue colors. Very dark and amateur tattoos usually respond considerably well to this laser type. Medical tattoos can also have a good response. 2 After treatment with this laser type, transient hypopigmentation that resolves spontaneously in variable periods can occur (Figure 1).

Zelickson et al. carried out a study of 47 black or blue tattoos treated simultaneously with QS Ruby, QS Nd:YAG and QS Alexandrite lasers, with QS Ruby showing superior results. Kilmer and Anderson also demonstrated that QS Ruby laser is effective in treating green ink, although other studies have shown that QS Alexandrite treats this color more efficiently. [11,12]

QS Nd:YAG laser has a wavelength of 1,064 nm, emits green light and, through the KTP crystal (potassium titanyl phosphate), also doubles the 1,064 frequency, emitting a 532nm wavelength. This versatility allows for the treatment of dark pigments (such as black and dark blue) using 1,064nm; red, yellow, and orange pigments can also be treated with 532nm.

The longer wavelength lends greater penetrating power to this type of laser, thus better protecting the melanocytes of the epidermis, and as a result it is a laser type suitable for higher skin phototypes. Some studies comparing QS Ruby with QS Nd:YAG have demonstrated that the latter has less tendency to cause blisters and less chance of residual hypopigmentation 13 (Figure 2).



Figures 1 **A** and **B:** Dark-coloredtattoo showing small area of hypopigmentation, treated with QS Ruby laser.

Figure 2: A and B: Dark-colored-tattoo treated with QS Nd:YAG laser.

Kilmer et al. conducted a study of 39 tattoos treated with QS Nd:YAG laser, with fluences of 6 to 12j/cm2.A response of 75%was obtained for the black pigment in 77% of treated tattoos, in addition to a 90% clearance in 28% of the patients after four sessions, without secondary hypopigmentation.[14]

As already mentioned, QS Nd:YAG's wavelength can be doubled to 532nm with the use of KTP.This wavelength is well absorbed by red, orange, and yellow pigments. This finding was published by Anthony and Harland, who conducted a study in which seven patients with an allergy to red tattoo pigment were treated. 532nm QS Nd:YAG was used in conjunction with topical corticosteroids with good response.[15] It is worth noting that this wavelength is absorbed by epidermal melanocytes, therefore, a chance of hypochromia exists with this laser type.

QS Alexandrite laser was launched in 1993 by Anderson et al. It has a 755nm wavelength. Fitzpatrick and Goldman published a series of 25 patients with professional and amateur tattoos with a 95% response when used for black and blue tat-

toos, with an average of 8.9 sessions.[16] This laser was proven superior to QS Ruby and QS Nd:YAG for the removal of green pigment. Nevertheless, as it is well absorbed by epidermal melanocytes, it also brings with it the risk of residual hypochromia. [12]

Generally, darker and amateur tattoos respond well to all three types of lasers mentioned above, for, by definition, the black color absorbs the wavelengths of all visible light. Red and green pigments are well absorbed by 532nm QS Nd:YAG and 755nm QS Alexandrite, respectively. However, modern tattoos are often composed of a mixture of colors that can be complex and highly variable, with very similar colors even having completely different compositions, and thus very different absorption spectra. The variation in chemical composition and absorption spectrum can result in tattoos that are resistant and even unresponsive to laser treatment.

Colors such as yellow and orange are known to be very resistant, and colors such as red and green have a highly variable response. There is no theory that explains this incomplete response. It is believed that the wavelength used is not adequate for those colors.[14]

The paradoxical darkening after tattoo removal laser sessions is also described. Peach et al. completed a study involving 184 non-black tattoos and observed a change of color in 33 of them. That alteration ranged from light gray to a complete darkening of the tattoo. The tattoos treated contained white, yellow, and shades of red pigments, becoming gray or completely dark after the sessions.[17] The exact mechanism that explains this change in color is not known. Cosmetic tattoos in shades of red and brown usually contain iron oxide in their composition and the oxidation of this component following QS Ruby laser sessions has already been demonstrated in vitro.[18]

The titanium dioxide found in white and shades of red tattoos is also responsible for the poor response to lasers. Titanium dioxide corresponds to 95% of the pigment in white tattoos, which in turn are used in conjunction with other tattoos to highlight color and brightness. 19 Some cases of resistance to green and blue are also attributed to the presence of titanium dioxide.[19]

In certain cases, treatment with ablative lasers can be indicated to remove pigments that have a risk of darkening or those resistant to treatment. 20

Complications after laser treatment for tattoos, such as dermatitis, granulomatous reactions, lichenoid reactions, and pseudolymphomatous reactions, including lymphadenomegalias, have been reported.[21-23] Moreover, there is a concern about the pigments' degradation following laser. Vasold et al. recently showed the formation of products containing the "Azo" radical, which is known to be carcinogenic and cytotoxic.[24]

Considerations regarding the treatment

The patient must be informed about the number of sessions required to remove the tattoo (six to ten, or possibly more sessions) and about the possibility of their incomplete removal. The number of sessions depends on the tattoo's color, and the age and depth of the pigment.[2]

It is important to instruct patients about protection against the sun—since melanin absorbs the laser and therefore there is a greater chance of damage to adjacent skin, with blistering, hypopigmentation, and scarring. If the patient is tanned or has a higher phototype, 1,064nm QS Nd:YAG is recommended, for it has a greater protective effect of epidermal melanocytes, due to the longer wavelength.[2] It is also important to pay close attention to the spot size of the device used in the treatment—the larger the spot size, the less energy will be deposited superficially in the skin and the lower the chance of causing damage to epidermal melanocytes. In patients with higher phototypes or who are tanned, skin-whitening treatment is recommended before the sessions. These treatments can be carried out with creams containing tretinoin, hydroquinone, and corticosteroids (triple combination).

Regarding any medication that may interfere with the effect of the laser, patients with rheumatoid arthritis who use a gold salts treatment may develop chrysiasis due to the exposure to laser. Patients taking isotretinoin should discontinue its use six months before the start of treatment in order to reduce the chance of formation of hypertrophic scars. Recent studies, nonetheless, have not suggested that isotretinoin may increase the chance of alteration in the healing process.

Anesthesia before the sessions is indicated, with the possible use of topical anesthetics in the form of creams with 5% lidocaine, with occlusion before the session or use of infiltrative and even regional block anesthesia. Cooled air can be used during the session to provide comfort. When the tattoo is considerably large, it is recommended that it be divided into parts, treating one part per session.

The color of the tatoo and the patient's phototype will be the main criteria in selecting the laser type to be used. As already indicated, QS Ruby, (1,064nm) QS Nd:YAG and QS Alexandrite are the most effective lasers in the treatment of dark blue and black tattoos. The carbon contained in the pigment of amateur tattoos also responds well, typically requiring fewer treatments than colored professional tattoos. However, in patients with higher phototypes,1,064nm QS Nd:YAG laser is indicated, as the longer wavelength interacts less with the epidermal melanin, resulting in a lower probability of hypopigmentation.

Colorful tattoos have unpredictable responses to treatment. In general, QS lasers will treat most of the colors, even though certain colors may be highly resistant to treatment (particularly yellow and orange).

Some lasers can treat certain colors more effectively—as 532nm QS Nd:YAG and QS Alexandrite lasers for red and green pigments, respectively—but as tattoo pigments are complex compounds with varying compositions, the successful treatment of colorful tattoos is often difficult. As the response of a tattoo to laser cannot be predicted, a test point can be indicated at the physician's discretion before the full treatment.

During the session, the laser will cause the "whitening out" of the color in the treated area. This phenomenon seems to be attributed to the vapor and gas bubbles (frost) resulting from

the fast heating of the tissue, which usually resolves 20 minutes after the session.[25,26] It indicates the end point of the session, and, if not observed, it is likely that the treatment has not been enough. It is also common to observe petechiae and even purpura following laser sessions.

The formation of crusting that lingers seven to ten days is common in the period immediately following the treatment. The patient should be instructed about the appropriate dressing of the wound in order to minimize the risk of infection, and about protection against exposure to the sun. In the case of formation of blisters, the patient must be instructed not to rupture them outside of a sterile environment. A new session can be carried out at an average interval of four weeks.

A very common mistake when performing tattoo removal with lasers is the reduction of the spot size and increase of the fluence when the tattoo becomes more resistant to the treatment. It is important to bear in mind that in those cases, decreasing the spot size will entail a more superficial, and consequently more aggressive laser, therefore increasing the risk of scarring. In such cases it is often even preferable to change the laser type, given that many Q-Switched lasers absorb black or any other type of pigment.

In most cases, the treatment of tattoos will occur in multiple sessions. More recently, studies were carried out that suggest multiple treatments in the same session, spaced long enough to resolve the frosting effect (usually 20 minutes). Kossida et al. conducted a study in which a black tattoo underwent four passes of QS Alexandrite laser, separated by 20-minute intervals. After three months, the tattoos that underwent that protocol showed better response than those that underwent a single application. This technique became known as R20.[27]

Other techniques described could serve as adjuvants to therapy with laser. Weiss et al., for instance, described good results using QS Ruby in conjunction with CO_2 laser for removing tattoos. They believe that the CO_2 laser would provide a type of abrasion of the tissue containing the tattoo, thus stimulating the inflammatory response of macrophages for removing the pigment. 28 Also, the use of imiquimod combined to QS laser has been reported in two studies with humans with better response than that of the isolated use of laser. [29,30]

Scheibner et al. carried out a study using QS Ruby for the treatment of 163 tattoos (101 amateur and 62 professional tattoos). A 5-8mm spot size and 2 to 4J/cm^2 fluence was used. On average three sessions were carried out for each lesion. In this study it was possible to observe that amateur tattoos responded better than the professional tattoos. There was complete resolution of 4 amateur tattoos, while 84 responded almost completely, with significantly decreased pigment in 11, and only 2 with unsatisfactory response. In the group of professional tattoos, 2 achieved complete response, 5 responded almost completely, 18 had a significant decrease of pigment, 25 presented minimal response, and 12 had almost no response. Professional tattoos contained colored pigments (yellow, red, green) that responded less than black pigment. Those authors did not report any cases of scarring after the treatment. [31]

How to avoid complications

Tissue damage: The main parameters related to the damage of tissue are the use of appropriate wavelength and the fluence of the laser. The fluence is a measure of the energy density, measured in J/cm2. Ideally, the minimum fluence necessary to cause the whitening of the lesion should be used. With the use of very high fluences, the skin absorbs great amounts of energy and the formation of blisters and scars are possible.

Greater caution must be taken when using high fluences in skin with darker phototypes, for the laser is more intensely absorbed in such cases, increasing the risk of undesired side effects. In darker phototypes, the most suitable laser is the 1,064nm QS Nd:YAG, which has greater penetration and protects the epidermis.

Paradoxical darkening: Cosmetic tattoos are made from a mixture of red, white, brown, and black pigments. Many of these tattoos, when treated with Q-switched lasers, exhibit a paradoxical darkening immediately after the treatment. White tattoos also exhibit this behavior due to the presence of zinc and titanium dioxide. When the paradoxical darkening of a tattoo that is being treated occurs, a number of measures can be taken. The sessions can be carried on using QS laser, or ablative lasers can be used and even the surgical removal of the lesion can be used in more resistant cases. There are reports with good outcomes for cases with the use of QS Nd:YAG in red or brown tattoos, although with an unfavorable response for yellow and white tattoos. It is worth noting that white tattoos almost always darken when exposed to laser, and in such cases it is possible to consider the association with ablative lasers, such as 10,600nm CO2 or 2,940nm Erbium:YAG.

Traumatic tattoos: Tattoos resulting from trauma usually contain carbon and graphite, and usually respond very well to all types of QS lasers. If the particles are too large, a nanosecond laser may not be enough, with ablative lasers like Erbium:YAG being recommended in those cases. 30

A great deal of caution must be taken with tattoos resulting from explosives, for the laser's energy can be enough to trigger the explosion of these particles, which are flammable and will result in scarring (pock-like).[2]

Allergic Reactions: The color to which patients have the most allergic reaction is red. However, as a point of caution, red can often be concealed in a mixture with other colors, for instance, with white to form a pink pigment. An allergy in such a case can manifest as eczema, which can become an intensely pruriginous nodule. Yellow tattoos can also cause photoallergies for they contain cadmium, which is a highly photoallergenic compound. Q-switched laser treatment of tattoos producing an allergic response is not recommended, as there is the possibility of triggering a systemic allergy, including anaphylactic shock. In such cases intralesional infiltration of corticosteroid is recommended, with some cases described with the use of ablative laser (CO_2). [32-37]

ADVANCES

Picosecond lasers: This laser type has a shorter pulse duration than that of Q-switched lasers. This shorter duration allows the laser to reach the pigment more effectively, and with less interaction with surrounding tissues. An article by Ross et al. demonstrated that 12 of 16 black tattoos treated using 1,046nm Nd:YAG obtained a better response with one pulse with duration of 35 picoseconds than one pulse with duration of 10 nanosseconds. In that study, 16 tattoos underwent four treatments with four-week intervals. In 12 of the 16 tattoos, the picosecond laser showed better results.[33]

Also, substances that enhance the skin's optical properties are being developed, allowing lasers to more easily reach tattoos in the dermis. These topical or injectable substances are being developed with the aim of reducing the dispersion of light due to dermal collagen, allowing better removal of tattoos with fewer side effects.[35]

New Pigments: Since 1999 a new type of tattoo pigment has been marketed in the United States—the Infinitink® (Freedom Ink, USA), created specifically for obtaining better response to laser treatment. It is composed of bioabsorbable dyes encapsulated in polymethylmethacrylate (PMMA) spheres. These granules also contain additional pigments specially designed for absorption by certain wavelengths.[2] Tattoos created with Infinitink® can be removed in a much shorter time than traditional tattoos.

CONCLUSION

The removal of tattoos was revolutionized with the invention of lasers, and the improvement of that technology has led to better and more predictable results. Nevertheless, more research regarding the safety of tattoo pigments is still needed. Currently, studies are more focused on developing faster lasers (picosecond) and on the more efficient targeting of tattoo pigment by lasers. In the future, these new technologies will generate safer and more effective procedures.

It is important to note that there is no legal requirement for manufacturers to disclose the ingredients of pigments or to use a pure formulation in the dyes used in tattoos. In addition to being a health risk, this makes the removal of a tattoo an even more challenging procedure. Knowledge of the formulation of these pigments could help guide treatments and predict the likelihood of a response or change in the color of tattoos.

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Questions for continuing medical education CDMS

1. The following are indicated for tattoo removal, except:
A) 1,064nm QS Nd:YAG
B) QS Ruby
C) QS Alexandrite
D) Intense Pulsed Light
E) 532 nm (KTP) QS Nd:YAG

2. Which is the correct correlation/association between the columns:

1 - QS Nd:YAG	a- 755nm	d- green light
2 – QS Ruby		b- 694nm e- greenish light
3 - QS Alexandrite	c- 1,064nm	f- red light

A) 1cd, 2be, 3af
B) 1cf, 2ad, 3be
C) 1cd, 2bf, 3ae
D) 1cf, 2ae, 3bd
E) 1cd, 2ae, 3bf

3. Which pigments show a better response with QS Ruby?
A) Dark, black
B) Green
C) Blue
D) Red
E) Yellow

4. Which laser is the best option for removing red pigment?
A) QS Ruby
B) 532nm QS Nd:YAG
C) 1,064nm QS Nd:YAG
D) QS Alexandrite
E) Alternatives A and D are correct

5. Which laser has a better indication for the removal of tattoos in higher skinphototypes?
A) QS Ruby
B) QS Alexandrite
C) QS Nd:YAG
D) Intense Pulsed Light
E) CO2 laser

6. Which laser is the best option for removing green pigment?
A) QS Ruby
B) 532nm QS Nd:YAG
C) 1,064nm QS Nd:YAG
D) QS Alexandrite
E) Laser Diode

7. Which pigments tend to be more resistant to laser treatment?
A) Yellow and green
B) Yellow and orange
C) Orange and red
D) Red and green
E) Black and green

8. Which of the following are complications described in the treatment of tattoo removal with lasers:
A) Dermatitis
B) Granulomatous reactions
C) Lichenoid reactions
D) Lymphadenomegaly
E) All of the above

9. What are the main criteria in choosing the type of laser for use in tattoo removal?
A) Patient'sphototype
B) Color(s) of the tattoos
C) Tattoo type: amateur, professional, medical
D) Answers A and B are correct
E) Answers A and C are correct

10. Which is the correct correlation/association between the columns:

Risk of:

1) Traumatic tattoo	a) Allergic reaction
2) Aesthetic tattoo	b) Explosion of flammable particles
3) Red tattoo	c) Paradoxical darkening
4) Use of high fluences	d) Formation of blisters and scarring

A) 1d, 2d, 3c, 4b
B) 1b, 2c, 3a, 4d
C) 1b, 2a, 3d, 4c
D) 1b, 2a, 3c, 4d
E) 1d, 2c, 3a, 4b

Key:
Photography in dermatologic surgery and cosmiatry—Part II. 2013, 5 (3):189-98.

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

Answers must be submitted online 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.

Article
Original

Variation of melanin levels in the skin in areas exposed and not exposed to the sun following winter and summer

Variação dos níveis de melanina da pele em áreas expostas e não expostas ao sol após inverno e verão

Authors:
Doris Hexsel[1]
Patrícia Caspary[2]
Taciana Dal Forno Dini[3]
Juliana Schilling-Souza[4]
Carolina Siega[5]

[1] Dermatologist Physician, and Preceptor at the Dermatology Service of the Pontifícia Universidade Católica do Rio Grande do Sul (PUC-RS); Principal Investigator at the Centro Brasileiro de Estudos em Dermatologia—Porto Alegre (RS), Brazil

[2] Specialist from the Sociedade Brasileira de Dermatologia (Brazilian Dermatology Society), Master in Medicine and Health Sciences, PUC-RS; Co-investigator at the Centro Brasileiro de Estudos em Dermatologia—Porto Alegre (RS)

[3] Internist and Dermatologist Physician, Specialist from the Sociedade Brasileira de Dermatologia (Brazilian Dermatology Society); PhD in Medical Sciences from the Federal University of Rio Grande do Sul (UFRGS); Coordinator of the Cosmetic Dermatology Sector of the Specialization Course in Dermatology at PUC-RS—Porto Alegre (RS), Brazil

[4] Pharmacist; Research Coordinator at the Centro Brasileiro de Estudos em Dermatologia—Porto Alegre (RS)

[5] Biologist; Research Coordinator at the Centro Brasileiro de Estudos em Dermatologia—Porto Alegre (RS)

Correspondence:
Centro Brasileiro de Estudos em Dermatologia
Dr. Timóteo 782—Moinhos de Vento
Cep: 90570-040—Porto Alegre—RS, Brazil
E-mail: doris@hexsel.com.br

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Study performed at the Centro Brasileiro de Estudos em Dermatologia—Porto Alegre (RS), Brazil.

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ABSTRACT

Introduction The pigment mainly responsible for the color of the skin, melanin is directly influenced by exposure to sunlight.

Objective: The present study assessed the effects of solar radiation on the levels of melanin in areas exposed and not exposed to the sun, taking into consideration the seasonality of exposure.

Methods: Melanin levels were evaluated on the forehead, sacral region, and forearm, in the post-summer and post-winter periods, using spectrophotometry.

Results: The levels of melanin after winter were lower than those after summer in the forehead (168.1 vs. 177.0), sacral region (132.0 vs. 140.4), and forearm (218.7 vs. 260. 4), with a statistically significant reduction only in the forearm ($p<0.0001$). Additionally, erythema was significantly less intense in the forearm and forehead ($p<0.0001$ and $p=0.002$) after winter than after summer.

Conclusion: The significant reduction of melanin levels in the forearm after winter reinforces the influence of seasonality on skin pigmentation changes to body areas exposed to the sun without protection. The small variation in the levels of melanin found in the unexposed area (sacrum) confirms that the effect of exposure to the sun on the levels of melanin is predominantly local. Increased production of melanin is directly related to local exposure to UV rays.

Keywords: melanins; erythema;solar radiation; pigmentation.

RESUMO

Introdução: *A melanina, principal pigmento responsável pela cor da pele, sofre influência direta da exposição aos raios solares.*

Objetivo: *Este estudo avaliou os efeitos dos raios solares nos níveis de melanina em áreas expostas e não expostas à radiação solar, considerando a sazonalidade.*

Métodos: *Os níveis de melanina foram avaliados na fronte, região sacra e antebraço, nos períodos pós-verão e pós-inverno, através de espectrofotometria.*

Resultados: *Os níveis de melanina após o inverno foram menores que após o verão na fronte (168,1 vs. 177), região sacra (132 vs. 140,4) e antebraço (218,7 vs. 260,4), sendo a redução estatisticamente significativa apenas no antebraço ($p<0,0001$). O eritema foi significativamente menor no antebraço e na fronte ($p<0,0001$ e $p=0,002$) após o inverno do que após o verão.*

Conclusões: *A redução significativa dos níveis de melanina após o inverno no antebraço reforça a influência da sazonalidade na pigmentação da pele nas áreas de exposição solar sem uso de proteção. A pequena variação dos níveis de melanina verificado na área não exposta (sacro) confirma que a repercussão da exposição solar nos níveis de melanina é predominantemente local. O aumento da produção de melanina é diretamente relacionado à exposição local aos raios UV.*

Palavras-chave: *melaninas; eritema; radiação solar; pigmentação.*

INTRODUCTION

Skin color results from the presence of pigments, such as hemoglobin, carotenoids, and especially, melanin.[1] The quality and amount of melanin produced by melanocytes are the main determinants of cutaneous pigmentation.[2] Melanin is a protein whose main role is to protect DNA from the harmful action of solar radiation, absorbing and diffusing ultraviolet rays (UV).[1,3] There are two types of melanin: the constructive (determined by genes and not dependent on the exposure to the sun), 4 and the optional (produced by the body after exposure to UV rays).[1]

The increase in melanin production after exposure to UV rays is a photoprotective response of melanocytes and keratinocytes, achieved through a cascade of chemical reactions that result in, among other things, the increased expression of hormones, especially the melanocyte stimulating hormone melatonin. 5 When excessive, exposure to the sun can cause or worsen some important alterations in pigmentation, such as melasma,[6] post-inflammatory hyperpigmentation,[7] solar lentigines,[8] and can also lead to the development of cutaneous neoplasms.

The dose of UV rays that reaches the skin depends on the change of the seasons, among other factors. The irradiation of UVB rays, for instance, is much higher in summer than in winter. 9 Moreover, parameters like latitude also influence the intensity of the UV rays that reach the surface of the earth. 9 The city of Porto Alegre (RS), Brazil, where the study was carried out, experiences well-defined seasons, making it a favorable location for obtaining accurate results regarding the seasonal variation in the levels of melanin.

It is known that activation of melanocytes in order to produce melanin, which is caused by exposure to sunlight, occurs in body sites where there has been direct solar incidence. It is unknown however, whether the cutaneous expression of melanin remains restricted to the exposed locations or if it also occurs in areas where there was no direct solar incidence, as a result from increased serum levels of hormones, such as melatonin. The present study was developed to evaluate the effects of solar radiation on the levels of melanin in body areas exposed and not exposed to solar radiation, taking into account the specific season of the year.

METHODS

A prospective observational study was conducted in 2009 and 2010. Patients were recruited from a pre-existing Centro Brasileiro de Estudos em Dermatologia—CBED's (Brazilian Center for Studies in Dermatology) database. Prior written consent regarding participation in the study was obtained from all patients. The protocol of the study was approved by the Ethics Committee of the Hospital Moinhos de Vento, in Porto Alegre (RS), Brazil.

The main inclusion criteria were: individuals older than 18, Fitzpatrick skin phototypes I to IV, and absence of prior exposure to artificial sources of UV radiation. Exclusion criteria included: pigmentation disorders, topical treatments that might interfere with skin pigmentation, or having undergone other cosmetic treatments or surgeries in the assessed sites.

The patients attended the research center on two occasions, with one visit during the months of March and April (post-summer period) and another in September or October (post-winter period). The interval between visits was six months for all researched individuals. On both visits, skin pigmentation was assessed using a spectrophotometer (Mexameter®, Courage-Khazaka, Cologne, Germany), a device that provides objective measures of the levels of melanin and erythema in the skin.

Three areas were evaluated in each patient:

- the anterior part of the forearm, 8 cm above the wrist, measured from the styloid process of the ulna (an area exposed to direct sunlight only during the summer)
- the forehead, 4 cm below the hair's implantation line (an area exposed to direct sunlight throughout the year)
- the sacral region, located 10 cm below the midpoint between the posterior iliac crests (an area not exposed to direct sunlight at any time of year)

Statistical Analysis

The data were described using mean value and standard deviation for continuous variables and as percentages for categorical data. The data for melanin and erythema were compared over time through a paired t-test. The correlation between the values of melanin and erythema levels was calculated through the Pearson's correlation coefficient. The statistical analyses were performed using the SPSS 16.0 software (Chicago IL).

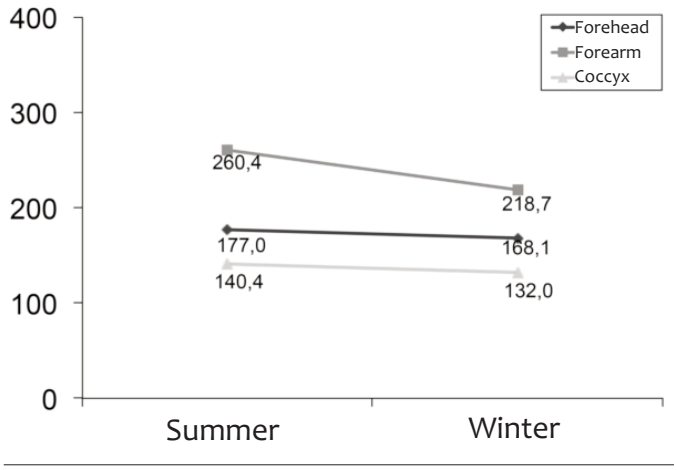
RESULTS

Thirty-four female patients were included in the study. Most patients were classified as phototype III (38.2%) and the mean value of their ages was 38.4 ± 11.6 years. The objective evaluations of pigmentation indicated that the levels of melanin decreased after the winter as compared to those seen after the summer, in all body areas (Graph 1). However this reduction was statistically significant only in the forearm ($p < 0.0001$), an area that is exposed to the sunlight especially in the summer.

Regarding the levels of erythema, there was also a statistically significant reduction in the forearm and forehead ($p < 0.0001$ and $p = 0.002$, respectively) when comparing the results obtained after the summer and after the winter. The sacral region showed a slight increase in erythema after the winter, nevertheless with an absence of a significant difference when this value was compared to that presented after the summer (Graph 2).

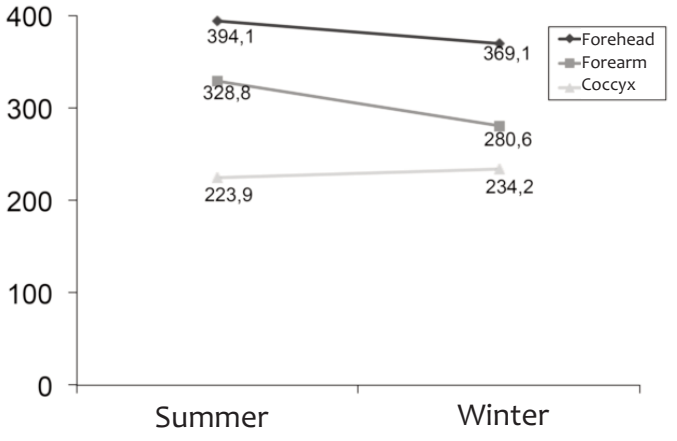
After the summer, a positive correlation between the amounts of melanin and erythema in the forehead ($r = 0.512$; $p = 0.002$), and a strong positive correlation between the values for melanin and erythema in the forearm and sacrum were verified ($r = 0.744$; $p < 0.0001$ and $r = 0.835$; $p < 0.0001$ respectively). After the winter, the same correlation pattern was observed: there was a positive correlation between the values for melanin and erythema in the forehead ($r = 0.485$; $p = 0.004$) and a strong positive correlation between the values for melanin and erythema in the forearm and sacrum ($r = 0.809$; $p < 0.0001$ and $r = 0.719$; $p < 0.0001$ respectively).

Graph 1: Melanin levels



Melanin levels after the summer and after the winter, evaluated in the forehead, forearm, and coccyx

Graph 2: Erythema levels



Erythema levels after the summer and after the winter, evaluated in the forehead, forearm and coccyx

DISCUSSION

Studies evaluating the response of melanin production after UV exposure have already been carried out. 10-12 Nevertheless, the present study is the first that objectively evaluates through spectrophotometry whether there is a systemic expression of melanin after the exposure to or in the absence of direct sunlight, taking into account seasonal variation.

As expected, the present study revealed lower values for melanin levels after the winter as compared to those observed after the summer, with those values showing to be significantly lower in the forearm, a body site that is usually exposed to the sunlight during the summer and protected during the winter. An interesting finding was that although the face has also presented lower melanin levels after the winter (177.0 vs. 168.1), this reduction was not statistically significant. This might be due to the fact that the face is always exposed to the sunlight and the patients have maintained the same habits of using or not using sunscreen throughout the year. These results are similar to those found by Roh et al., 10 who have also observed significant seasonal variation of melanin in the arm, as well as have Lock-Andersen and Wulf, 11 who observed considerable seasonal variation in skin pigmentation of body areas exposed to the sun.

Another important finding was that there was no significant variation in the levels of melanin in the sacral region, a body site that is not usually exposed to direct sunlight anytime of the year. This supports the idea that increased levels of melanin are, above all, a predominantly local effect of exposure to sunlight. Regarding the levels of erythema, there was a significant decrease at the end of winter, in the forearm and forehead, which are body sites with greater seasonal exposure. The levels of melanin and erythema were positively correlated in this study, indicating that the higher the values of melanin, the higher the values observed for measurements of erythema.

The device used in the study's evaluations (Mexameter®) allowed for the objective checking of the levels of melanin and erythema, since it quantifies those two components that are responsible for the color of the skin on a scale from 0 to 999. The narrow-band reflectance spectrophotometry is a sensitive, reproducible, and specific method for taking objective measurements of the color of the skin, allowing the quantification of small differences.[13,14]

CONCLUSIONS

The increase in production of melanin is directly related to local exposure to sunlight. The same effect was not observed in areas that were not directly exposed to sunlight.

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Article
Original

Epidemiological profile of patients with periorbital hyperpigmentation, at a dermatology specialist center in southern Brazil

Perfil epidemiológico dos pacientes com hipercromia periorbital em um centro de referência de dermatologia do Sul do Brasil

Authors:
Cristiane Lüdtke[1]
Daniela Moraes Souza[1]
Magda Blessmann Weber[2]
Aline Ascoli[3]
Fernanda Swarowski[3]
Cynthia Pessin[4]

[1] Dermatologist Physician at private practice—Porto Alegre (RS), Brazil
[2] Associate Professor of Dermatology at the Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA)—Porto Alegre (RS), Brazil
[3] Intern at the Department of Dermatology, UFCSPA—Porto Alegre (RS)
[4] Dermatology Resident Physician, UFCSPA—Porto Alegre (RS)

ABSTRACT

Introduction: Periorbital hyperchromia or "dark circles" is a common complaint, due to the fact that it interferes with patients' self-esteem.

Objective: To evaluate the prevalence of periorbital hyperchromia and its possible etiopathogenetic factors in a population sample drawn from a state and university dermatology service in Porto Alegre, Brazil.

Methods: Cross-sectional, prospective study. Data collection questionnaire given to patients who visited the Dermatology Department of UFCSPA, from November 2011 to April 2012.

Results: From a total of 220 investigated patients, there was a predominance of women with skin phototypes 2 and 3 and a mean age of 42.2 years. The use of sunscreen and corrective makeup were seen in 59.8% and 40.4% of studied patients, respectively. Presence of septal deviation was observed in 6.8% of patients, snoring at night in 48.4%, asthma in 15.1%, rhinitis in 44.7%, atopic dermatitis in 11.2%, mouth breathing in 20.1% and other types of allergy in 28.6%. Half of the sample mentioned sleeping 5 to 7 hours per night. Smoking, alcohol consumption, and physical activity were reported by 19.2%, 32.9% and 42.9% of patients, respectively. A family history of dark circles was described in 63.7% of cases.

Conclusions: periorbital hyperchromia predominated in women of low skin phototypes, during their 4th decade of life and who reported daily use of sunscreen, physical inactivity, alcohol consumption, smoking habit, allergies, sleep deprivation, and a family history of dark circles.

Keywords: eyes; quality of life; dermatology.

RESUMO

Introdução: *A hipercromia periorbital ou "olheira" é queixa comum por interferir na autoestima dos pacientes.*

Objetivo: *avaliar a prevalência de hipercromia periorbital e seus possíveis fatores etiopatogênicos, em amostra populacional de um serviço de dermatologia público e universitário de Porto Alegre.*

Métodos: *Estudo transversal, prospectivo. Questionário de coleta dos dados aplicado em pacientes que se consultaram no Serviço de Dermatologia da UFCSPA entre novembro de 2011 a abril de 2012.*

Resultados: *Total de 220 investigados, com predomínio de mulheres com fototipos 2 e 3, e média de idade de 42,2 anos. O uso de fotoprotetor e de maquiagem corretiva foi visto em 59,8% e 40,4%, respectivamente. Foram observados presença de desvio de septo em 6,8% dos pacientes; ronco à noite, 48,4%; asma, 15,1%; rinite, 44,7%; dermatite atópica, 11,2%; respiração bucal, 20,1%; e outro tipo de alergia, 28,6%. Metade da amostra mencionou dormir de cinco a sete horas por noite. Tabagismo, etilismo e atividade física foram referidos em 19,2%, 32,9% e 42,9%, respectivamente. História familiar de olheiras foi descrita em 63,7%.*

Conclusões: *A hipercromia periorbital predominou em mulheres na quarta década de vida, com fototipos baixos, que referiam uso diário de fotoprotetor, sedentarismo, etilismo, tabagismo, alergias, privação do sono e história familiar de olheira.*

Palavras-chave: *olhos; qualidade de vida; dermatologia.*

Correspondence:
Dr. Magda Blessmann Weber
R. Neuza G. Brizola, 495/301
Cep: 90460-230—Porto Alegre—RS, Brazil
E-mail: mbw@terra.com.br

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INTRODUCTION

Periorbital hyperchromia, peripalpebral hyperchromia, dark eyelids, dark eye circles or simply "dark circles", despite being a mere difference in color between the palpebral skin and the rest of the facial skin, can have a major impact on the quality of life by causing an appearance of fatigue and premature aging.[1-4] There are two types of dark circles: vascular and melanic, nevertheless it is believed that most have mixed components, with melanin and hemosiderin being found in almost all types of dark circles, to a greater or lesser degree.[2]

Vascular dark circles, the predominant type, have an autosomal dominant inheritance pattern. They usually appear earlier in life, during childhood or adolescence. They are more common in ethnic groups that include people of Arabic, Turkic, Indian, or Iberian backgrounds. The diagnosis of this type of dark circles is carried out by applying traction to the lower eyelid, making it more transparent and therefore easier to view the vessels underneath the skin.[2-4] In this type of periorbital hyperchromia there is no change in the color of the skin, however the eyelid has a darker hue due to the visible presence of dilated vessels. It is believed that cutaneous hyperchromia occurs due to the deposition of hemosiderin when there is dermal blood extravasation.[2] Smoking, consumption of alcohol, mouth breathing, sleep deprivation, the use of vasodilator drugs, prostaglandin analogues based eye drops, contraceptives, chemotherapy and antipsychotics are factors that can contribute to this process through the stasis of blood vessels, leading to a change of color in the area. Moreover, the presence of conditions that involves the retention of water and eyelid edema (thyroid, kidney, heart, and lung diseases) cause a worsening of the unaesthetic appearance of dark circles. The ideal treatment should include the discontinuation of possibly identified triggering factors, the removal of preformed hemosiderin, and photoprotection.[2-4]

The predominantly melanic periorbital hyperchromia typically affects older people with higher skin types, however it can also occur in patients with lower skin types (also usually elderly) as a result of excessive and cumulative exposure to the sun.[3]

In the literature, there is little dissemination of epidemiological data and factors associated with periorbital hyperchromia. The present study is aimed at evaluating those variables in patients with dark circles.

OBJECTIVES

To assess the prevalence of periorbital hyperchromia and possible pathogenetic factors in a population sample of a public dermatology service of a university in southern Brazil.

METHODS

A prospective cross-sectional study was conducted at the public dermatology service of the Universidade Federal de Ciências da Saúde de Porto Alegre (RS), Brazil. The study was approved by the research ethics committee of the institution where the study was conducted.

Patients who attended medical appointments at the service from November 2011 to April 2012 with complaints of dark circles were invited to participate. All were clarified by the interviewer as to the purpose of the study and about the protection of their privacy, ensuring their anonymity would be preserved in the presentation of the study's results. A term of free and informed consent was signed by all participants, who were then administered a questionnaire by the researchers in order to collect data.

The inclusion criteria for the study were: patients who attended the dermatology service, of both genders and all races, over 18-years-old, and who had signed the free and informed consent term, and agreed to participate in the study. Patients who did not agree to participate, did not sign the term of consent and were under 18-years-old were excluded.

Data collected included: age, gender, skin phototype, age of onset of dark circles, use of sunscreen and corrective makeup, previous treatments for dark circles, habit of snoring, presence of deviated septum, atopic dermatitis, asthma, rhinitis, comorbidities, use of mouth breathing device and continuous medications, in addition to the presence of dark circles in the family and number of hours of sleep per day.

The data were tabulated in an Excel database and distributed using the Kolmogorov-Smirnov test.

RESULTS

During the study, 220 patients were investigated. Of these, 78.2% (n = 172) were women. The mean age was 42.2 years (SD = ± 16.6 years), with a minimum of 18 and a maximum 84 years.

Regarding the age of onset of dark circles, the mean value was 23.2 years (SD ± 14.7 years). Regarding the phototype, the sample studied had greater participation of phototypes II (35.6%, n = 78) and III (32.0%, n = 70).

The use of sunscreen was reported by 59.8% (n = 131) of patients. Regarding the use of corrective makeup to camouflage dark circles, 40.4% (n = 88) of respondents reported its use, with most reporting daily use (43.0%, n = 37).

When asked whether they had undergone previous treatment, a small portion of the sample answered positively (2.8%, n = 6), informing that only topical cosmeceuticals had been used previously (Table 1).

Occurrence of deviated septum was observed in 6.8% (n = 15), nocturnal snoring in 48.4% (n = 106), asthma in 15.1% (n = 33), rhinitis in 44.7% (n = 98), and atopic dermatitis in 11.2% (n = 24).

Mouth breathing was reported by 20.1% (n = 44) of the investigated patients. Regarding the presence of some other type of allergy, 28.6% (n = 63) answered positively, with the most cited being mosquito bites (42.9%, n = 33) (Table 2).

Regarding hours of sleep, half of the sample (n = 107) reported sleeping 5 to 7 hours per day, with an average of roughly 7 hours per day (SD = 1.7 hours/day), a minimum of 1 and maximum of 12 hours per day.

Smoking habits were reported by 19.2% (n = 42) of the investigated patients, of which 54.8% (n = 23) reported smoking

Table 1: Absolute and relative distribution regarding gender, use of sunscreen, use of corrective makeup, previous treatment and skin phototype; mean values and standard deviation for age and the age of onset of "dark circles".

Variables	Total (n=220)	
Gender*		
Male	48	21,8
Female	172	78,2
Age		
Mean ± standard deviation	42,2 ± 16,6	
Median (range)	41,0 (17 – 84)	
Age of onset of dark circles NR = 13 (5.9%)		
Mean ± standard deviation	23,2±14,7	
Median (range)	20,0 (0 – 69)	
Use of sunscreen* NR = 1 (0.5%)		
yes	131	59,8
no	88	40,2
Use of corrective makeup* NR = 2 (0.9%)		
no	130	59,6
yes	88	40,4
Frequency of use* NR = 2 (2.3%)		
daily	37	43,0
3x a week	12	13,9
on special occasions	34	39,5
Previous treatment* NR = 8 (3.6%)		
no	206	97,2
yes	6	2,8
Which treatment NR = 1 (16.7%)		
2 Topical creams	5	100,0
Phototype* NR = 1 (0.5%)		
1 Very fair skin, always burns (always becomes red) and never tans	6	2,7
2 Fair skin, always burns (always becomes red) and sometimes tans	78	35,6
3 Lesser fair skin, sometimes burns (sometimes becomes red) and always tans	70	32,0
4 Pale brown skin, rarely burns (rarely becomes red) and always tans	41	18,7
5 Dark brown skin, never burns (never becomes red) and always tans	19	8,7
6 Dark skin, never burns (never becomes red) and always tans	5	2,3

* Results are presented in the format n(%),with percentages obtained based on the total number of valid cases

11 to 20 cigarettes daily (median = 20 cigarettes/day). It was also verified that 13.2% (n = 29) of the patients being investigated were ex-smokers.

As for drinking habits (ethylism), 32.9% (n = 72) of respondents reported drinking alcohol once or twice a week (84.3%, n = 59).

Practicing some physical activity was reported by 42.9% (n = 94) of the respondents, with 43.3% (n = 39) carrying it out three or four times a week (Table 3).

Regarding the presence of dark circles in the family, 63.7% (n = 137) of patients responded affirmatively. As for the degree of kinship, the most frequently cited were parents (52.5%, n = 72), children (29.2%, n = 40), and siblings (21.8%, n = 30) (Table 4).

The presence of comorbidities was seen in 31.8% of the sample, with the most frequent being arterial systemic hypertension (55%), diabetes mellitus (13.3%) and dyslipidemia (11.7%) (Table 5). The continuous use of medications was reported by 25.9% of respondents, with the most frequently cited being beta-blockers (29.8%) and the angiotensin converting enzyme inhibitor (22.8%) (Table 6).

DISCUSSION

Periorbital hyperchromia, also called dark circles, is more often observed in women—particularly in brunettes—being caused by physiological and genetic factors.[1]

Table 2: Absolute and relative distribution for deviated septum, nocturnal snoring, use of breathing device, asthma, rhinitis, atopic dermatitis and other allergies.

Variables*	Total (n=220)	
Deviated septum * NR = 1 (0.5%)		
No	202	92,2
Yes	15	6,8
Not Specified	2	1
Snores at night* NR = 1 (0.5%)		
No	106	48,4
Yes	121	51,1
Not Specified	1	0,5
Use of oral breathing device* NR = 1 (0.5%)		
Yes	44	20,1
No	175	79,9
Asthma* NR = 1 (0.5%)		
Yes	33	15,1
No	186	84,9
Rhinitis* NR = 1 (0.5%)		
Yes	98	44,7
No	121	55,3
Atopic dermatitis* NR = 6 (2.7%)		
Yes	24	11,2
No	190	88,8
Occurrence of allergy		
No	157	71,4
Yes	63	28,6
Which allergy?		
1 - Mosquito bite	33	42,9
2 - Metal	9	11,7
3 - Medications	7	9,1
4 - Food	6	7,8
5 - Enamel	4	5,2
6 - Cleaning products	3	3,9
7 - Perfume	3	3,9
8 - Dust	3	3,9
9 - Makeup	2	2,6
10 - Animal hair	2	2,6
11 - Urticaria	1	1,3
12 - Hair dye	1	1,3
13 - Mercury	1	1,3
14- Wool	1	1,3
15 - Building and construction materials	1	1,3

* Results are presented in the format n(%), with percentages obtained based on the total number of valid cases

In the present study—and in line with the literature—the majority of patients were female. Regarding phototypes, the study group had a concentration of types II and III, a fact that differs from many studies. These results may be due to the population studied, primarily Caucasian, as demonstrated by the prevalence of skin phototypes II and III.

Regarding the age, periorbital hyperchromia can start in childhood or in adulthood. In the first case, it usually has a pattern of family heritage, being mostly vascular. In the second case, it is mostly melanic.[2] Most dark circles, however, have mixed components.[2] In the present study, most patients were adults who experienced the onset of periorbital hyperchromia in late adolescence. In those cases, it was impossible to determine whether the onset was related to melanic or vascular predominance, because the patients were not classified by their type of dark circles. However, the majority had a family history, which favors the vascular component. As for the use of suns-

Table 3: Absolute and relative distribution for hours of sleep, smoking, ethylism and physical activity; and central tendency and variability measures for hours of sleep

Variables	Total (n=220)	
Hours of sleep per day* NR = 6 (2.7%)		
From 1 to 4	13	6,1
From 5 to 7	107	50,0
From 8 to 12	94	43,9
Hours of sleep		
Mean ± standard deviation	7,1±1,7	
Median (range)	7 (1-12)	
Smoking* NR = 1 (0.5%)		
Yes	42	19,2
Amount		
From 1 to 10	10	23,8
From 1 to 20	23	54,8
More than 20	9	21,4
Ex-smoker	29	13,2
Amount		
From 1 to 10	12	41,4
From 11 to 20	6	20,7
More than 20	11	37,9
No	148	67,3
Ethylism* NR = 1 (0.5%)		
Yes	72	32,9
No	146	66,7
Quantity (days/week)		
From 1 to 2	59	84,3
From 3 to 4	7	10,0
From 5 to 7	4	5,7
Physical activity* NR = 1 (0.5%)		
No	125	57,1
Yes	94	42,9
Frequency (days/week) NR = 4 (4.2%)		
From 1 to 2	21	23,3
From 3 to 4	39	43,3
From 5 to 7	30	33,3

* Results are presented in the format n(%), with percentages obtained based on the total number of valid cases.

Table 4: Absolute and relative distribution for dark circles in the family.

Variables	Total (n=220)	
	n	%
Dark circles in the family* NR = 5 (2.3%)		
No	78	36,3
Yes	137	63,7
Degree of kinship		
1 - Parents	72	52,5
2 – Children	40	29,2
3 – Siblings	30	21,8
4 – Nephews	7	
5 – Uncles/aunts	7	
6 – Cousins	3	
7 – Grandchildren	1	
8 - In-laws	8	
9 – Grandparents		
10 – unspecified	2	7

* Results are presented in the format n(%), with percentages obtained based on the total number of valid cases.

Table 5: Absolute and relative distribution of health problems

Variables	Total (n=220)	
Health Problems		
No	150	68,2
Yes	60	31,8
Health Problems		
1 – Hypertension	33	55,0
2 - *Diabetes Mellitus*	8	13,3
3 –Dyslipidaemia	7	11,7
4 – Psoriasis	6	10,0
5 –Hypothyroidism	6	10,0
6 – Epilepsy	5	8,3
7 – Depression	4	6,7
8 - COPD (chronic obstructive pulmonary disease)	3	5,0
9 – Arthrosis9 - artrose	2	3,3
10 – Cardiopathy	2	3,3
11 – Osteoporosis	2	3,3
12 - Systemic Lupus Erythematosus	2	3,3
13 - Hiatal hernia	1	1,7
14 – Cholelithiasis	1	1,7
15 - Kidney transplant	1	1,7
16 - Hepatitis C virus	1	1,7
17 – Endometriosis	1	1,7
18 – Obesity	1	1,7
19 – Onychomycosis	1	1,7
20 – Neoplasia	1	1,7
21 - Benign Prostatic hyperplasia	1	1,7
22 – Anemia	1	1,7
23 - Herpes simplex	1	1,7
24 - Monoclonal gammopathy	1	1,7
25 - Irritable bowel syndrome	1	1,7
26 - Polycystic ovary syndrome	1	1,7
27 - HIV virus	1	1,7
28 -Bronchial asthma	1	1,7
29 - Disc herniation	1	1,7
30 - Pulmonary hypertension	1	1,7
31 – Liver disease	1	1,7
32 – Rosacea	1	1,7
33 – Migraine	1	1,7

* Results are presented in the format n(%), with percentages obtained based on the total number of valid cases.

creen, it is known that the product acts in preventing dark circles.[5] In the present study, daily use of sunscreen was relatively frequent, probably due to the intention of the patients to better control the condition.

Conditions such as smoking, physical inactivity, ethylism, deviated septum, asthma, rhinitis, atopic dermatitis and other allergies, mouth breathing and sleep deprivation can contribute to palpebral hyperchromia due to the stasis of blood vessels.[2,6] In the present study, those factors were found in a considerable part of the sample, further strengthening their correlation with the presence of dark circles. Regarding the presence of diseases most frequently associated with periorbital hyperchromia (thyroid, kidney, heart, and lung diseases), they were rarely reported by the studied patients. In the present study, the most frequently mentioned comorbidities were arterial systemic hypertension, diabetes mellitus, and dyslipidemia—conditions that can develop into some of the already mentioned diseases. The use of vasodilators, prostaglandin analogues eye drops, chemotherapeutic agents, contraceptives and antipsychotics, all of which, according to the literature, usually contribute to periorbital hyperchromia, have also been rarely reported in the studied sample.[2,3] The medications more frequently informed were beta-blockers

Table 6: Absolute and relative distribution for the use of medication

Variables	Total (n=220)	
Use of medication		
No	163	74,1
Yes	57	25,9
Which medicines?		
1 - Betablocker	17	29,8
2 - Angiotensin converting enzyme inhibitor	13	22,8
3 - Glibenclamide	10	17,5
4 - Statin	9	15,8
5 - Diuretic	9	15,8
6 - Metformin	4	7,0
7 - Acetylsalicylic acid	5	8,8
8 - Oral contraceptive	7	12,3
9 - Levothyroxine	6	10,5
10 - Calcium channel antagonist	5	8,8
11 - Anticonvulsant	3	5,3
12 - Serotonin reuptake inhibitor	3	5,3
13 - Benzodiazepines	3	5,3
14 - Immunosuppressants (tacrolimus, mycophenolate, prednisone)	2	3,5
15 - Formoterol fumarate + budesonide (inhaler)	2	3,5
16 - Calcium carbonate	2	3,5
17 - Salbutamol	1	1,8
18 - Insulin	1	1,8
19 - Fluoxetine	1	1,8
20 - Beta agonist of short duration	1	1,8
21 - Omeprazole	1	1,8
22 - Budesonide nasal spray	1	1,8
23 - Hydroxychloroquine	1	1,8
24 - Fibrate	1	1,8
25 - Renin angiotensin II antagonist	1	1,8
26 - Amitriptyline1	1,8	

* Results are presented in the format n(%), with percentages obtained based on the total number of valid cases.

and angiotensin converting enzyme inhibitors, probably due to the predominance of cases of hypertension in the studied population.

CONCLUSION

In the present study, periorbital hyperchromia was more frequently observed in women in their 40's, with low skin phototypes, who reported daily use of sunscreen, sedentary habits, sleep deprivation, and family history of dark circles. Despite this epidemiological profile being similar to that described in the literature, further studies are necessary in order to allow dermatologists to develop better management strategies for this condition, thereby contributing to improvements in the patients' self-esteem and quality of life.

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Article
Original

Use of non-ablative fractional 1,340nm Nd:YAP laser in the treatment of nodulocystic acne resistant to isotretinoin

Uso do laser fracionado não ablativo Nd-YAP 1.340nm no tratamento da acne nódulo cística resistente à isotretinoína

Authors:
Carlos Roberto Antonio[1]
João Roberto Antonio[2]
Guilherme Bueno de Oliveira[3]
Livia Arroyo Trídico[4]
Mariana Perez Borim[5]

[1] Dermatologist Physician from the Faculdade de Medicina de São José do Rio Preto (FAMERP)—São José do Rio Preto (SP), Brazil; Dermatology Instructor, FAMERP; Responsible Physician, Dermatologic Surgery, Dermatology Service, Hospital de Base, FAMERP

[2] PhD in Health Sciences from the FAMERP—São José do Rio Preto (SP), Brazil; Professor Emeritus, Head of the Dermatology discipline, FAMERP—São José do Rio Preto (SP), Brazil; Head of the Department of Dermatology, Hospital de Base, FAMERP—São José do Rio Preto (SP)

[3] Dermatologist Physician from the FAMERP—São José do Rio Preto (SP), Brazil; Preceptor at the Dermatology Ambulatory of the FAMERP—São José do Rio Preto (SP)

[4] Dermatology Resident Physician at the FAMERP—São José do Rio Preto (SP)

[5] Final-Year Undergraduate Medicine student at FAMERP—São José do Rio Preto (SP)

Correspondence:
Dr. Carlos Roberto Antonio
R. Silva Jardim, 3114—Centro
Cep: 15010-060–São José do Rio Preto—SP, Brazil
E-mail: carlos@ipele.com.br

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ABSTRACT

Introduction: Acne is one of the most prevalent skin conditions, representing a constant challenge to dermatologists, especially in severe cases as nodulocystic acne, which can be resistant to medicament based treatment. Traditional therapy includes topical and oral drugs that are not always effective and often lead to bacterial resistance and side effects. The use of lasers in the treatment of inflammatory acne has increased lately due to the ease, clinical efficacy, and minimal side effects of this type of therapy.

Objective: To evaluate the effects of fractional laser in patients with nodulocystic acne resistant to treatment with isotretinoin.

Methods: Application of laser therapy sessions with Nd:YAP in 9 patients. Assessment of the degree of patient satisfaction and comparison of photographs taken before and after treatment by dermatologists not linked to the study.

Results: Average reduction of 65% in inflammatory lesions, satisfaction of all patients who underwent treatment, and approval in the assessment carried out by dermatologists.

Conclusions: The fractional Nd:YAP laser was proven effective in the treatment of inflammatory acne and may represent a new therapeutic option for this pathology, especially for patients who do not respond to conventional treatment.

Keywords: acne vulgaris; lasers; laser therapy.

RESUMO

Introdução: *A acne é uma das afecções da pele mais prevalentes, representando constante desafio aos dermatologistas, principalmente em casos graves, como a acne nódulo- cística, que pode apresentar resistência ao tratamento medicamentoso. A terapia tradicional inclui medicamentos tópicos e orais, que nem sempre são eficazes e muitas vezes provocam resistência bacteriana e efeitos colaterais. O uso do laser no tratamento da acne inflamatória cresceu ultimamente devido à facilidade desse tipo de terapia, a sua eficácia clínica e aos mínimos efeitos adversos.*

Objetivo: *Avaliar a ação do laser fracionado em pacientes com acne nódulo-cística resistente ao tratamento com isotretinoína.*

Métodos: *Realização de sessões de laserterapia com Nd:YAP em nove pacientes. Avaliação do grau de satisfação dos pacientes e comparação de fotografias realizadas antes e após o tratamento por dermatologistas não vinculados ao estudo.*

Resultados: *Redução média de 65% das lesões inflamatórias, satisfação de todos os pacientes submetidos ao tratamento e aprovação na avaliação realizada pelos dermatologistas.*

Conclusões: *O laser fracionado Nd:YAP mostrou-se eficaz no tratamento da acne inflamatória, podendo representar nova opção terapêutica para essa patologia, principalmente para os pacientes que não respondem ao tratamento convencional.*

Palavras-chave: *acne vulgar; lasers; terapia a laser.*

INTRODUCTION

Acne is one of the most common dermatological conditions, accounting for 30% of dermatological complaints.[1-3] It affects most people at some point in their life, being prevalent in adolescents and affecting 85% of individuals between 12 and 24 years old.[4,5]

It is an inflammatory dermatosis of the pilosebaceous unit, whose pathogenesis is multifactorial. The main contributing factors for its development include follicular hyperkeratinization, increased production of sebum by the sebaceous glands, bacterial colonization of the follicle by Propionibacterium acnes (P. acnes) and the release of inflammatory mediators in the follicle and adjacent dermis.[6]

Drug options can be topical or systemic. The treatment of mild acne is topical, encompassing retinoids, benzoyl peroxide, azelaic acid, and topical antibiotics, and demands frequent applications. Moderate acne requires long-term treatment with oral antibiotics, and may be associated with bacterial resistance. Severe, nodular cystic acne requires the use of oral isotretinoin, a medication associated with significant advancement in the treatment of acne, however it can present side effects such as teratogenicity, lip dryness, dry skin, epistaxis, erythema and/or dermatitis on the face, myalgia, constipation, and elevation of plasmatic lipids, in addition to the possibility of resistance to the action of active principles.[2,7]

Despite the availability of various treatments, there are cases of difficult management, especially the most severe, such as nodularcystic acne, where in spite of the new therapies, lesions often continue to arise.[8,9] In such extreme cases, light and laser-based treatments have become an alternative to topical and oral medications in recent years, since they seem to reduce inflammatory acne lesions, acting on the major physio-pathological factors.[2]

Some studies have reported success in treating inflammatory acne with laser therapy such as 10-12 intense pulsed light (IPL), dye lasers (PDL),[13,14] diode lasers,[15] KTP (potassium titanyl phosphate), erbium glass laser, radiofrequency, and photodynamic therapy[1,2] being cited as examples. Positive results obtained with laser therapy can be explained by the action on the *P. acnes* bacteria and the inflammatory activity by the sebaceous gland.[2]

In light of the success of various types of lasers in treating acne[16,17] the authors sought to evaluate the use of a new non-ablative fractional technology in nodularcystic acne, the 1,340nm Nd:YAP laser (Neodimiun:Ytrium Aluminum Perovskite), since itsindication in acne has up until now been restricted to the correction of scars.[16] The present study was aimed at investigating the benefits of this laser in the treatment of difficult to control, oral isotretinoin treatment-resistant acne.

METHODOLOGY

Patients above 14 years of age, with nodularcystic acne, treated at the Acne Ambulatory of the Dermatological Surgery and Laser Therapy Unit, Dermatology Department of the Faculdade de Medicina de São José do Rio Preto (FAMERP),São Paulo, Brazil, took part in a clinical interventionist study, from September 2012 to June 2013. Inclusion criteria included presence of nodular cystic acne active in the facial region, resistant to oral isotretinoin; absence of the use of any other treatment for acne for at least 90 days. Exclusion criteria included: pregnancy, patients under 14-years-old, patients bearing any other type of infection or skin condition or herpes active in the studied region, and those with a sensitivity to light. Those who met the selection criteria and agreed to participate in the research project signed a Free and Informed Term of Consent. The project was approved by the Ethics Committee of FAMERP.

Each patient underwent a variable number of sessions (two to six), according to clinical indication and at 28-30 day intervals. The laser device used was the 1,340nm Nd:YAP (Etherea®, Industra Technologies Indústria e Comércio Ltda, São Carlos,SP, Brazil), 100mtz (thermal microzones), energy = 100mJ, 3ms and 8mm tip. The patient received one application of this fractional laser per session. The anatomical pathological examination was performed through the incisional biopsy technique, using a 3mm punch. This procedure was carried out before the treatment and after the last laser session,at the same location. The number of sessions was determined by the patient's clinical improvement.

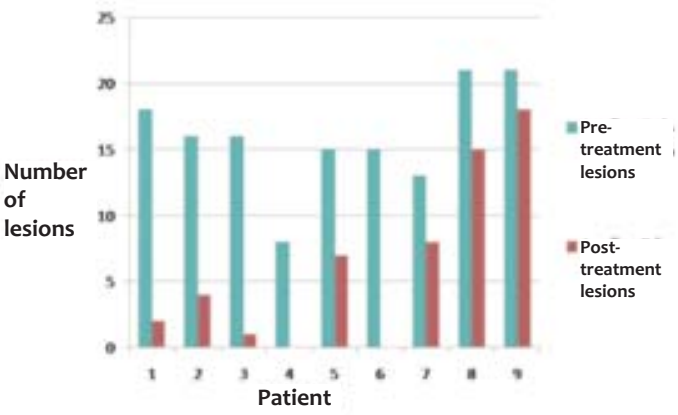
The evaluation of outcomes was performed through comparison of photographs taken before and after the treatment with fractional laser for each patient. The images were analyzed by two dermatologist physicians not related to the study and who were responsible for assigning scores from 0 to 3 (0 = worsening, 1 = absence of improvement, 2 = moderate improvement, 3 = significant improvement), after comparing the two photographs. The patients also provided information on their degree of satisfaction with the treatment (0 = dissatisfied, 1 = somewhat satisfied, 2 = satisfied, 3 = very satisfied). In addition, the lesions were counted on day zero and after the last session.

RESULTS

Nine male patients underwent laser treatment for nodular cystic acne resistant to isotretinoin. The mean value of the patients' age was 20 (range = 16 to 27). The patients had an average of 16 lesions in the face before the treatment (range = 8 to 21), with standard deviation.[3,7,8]

The number of laser sessions performed on the patients ranged from 2 to 6 (2 sessions in one patient, 3 sessions in three patients, 4 sessions in four patients and 6 sessions in one patient), according to clinical indication. As a result, after the treatment, six acne lesions lingered on average, ranging from 0 to 18, with a standard deviation of 6.20 (Graph 1).

Considering the average number of lesions existing before the treatment (16 lesions) and comparingit to the average number of lesions after the treatment (6 lesions), it was observed that there was an average decrease of 65% of lesions. The highest percentage of lesion reduction was found in patients who had at least 4 laser sessions, with an average reduction of 82%, while in those who underwent a maximum of 3 sessions, lesions reduced on average 45%.



Graph 1: Number of acne lesions present before and after the treatment

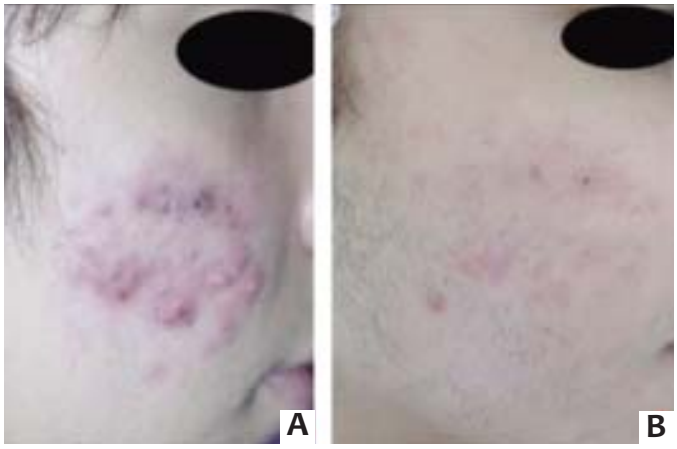
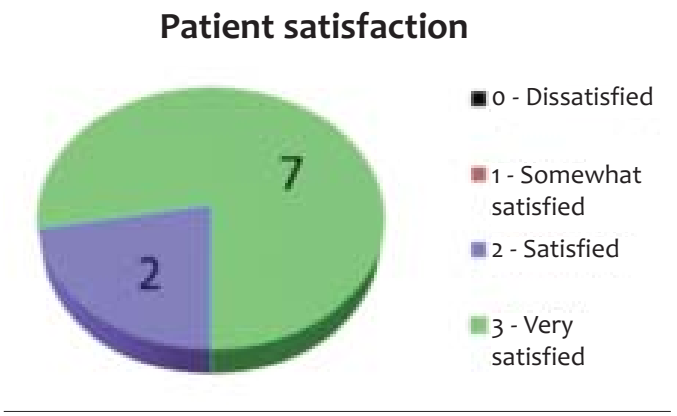


Figure 1: Acne lesions before the treatment **(A)** and after the treatment **(B)**



Graph 2: Level of satisfaction of patients after treatment

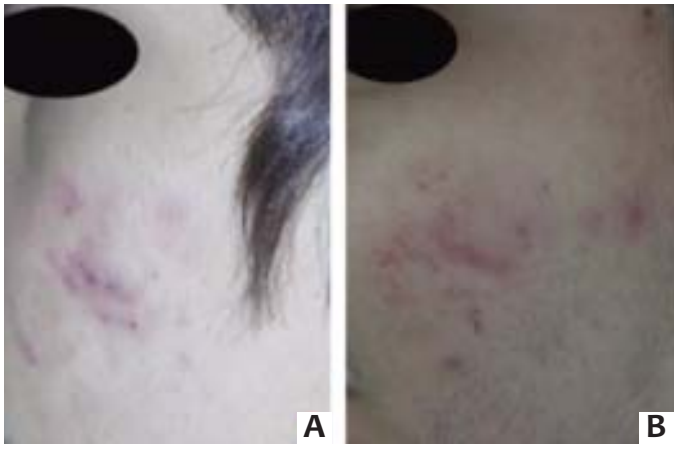


Figure 2: Acne lesions before the treatment **(A)** and after the treatment **(B)**

The degree of satisfaction assessed subjectively by the patients was as follows: 7 patients reported being very satisfied (degree of satisfaction 3), 2 patients reported being satisfied (degree of satisfaction 2) and no patient was somewhat satisfied or dissatisfied (degrees of satisfaction 1 and 0, respectively) (Graph 2). The objective analysis of photographs (Figures 1 to 3) carried out by the two dermatologist physicians not related to the study was rated as follows: Physician 1 rated 6 patients with significant improvement and 3 patients with moderate improvement. Physician 2 rated 5 patients with significant improvement, 3 patients with moderate improvement and 1 patient with absence of improvement. (Graph 3) The physicians had differing opinions only regarding 2 patients, with one of them being rated with significant improvement by Physician 1 and moderate improvement by Physician 2,while the other was rated with moderate improvement by Physician 1 and absence of improvement by Physician 2. In aggregate terms, the physicians had the same opinion in 78% of patients, with Physician 2 rating photographs of two patients with a lesser degree of improvement when compared tothe rating attributed by Physician1 to the same patients.

Before the treatment, the anatomical pathological examination revealed lymphocytic inflammatory infiltrate and thick and disorganized collagen fibers. After the last session, it showed a significant reduction in the inflammatory infiltrate and that collagen fibers were organized (Figure 4).

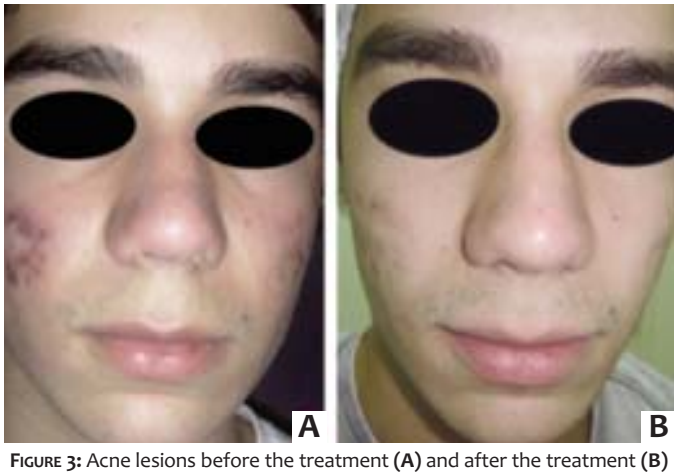


Figure 3: Acne lesions before the treatment **(A)** and after the treatment **(B)**

As an adverse reaction to the treatment, the 9 patients presented only pain and mild erythema after the application of

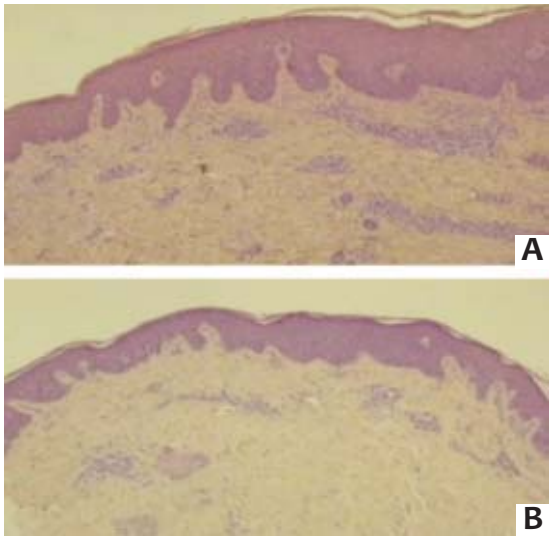
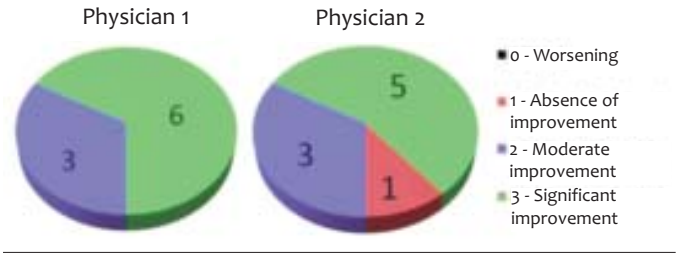
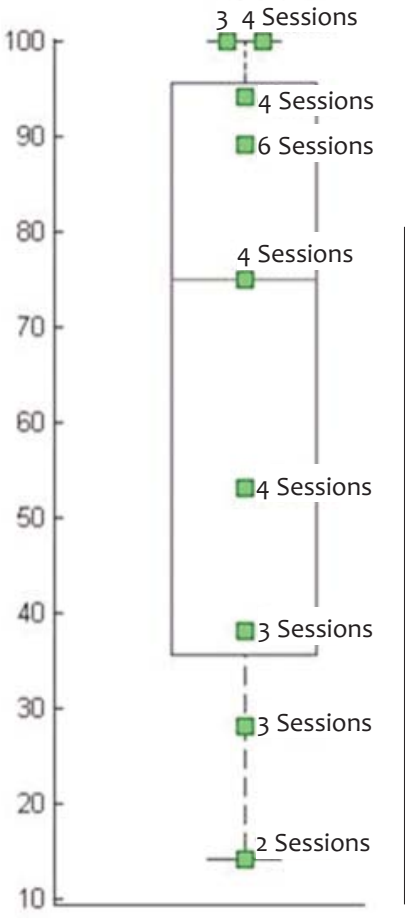


Figure 4: Histology before the treatment **(A)** and after the treatment **(B)**



Graph 3: Comparative analysis of photographs carried out by two dermatologist physicians before and after the treatment



Graph 4: Box plot of the distribution of the percentage of reduction of lesions according to the number of sessions of laser therapy performed

non-ablative fractional laser. No severe, adverse effects were observed in any of the patients.

DISCUSSION

Laser therapy for inflammatory acne is an alternative treatment mainly for patients who do not respond to conventional treatment. It is associated with minimal side effects, and is therefore an option for patients who have moderate and severe acne.[18] According to Rai and Natarajan, advances in laser therapy for inflammatory acne have been reported. Notwithstanding, the development of clinical studies is necessary in order to determine its effectiveness in the different types of laser therapy.[18]

The present study demonstrated that there was a significant reduction in the number of acne lesions after treatment with 1,340nm Nd:YAP laser. The reduction in the number of lesions was on average 65%. In addition, the greater the number of sessions performed, the higher the percentage of reduction, since the patients who underwent more than four sessions showed an 82% reduction in the number of lesions on average, evidencing an important response to the therapy (Graph 4). It was also possible to observe that two patients had 100% improvement in the number of lesions, meaning that it was not possible to observe nodular cystic acne lesions in those patients after the laser treatment.

Due to the psychosocial impact caused by acne, 19,20 the present study showed the relevance in asking about the degree of patient satisfaction, for the majority reported great satisfaction with the treatment, and no patient was somewhat satisfied or unsatisfied. It was possible to note that, in addition to the reduction in the number of lesions, the use of fractional laser also provided physical and psychological well-being.

From a medical standpoint, the therapy with fractional laser proved effective in treating acne, for in the evaluation performed by dermatologist physicians not related to the study, very close and positive opinions were obtained. Another factor contributing to the efficacy was an important histological improvement after the laser therapy, with the decrease of inflammatory infiltrate and the reorganization of collagen fibers. Furthermore, no significant adverse effects were observed, ensuring the method's safety.

CONCLUSION

Nodular cystic acne resistant to isotretinoin is a condition capable of having psychosocial impacts on patients, requiring effective methods for its management. The authors concluded that the treatment with non-ablative fractional 1,340nm Nd:YAP laser was effective and safe for that indication and can be a good option. Further studies are necessary in order to consolidate the authors' conclusion. ●

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Article
Original

Analysis of improvement of the clinical signs of skin aging with assistance of intradermotherapy: clinical, photographic, and ultrasonographic analyses

Análise da melhora dos sinais clínicos do envelhecimento cutâneo com o uso da intradermoterapia: análise clínica, fotográfica e ultrassonográfica

Authors:
Magda Expósito de Oliveira[1]
Meire Gonzaga[1]
Marisa Gonzaga da Cunha[2]
Ayrton Roberto Pastore[3]
Carlos A. Machado[4]

[1] Dermatologist Physician; Preceptor, Cosmetic Dermatology, Faculdade de Medicina do ABC (FMABC)—Santo André (SP), Brazil

[2] Dermatologist Physician; Responsible Physician, Cosmetic Dermatology, FMABC—Santo André (SP)

[3] Full Professor, Department of Radiology, Universidade de São Paulo (USP)—São Paulo (SP), Brazil

[4] Full Professor of Dermatology, FMABC—Santo André (SP)

ABSTRACT

Introduction: *Intradermotherapy with poly-revitalization is an additional therapeutic option for the treatment of photodamage.*

Objective: *To evaluate the efficacy of intradermotherapy treatment and skin rejuvenation results due to the use of injectable poly-revitalizing substance constituted of antioxidants, vitamin complexes, amino acids, coenzymes, and hyaluronic acid without crosslinking.*

Method: *A retrospective, monocentric, open and non-comparative clinical study with 30 female patients who underwent 5 applications of injectable poly-revitalizing substance in the face. The photographs were analyzed and compared by blinded investigators and the medical professional who applied the treatment. Dermal thickness and density were analyzed and compared through ultrasonography.*

Result: *Increased dermal thickness and density verified through ultrasonography. Clinical improvement was observed through pre- and post-application photographs.*

Conclusion: *Intradermotherapy with the studied poly-revitalizing substance was proven to be a good therapeutic option for the treatment of photodamage.*

Keywords: *skin aging; mesotherapy; ultrasonography.*

RESUMO

Introdução: A intradermoterapia com polirrevitalização é opção terapêutica adicional para o tratamento do fotodano.

Objetivo: Avaliar a eficácia do tratamento e rejuvenescimento cutâneo, com o uso de polirrevitalizante injetável composto por antioxidantes, complexos vitamínicos, aminoácidos, coenzimas e ácido hialurônico sem crosslinking, através da intradermoterapia.

Método: Foi desenhado estudo clínico monocêntrico retrospectivo, não comparativo e aberto, com 30 pacientes do sexo feminino, submetidas a cinco aplicações de polirrevitalizante injetável na face. As fotos foram analisadas e comparadas por investigador cego e pelo médico aplicador. Através do exame ultrassonográfico, foram analisadas e comparadas espessura e densidade dérmica.

Resultado: Houve aumento da espessura e densidade dérmica através da ultrassonografia. A melhora clínica foi observada através das fotos pré e pós-aplicação.

Conclusão: A intradermoterapia com o polirrevitalizante estudado mostrou-se boa opção terapêutica ao fotodano.

Palavras-chave: envelhecimento da pele; mesoterapia; ultrassonografia.

Correspondence:
Dr. Magda Expósito de Oliveira
Av. Gabriel de Rezende Passos, 500—11o andar / G. 1,116—Moema
Cep: 04521-022—São Paulo—SP, Brazil
E-mail: mexposito@uol.com.br

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INTRODUCTION

Skin aging is a multifactorial process,[1] classically divided into intrinsic aging (genetically determined and caused by cellular degeneration that occurs progressively from birth as the result of genetic, [2,3] hormonal [4,5] and environmental 1 factors) and extrinsic aging (which is called photoagingand is caused by the cumulative results of various effects, in particular chronic exposure to ultraviolet (UV) radiation 1 but also other factors such as smoking, pollution, infrared radiation, and poor nutrition).[6]

UV radiation produces a sequence of alterations in the skin layers, starting with DNA damage and culminating with the fragmentation of collagen and other extracellular matrix proteins. In the epidermis, it causes damage to DNA, proteins, and lipids, interfering with cell growth and differentiation through the activation of various cell surface receptors.[1] Such damage can lead to acute and transient responses (such as inflammation, formation of sunburn cells, and pruritus) but also delayed chronic responses (such as photodamage, immunosuppression, and carcinogenesis).[1] Chronic alterations are clinically manifested through dryness and pigmentation and keratinization changes. The flattening of the dermal-epidermal junction reduces epidermal nourishment and hydration.[7]

The particles resulting from the fragmentation of collagen and other extracellular matrix proteins, promote the synthesis of metalloproteinases (MMPs), which exacerbate the damage to the ground substance.[8] As a result, they cause epidermal and dermal alterations, affecting cellular components and the extracellular matrix with the loss of collagen fibers and the accumulation of disorganized elastic fibers. The activation of MMP enzymes, especially collagenase, is responsible for alterations in the collagen, as well as direct aggression to fibroblasts, with the interruption of the synthesis of new collagen.[1,2] Free radicals also play an important role in cutaneous aging.[1,2] Oxidative stress is caused by an imbalance between the formation of free radicals—which is caused by oxygen metabolism—and the action of antioxidant defense systems.

Free radicals damage cell structures such as membranes, DNA segments, collagen, and elastic fibers. The accumulation of these molecular alterations, particularly in proteins, constitutes the basis of cellular aging 2 and results in the clinical signs of photodamage, such as a decrease inthe skin's thickness, appearance of fine wrinkles, loss of elasticity, vascular fragility, and pigmentary and keratinization alterations. 1 Enzymes that minimize oxidative damage are the superoxide dismutase, catalase, glutathione peroxidase, glutathione transferase, peroxidases and thiol-specific antioxidant enzymes. Combined with low molecular weight compounds (such as ascorbate, glutathione, beta-carotene, alpha-tocopherol, bilirubins and uric acid), they serve as free radical sweepers.[2]

Water is essential for cellular functions and plays a key role in the differentiation process, desquamation, and final appearance of the skin. The factor that allows skin to stay healthy, with flexibility and elasticity, is the balance that exists in the hydration mechanism and in the body's ability to promote cell renewal. The small loss of water that occurs in the deeper layers hydrates the more superficial layers, facilitating enzymatic reactions that allow the maturation of the stratum corneum (EC). The concentration of water in the deep epidermis depends on the patient's age, anatomical location, and the time of year (season). Maintenance of the water gradient across the epidermis is regarded as the basic and fundamental measure in anti-aging treatment.[9]

The maintenance of the EC's optimum level of hydration depends on several factors. One of the most important is a complex mixture of soluble compounds in low molecular weight water, formed by amino acids, which result fromthe protein degradation of corneocytes, whose composition is regulated by the level of epidermal hydration.[10] They are referred to as the natural moisturizing factors (NMF).

Cutaneous hydration is also maintained by the presence of the ground substance in the dermis. The ground substance is composed of glycoproteins and proteoglycans, including hyaluronic acid, which is a glucosamine polysaccharide synthesized in the cell membranes of the fibroblasts and eliminated into the extracellular medium, where it plays an important role in maintaining hydration, in cutaneous filling, in the modulation of inflammatory cells and the sweeping of free radicals, through the maintenance of intercellular hydric balance.[10]

Therefore, as a result of the oxidative process induced by UV radiation and intrinsic aging, alterations of the components of the connective tissue occur (such as a reduction in the number and activity of fibroblasts, with consequent reduction and disorganization of collagen and elastin fibers), in addition to a decrease in hyaluronic acid. Such alterations are responsible for many of the morphological and mechanical alterations that result in the formation of fine wrinkles, loss of elasticity, dryness, loss of skin tone and strength.

One of the proposed treatments for improvement of fine wrinkles, brightness, firmness, hydration, and overall appearance of the skin is the application of the compound NCTF 135 HA (registered in ANVISA, the Brazilian National Health Surveillance Agency, under the number 80279420034), which contains 12 vitamins (ascorbic acid, biotin, pantothenic acid, folic acid, inositol, nicotinamide, pyridoxine, riboflavin, thiamine, tocopherol, retinol); 23 amino acids which act directly on the synthesis of collagen and elastin (alanine, arginine, aspartic acid, asparagine, glutamine, glutamic acid, cystine, glycine, histidine, hydroxyproline, proline, lysine, leucine, serine, taurine, and others); 6 minerals which act in hundreds of enzymatic reactions and are essential to cellular function (calcium and potassium hydrochlorides, magnesium sulfate, sodium acetate, sodium hydrochloride, sodium dihydrogen phosphate); 6 coenzymes which act as biochemical activators and increase the rate of tissue repair (TPP, CoA, FAD, NAD, NADP, UTP and dinucleotide phosphatase); 5 nucleic acids which regulateand command protein synthesis; glutathione, which is a reduction agent; and hyaluronic acid (5mg/ml), with a hygroscopic action that secures large amounts of water.

Vitamins A, C, E, and B complex are important in the regulating and sweeping of free radicals, as enzyme cofactors in the synthesis of collagen, skin hydration, and also for controlling the overproduction of melanin.[11-19] Ascorbic acid (vitamin C) is essential in the synthesis of collagen and participates in the regeneration of the tocopherol (vitamin E) system, helping to maintain the plasma antioxidant capacity. 15 Vitamin E protects the membrane lipids from oxidation.[11] Vitamin K acts on microcirculation and acts as a ligand for receptors.[18] It also contains amino acids and polynucleotides that promote hydration and stimulate fibroblast activity. Sodium, potassium, calcium and magnesium act as catalysts for many enzymes. Organic silicon induces collagen synthesis.[19] Non cross-linked hyaluronic acid, although somewhat unstable and with a short half-life, acts as an epidermal 20 and dermal moisturizer and can stimulate its own biosynthesis through fibroblasts, which explains its longer lasting effect.[21]

Application through an intradermal route, known as intradermotherapy, is a medical procedure introduced in France by Pistor in 1958. It is a way of administering substances with well-established mechanisms of action, in low doses, directly in the area being treated, without significant side effects.[22] It has beenused safely in Europe for over 30 years with good results. In this particular case, it involves the application of biocompatible and absorbable substances, with already established effects, necessary in the sweep of free radicals, dermal hydration, and for the elaboration of the extracellular matrix components by fibroblasts.

Therefore, intradermotherapy with the described product is indicated in cases of mild to moderate histological aging, both intrinsic and photoaging based, and as a preventionfor cutaneous aging. It is contraindicated for the treatment of expression wrinkles and as an isolated treatment for anatomical facial aging, where it can be used as an adjuvant therapy.

METHODS

A monocentric, retrospective, non-comparative, open clinical study was carried out at the Cosmetic Dermatology Ambulatory of the Dermatology Discipline, at the Faculdade de Medicina do ABC, Santo André (SP), Brazil, with the aim of evaluating the efficacy of the treatment for skin rejuvenation with a combination of antioxidants, vitamin complexes, amino acids, coenzymes, and noncross-linked hyaluronic acid. The treatment was carried out in five superficial and deep intradermal applications of the product, with intervals of 15 days between the first three sessions and of 1 month between he last two sessions. The study was conducted in accordance with the ethical principles originating from the Declaration of Helsinki.

Inclusion criteria

Thirty female patients aged 40-55 years, with signs of mild to moderate photoaging were assessed. Following the routine of the Institution's Dermatology Service, all signed the Free and Informed Term of Consent (FITC), after receiving a full explanation about the product. The selected patients used only sunscreen during the treatment period.

Exclusion criteria

Exclusion criteria for the study were menopause, pregnancy, breast-feeding, bleeding disorders and use of anticoagulants, history of allergic reactions to the formulation's components, and systemic or cutaneous diseases that could interfere with the evaluation of the effectiveness of the product.

Photographs of each patient were taken from the frontal position, and right (R) and left (L) profiles for posterior comparison; patients answered a questionnaire about the perceived quality of the skin through self-assessment, including parameters such as brightness, hydration, firmness, fine wrinkles, and overall appearance, with factors ratedfrom 0 to 10; the physician applying the product also answered a predetermined questionnaire aimed at assessing those parameters, also with scores from 0 to 10; the patients underwent an ultrasound examination of skin from various regions of the face, always performed by the same physician, in a laboratory specializing in radiology (Laboratório Cetrus, unidade SãoPaulo (SP), Brazil), with a 18MHz linear transducer (Mylab 40™—Esaote, Italy).

Application technique

After a thorough cleaning, the entire face was treated using an intradermal route, with a combination of techniques: a) point-to-point technique (1ml), with spaces of about 5mm between them, penetrating 2-4mm; b) nappage technique, where multiple punctures are performed rapidly, superficially and close to one another (1ml); and c) deep intradermal technique with 30G1/2 needle, at 4-7mm from the surface, injecting 0.01ml per point in the nasogenian folds and mandibular regions (1ml).

Five applications were performed (Days 0, 15, 30, 60 and 90), always followed by advice to the patients not to use any topical product for at least two hours.

Evaluation

Fifteen days after the last session, two questionnaires were issued again: one assessing the perceived clinical effectiveness, to be answered by the physician applying the product and the patient, which contained the same issues as the initial questionnaire with rates from 0 to 10; and another assessing the safety of the procedure, focusing on the description of adverse effects.

A new ultrasound skin examination was performed in predetermined areas of the face, in addition to new frontal and profile photographs, 30 days after the last application.

The photographs were analyzed and compared by a physician who did not participate in the study, but who also answered the questionnaire previously given to the physician who applied the product. The ultrasounds were compared in terms of dermal thickness and density.

The analysis of the results of each patient considered:

- The evaluation of individual patients with rates from 0 to 10 for the items: brightness, hydration, firmness, fine wrinkles, and overall appearance;
- The participating physician rates for those items;
- The external investigator physician's rates for those items;
- The results from the sonographic measurements of various facial points.

RESULTS

The rates for final results assessing the improvement in each of the evaluated items, attributed by the patients and participating and observing physicians 30 days after the last application, are shown in Table 1.

Regarding dermal thickness, measurements were carried out using 30MHz ultrasound in several areas of the face before and 117 days after the first application. The measurements are exemplified in Figures 1A and 1B and in Figures 2A and 2B, where the superficial dermis is hypoechogenic (gray) and the deep dermis is echogenic (white). The measurements were analyzed separately in their respective areas, as shown in Tables 2 to 4.

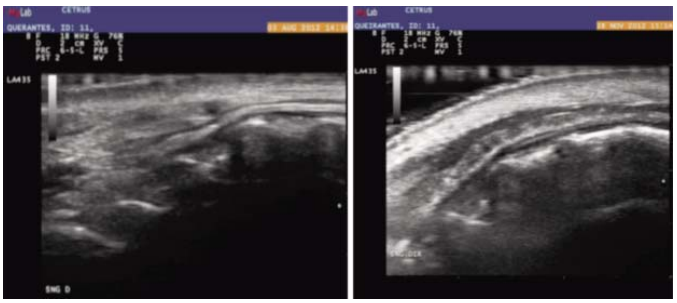
In the statistical analysis the paired t-test was applied, with the measurement of the skin's thickness being taken before and after 2 applications of the medicament. The following parameters were used:

- H0 or null hypothesis: states that there is no difference between the thickness before and after application;
- H1: implies significant alteration between the time before and after the applications.

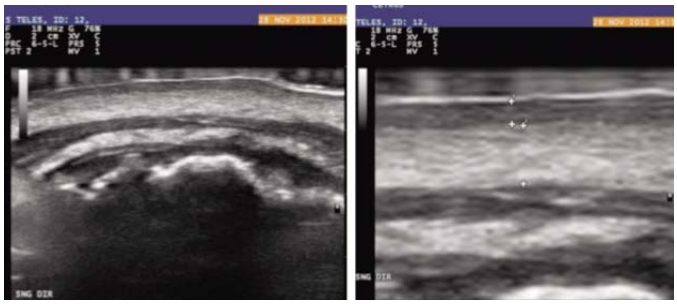
The test used a normal, two-tailed model for the distribution of values, with alpha = 0.05%. In light of the values and determining a strength of 80%, the sample size of 30 patients was considered sufficient. Tables 1, 2, and 3 show the measurements of the dermis in the skin ultrasonography before and 15 days after the last application, with their respective standard

Table 1: Rates attributed to the improvement in each of the items analyzed, with 0 = absence of response, 1 to 4 = little improvement, 5 to 6 = moderate improvement, 7 to 8 = good improvement and 9 to 10 = significant improvement, with the percentage of patients

	RATE	PATIENT %	APPLICATOR %	EXAMINER %
BRIGHTNESS	0 a 4	0	0	0
	5 a 6	13,33	0	0
	7 a 8	30	76,66	36,67
	9 a 10	56,67	23,34	63,33
HYDRATION	0 a 4	0	0	0
	5 a 6	10	0	0
	7 a 8	23,33	83,33	36,67
	9 a 10	66,67	16,67	63,33
FIRMNESS	0 a 4	0	0	0
	5 a 6	6,67	0	0
	7 a 8	33,33	90	36,67
	9 a 10	60	10	63,33
FINE WRINKLES	0 a 4	13,33	20	0
	5 a 6	26,67	40	0
	7 a 8	43,34	40	43,33
	9 a 10	16,66	0	56,67
GENERAL APPEARANCE	0 a 4	0	3,33	0
	5 a 6	10	6,67	0
	7 a 8	53,34	60	50
	9 a 10	36,66	30	50



Figures 1A and 1B: Before, and 117 days after ultrasound. The dermis is thickened more clearly in the deep dermis (echogenic/white), demonstrating a positive response to the treatment



Figures 2A and 2B: Ultrassonography before and 117 days after the treatment. The dermis is thickened more clearly in the deep dermis (echogenic/white), demonstrating a positive response to the treatment

Table 2: Measurements of the forehead, R and L orbits

P	FOREHEAD			R ORBIT		L ORBIT			
	Pre-application (mm)	Post-application (mm)	Deviation	Pre-application (mm)	Deviation	Post-application (mm)	Post-application (mm)	Desvio	
1	0,55	1,4	-0,85	0,43	1,7	-1,27	0,59	2,2	-1,61
2	0,89	1,89	-1	0,64	1,74	-1,1	1	1,31	-0,31
3	0,52	1,62	-1,1	0,3	1,13	-0,83	0,51	1	-0,49
4	0,63	1,6	-0,97	0,94	1,7	-0,76	0,82	1,98	-1,16
5	0,98	1,82	-0,84	1,4	1,62	-0,22	0,39	1,87	-1,48
6	0,72	2,02	-1,3	1,1	1,74	-0,64	0,81	1,44	-0,63
7	2,1	3,3	-1,2	0,93	1,49	-0,56	0,85	2,08	-1,23
8	0,73	1,78	-1,05	0,6	1,3	-0,7	0,57	0,92	-0,35
9	0,34	1,58	-1,24	0,74	1,16	-0,42	0,76	1,19	-0,43
10	0,47	1,5	-1,03	0,68	1,79	-1,11	0,38	1,33	-0,95
11	0,6	1,73	-1,13	0,9	1,43	-0,53	0,64	1,89	-1,25
12	0,85	1,43	-0,58	0,55	1,83	-1,28	0,34	1,01	-0,67
13	0,64	1,62	-0,98	0,76	2,51	-1,75	0,72	1,27	-0,55
14	0,39	1,26	-0,87	0,68	1,11	-0,43	0,64	1,08	-0,44
15	1	2,6	-1,6	0,6	1,19	-0,59	0,59	1,15	-0,56
16	0,34	2,16	-1,82	0,6	2,18	-1,58	0,73	1,63	-0,9
17	1,9	1,65	0,25	0,7	2,05	-1,35	0,89	1,46	-0,57
18	0,72	1,95	-1,23	0,98	1,7	-0,72	1	1,58	-0,58
17	0,95	2,19	-1,24	1,15	1,84	-0,69	1,2	1,51	-0,31
20	0,72	1,47	-0,75	0,47	1,85	-1,38	0,51	1,46	-0,95
21	0,42	1,69	-1,27	0,55	1,03	-0,48	0,65	1,5	-0,85
22	0,7	2,25	-1,55	0,6	1,32	-0,72	0,52	1,71	-1,19
23	0,59	1,9	-1,31	0,72	0,95	-0,23	0,6	1,41	-0,81
24	0,81	1,73	-0,92	0,94	1,57	-0,63	0,85	1,38	-0,53
25	0,56	1,53	-0,97	0,55	1,74	-1,19	1	1,5	-0,5
26	0,47	1,58	-1,11	0,77	1,48	-0,71	0,55	1,28	-0,73
27	0,52	1,89	-1,37	0,85	1,48	-0,63	1	1,43	-0,43
28	0,8	1,96	-1,16	0,34	1,89	-1,55	0,95	2,45	-1,5
29	0,34	1,21	-0,87	0,55	1,14	-0,59	0,6	1,33	-0,73
30	0,67	1,89	-1,22	0,89	1,63	-0,74	0,77	1,57	-0,8
	Mean	-1,076		**Mean**	-0,846		**Média**	-0,783	
	Variance	0,130135172		**Variance**	0,166707586		**Variance**	0,131621	
	Standard-deviation	0,360742529		**Standard-deviation**	0,408298403		**Standard-deviation**	0,368998178	

deviations. The measurements were performed on the forehead, R and L periorbital regions, R and L malar regions, R and L nasogenian folds (NGF), and R and L mandibular regions.

The results of the statistical analysis of the measurements obtained through skin ultrasonography demonstrated that all areas studied showed significant differences after the application, concluding that within the three month period the application of the medicament through intradermotherapy has modified the skin's thickness.

Therefore, the observations of the patients, participating lead physician, and blinded observer physician implied rates that ranged from 7 to 10, indicating answers from good to excellent (Figures 3 to 6).

DISCUSSION

Clinical signs of cutaneous aging are the result of alterations that the skin undergoes under the influence of UV radiation, the environment (such as pollution), eating and personal habits, and life style (such as smoking and stress, hormone levels and genetics). The loss of brightness and presence of sagging, and dryness in addition to the appearance of fine wrinkles, are the first signs of aging, leading many patients to seek treatment. In these cases, improvement in hydration and intake of nutrients often become the most effective measures, yielding long-lasting results.

Despite the fact that treatment with intradermotherapy has been used in France for more than 30 years, its results are still being questioned due to the lack of comparative studies with data taken both before and after the application to prove its efficacy. Several authors question the clinical improvement resulting from this treatment.[24]

The present study was aimed at analyzing and confirming whether or not the benefits of skin rejuvenation treatment with a combination of antioxidants, vitamin complexes, amino acids,

Table 3: Measurements of the R and L malar regions, and R and L nasogenian folds (NGF)

P	R MALAR			L MALAR			R NGF			L NGF		
	Pré	Post	Deviation	Pré	Post	Deviation	Pré	Post	Deviation	Pré	Post	Deviation
1	0,56	1,76	-1,2	0,64	1,84	-1,2	1,4	2,5	-1,1	2,3	2,8	-0,5
2	1,62	1,66	-0,04	1,8	1,62	0,18	0,7	1,98	-1,28	1,8	2,15	-0,35
3		1,26	-0,44	0,47	1,35	-0,88	1,88	2,01	-0,13	1,8	3,41	-1,61
4	0,47	1,74	-1,27	0,55	1,66	-1,11	1,7	2,63	-0,93	1,4	2,8	-1,4
5	0,72	2,01	-1,29	0,76	1,63	-0,87	1,3	3,4	-2,1	0,39	2,86	-2,47
6	1,3	1,97	-0,67	1,1	1,74	-0,64	1,6	3,66	-2,06	1,8	4,13	-2,33
7	1,8	2,4	-0,6	1,54	2,25	-0,71	2,4	3,1	-0,7	2	2,6	-0,6
8	1,54	1,94	-0,4	0,64	1,6	-0,96	1,1	2,48	-1,38	1,3	1,89	-0,59
9	1,55	1,6	-0,05	1	1,33	-0,33	2,2	2,59	-0,39	2,8	5,03	-2,23
10	1,69	1,86	-0,17	0,42	2,07	-1,65	2,1	3,24	-1,14	1	3,34	-2,34
11	2,4	1,56	0,84	2,1	1,71	0,39	2,1	3	-0,9	1,8	2,6	-0,8
12	0,55	1,8	-1,25	0,72	1,65	-0,93	1,5	3,09	-1,59	2,3	3,32	-1,02
13	0,85	1,77	-0,92	1,3	1,59	-0,29	1,4	2,67	-1,27	1,4	2,83	-1,43
14	1,41	1,65	-0,24	1,41	1,32	0,09	1,51	2,69	-1,18	2,1	2,75	-0,65
15	1,62	2,6	-0,98	1,68	1,55	0,13	2,76	3,02	-0,26	3,1	2,52	0,58
16	1,1	2,33	-1,23	0,76	1,73	-0,97	1,73	2,01	-0,28	0,9	2,22	-1,32
17	1,65	1,59	0,06	1,1	1,49	-0,39	0,77	2,48	-1,71	1,2	3	-1,8
18	0,68	1,54	-0,86	0,56	1,53	-0,97	1,8	2,43	-0,63	1,38	3,24	-1,86
19	1,1	1,82	-0,72	1,1	1,71	-0,61	1,7	2,16	-0,46	1,7	1,68	0,02
20	1,3	1,91	-0,61	0,89	1,75	-0,86	0,98	1,91	-0,93	1,7	2,7	-1
21	1,72	1,88	-0,16	1,18	1,76	-0,58	1,3	2,67	-1,37	1,7	2,84	-1,14
22	1,52	2,1	-0,58	1,11	1,86	-0,75	2,21	4,2	-1,99	2,7	2	0,7
23	0,38	1,46	-1,08	0,51	1,15	-0,64	1,7	3,01	-1,31	1,9	3,09	-1,19
24	1,31	1,97	-0,66	0,64	1,55	-0,91	2,39	2,77	-0,38	2,2	1,88	0,32
25	0,73	1,97	-1,24	0,47	1,35	-0,88	2	2,93	-0,93	1,1	3,6	-2,5
26	0,81	1,37	-0,56	0,85	1,38	-0,53	1,8	2,62	-0,82	1,4	3,4	-2
27	1,3	2,5	-1,2	0,77	2,19	-1,42	1,3	2,28	-0,98	1,4	2,4	-1
28	0,72	1,77	-1,05	0,52	1,84	-1,32	1,6	2,25	-0,65	1,4	3,44	-2,04
29	0,6	1,61	-1,01	0,93	1,05	-0,12	2,1	2,53	-0,43	1,2	1,96	-0,76
30	2,23	2,17	0,06	1,63	1,58	0,05	2,06	3,15	-1,09	3,1	2,1	1
		Mean	-0,650666667		Mean	-0,656		Mean	-1,012333333		Mean	-1,077
		Variance	0,271447816		Variance	0,249369655		Variance	0,288377126		Variance	0,932311379
		Standard-deviation	0,521006541		Standard-deviation	0,499369257		Standard-deviation	0,537007566		Standard-deviation	0,965562727

coenzymes and noncross-linked hyaluronic acid can be confirmed, based on the opinion of the patients and the physician who applied the product, taking into considerationthe parameters of brightness, hydration, texture, and overall appearance of the skin of patients with mild to moderate clinical signs of photoaging. The analysis of photographs carried out before, during, and after the treatment also reinforces the critical analysis, which the study is intended to perform.

Ultrasonography of the skin with the 18MHz transducer proved an excellent way of assessing epidermal and dermal thickness, as seen in the photographs, due to its high resolution. This also facilitated the carrying out of studies aimed at analyzing the skin's thickness, since skin biopsies have always been very difficult to implement, for the patients are often not willing to undergo tests that leave scars.

In most patients, the ultrasound study demonstrated increased dermal thickness and dermal rearrangement, with the reorganization of fibers, which explains the improvement in skin texture, fine wrinkles, and acne scars, as observed in one of the patients.

The statistical analysis has shown that 30 patients (n = 30) is a suitable sample to assess the effectiveness of the treatment and the analysis of sonographic measurements in the periods before and after the treatment; it has also shown that there has indeed been improvement in dermal thickness with intradermal injections of the compound in association with antioxidants, vitamin complexes, amino acids, coenzymes, and noncross-linked hyaluronic acid.

The mean values of the scores assigned in the questionnaires by the patients, the physician who applied the product, and

Table 4: Measurements of the R and L mandibular regions

P		MANDIBULAR D			MANDIBULAR E	
	Pre-application (mm)	Post-application (mm)	Deviation	Pre-application (mm)	Post-application (mm)	Deviation
1	0,51	1,13	-0,62	0,51	1,3	-0,79
2	0,43	1,24	-0,81	0,51	1,36	-0,85
3	0,26	0,87	-0,61	0,32	1,14	-0,82
4	0,43	1,92	-1,49	0,56	1,66	-1,1
5	0,39	1,56	-1,17	0,43	1,44	-1,01
6	0,47	1,83	-1,36	0,9	1,51	-0,61
7	0,35	2,02	-1,67	0,68	1,98	-1,3
8	0,52	1,2	-0,68	0,47	1,12	-0,65
9	0,6	1,38	-0,78	0,47	1,01	-0,54
10	0,51	2,03	-1,52	0,34	1,26	-0,92
11	0,55	1,35	-0,8	0,38	1,61	-1,23
12	0,56	1,23	-0,67	0,43	1,41	-0,98
13	0,25	1,42	-1,17	0,43	1,32	-0,89
14	0,39	1,05	-0,66	0,81	1,36	-0,55
15	0,65	1,64	-0,99	0,48	1,6	-1,12
16	0,37	1,45	-1,08	0,41	1,59	-1,18
17	0,47	1,42	-0,95	0,47	1,58	-1,11
18	0,55	1,7	-1,15	0,42	1,26	-0,84
19	0,43	1,66	-1,23	0,43	1,4	-0,97
20	0,68	1,3	-0,62	0,72	1,33	-0,61
21	0,51	1,5	-0,99	0,47	1,55	-1,08
22	0,42	1,7	-1,28	0,55	1,66	-1,11
23	0,59	1,2	-0,61	0,55	1,1	-0,55
24	0,47	0,85	-0,38	0,49	0,47	0,02
25	0,73	1,5	-0,77	0,6	1,39	-0,79
26	0,34	1,37	-1,03	0,34	1,43	-1,09
27	1	1,74	-0,74	1,2	1,87	-0,67
28	0,34	1,45	-1,11	0,51	1,57	-1,06
29	0,42	0,97	-0,55	0,6	1,03	-0,43
30	0,26	1,97	-1,71	0,38	1,17	-0,79
	Mean	-0,973333333		**Mean**	-0,854	
	Variance	0,122664368		**Variance**	0,081128276	
	Standard-deviation	0,350234732		**Standard-deviation**	0,284830258	

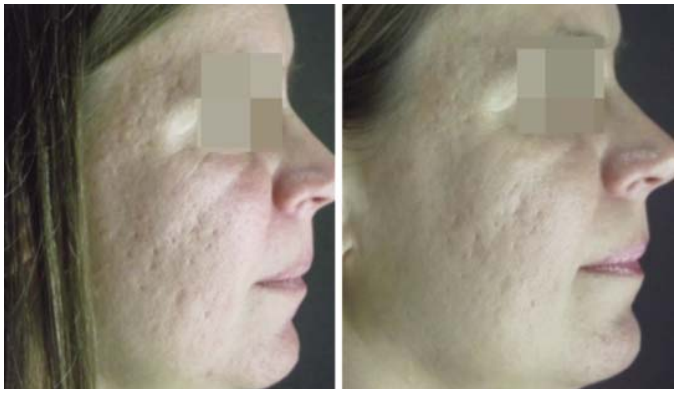


Figure 4: Pre- and post-application: note the improvement in texture and fine wrinkles.

the blinded examiner physician have shown that most patients treated with superficial and deep intradermal injections (intradermotherapy) of the compound were very satisfied with the treatment. A fact that attracted attention was that several patients with melasma reported improvement with the treatment.

Regarding the safety, the analysis has shown that there was no occurrence of major side effects other than the formation of small hematomas that resolved quickly. Pain during application did not constitute an obstacle to the execution of the treatment.

CONCLUSION

As with any other technique, it is important to analyze the benefits, safety, efficacy, and standardization of intradermotherapy regarding its indication as a treatment. A proper selection of patients seems critical to its outcome. Its best indication seems to be related to patients with early signs of photodamage and

Figure 5: Pre- and post-application: note the improvement in melasma

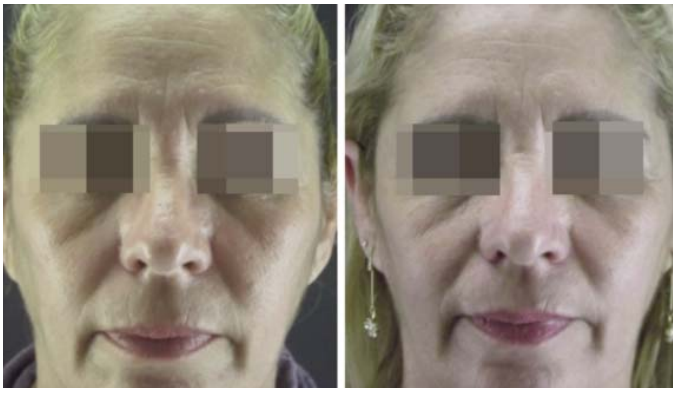


Figure 6: Pre- and post-application: note the improvement in wrinkles and brightness

who have mild to moderate skin dehydration, in addition to formation of fine wrinkles. The authors suggest that further studies be conducted to evaluate the efficacy of the studied technique in the treatment of melasma.

In thepresent study it was possible to observe that the intake of antioxidants (vitamins C, E, and glutathione), tissue nutrients in the form of vitamins (C, E, and B complex), coenzymes, nucleic acids, amino acids and hyaluronic acid without crosslinking, proved to be considerably effective for the improvement of dermal thickness and the reorganization of fibers, culminating with the improvement of mild to moderate signs of photodamage. ●

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Article
Original

Palpebral reconstruction of the ear helix with chondroperichondrial graft: experience of a Mohs micrographic surgery specialist center

Reconstrução Palpebral com Enxerto Condro-pericondral de Hélice de Orelha. Experiência de um Centro de Referência em Cirurgia Micrográfica de Mohs

Authors:
Frederico Hassin Sanchez[1]
Eduardo Lerner[2]

[1] Head of the Centro de Cirurgia Micrográfica do Rio de Janeiro; Preceptor, Dermatologic Surgery Fellow Program, Hospital Federal de Bonsucesso (UFB)—Rio de Janeiro (RJ); Technical Manager, Clínica Catarinense de Dermatologia—Chapecó (SC), Brazil
[2] Ophthalmologist Physician, Hospital da Polícia Militar—Rio de Janeiro—(RJ), Brazil; Contributor Physician, Centro de Cirurgia Micrográfica do Rio de Janeiro—Rio de Janeiro (RJ), Brazil

ABSTRACT

Introduction: The lower eyelid is often the site of basal cell carcinomas, with Mohs micrographic surgery (which allows precise histological control with maximum tissue preservation) being the ideal method for their treatment. Tumors that invade the posterior lamella cause full-thickness defects of the lower eyelid, for which several reconstruction techniques have been described with composite grafts. However, few authors use the helix of the ear as a donor area.

Objective: To describe the applicability of ear helix composite grafts in the reconstruction of the lower eyelid.

Methods: Retrospective study of a series of 6 cases of basal cell carcinoma in the lower eyelid, with tarsal invasion, operated through Mohs micrographic surgery in a private specialist service in the city of Rio de Janeiro, Brazil. All patients had full-thickness defects, and had undergone reconstruction of the posterior lamella through chondroperichondrial graft of the ear helix. The anterior lamella was reconstructed with the remaining eyelid tissue mobilization or with an advancement flap. Patients were assessed for functional capacity and aesthetics.

Results: There was complete adaptation of the perichondrium to the conjunctiva, after contact with the eyeball for 8 weeks. All patients with mild escleral show without ectropion.

Conclusions: Despite the small sample, all patients had excellent cosmetic and functional results.

Keywords: eyelid neoplasms; carcinoma, basal cell; Mohs surgery; ear cartilage.

RESUMO

Introdução: *A pálpebra inferior frequentemente é sede de carcinomas basocelulares, sendo ideal para seu tratamento a cirurgia micrográfica de Mohs, que permite controle histológico preciso, com máxima preservação tecidual. Os tumores que invadem a lamela posterior, causam defeitos de espessura total da pálpebra inferior, para cuja reconstrução têm sido descritas várias técnicas com enxertos compostos; poucos autores, porém, utilizam a hélice da orelha como área doadora.*

Objetivo: *Descrever a aplicabilidade do enxerto composto de hélice da orelha nas reconstruções de pálpebra inferior.*

Métodos: *Estudo retrospectivo de série de seis casos de carcinoma basocelular em pálpebra inferior, com invasão tarsal, operados pela cirurgia micrográfica de Mohs, em serviço privado de referência nessa técnica no município do Rio de Janeiro, Brasil. Todos os pacientes apresentavam defeitos de espessura total e tiveram reconstrução da lamela posterior através de enxerto condro-pericondral de hélice da orelha. A lamela anterior foi reconstituída com mobilização do tecido palpebral remanescente ou com retalho de avanço. Os pacientes foram avaliados em relação à capacidade funcional e estética.*

Resultados: *Houve completa adaptação do pericôndrio à conjuntiva, após contato com o globo ocular durante oito semanas. Todos os pacientes evoluíram com discreto escleroshow, sem ectrópio.*

Conclusões: *Apesar da amostragem pequena, todos os pacientes tiveram excelentes resultados cosméticos e funcionais.*

Palavras-chave: *pálpebras; carcinoma basocelular; cirurgia de Mohs; cartilagem da orelha.*

Correspondence:
Centro de Cirurgia Micrográfica do Rio de Janeiro
Dr. Frederico H. Sanchez
R. da Assembéia, 10 / Sala 2,807—Centro
Cep: 20011-000—Rio de Janeiro—RJ
E-mail: fredhsanchez@gmail.com

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INTRODUCTION

Various skin tumors can affect the lower eyelid and extend up to the tarsal region. Basal cell carcinoma (BCC) is the most common skin cancer, accounting for approximately 80-95% of all malign neoplasms of the eyelid. [1,2]

The treatment of choice for non-melanoma tumors of the eyelid is Mohs micrographic surgery (MMS), which achieves higher cure percentages with lower recurrence rates.[3] It allows greater economy of healthy tissue around the tumor, favoring the preservation of important structures and surgical reconstruction. [1-3]

The lower eyelid has protective and lubricatingfunctions forthe eyeball, in addition to playing an important aesthetic role. Total-thickness defects of the eyelid require the reconstruction of two basic elements: the anterior lamella (which consists of skin, subcutaneous tissue, and orbicularis muscle), and the posterior lamella (which consists of the tarsus and palpebral conjunctiva).[3,4] The lower tarsus is a dense conjunctive structure which lends mechanical support and stability to the eyelid,[4] maintaining its shape and promoting the eyelid's adaptation to the curvature of the eye, in addition to containing the meibomian glands, which secrete a sebaceous material important for lubricating the cornea.[1,3] It is connected medially to the medial canthal tendon (or ligament) and laterally to the lateral canthal ligament, both ofwhich insert into the orbital rim.

Tumors invading the tarsal plate promote total-thickness surgical defects of the eyelid, with defects ofup to one-thirdthe size of the total length of the lower eyelid generally capable of being closed. When tumors exceed this size, however, surgical reconstruction through the preparation of flaps and/or grafts is required, representing a major challenge for dermatologic surgeons.[5,6]

For reconstructing the posterior lamella, several graft options—such as jugal mucosa grafts, mucosal grafts from the hard palate,[7,8] chondro-mucosal grafts from the nasal septum 8 and more recently, on an experimental level, nail plate xenografts in animal models for tarsal reconstruction 9—have been described.

The ear chondro-perichondrial graft was first described by Matsuo in 1987, using the auricular concha as the donor site for reconstructing the posterior lamella, combining it with a flap of adjacent skin to repair the anterior lamella.[4] Many surgeons have used the auricular concha as the donor area since then. In the presentstudy, the authors propose the use of the ear helix as the donor site due to its reduced thickness, greater malleability of cartilage and, consequently, better adaptationto the eyeball, as compared to the auricular concha's cartilage.

OBJECTIVE

To demonstrate the applicability of this eyelid reconstruction technique, with a chondro-perichondrial composite graft of the helix of the ear, when there is loss of the lower tarsus after MMS.

METHODS

Six female patients who had undergone MMS for treatment of BCC in the lower eyelidwith invasion of the tarsus between January 2011 and April 2013, were selected. All underwent surgical reconstruction withcartilage of the ear helixand perichondrium grafts. The surgical procedures were performed at the Centro de Cirurgia Micrográfica do Rio de Janeiro, Brazil (Micrographic Surgery Center of Rio de Janeiro), a renowned private specialist center in MMS.

Four patients had recurrent BCC—with 1 having undergone operation twice using the traditional surgical method, with the tumor recurring less than one year from the last intervention (Figure 1). One of the patients had undergone topical chemotherapy with imiquimod and previous electrocautery (Figure 2). The other 2 had undergone prior surgical procedures, which, however, they were not able to describe with precision. All patients had their lesions previously biopsied, with the histological report describing nodular BCC in three cases, micronodular BCC in one case and infiltrative BCC in two cases. After excision of the lesions through MMS and successive stages of surgical increase of free margins, there was a loss of about three-quarters of the tarsal area in 3 patients (Figure 2) and approximately two-thirds of the lower tarsus in 3 patients (Figure 1).

The first phase of palpebral reconstruction was initiatedwith the aim of reconstructing the posterior lamella. The surgical defect was duly measured, and the donor area in the ipsilateral ear helix marked with a dermographic pen. A small fusiform incision with the same length as that of the receiving area was carried out at the anterosuperior part of the helix of the ear, in the scaphoid fossa region, located between helix and antihelix. Aband of cartilage with perichondrium, approximately 3 to 4mm wide, was carefully dissected and harvested to be grafted onto the lower eyelid. The band of cartilage that was partly covered with perichondrium was placed in contact with the eyeball (Figure 2). The graft was attached to the medial and lateral canthal tendons, which remained in the operated eyelid. The lower part of the graft was attachedto the retractor muscle of the lower eyelid using 7.0 poliglecrapone absorbable suture (Caprofyl®, Ethicon, Johnson & Johnson or Monocryl® Polysuture). Patients were asked to move the eyeball up and down in order to assess the perfect adaptation of the graft in contact with the eyeball, thereby avoiding keratitis and corneal ulceration.

After the attachment of the graft, the second phase of palpebral reconstruction was initiated, with the aim of reconstructing the anterior lamella. Usually, a myocutaneous flap or a simple advancement of the orbicularis muscle and skin remaining in the lower eyelid are positioned over the graft for nourishment purposes. In the present study, only 1 patient underwent a simple advancement flap to cover the graft. The other underwent reconstruction of the anterior lamella with the simple displacement of the tissue remaining in the lower eyelid. The skin was sutured to the superior part of the graft. A Frost suture was carried out to prevent retraction and the formation of

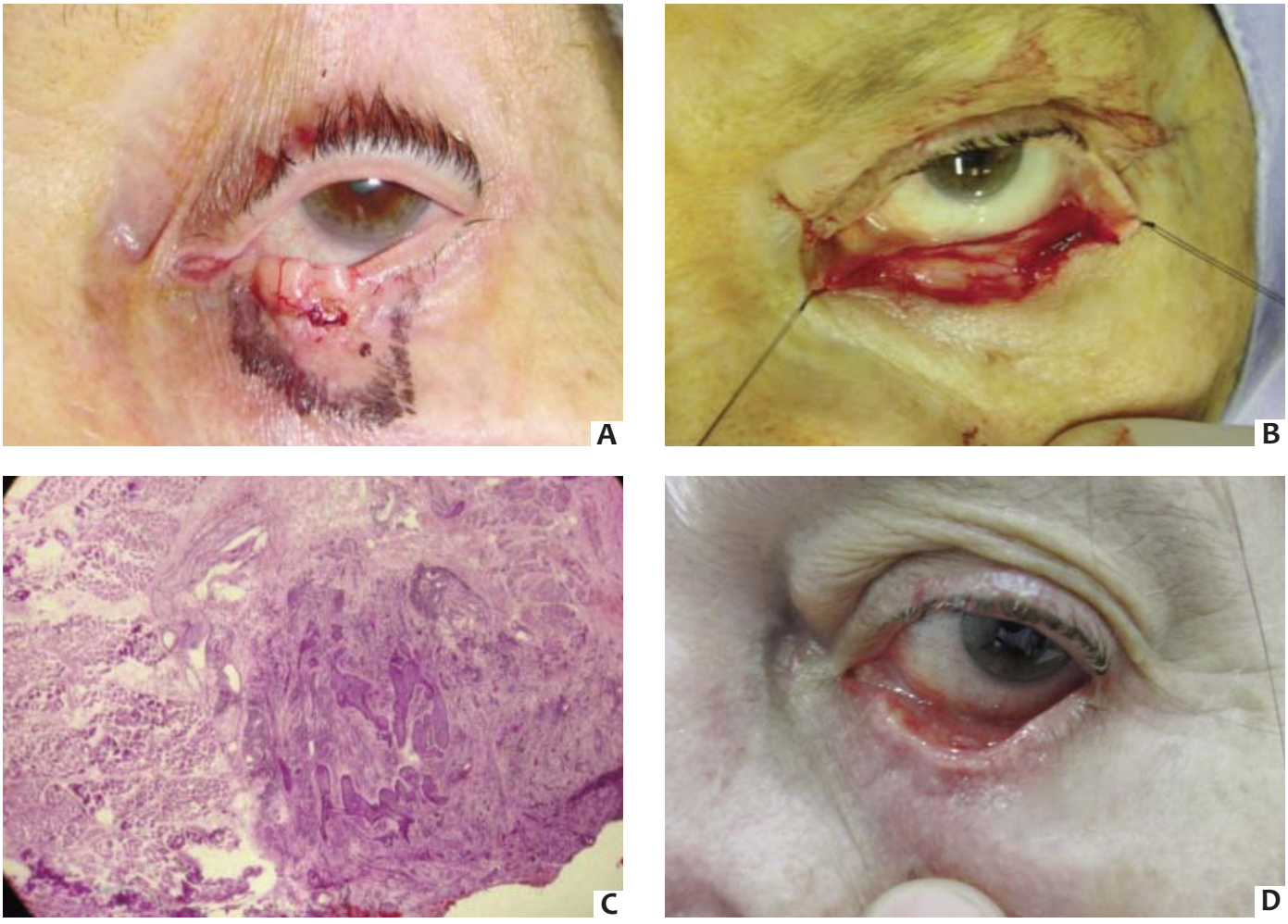

Figure 1: A - Patient 1:BCC in the lower eyelid; **B** - Patient 1:Total-thickness surgical defect of the eyelid with a loss of more than one-third of the tarsal plate; **C** – Patient 1: Peri-operative histological examination showinga positive surgical margin with infiltrating BCC; **D** - Patient 1: Complete epithelialization of the perichondrium eight weeks after surgery, with excellent functional and aesthetic results

ectropion. This type of suture is indicated when excessive traction occurs in the skin (Figure 2).

The donor area in the ear's scaphoid fossa was primarily sutured with nylon monofilament, leaving a virtually unnoticeable scar (Figure 3).

The patients were instructed to use lubricant eye drops several times a day and retinol acetate and chloramphenicol based ophthalmic ointment overnight. This decreases the discomfort caused by the friction of the perichondrium with the eyeball andalso red-eye syndrome, which occurs in the first weeks.

RESULTS

During MMS, histological analysis showed BCC with a mixed histologic pattern in 3 patients (in a nodular and infiltrative pattern (Figure 1) in the same lesion), 1 with a purely nodular pattern, and 2 patients whose tumors were not observedduring surgery due to the fact that free margins were obtained in the first surgical stage. Surgical margins free from neoplasms were obtained after two amplification stages in 3 patients, and three required in 1 patient. All patients developed with complete adaptation of the chondro-perichondrial graft, with minimal ocular discomfort in the first few weeks, and total transformation of the perichondrial tissue in contact with the eyeball into conjunctiva (through metaplasia), after eight weeks (Figure 1).

There was a slight retraction of the lower eyelid in all cases, causing subtle scleral show, but at an aesthetically acceptable level and with no degree of ectropion (Figure 2). None of the patients had recurrence as ofthe date the present article was written, with a post-operative follow-up time of 6 to 32 months.

DISCUSSION

MMS has confirmed its importance as the gold standard in the treatment of palpebral tumors due to the fact that it allows a precise histological control of surgical margins.

Several techniques have been described for the recons-

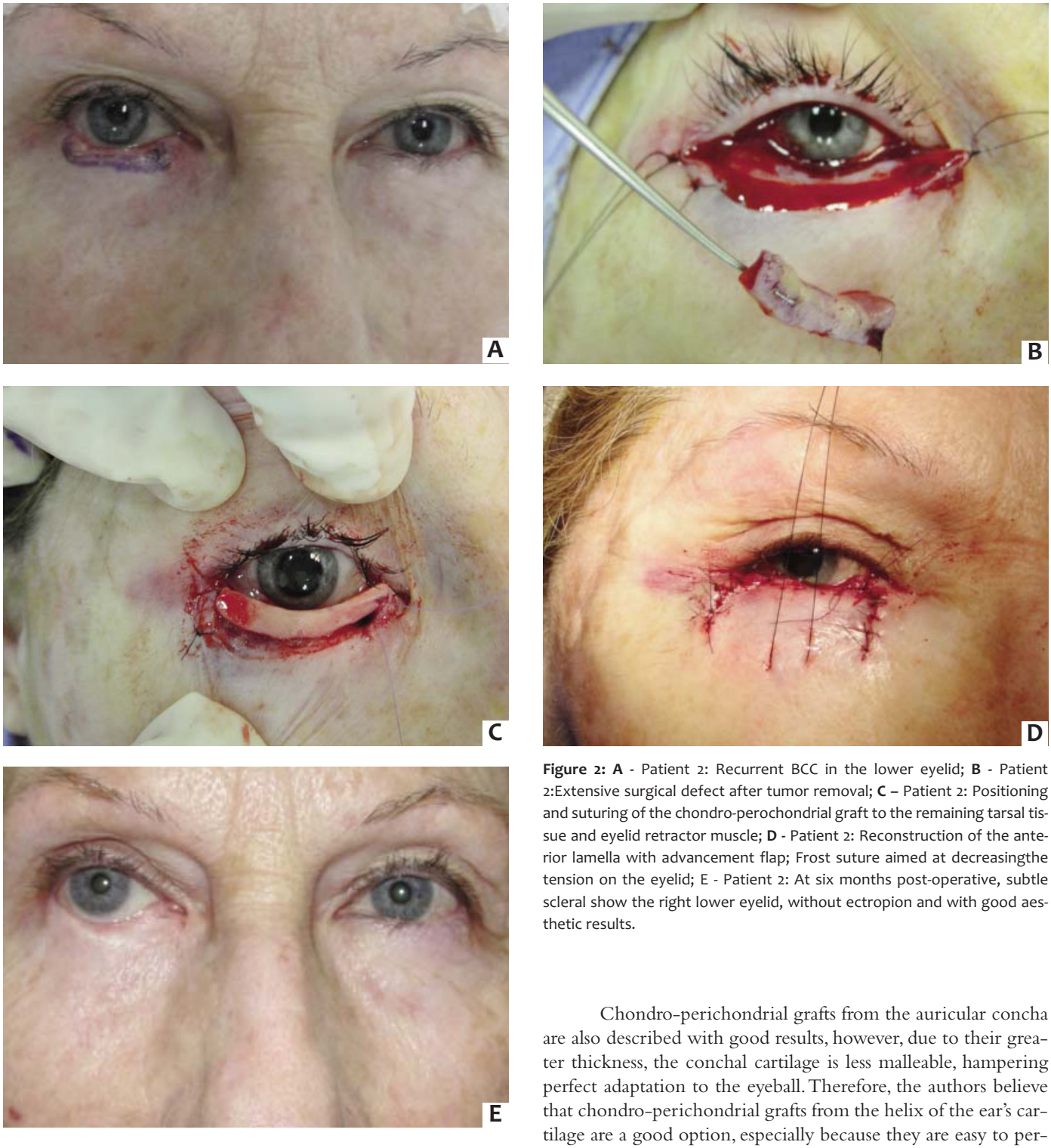

Figure 2: A - Patient 2: Recurrent BCC in the lower eyelid; **B** - Patient 2:Extensive surgical defect after tumor removal; **C –** Patient 2: Positioning and suturing of the chondro-perochondrial graft to the remaining tarsal tissue and eyelid retractor muscle; **D** - Patient 2: Reconstruction of the anterior lamella with advancement flap; Frost suture aimed at decreasingthe tension on the eyelid; E - Patient 2: At six months post-operative, subtle scleral show the right lower eyelid, without ectropion and with good aesthetic results.

truction of the posterior lamella. Mucosal only grafts, such as in the case of hard palate grafts, do not provide sufficient mechanical stability withthe occurrence of large defects of the lamella.[4,5] Composite grafts of cartilage/mucosa from the nasal septum are classically described in the literature with good results, but nevertheless they are technically difficult to harvestfrom the donor area. [4,5]

Chondro-perichondrial grafts from the auricular concha are also described with good results, however, due to their greater thickness, the conchal cartilage is less malleable, hampering perfect adaptation to the eyeball. Therefore, the authors believe that chondro-perichondrial grafts from the helix of the ear's cartilage are a good option, especially because they are easy to perform and adapt well to the eyeball. The technique described in the present study dismisses the need for a mucosal graft, since the perichondrium that remains in direct contact with the eyeball undergoes metaplasia and turns into a tissue similar to that of the conjunctiva. These findings are consistent with publications that demonstrate the importance of the perichondrium in the epithelialization process and the speed of transformation of the tissue into conjunctiva, which is superior when compared to

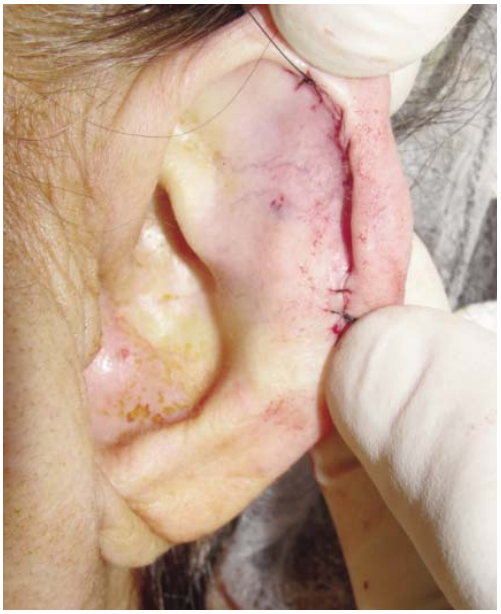

Figure 3: Donor area from the helix of the ear

cartilage only, perichondrium-free grafts. [10,11]

Furthermore, the chondro-perichondrial graft from the ear helix satisfactorily replaces the lost tarsal tissue, providing mechanical support and allowing foradequate palpebral mobilization and occlusion. [4,11]

CONCLUSION

Although the present study has worked with a small sample size, the technique described proved an excellent choice for extensive palpebral reconstructions in cases involving loss of the posterior lamella. This is due to the fact that it provided adequate stability and mobility to the eyelid, with the complete transformation of the perichondrium into conjunctival tissue in a few weeks, with minimal post-operative discomfort, and with excellent functional and aesthetic results.

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Artigo Original

Distensible acne scar correction using hyaluronic acid enhanced with LED lighting

Técnica de correção de cicatrizes distensíveis de acne com ácido hialurônico, otimizada com iluminação de LED

Authors:
Carlos Roberto Antonio[1]
Marina Garcia Nicoli[2]

[1] Head Instructor, responsible for Dermatologic Surgery discipline, Faculdade Estadual de Medicina de São José do Rio Preto (FAMERP)—São José do Rio Preto (SP), Brazil

[2] Undergraduate Medical Student, FAMERP—São José do Rio Preto (SP)

ABSTRACT

Introduction: The best option for treating distensible acne scars is cutaneous filling, however many such lesions cannot be seen properly under traditional lighting.

Objective: To investigate whether an LED light spot helps in the technique of filling acne scars with hyaluronic acid.

Methods: Twelve patients were treated with and without the diagonal and posterior focus of LED lighting. The patients themselves and two physicians deemed that the treatment has provided improvement. The median percentage of improvement attributed by the patients was 60% (without LED lighting) and 70% (with LED lighting).

Results: The average median percentage of improvement attributed by the physicians was 55.0% / 65.0% (without LED lighting) and 70.0% / 72.5% (with LED lighting).

Conclusion: The use of diagonal and posterior LED light spots enhances outcomes and patient satisfaction rates.

Keywords: acne vulgaris; cicatrix; hyaluronic acid.

RESUMO

Introdução: *A melhor opção para tratamento das cicatrizes de acne distensíveis é o preenchimento, porém muitas dessas lesões não são adequadamente visualizadas na iluminação tradicional.*

Objetivo: *Investigar se o foco de luz de LED favorece a realização da técnica de preenchimento com ácido hialurônico em cicatrizes de acne.*

Métodos: *Doze pacientes foram tratados com e sem foco diagonal e posterior de luz de LED. Os próprios pacientes e dois médicos atribuíram percentual de melhora. As medianas dos percentuais de melhora atribuídos pelos pacientes foram 60% (sem LED) e 70% (com LED).*

Resultados: *Medianas dos percentuais atribuídos pelos médicos foram 55%/65% (sem LED) e 70%/72,5% (com LED).*

Conclusão: *o uso do foco de luz LED em posição diagonal e posterior otimiza os resultados e os índices de satisfação dos pacientes.*

Palavras-chave: *acne vulgar; cicatriz; ácido hialurônico.*

Correspondence:
Dr. Carlos Roberto Antonio
R. Silva Jardim, 3.114, Centro
Cep: 15010-060—São José do Rio Preto—SP, Brazil
E-mail: carlos@ipele.com.br

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INTRODUCTION

Acne scars represent a major complaint in the dermatologist's office. In the past, the management of such scars was a challenge; nowadays, there are many treatment options.

According to their characteristics, acne scars can be classified into elevated, dystrophic, and depressed.[1] Depressed scars can be subdivided into distensible (where significant improvement can be observed with almost complete disappearance when the skin is stretched) and non-distensible (where no improvement is observed when the skin is stretched). In turn, distensible scars can be retractable (they present moderate fibrosis when strained) or non-retractable (without fibrosis).[1]

The best treatment option for non-retractable distensible scars is cutaneous filling. Retractable distensible scars are treated through a process called subcision, in which fibrous bands beneath the scar are ruptured by using needles with cutting tips.[2] The treatment can be supplemented with hyaluronic acid filling and/or fractional lasers. Hyaluronic acid, a natural polysaccharide, is a component of the connective tissues of all mammals.[3] It has a similar chemical structure in all species and a minimum potential for immunologic reactions.[4] Due to the fact that it is natural and degrades gradually, problems associated with rejection and granulomatous reactions are rare, and it can be easily dissolved using hyaluronidase.[5]

By treating non-retractable distensible acne scars with hyaluronic acid, it is possible to verify that the presence of light has an influence on their visualization. These lesions become more evident if a spotlight is positioned diagonally and posteriorly to the patient. An LED (Light Emitting Diode) is a semiconductor electronic component that converts electrical energy into light—unlike other types of lamps that use ultra-violet metallic filaments, radiation, or gas discharge. The light emitted by LEDs is intense and cold. In addition to its effectiveness, the great usefulness of LEDs in dermatology is linked to the fact that they do not cause warming either of the skin of the treated area or in the professional who is applying it.[6]

Thus, the present study was aimed at verifying the efficacy of the use of LED lighting in order to improve the results of filling procedures. In this way, a spotlight positioned diagonally and posteriorly to the patient during the procedure, allows for a better visualization of the shadows and reliefs of scars. As a result, it was possible in fact to note an enhancement in the visualization of the appearance of the scars. The observation started under regular yellow lighting, which was then replaced by LED lighting.

There are no reports in the literature regarding the use of this device to assist the treatment of distensible scars.

METHODS

From March 2008 to May 2010,[12] patients with depressed, distensible, non-retractable acne scars were recruited for the present prospective comparative study that was performed within the ethical standards regulated by the Declaration of Helsinki.

Smokers, those on anticoagulants, or those with elevated or non-distensible scars were excluded.

The treatment was performed exclusively using intradermal injections of monophasic reticulate crosslinked hyaluronic acid in the concentrations of 24 mg/ml and 25 mg/ml. Scars on both sides of the face were treated, in the following sequence:

- application of filling substance with the visualization of scars under yellow light from a diagonal and posterior position, followed by the evaluation of the corrected scars
- application of filler substance with the visualization of scars under LED lighting from a diagonal and posterior position, followed by the evaluation of the corrected scars

Photographic records were made in standardized positions—frontal and 45° and 90° profiles—with the same camera, before and after the two applications.

The evaluation of results was carried out through questionnaires completed by patients who attributed a percentage of improvement (in parameters from 0 to 100, gradations of 5%) for the scars treated without LED lighting (during the procedure) and with the assistance of LED lighting (immediately after application).

In addition, two physicians not related to the study evaluated the percentage of improvement during the procedure without LED lighting and immediately after application with LED lighting. The degree of improvement of distensible scars was classified as excellent (76-100%), good (51-75%), moderate (26-50%), or poor (0-25%).

RESULTS

The positioning of the LED spot lighting (diagonal and posterior to the patient) is shown in figure 1. Figures 2 and 3 illustrate the visualization of acne scars without the spot and with the LED lighting spot before the filling procedure, respectively. Figures 4 and 5 show, respectively, the visualization of acne scars after the filling procedure, without the spot and with the

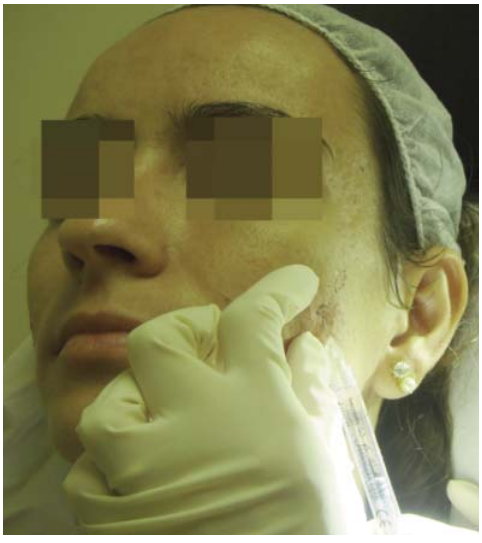


Figure 1: Positioning of the LED spotlight (diagonal and posterior to the patient).

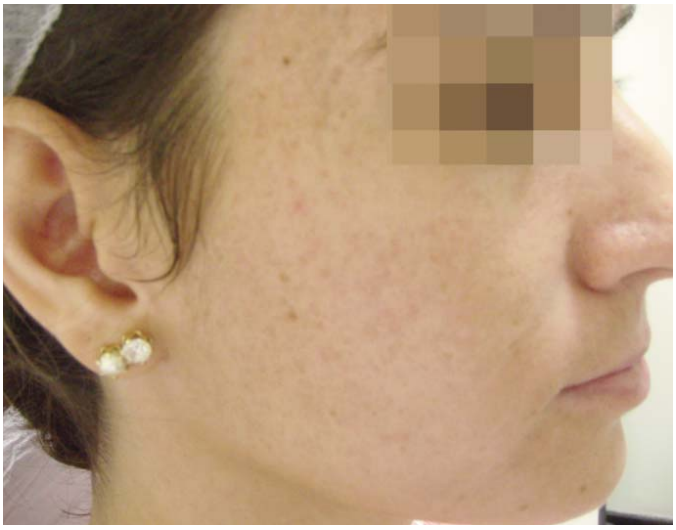


Figure 2: Visualization of acne scars without the LED spotlight, before the filling procedure

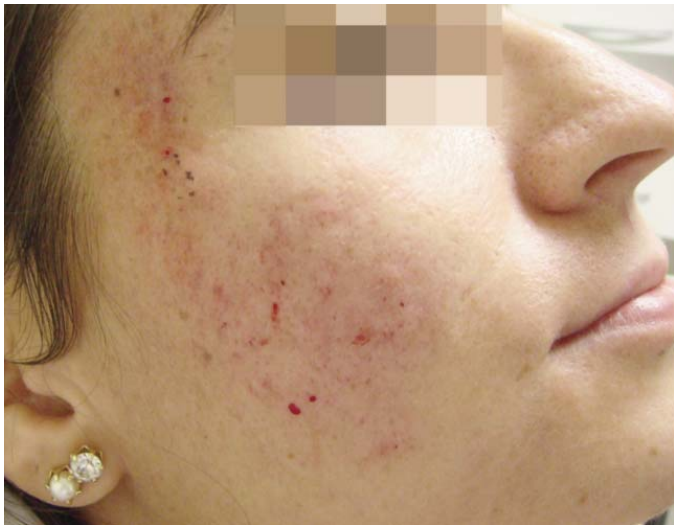


Figure 3: Visualization of acne scars with the LED spotlight, before the filling procedure

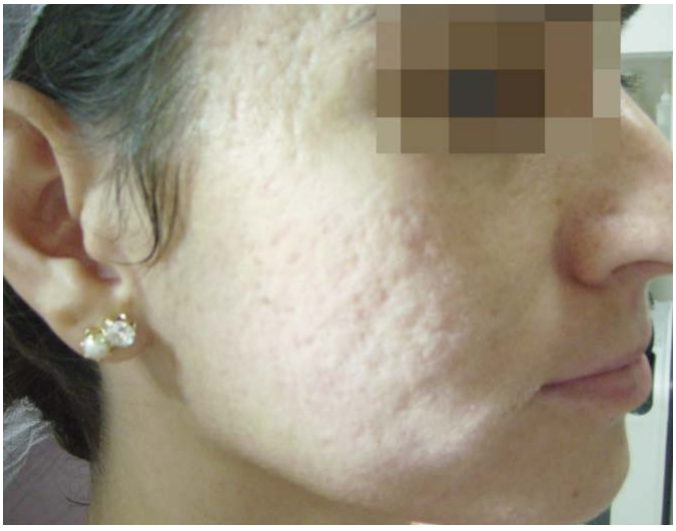


Figure 4: Visualization of acne scars without the LED spotlight, after the filling procedure

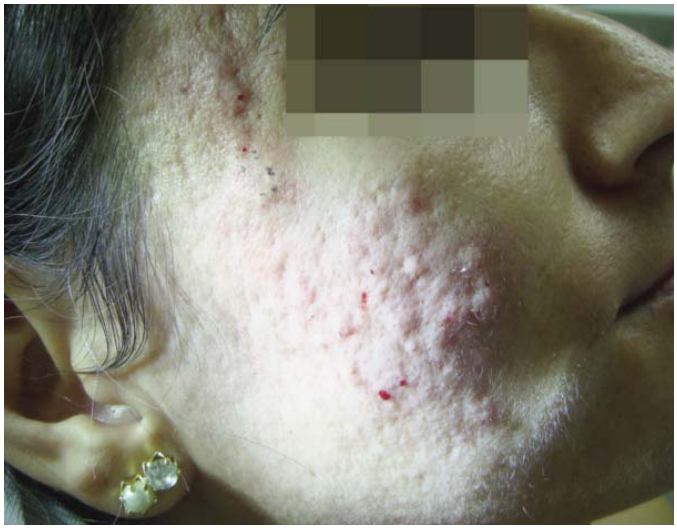


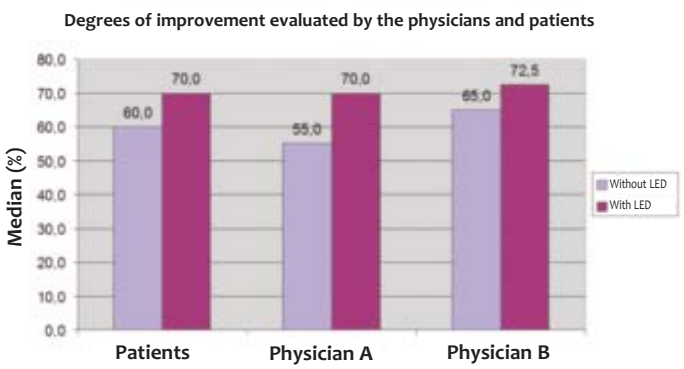
Figure 5: Visualization of acne scars with the LED spotlight, after the filling procedure

LED lighting spot. It is possible to note that the use of the spot in this positioning provides better visualization of the areas that need correction.

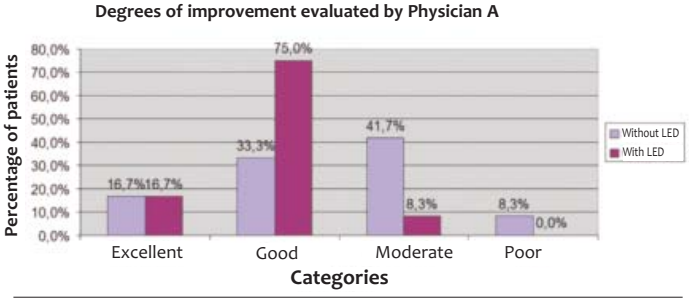
In the present study, the percentage of improvement obtained was higher when the scars were treated with the assistance of LED lighting. Only one patient did not notice the difference between the treatments with and without LED. None of the patients assigned a higher degree of improvement to the treatment without the LED.

The median of the percentages of improvement attributed by patients after the treatment without the use of LED lighting was 60%. Using LED, the median of the percentages of improvement was 70%. The median of percentages of improvement evaluated by the physicians after the treatment without LED lighting was 55% (Physician A) and 65% (Physician B); after the treatment with LED lighting, the medians were 70% (Physician A) and 72.5% (Physician B). This data is illustrated in Graph 1.

The obtained percentages of improvement were categorized as excellent, good, moderate, and poor outcome. One patient (8.3%) rated the outcome of the filling with hyaluronic acid without LED as excellent, 6 patients (50%) classified it as good, 4 (33.3%) as moderate, and 1 (8.3%) as poor. After the treatment using LED lighting, 5 patients (41.7%) rated the out-



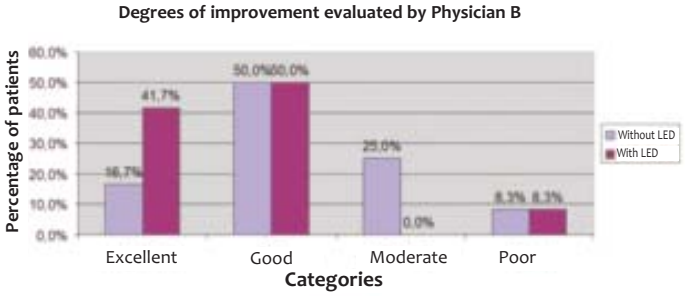
Graph 1: Medians of the degrees of improvement after the filling procedure with hyaluronic acid, with and without use of the LED spotlight, attributed by two physicians and the patients themselves



Graph 2: Percentage of degrees of improvement in acne scars attributed by Physician A to the patients after the filling procedure with hyaluronic acid, with and without the LED spotlight

come as excellent, 6 (50%) as good, and 1 (8.3%) as poor.

Regarding the degree of improvement attributed by the physicians, Physician A (Graph 2) rated the outcome of the filling with hyaluronic acid without LED as excellent in 2 patients, good in 4, moderate in 5, and poor in 1 patient. After the treatment with the LED spotlight, Physician A rated the outcome as excellent in 2 patients, good in 9, and moderate in 1 patient. In turn, Physician B (Graph 3) evaluated the outcome



Graph 3: Percentage of degrees of improvement in acne scars attributed by Physician B to patients after the filling procedure with hyaluronic acid, with and without the LED lighting spot

without LED light as excellent in 2 patients, good in 6, moderate in 3, and poor in 1 patient. The outcome of the treatment using LED was rated by Physician B as excellent in 5 patients, good in 6, and poor in 1 patient.

DISCUSSION

The treatment of acne scars constitutes a challenge, 6-8 and the correct classification of the latter determines the success of the first. Distensible scars respond to hyaluronic acid fillings with excellent outcomes, however many are not adequately visualized due to inadequate lighting during the procedure.

The authors evaluated the perception of improvement of acne scars (distensible and non-retractable), represented by percentages of improvement in 12 patients treated with hyaluronic acid filler, in two stages: firstly without the use of LED, and secondly, with the use of a diagonal and posterior spot of LED lighting during the application. The outcomes show that the percentage of improvement was greater in the group treated with an LED spotlight. The satisfaction of patients with cutaneous filling procedures can be 90% when the indication is criterious. 6 LED lighting facilitates the application in the correct location, as lesions presenting distensibility or depression are better—and sometimes only—visualized when subjected to diagonal lights that promote shade.

The use of diagonal lighting with LED enables an accurate and detailed view of the scars, optimizing the outcome and promoting a higher patient satisfaction rate.

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Article
Original

Comparative, randomized study to evaluate a dermocosmetic containing a complex reparative for the skin barrier, for use in post-cosmiatric treatment

Estudo comparativo e randomizado para avaliação de dermocosmético contendo um complexo reparador de barreira nos cuidados da pele após tratamento cosmiátrico

Authors:
Carlos D'Apparecida Santos Machado Filho[1]
Tereza Cristina dos Santos[2]
Ana Paula Licati Juberto Rodrigues[2]
Marisa Gonzaga da Cunha[3]

[1] Full Professor of Dermatology, Faculdade de Medicina do ABC (FMABC)—Santo André (SP), Brazil

[2] Dermatocosmiatry Graduate Candidate, FMABC—Santo André (SP)

[3] Dermatologist Physician, responsible for the postgraduate program in Dermatocosmiatry, FMABC—Santo André (SP)

ABSTRACT

Introduction: Cosmiatric procedures are common in dermatology and products with moisturizing action are recommended in the post-procedure period in order to accelerate reepithelialization.

Objective: To evaluate a formulation containing a skin barrier reparative complex, applied in the period after chemical exfoliation, used to reduce discomfort and improve skin hydration.

Methods: Comparative, randomized clinical study with 52 volunteer patients. The patients were divided into two groups and had all undergone exfoliation with 5% retinoic acid. Clinical assessment and biophysical technique measurements were performed during visits 1 (D0) to 6 (D7), using the test product in combination with sunscreen (Group I) or sunscreen only (Group II).

Results: The group treated (Group I) showed better improvement of desquamation and dryness at all visits, with a statistical significance ($p<0.05$) for a reduction in desquamation in D4 and in D7. In the assessment of hydration, the treated group (Group I) achieved better results than the control (Group II), with statistical significance in D2, D3, and D4 ($p<0.05$).

Conclusions: The use of the studied formulation was proven effective in improving symptoms and hydrating skin after cutaneous chemical exfoliation.

Keywords: *chemexfoliation; skin; cosmetics.*

RESUMO

Introdução: *Os procedimentos cosmiátricos são comuns na dermatologia, e produtos com ação hidratante são recomendados no período após o procedimento, com a finalida de de acelerar a reepitelização.*

Objetivo: *Avaliar formulação contendo complexo reparador de barreira, aplicada no período após esfoliação química, para redução do desconforto e melhora da hidratação da pele.*

Métodos: *Estudo clínico comparativo, randomizado com a inclusão de 52 voluntários, divididos em dois grupos, submetidos à esfoliação com ácido retinoico a 5%. Medidas de avaliação clínica e técnicas biofísicas foram realizadas durante as seis visitas (D0 a D7), com o uso do produto em teste associado ao protetor solar no grupo I ou o uso do protetor solar puro no grupo II.*

Resultados: *O grupo tratado apresentou melhor evolução da descamação e do ressecamento em todas as visitas, com significância estatística ($p<0,05$) para redução da descamação em D4 e D7. Na avaliação da hidratação, o grupo tratado obteve melhores resultados do que o controle, com significância estatística em D2, D3 e D4 ($p<0,05$).*

Conclusões: *O uso da formulação estudada demonstrou ser eficaz na melhora dos sintomas e da hidratação da pele após a realização de esfoliação química cutânea.*

Palavras-chave: *abrasão química; pele; cosméticos.*

Correspondence:
Dr. Tereza Cristina dos Santos
R. Voluntários da Pátria, 3.880, 73—B
Cep: 02402400—São Paulo—SP, Brazil
E-mail: terezacscelidonio@gmail.com

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INTRODUCTION

Current dermatological practice presupposes the development of different therapeutic procedures for the treatment of facial aging.[1]

From within the existing dermatologic armamentarium, it is possible to cite procedures that exert some degree of exfoliation or abrasion on the skin, such as chemical peels, lasers, and other technologies that employ light and microdermabrasion.[1]

With all of these exfoliating procedures, there is an intentional generation of damage to the cutaneous barrier in order to promote the repair of the epidermis and increased cell renewal, all aimed at producing aesthetic benefits.[1]

By promoting damage (chemically, physically, or mechanically) to the stratum corneum or epidermis, some degree of irritation—which translates into erythema and/or edema, in addition to desquamation of greater or lesser intensity—is expected to occur clinically, depending on the depth of the damage. Facial chemical exfoliation is a well-established procedure in which the dermatologist uses some agent (usually acids) that produces aggression to the skin, with consequent damage to the cutaneous barrier.[2]

There are different types of chemical exfoliation (or peels) used in dermatologic practice, with the most common being superficial peels performed with the use of retinoids and hydroxy acids.[1,2]

Retinoic acid peeling has been proposed in the literature as an option with high tolerability and low rates of adverse reactions.[3]

The presence of desquamation and dryness is observed in most patients, with the possible occurrence of mild erythema.[3-8] The desquamation process is usually more intense between the third and seventh day after the application of tretinoin (retinoic acid).

In the period immediately subsequent to the performing of the procedure, it is recommended that the dermatologist instruct the patient in the use of sunscreen and moisturizing agents that are able to provide a restorative action on the cutaneous barrier. This helps to relieve symptoms (such as burning, scaling, and erythema) and promotes the quick and efficient repair of the superficial structures of the epidermis—in particular the stratum corneum.[9]

Among the agents with a moisturizing and repairing effect on the cutaneous barrier, the use of sodium PCA, panthenol, dimethicone, cyclopentasiloxane, and karité butter stand out.[10]

The present study was aimed at evaluating, on a comparative basis, the efficacy and safety of a dermo-cosmetic formulation (test product) associated with the use of sunscreen versus the isolated use of sunscreen, in the care of the skin that had undergone cosmiatric procedures (facial chemical exfoliation). Evaluations were based on clinical and instrumental measurements of corneometry and evaporimetry (TEWL).

METHODS

A clinical, comparative, randomized, and monocentric study was carried out with the assistance of clinical and instrumental evaluation.

After the approval by the Research Ethics Committee (REC), 64 volunteers (52 women with ages between 35 and 65 years) were recruited during the period March-June 2013 who were undergoing cosmiatric treatment, which included plans for facial peeling with retinoic acid. All volunteers expressed their willingness to participate in the study by signing the Free and Informed Term of Consent (FITC) prior to undergoing any procedure planned in the protocol.

In order to ensure the eligibility of volunteers, in addition to meeting the characteristics of the population, they could not present with any of the following criteria: pregnancy or potential risk of pregnancy, lactation, use of topical or systemic anti-inflammatory medications and/or immunosuppressants, antihistamines for up 15 days before the start of the study, previous reaction to cosmetic products for the facial area, atopic or allergic history, local and/or disseminated active skin conditions that could interfere with the study results, pathologies that could cause immune suppression, intense exposure to the sun 15 days before inclusion in the study, and any other condition deemed by the volunteer investigator reasonable for disqualification.

After initial clinical evaluation for the verification of the eligibility criteria and photographic records, all volunteers underwent measurements of skin hydration (through the corneometry technique) and integrity of the cutaneous barrier (by measuring transepidermal water loss through evaporimetry) as described below.

Evaporimetry: the Tewameter® TM 300 (Courage & Khazaka) device was used to quantify the transepidermal water loss and, consequently, the functional integrity of the stratum corneum. The greater the integrity of the cutaneous barrier, the lesser the transepidermal water loss.

Corneometry: the Corneometer® MPA 580 (Courage & Khazaka) device was used to assess the hydration level by measuring the electrical conductivity in the skin, which takes place due to the presence of water. The higher the electrical conductivity measured, the higher the water content that is present in the skin's surface.

Measurements were carried out in the treated area (face) and in the control area (without treatment and previously defined as the volar aspect of the right and left forearm) for all instrumental evaluations.

Later on, the volunteers underwent peeling with 5% retinoic acid in hydroalcoholic vehicle, performed by a dermatologist physician. The volunteers were instructed to remove the product four hours after the application.

At the end of the session, the volunteers were randomly divided into two sub-groups, namely:

Group I—Application of standard sunscreen every two hours + study product, applied twice daily.

Group II—Application of standard sunscreen every two hours.

The products were distributed to the volunteers to be applied at home, along with a guidance booklet on how to use them.

The volunteers returned on the following days: D1 (24 hours), D2 (48 hours), D3 (72 hours), D4 (96 hours), D5 (120 hours) and D6 (7 days).

At the intervening and final visits, corneometry and evaporimetry measurements, in addition to clinical assessments, were carried out in the treatment areas and under the conditions defined at the initial visit.

The clinical evaluation consisted of observing the clinical characteristics of the facial skin based on the parameters erythema, dryness, and desquamation, grading it with the assistance of a four-point scale (0-3).

The test product (Cetaphil Advanced,® Galderma, Brazil), is a dermocosmetic that has a hydrating and reparative effect on the cutaneous barrier, which contains ERC-5® complex (whose composition includes the agents sodium PCA, panthenol, dimethicone, cyclopentasiloxane, and karité butter emulsion). One unit of the product was supplied to each volunteer in Group I (treated), along with sunscreen, for exclusive use during the study period.

The standardized sunscreen for both Groups was dispensed with SPF 30.

RESULTS

Of the 64 volunteers initially evaluated, 52 were randomized and started the study, with 26 volunteers allocated to each group.

Fifty volunteers completed the study: 24 in Group I and 26 in Group II.

One volunteer withdrew from participation for personal reasons, and the other presented with a mild contact dermatitis condition, and was discontinued from the study.

There were no other reports of adverse events.

Figure 1 shows the flowchart of volunteers, according to the CONSORT standard.[11]

Only volunteers who completed the study were considered for the evaluation of efficacy.

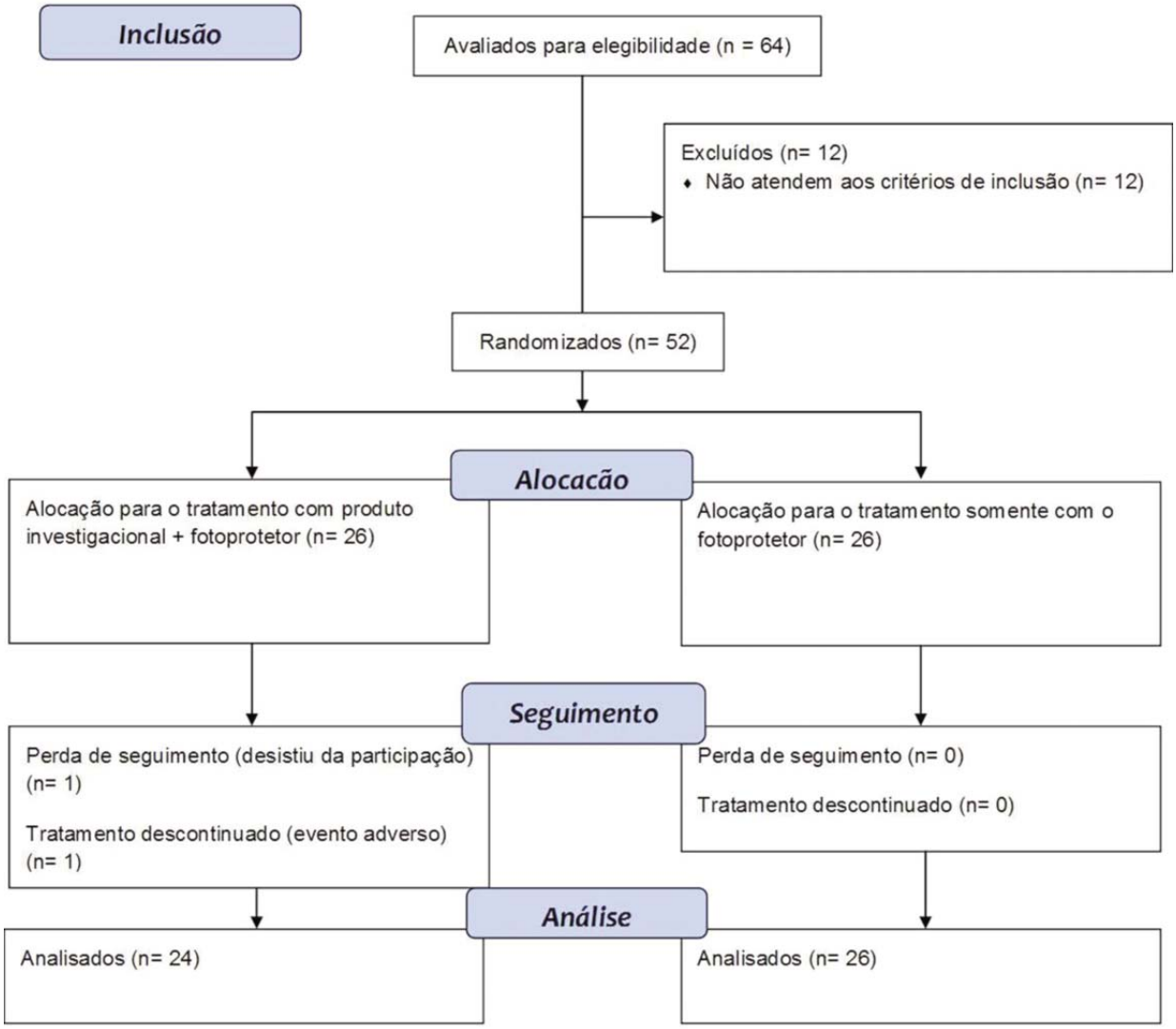
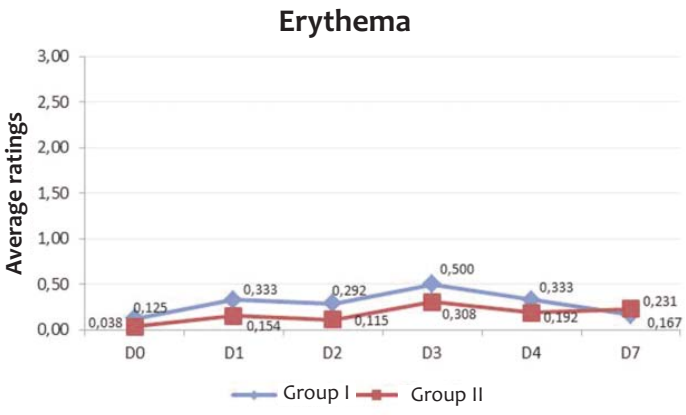
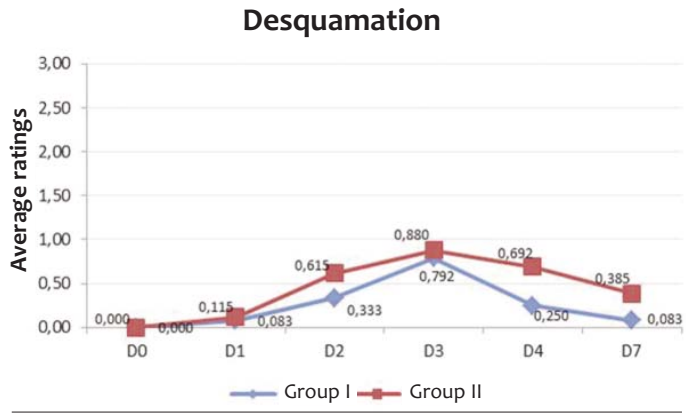


Figure 1: shows the flowchart of volunteers, according to the CONSORT standard.[11]



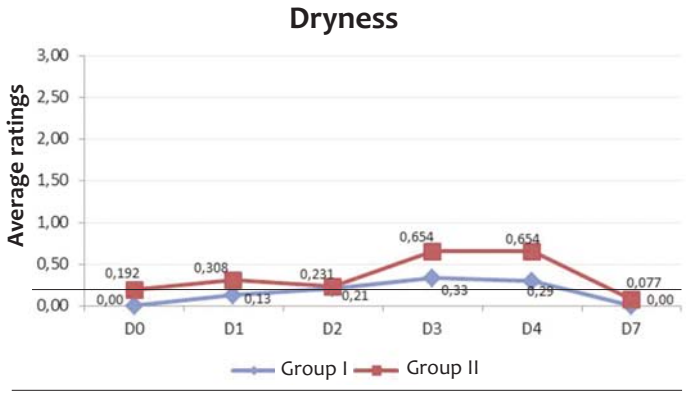
Average ratings for erythema according to the clinical evaluation, where:
0 = absent, 1 = mild, 2 = moderate, 3 = intense

Graph 1: Variation of erythema at the return visits



Average ratings for desquamation according to the clinical evaluation, where:
0 = absent, 1 = mild, 2 = moderate, 3 = intense.

Graph 2: Variation indesquamationat the return visits



Average ratings for dryness according to the clinical evaluation, where:
0 = absent, 1 = mild, 2 = moderate, 3 = intense.

Graph 3: Variation in dryness at return visits

1-Clinical Assessment

Graphs 1, 2, and 3 show the average score for clinical evaluation of erythema, desquamation, and dryness, respectively, in the different experimental times:

The graphical analysis shows that Group I has higher results (lower average) as compared to Group II in the parameters desquamation and dryness in most experimental time periods. For the parameter erythema, slightly higher values were observed in Group I as compared with Group II, except for in the final evaluation (D7).

The results of the two groups were compared using the Mann-Whitney test, as shown in Table 1:

It is important to note that there is a statistically significant difference between Groups for desquamation on D4 and D7, when Group I had lower averages than those in Group II. There was no statistically significant difference between the groups for the parameters erythema and dryness.

2-Instrumental Effectiveness through Corneometry

The results of the evaluation of skin hydration through the corneometry technique are expressed in a corneometric index, a unit intrinsic to the device used to measure it.

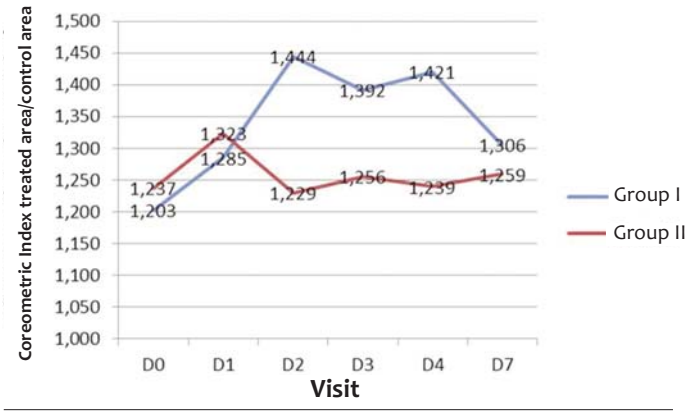
In order to eliminate environmental and extrinsic variation from the study, the correlation between the corneometric index of the treated area (face) and the control area (forearm) must be analyzed.

Graph 4 shows the variation of the corneometric index in different experimental times.

Table 1: Results of the comparison test between the groups for clinical evaluation

Experimental time	Parameter	P Value	Conclusion**
D1	Erythema	0,467	does not reject the hypothesis*
D2	Erythema	0,611	does not reject the hypothesis
D3	Erythema	0,575	does not reject the hypothesis
D4	Erythema	0,630	does not reject the hypothesis
D7	Erythema	0,179	does not reject the hypothesis
D1	Desquamation	0,723	does not reject the hypothesis
D2	Desquamation	0,076	does not reject the hypothesis
D3	Desquamation	0,505	does not reject the hypothesis
D4	Desquamation	0,004	rejects the hypothesis
D7	Desquamation	0,014	rejects the hypothesis
D1	Dryness	0,976	does not reject the hypothesis
D2	Dryness	0,579	does not reject the hypothesis
D3	Dryness	0,351	does not reject the hypothesis
D4	Dryness	0,188	does not reject the hypothesis
D7	Dryness	1,000	does not reject the hypothesis

*Hypothesis: There is no difference between the groups.
**Level of significance = 5%.



Average Corneometric Index (treated area/control area) for both groups at experimental times

Graph 4: Variation of the corneometry measurements at the return visits

The percentage of variation in skin hydration between experimental times when compared to D0 (before the peel), is presented in Table 2. Negative values correspond to a reduction in skin hydration.

It is possible to observe (both in the table and graphically) that there is a significantly distinct behavior between the groups, with Group I's results being higher than those of Group II at all time points, except for the variation between D1 and D0, where the results were similar.

In order to compare the groups, Table 3 shows the statistical analysis of the corneometric index variation of the treated area/control area, relative to the baseline, between the various intermediate and final visits, using the Student's t-test.

Table 2: Percentage change in the difference of skin hydration between experimental time points compared to D0, measured through corneometry

	Areas/Time point	D0-D1	D0-D2	D0-D3	D0-D4	D0-D7
GROUP I	Treated/Control	6,49	19,69	15,34	17,75	8,21
GROUP II	Treated/Control	6,98	-0,60	1,52	0,20	1,81

Table 3: Student's t-test results for the comparison of treated areas between Groups I and II

Time points	P value	Conclusion**
D0-D1	0,828	does not reject the hypothesis *
D0-D2	0,001	rejects the hypothesis
D0-D3	<0,001	rejects the hypothesis
D0-D4	0,003	rejects the hypothesis
D0-D7	0,101	does not reject the hypothesis

* Hypothesis: There is no difference between the groups.
** Level of significance = 5%.

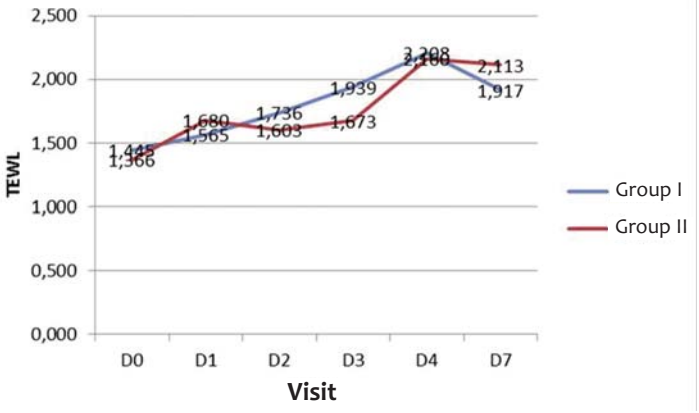
It is important to note that there is a statistically significant difference in D2, D3, and D4 in the treated area, with Group II showing inferior results when compared to Group I.

3—Instrumental Effectiveness through Evaporimetry

The results of the assessment of the transepidermal water loss of the skin through the evaporimetry technique are expressed in grams per square meter per hour (g/m2/h). In order to eliminate environmental and extrinsic variation from the study, it is necessary to study the correlation between the transepidermal water loss treatment in the treated area (face) and in the control area (forearm). Graph 5 shows the values for the transpidermal water loss (TEWL) in the different experimental times. The results of the percentage change in transepidermal water loss between the time points when compared with D0 (before the peeling) are presented in Table 4.

It is possible to observe increased evaporimetry measures in both groups. The development of that progression showed a distinct behavior between groups, being more marked in the early days in Group I, and more marked in the last days in Group II. At the end of the study, Group I had absolute and relative results superior to those of Group II.

Table 5 shows the statistical analysis between the groups, in the variation of the transepidermal water loss of the treated area/control area in different visits, as compared to baseline, using the Student's t-test.



Average transepidermal water loss (treated area/control area) for both groups at experimental times

Graph 5: Variation of the evaporimetry measurements atthe return visits

Table 4: Percentage change in the difference of skin hydration between experimental time points compared to D0, measured through evaporimetry

	Areas/Time point	D0-D1	D0-D2	D0-D3	D0-D4	D0-D7
GROUP I	Treated/Control	8,28	20,15	34,19	52,81	32,67
GROUP II	Treated/Control	22,93	17,34	22,47	58,10	54,65

Table 5: Student's t-test results for the comparison of treated areas between Groups I and II

Time points	P value	Conclusion**
D0-D1	0,069	does not reject the hypothesis *
D0-D2	0,321	does not reject the hypothesis
D0-D3	0,482	does not reject the hypothesis
D0-D4	0,760	does not reject the hypothesis
D0-D7	0,375	does not reject the hypothesis

* Hypothesis: There is no difference between the groups.
** Level of significance = 5%.

It is important to note that there was no statistically significant difference between the groups.

DISCUSSION

Superficial exfoliative procedures are common in the dermatological practice.

The purpose of these procedures is to promote a reduction in the thickness of the stratum corneum and/or deeper layers of the epidermis, inducing cell renewal and reducing the unaesthetic appearance of superficial dyschromic or hyperkeratotic lesions, leading to younger-looking skin.[1]

Of these procedures, the retinoic acid peel is the most frequent option among Brazilian dermatologists due to its practicality, low rate of adverse events, and the absence of restrictions on patients' daily activities, eliminating recuperation periods and time-off from work.[3]

Care after these procedures should include appropriate photoprotection (in order to reduce the risk of post-inflammatory hyperpigmentation) and the use of cutaneous barrier moisturizing and repairering agents (which can reduce desquamation, erythema and dryness, and at the same time, provide adequate hydration).

The present study was aimed at evaluating the ability of a topical product with 5% retinoic acid—used in the post-procedure period of peelings—to reduce signs and symptoms of exfoliation (erythema, dryness, and desquamation), simultaneously evaluating the water content and transepidermal water loss of the skin through instrumental measurements.

The study was conducted on a comparative basis, with the experimental group making use of the test product and standard sunscreen, while the control group used only the standard sunscreen.

The test product has moisturizing characteristics, exerting a reparative effect on the cutaneous barrier.

Fifty patients completed the study (per protocol population), with 24 of them having used both the sunscreen and the test product, and 26 the sunscreen only.

Regarding the clinical effects, it was possible to observe that the parameter erythema presented very low levels in both groups, (which is expected in patients who undergo retinoic acid peels), for being a superficial exfoliation. For that reason, no statistically significant difference between the groups was observed.

Desquamation is certainly the most observed event in patients undergoing retinoic acid peels, with dermatologist physicians often verifying this process peaking at between the third and fourth day of the procedure, possibly lasting from seven to ten days, depending on its intensity.

An expected progress of desquamation was found in the present study for both groups. Nevertheless, it was proved that Group I (treated with the test product and sunscreen) showed lower average desquamation as compared to Group II (treated only with sunscreen) at all time points, with statistical significance in the fourth and seventh days after the procedure. This demonstrates the added benefit that the use of the study product can offer in reducing desquamation.

Regarding the dryness sensation, it was possible to notice that the absolute rates for both groups were low. However when the two groups were compared, it was graphically possible to observe that Group I had lower average scores when compared to Group II. Statistical significance was not observed, probably due to the low values found in both groups.

The present study also sought to quantitatively evaluate the skin's hydration (carried out by measuring the skin's water content through corneometry) and transepidermal water loss (through evaporimetry).

When analyzing results for corneometry, it was possible to observe markedly distinct developments for the two groups.

It was evidenced that the treated group (Group I) showed superior results to those of Group II at all return visits, meaning that the use of a topical agent with moisturizing capacity can induce increased water content in the skin, resulting in improved hydration and contributing to a more effective recovery in the post-procedure period.

In the statistical evaluation between groups, it was observed that Group I was statistically superior to Group II in all intermediate visits (D2, D3, and D4), when compared to D0. In the first and last visits after the peeling procedure (D1 to D7), the improvement was not statistically significant.

The capacity to retain water, which is observed through the corneometry's results, demonstrates the test product's significant moisturizing capacity.

If the evaluation of the skin's water content (mainly promoted by products with high moisturizing and hygroscopicity properties) was carried out through corneometry assessments, the evaluation of transepidermal water loss was carried out by analyzing the corneum stratum's capacity for occlusion in preventing the evaporation of water from the skin's deeper layers to the environment.

Damaged skin—as it is after exfoliation—presents a rupture of the stratum corneum's structure, facilitating the evaporation of water, clearly evidenced by the evolution of evaporimetry curves of both groups.

Interestingly, the least favorable development observed in Group I (treated) in the early days of the study, is probably due to the greater supply of water on the skin's surface resulting from the use of the test product.

In other words, the supply of water provided by the hygroscopic power of the product (demonstrated in corneometry measurements) was the main factor for the increased evaporation of the water, noticed in the evaporimetry curves.

On subsequent days, however, the reparative effect of the test product on the barrier was evidenced through the improvement in the development of transepidermal water loss.

CONCLUSION

The use of the formulation containing the restorative complex ERC-5®, with hydrating and restorative action, demonstrated additional benefits in the post-procedure care of exfoliative techniques, resulting in the reduction of desquamation, promoting increased water content in the skin, and facilitating the structural recovery of the skin barrier. ●

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Poly-L-lactic acid: a biostimulating agent

Ácido Poli-L-Láctico: um agente bioestimulador

Review article

ABSTRACT

Poly-L-lactic acid (PLLA) is a biocompatible, re-absorbable, immunologically inert polymer that induces neocollagenesis through a subclinical inflammatory response. It is indicated for restoration of facial volume associated with facial lipoatrophy in immunocompetent or HIV-immunodeficient patients. In addition there are cosmetic indications for extra facial areas. For more than three decades it has been used in medical devices such as plates, screws, intraosseous and soft tissue implants, and as a biodegradable vector for drugs, in sutures and stents. The present article is aimed at presenting a literature review on the indications, application method, and complications of the use of PLLA.

Keywords: collagen; skin aging; rejuvenation

RESUMO

O ácido poli-L-láctico (PLLA) é polímero biocompatível, reabsorvível, imunologicamente inerte, que induz a neocolagênese através de resposta inflamatória subclínica, indicado para restauração do volume facial associado à lipoatrofia facial em pacientes imunocompetentes ou com imunodeficiência pelo vírus HIV, além das indicações cosméticas em áreas extrafaciais. Há mais de três décadas vem sendo usado em dispositivos médicos como placas, parafusos, implantes intraósseos, de tecidos moles, como vetor biodegradável para medicamentos, em fios de sutura e stents. Este artigo tem como objetivo apresentar uma revisão da literatura sobre indicações ao uso do PLLA, seu modo de aplicação e suas possíveis complicações.

Palavras-chave: *colágeno; envelhecimento da pele; rejuvenescimento.*

Authors:
Carlos D'Apparecida Santos Machado Filho[1]
Tereza Cristina dos Santos[2]
Ana Paula Licati Juberto Rodrigues[2]
Marisa Gonzaga da Cunha[3]

[1] Full Professor of Dermatology, Faculdade de Medicina do ABC (FMABC)—Santo André (SP), Brazil

[2] Dermatocosmiatry Graduate Candidate, FMABC—Santo André (SP)

[3] Dermatologist Physician, responsible for the postgraduate program in Dermatocosmiatry, FMABC-Santo André (SP)

Correspondence:
Dr. Tereza Cristina dos Santos
R. Voluntários da Pátria, 3.880, 73—B
Cep: 02402400—São Paulo—SP, Brazil
E-mail: terezacscelidonio@gmail.com

INTRODUCTION

The facial aging process starts slowly at around the age of 20, when the cell renewal rate slows down.[1] Nevertheless, the visible manifestations take years to be noticed and are determined by the depression of soft tissues, with the loss of muscle, subcutaneous and osseous tissues, and skin atrophy.[2,3]

Minimally invasive techniques for facial rejuvenation are performed with cutaneous fillers, volumizers, and enhancers,[4-6] and are a good option for many patients. Currently, cutaneous fillers can be classified into two categories: temporary or biodegradable products (which persist for months or a few years) and non-resorbable or permanent products.[7] Considering that the aging process is continuous, temporary fillers should be preferred.[2]

Poly-L-lactic acid (PLLA) was approved as a cutaneous filler in Europe in 1999, under the trade name of New-Fill. 8 In 2004 it was approved by the FDA in the U.S. with the brand name Sculptra (Dermik Laboratories, Sanofi Aventis, USA), for the treatment of HIV-associated lipoatrophy and for treating volume loss with an aesthetic purpose in 2009,[8-11] under the name Sculptra Aesthetic (Sanofi Aventis).[12,13] By 2006 over 150,000 patients had been treated[14,15] in more than 30 countries.[16]

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The PLLA is a synthetic molecule discovered by the Centre National de la Recherche Scientifique (CNRS), Lyon, France, in 1954. It is derived from lactic acid, which is naturally produced by muscle contraction. The product is marketed as a lyophilised powder in a sterile vial containing non-pyrogenic mannitol, sodium croscarmellose and microparticles of PLLA (97.5% of water)[17] measuring 40-63 microns in diameter and belonging to the family of alpha-hydroxy acids[13,18] produced from the fermentation of corn.[12] The size of the particles prevents them from being phagocytized by macrophages in the dermis or from passing through the walls of capillaries. Nonetheless, they are small enough to be injected with a 26G needle.[13]

The mechanism of action occurs through the stimulation of fibroblasts[4,13,15] in response to a subclinical tissular inflammation. It is this fibroplasia that produces the desired cosmetic result.[13] New collagen begins to form after one month and continues to increase for nine months to a year. In the sixth month many particles become porous and surrounded by macrophages. After this period there is no evidence of fibrosis and the PLLA particles disappear.[6,19] The product's degradation occurs through non-enzymatic hydrolysis into lactic acid monomers that are metabolized into CO2, H2O or incorporated into glucose. [1,14,16] With its half-life estimated at 31 days, PLLA is totally eliminated from the body in about 18 months. [20]

An increase of 4 to 6mm in the thickness of the dermis 5 has been demonstrated through Doppler ultrasound, evidencing the presence of support in the skin for 96 months.[6] An ultrasound study measured the skin thickness of 33 patients with HIV-associated lipoatrophy who were treated with 4 sessions of PLLA and showed a 151% increase in skin thickness at 12 months and a 196% increase at 24 months, confirming that the effect of neocollagenesis continues several months after the injection of the product.[21] Vega, Westminster, Blue Pacific and Apex, and, more recently Fitzgerald and Vleggaar,[13] and Rendon 21 have repeatedly demonstrated through prospective clinical studies that the duration of clinical effects may betwo years or more.

The best indication for the product is to use it as three-dimensional biostimulator 1,20 in patients seeking a natural look without the appearance of tiredness.[13] The PLLA is not injected directly into wrinkles or furrows, but diffusely in areas that are concave or in areas of shadow, caused by hypodermic and/or subcutaneous fat loss due to aging, weight loss, trauma, lipoatrophy secondary to diseases,[19] corticosteroid injection, and after facelift surgery. [22]

The use of PLLA should be avoided in certain facial areas, such as perioral and periorbital regions,[5,16] which are regions of muscle hypermobility,[23] and it is not indicated for filling the lips.[5,16] It promotes the improvement of facial contour, including jaw lines, nasolabial folds, temporal region, malar region 15 and the correction of marionette lines, and restores the harmonic shape of the face.

In 2009, Sadick and Palmisano 24 reported the case of a 60-year-old woman with acne scars who underwent several previous procedures, with success after seven PLLA sessions, corroborating a study by Beer,[25] who published the follow-up of 16 cases of moderate and severe acne scars[24] and varicella scars, with a significant reduction measured in distensible scars (2-3mm) after a similar number of sessions. Grimald et al. used the product in three sessions with the aim of increasing the thickness of the skin in a patient bearer of Parry-Romberg syndrome, in a procedure that followed the Coleman technique to reconstruct the three-dimensional projection of the face[26] or areas of asymmetry, as referred by Burgess.[14] Other areas have been treated, including the neck, [21] hands,[27-29] breast,[16,30] and atrophic scars.

Coimbra and Amorim[31] obtained good results with the sagging of arms in 16 women after treatment with PLLA.

It is worth noting that Vleggaar improved the appearance and contour of a patient with pectus excavatum[32] with three PLLA sessions, and Shulman et al. described the correction of thoracic deformity secondary to breast reconstruction after mastectomy, in a thin 63-year-old woman. The step formed between the implant and the skin was corrected with two vials per session, totaling four sessions.[33] Hamilton and Burgess published a discussion on the use of the product in melanodermic patients (Fitzpatrick IV to VI), with modifications of the technique—such as extended time between sessions and the injection of the product in different layers, like the subcutaneous, and small amounts over the bone of the maxilla and zygoma—achieving better aesthetic results.[34] The procedure proved to be safe in those patients.

The contraindications to the use of the product are: areas previously treated with permanent fillers such as silicone or polymethylmethacrylate,[3,11,20] and patients on aspirin, vitamin E, fish oil capsules, non steroidal antinflammatories and anticoagulants, the latter which should be discontinued ten days before the procedure.[3,5,27] The use of PLLA is also not approved in children, and pregnant or lactating women.[3] Other contraindications are: use of immunosuppressants, heavy smoking, and patients eager for immediate results. Patients with chronic use of immunosuppressants and anti-inflammatory drugs such as corticosteroids, should be treated with extreme caution, for suppressing the inflammatory response during the treatment with prednisone can lead to subtherapeutic response. After discontinuing or interrupting prednisone, an exaggerated response to PLLA may occur.[22]

The reconstitution of the product should be performed in distilled water (DW), ranging from 2 13 to 24 hours,[22,25] or even 72 hours before use[5,19] (which would facilitate the dilution), or up to seven days if diluted in DW with bactericidal, according to Palm.[11] Lam et al. emphasized that reconstructions of less than 12 hours increase the risk of nodules.[16]

Initially, the laboratory that manufactured New-Fill suggested dilution of the product in 3 ml of DW, [23] carried out 30 minutes prior to use, 3 which would imply greater risk of adverse effects.[18] Currently, other dilutions can be used, such as in five, [2,4,5,11,14,23,25] six, [22,34,35] seven, [5,8,11,12] eight [29] or 12ml, [27] supplemented or not with 1% or 2% lidocaine 32 of 1-4ml per vial. After hydrating the PLLA, the vials must be kept at rest up until the moment of use, preventing the deposition of particle agglomerates on their wall.[13] Since 2004, Rendon[22] dilutes in saline solution associated with lidocaine, providing a tumescent anesthetic effect and decreasing the discomfort, with a final volume of 6-8ml, [5,20]

with dilutions lower than 10ml being used in the face, [5,22] and of up to 16ml[11, 31] or 20ml[31] in extrafacial areas. Immediately before use, the product should be shaken vigorously in order to obtain a homogeneous suspension with few bubbles.

The stability of the product after reconstitution at room temperature is 72 hours, [5,16] although Sherman[22] believes that dilution in DW plus bactericidal allows its use within up to 30 days.[19,22]

For the application, skin antisepsis must be carried out with chlorhexidine, applying 4% lidocaine 30 minutes before. [4,22] Some authors carry out infraorbital nerve block with lidocaine, [6,14,34] in addition to mentonian nerves.[19,34] Sherman[22] applies ice packs before and after the injection of PLLA to decrease pain, stimulate vasoconstriction and reduce the formation of hematoma and echymosis. Pain is felt as the needle perforates the dermis or touches the periosteum. Fabi[11] and Goldman[12] treated 90 cases only with 1% lidocaine with 1:100,000 epinephrine, added to the solution.

Due to the fact that it is a procedure performed in series, with benefits gradually increasing over months, it is important to record the development with photographs (frontal, lateral, and oblique).[19] The area to be treated should be mapped in such a way that the areas in which applications will be carried out are identified. Convex areas should be marked in order not to be filled.[22]

The application technique consists of using a 1 to 3ml syringe and an 18G needle to withdraw the product from the vial. The needle used in the application itself is a 26G, with the product being applied between the deep dermis and hypodermis. Prior aspiration is carried out to avoid intravascular injection, with an entry angle into the skin of between 30° and 45°, with 0.1-0.2 ml of the product being slowly deposited in retroinjection. In order to prevent superficial deposits, which may cause the emergence of papules, the injection should be halted when ¾ of the needle becomes apparent.[22] The PLLA is applied in parallel lines or in the shape of an "X". The technique of filling in small bolus is employed in areas of very thin skin—such as the temples—in small volumes of 0.05ml, nevertheless the formation of nodules may take place.[22] According to Sherman, [22] the application should be implemented at a continuous pace and with continuous movement during the retroinjection, in order to prevent the deposition of bolus, which depending on the depth, can lead to the formation of papules or nodules. This observation is especially important for those with a beginner skill level for applying the product, who should always carry out aspiration before injection.[22] For areas of very thin skin, Sherman also prefers the tunneling technique, applying the product in small amounts, depositing between 0.025 and 0.05 ml, above the periosteum. For those who are already skilled in handling the product, he suggests applications in the shape of fans, consisting of multiple retrograde tunnels with few punctures to cover larger areas, such as the genian, pre-auricular, and mentum's lateral regions, nasogenian sulci, and the lateral region of the eyebrows.[19]

The treated area should be massaged immediately after the application in order to ensure an even distribution of the product. The application of ice at the site stimulates vasoconstriction and prevents echymosis. The syringe must be kept parallel to the skin's surface during application, which keeps the needle pervious during the procedure. The use of 3ml syringes with a content of 1ml makes for comfortable handling and allows its manipulation in a way that prevents the precipitation of PLLA and avoids the clogging of the needle.[22] Sherman still advises that the direction of the application of the product should be from top to bottom and from medial to lateral, in the face. The face must be treated globally, rather thanfilling only the cavities, thereby avoiding overcorrection. [3,13,16]

The application technique of PLLA varies according to each author's experience. Lowe et al. 4 published a retrospective study of 281 treated cases, where 0.05 ml of PLLA were deposited in the deep dermis or upper subcutaneous using tunneling retroinjection, in the shape of an "X" or that of a fan. 6 According to Beer, 15 this cross technique ensures better distribution of the product in the desired plane. Lam et al. 16 suggest that the "X" technique allows a better distribution of the product in addition to the fact that its application in the subcutaneous minimizes the risk of complications. They treat infraorbital and temporal areas with transcutaneous bolus 5 of 0.1ml per deposit in a dilution of 11ml. Lacombe [8,9] recommends that the application in the infraorbital margin be carried out with a long needle into the lateral of the orbit in small deposits, avoiding echymosis and the surfacing of the product across the muscle. For the lower half of the face he uses a long needle and application in the shape of fans 8 or an "X" in order to reduce the number of punctures. Fitzgerald and Vleggaar's treatment protocol 13 consists of carrying out the applications in the deep subcutaneous in the medial region of the cheeks and mentum, and in the superficial subcutaneous in the parotid and masseteric region, with the "X" or fan shape technique or using 0.1-0.3 ml/cm, in addition to supraperiosteal applications in the zygoma, maxilla, and mandible using 0.2-0.3 ml/cm. In the temporal region, the protocol recommends applying 0.3-0.5 ml/cm deposits of the product.

Palm and Chayavichitsilp 11 described modifications of the techniques used. Supraperiosteal injections in the temporal region, piriform aperture, zygoma and canine fossa, and bolus in the anterior mandibular sulcus. It is important to note that the application in the piriform aperture and mentum region is performed through intraoral access. They also perform PLLA applications in the bottom of the superior and inferior gingival sulcus. The authors claim to have been performing that technique for five years without any complication. When applying the product in the infraorbital margin, the needle is oriented from the genian region towards the orbit. The remainder is applied using the fan technique, as described above. Good results were reported by Hamilton and Burgess,[34] after application in different layers of the skin aimed at an adequate restoration of facial volume, resulting in a more youthful appearance. Small boluses are applied over the bone in the maxilla and zygoma, startingin the nasofacial sulcus. With the correction of the malar region, other regions of the maxilla also improve, with the application carried in the deep subcutaneous tissue.

Sadick et al. 27 treated the hands of 26 patients with subdermal and above-the-facial- plane deposits of 0.3-0.5ml, with 8-10ml dilutions. Coimbra and Amorim[31] published the report of a treatment in the medial region of the arms of 22 women,

where the linear retrograde technique was applied, with a dilution of 20ml and deposits of 0.05ml per point, with good improvement of local sagging.

Mazzuco et al.[21] described the first series of neck and breast rejuvenation cases in 2009, in which[33] patients received the application of PLLA in the neck in the dilution of 10ml, with 3 patients also receivingit in the breast. The technique used was that of small 0.05ml bolus with a distance of 1 cm between the dermis and subcutaneous tissue. Peterson and Goldman 30 used a 16ml dilution, with retrograde technique in a fan shape, for rejuvenating breasts. Kafler et al. presented a comparative study, conducted in the dermatology department of the Faculdade de Medicina do ABC (São Paulo, Brazil) in which 6 female patients underwent two PLLA treatments, with monthly intervals, in the inner part of the arms. In the right-hand side, the final dilution of the product was 20ml, and the technique used was the linear retrograde, with a final volume of 5ml. In the left-hand side, the final dilution of the product was 10ml, with point-to-pointapplication, and a total applied volume of 2.5ml. In the follow-up, 6 patients reported less pain in the right-hand side (i.e. side with greater dilution), with none noticing differences in the final results. Five described important degrees of improvement in sagging, and 1 reported moderate improvement.[36]

After each treatment, patients should be instructed to massage the area 5 times a day, for 5 minutes for 5 days [4,8,12,13,24,27,30] using emollient creams to minimize friction during massage. This procedure can be extended up to one month.[11] Massage ensures the distribution of the product and prevents the formation of papules and nodules.[5]

The interval between sessions is typically four [8,10,15] to eight[34] weeks, until the end of the treatment.[11] The total number of vials to be used is related to the surface area to be treated that requires volumization, [11,13] in addition to the patient's age, degree of lipoatrophy and sagging. Patients with more severe lipoatrophy may need 2 bottles per session 19 and up to 5 or more sessions to achieve the desired result, although most treatments require 1 bottle per session and 2 or 3 sessions.[19,22] According to Lacombe,[19] if the treatment is performed in the middle and lower third of the face, two vials are necessary. Some authors, like Goldman,[8] wait for an interval of 12 weeks after the 3rd session, in order to evaluate whether there is a need for additional treatment.

In order to increase tissular volume, the initial treatment yields a base with a new fibrosis matrix.[6] The final outcome will be achieved within a period varying from four to six months. [19] Due to the volume of the product's reconstitution, the patient will leave the practice with the appearance of having in fact undergonea filling procedure, with the understanding that such improvement will disappear in a few days and he or she should then wait for production of collagen to start in six to eight weeks.

Once volumization has been achieved, results can be maintained for three years or more.[19] According to Vleggaar,[32] PLLA appears to be stable for 30 to 40 months 23 after treatment. Salles et al.,[2] showed good results for 36 months in 40% of ten treated patients. According to the publication of Faces, 10 a prospective study of 290 HIV-seropositive patients undergoing treatment with PLLA, after two years 79% of them had Grade I (almost normal) in the James' scale, independent of phototype, age, or gender. In a 5-year retrospective follow-up study, Rendon 20 suggests that the duration of the results is dependent on the patient's age, initial dermal thickness and bone structure prior to treatment, with patients under 55-years-old presenting a prolonged duration.

Adverse reactions related to the use of PLLA, such as echymoses, hematomas, edema, papules, nodules, and granulomas, mainly appear at the sites of injection of the product. The reported incidence of papules ranges from 31-44% 10 in dilutions of 4ml or less; with higher rates—of around 13.9% or less—in dilutions greater than 5ml.[29,30,34]

Papules and nodules are mostly only palpable and not visible, and dependent on the application technique. They are related to large volumes injected superficially[37,38] or the non-interruption of the application before withdrawing the needle, 22 with the application of little diluted product[10,30,37,38] and use in areas with thin skin (such as the infraorbital,[18,37] perioral,[20] and temporal regions), and areas of hypermobility,[23] in addition to cases where massage is not performed after the procedure.[21,30] Intradermal injections should be avoided.[30] Sessions held at four to 6 week intervals 30 minimize the formation of nodules. Papules are usually transient and disappear spontaneously through the phenomenon of transepidermal elimination.[22] In the Faces publication, 10 76.9% of papules and nodules were resolved spontaneously after two years. In the experience of Sherman, topical retinoids (0.025%-0.1% tretinoin) and superficial chemical peels (glycolic, lactic, mandelic, or salicylic acids) can help resolve or prevent the formation of papules.

It is important to differentiate papules, nodules, and granulomas after treatment with PLLA. A nodule may be visible or not, painful or not, 9 hardened with a clear boundary between it andthe surrounding tissue, with a size that does not change up until it is reabsorbed, treated, or removed.[16] Typically, it only appears several weeks after injection, and[16] represents a PLLA grouping.[16] The coalescence of these particles can be broken with the fragmentation of the nodule and injection of saline solution (SS) using a Luer-Lok syringe, 1-3ml of 0.9%SS with 25G needle to hydrate and redistribute the particles, followed by aggressive massage, 16—all of which can be repeated weekly until improvement of the situation,[16,21,22] which resolves in 80% of cases. 2 Non-visible and untreated nodules tend to remain stable for two, 8 three, 32 or more years.

Although PLLA is an inert substance, it can still stimulate foreign body reaction.[18] The function of these reactions is to isolate and prevent the migration of particles that cannot be readily removed by phagocytosis and enzymatic degradation.[9]

Granulomas can be characterized by particle aggregates of chronic inflammatory cells forming nodules, typically of a few millimeters in diameter. What distinguishes granulomas from other components of the inflammatory response is a collection of macrophages and epithelioid cells, usually surrounded by lymphocytes. In granulomas, macrophages are modified into giant multinucleated cells.[9] Histologically, nodules consist of

fluid droplets or microparticles of various sizes that are: irregularly shaped; 7 birefringent under polarized light; 39 surrounded by a foreign body in a reactive state;[9,16] with macrophages and giant multinucleated cells[7,18,37] and few inflammatory cells.[17] Granulomas are delayed nodules, which appear several months after application, and which may be treated with intralesional corticosteroid of 0.02-0.04 ml triamcinolone.[16,22] These applications can be repeated at intervals of 2 to 4 weeks. If not resolved, they can be removed surgically. Goldman, 8 who has treated more than 1,000 patients with PLLA, makes it a practice not to leave non-visible nodules to disappear spontaneously, since the application of intralesional corticosteroids may cause dissolution of perinodular fat, making them more evident. As an alternative, he opts for a surrounding application of hyaluronic acid to make them less evident. The reported incidence of granulomas related to the use of PLLA is low: 0.01-0.1% (Vleggaar described six granulomas in 3,000 treated patients).[16]

Treatment of granuloma can also be carried out with the use of corticosteroid therapy 16 (orally with prednisone 60mg/day, 40 intralesionally with triamcinolone acetonide 40mg/ml every three weeks for a total of 1 to 10 applications, 28 or intramuscularly), minocycline[9,28,40] as an anti-inflammatory, immunomodulator and with antigranulomatous properties.[9] Another option is to use 5-fluorouracil[9,40] (50mg/ml) isolated or combined with 1mg/ml triamcinolone acetonide or 7mg/ml betamethasone, which can reduce the skin atrophyrate. 16,40 Another effective combination is 1/3 of 5-fluorouracil (1.6 ml), 1/3 of betamethasone (3.5 mg) and 1/3 lidocaine. 16 Vleggaar has reported success with intralesional injections of 0.4 ml of 5-fluorouracil with 0.6 ml triamcinolone acetonide (10mg/ml), weekly for 4 weeks, in addition to oral corticosteroids of 100 mg minocycline daily for 8 weeks.[16] In the beginning of the treatment, other authors use a combination of two antibiotics, such as second-generation cephalosporin and third-generation macrolide, for seven days.[28] Surgical excision is more difficult due to the absence of a clear boundary between the healthy tissue and tissue affected by the granulomatous reaction.[16,28] In 2008, Goldman reported 4 cases offemale patients who were all heavy smokers who had granulomas in the lip region and who had all been treated for 2 to 6 months with PLLA; each hadsubsequently undergone antibiotic therapy and intralesional corticosteroids—with one of them also undergoing drainage of multiple abscesses.[41]

In 2009, Alijotas-Reig et al.[17] published a report on adverse effects in 10 patients treated with PLLA where the following had occurred 15 months after receiving the application of poly-L-lactic acid: 3 patients with inflammatory nodules, 1 with papules and nodules, 5 with nodules and facial edema, and 1 with inflammatory nodules on the face and with erythematous papules in the arms and legs (with a histological diagnosis of sarcoid reaction). In the last case, the patient had undergone an implantation of hyaluronic acid and methacrylate 36 months before the application of PLLA. The patient was treated with hydroxychloroquine, prednisone, and ibuprofen. Although the time elapsed between these two procedures and the appearance of adverse effects after PLLA had been long, the question of whether this granulomatous reaction was caused by the interaction of the two lingers. In theory two or more different antigenic stimuli can increase the risk of abnormal immune response and produce immune-mediated adverse effects. In vitro, all bioimplants can cause a foreign-body reaction based on macrophage activation and induction of T-cells. Theoretically, the development of the collagen network coincides with the decrease in inflammatory reaction, however the so-called stable granulomas may evolve into a progressive granulomatous reaction after minor trauma or infections. In this clinical series, 2 of the patients who had nodules and edema had also been treated with permanent implants.

Other rare complications that need to be mentioned are: 1 case of amaurosis and one case of angioedema post-PLLA. The first refers to a 43-year-old HIV-seropositive man who received PLLA in the lateral nasal and periorbital regions, who had amaurosis caused by intra-arterial injection into the ophthalmic artery. This patient had undergone rhinoplasty, which can be an additional risk factor due to the impairment of the anastomoses of the ophthalmic artery.[42] The other is the case of a 59-year-old woman without previous history of allergies, then using lisinopril, who underwent application of PLLA in the face and of hyaluronic acid with lidocaine in the lips. Two hours later, the patient developed significant edema in the lips and perioral region, having being hospitalized and properly treated. In that case, it was not clear whether the angioedema was caused by histamine release (either due to the trauma linked to the needle or to the intradermal injection of the product) in individuals who were predisposed and in use of angiotensin-converting enzyme inhibitors, or whether it was caused by the cutaneous filling substances. The authors attributed it to the PLLA, for the patient had previously undergone another application of hyaluronic acid without any complication.[43]

There are several proposals of treatments adjuvant to PLLA aimed at obtaining harmonious aesthetic outcomes. If the treated area presents photodamage, the application of pulsed light or non-ablative fractional laser can be performed in the same session, provided it precedes that of the PLLA (in order to avoid contamination of the tips of the device with blood) 8 without increasing the risk of adverse effects related to the association.[12] Lowe 23 suggests the association of other treatments, such as the application of hyaluronic acid and botulinum toxin, laser resurfacing, and radiofrequency. Others[11,20] associate hyaluronic acid or calcium hydroxylapatite, provided the application procedures are performed with an interval of 30 days.

Several studies [11,12,13] show high rates of patient satisfaction after treatment with PLLA. Vleggaar reported that 95.1% of patients were satisfied with the results, while Hanke et al. and Salles reported 89.5% and 60.0% patient satisfaction, respectively.[11]

CONCLUSION

Poly-L-lactic acid is a safe and effective product for the volumization of the face, correction of unaesthetic scars, and for the treatment of sagging, with predictable and good aesthetic results, provided that it is properly prepared and used. ●

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Dermoscopy of pigmented lesions of the face: a diagnostic challenge

Dermatoscopia das lesões pigmentadas na face: um desafio diagnóstico

Diagnostic imaging

ABSTRACT

Dermoscopy of lentigo maligna on the face has reliable and well-tested parameters for its diagnosis. However, some benign lesions such as pigmented actinic keratoses have dermoscopic aspects that are common in malignant lentigo, making the correct diagnosis difficult. This fact often leads to unnecessary excisions of benign lesions. The present article discusses these morphological parameters in light of the dermoscopic analysis of the commonalities between lentigo maligna and pigmented actinic keratosis, also touching upon the aspects already described for the diagnosis of pigmented actinic keratoses.

Keywords: Dermoscopy; Hutchinson's melanotic freckle; keratosis, actinic; face.

RESUMO

A dermatoscopia do lentigo maligno na face tem parâmetros confiáveis e bem testados para sua diagnose. Algumas lesões benignas, como as queratoses actínicas pigmentadas, apresentam, contudo, aspectos dermatoscópicos comuns aos lentigos malignos, dificultando a correta diagnose. Isso muitas vezes leva a excisões desnecessárias de lesões benignas. Este artigo discute esses parâmetros morfológicos no escopo de analisar os pontos em comum entre lentigo maligno e queratose actínica pigmentada com a dermatoscopia, assim como coteja os aspectos já descritos para a diagnose das queratoses actínicas pigmentadas.

Palavras-chave: *dermoscopia; sarda melanótica de Hutchinson; ceratose actínica; face.*

Authors:
Mauricio Mendonça do Nascimento1
Danielle Ioshimoto Shitara2
Sergio Yamada1

[1] Physician Member of the Dermoscopy Group of the Department of Dermatology, Universidade Federal de São Paulo (UNIFESP)—São Paulo (SP), Brazil

[2] Graduate Translational Medicine Program Candidate, UNIFESP—São Paulo (SP), Brazil

Correspondence:
Dr. Mauricio Mendonça do Nascimento
Av. Ibirapuera, 2.097 / conj. 201
Cep: 04029-1000—São Paulo—SP
E-mail: maumennas@uol.com.br

INTRODUCTION

Dermatoscopic examination of pigmented lesions on the face differs from usual dermoscopy due to the absence of a pigmented network at this location. Instead, it observes a pseudo-network, and also there are some well-established parameters for the diagnosis of lentigo maligna (LM) in the face.[1] (Table 1) Pigmented actinic keratoses (PAK) on the face are usually a diagnostic pitfall in the differentiation of LM. The present article describes some cases of dermoscopic images of doubtful PAKs with LM findings, as well as typical LM and PAK findings, which may be of assistance in the differential dermoscopic diagnosis.

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Table 1: Dermoscopic findings of lentigo maligna 1
Asymmetrically pigmented follicular openings
Dark rhomboidal structures (brown or black)
Slate-gray globules
Slate-gray dots

COMMENTS

Both the LM (Figure 1) and the PAK (Figure 2) may have the same appearance, except for the dark blurs.[2] The literature has described dermoscopic parameters that suggest the diagnosis of PAK rather than that of LM, with a rougher surface, due to hyperkeratosis associated with this type of lesion, the presence of multiple lesions (sign of the surroundings), a more regular architecture of the dots, hypodense holes in the pseudonetwork or the "strawberry" pattern (Figure 3).[3-5] These aspects of the PAK have already been tested for their diagnostic validity against LM,[4,5] with a prominent "strawberry" pattern found in the PAK, but not in the LM.[4] Given that the dermoscopy consensus establishes that a single dermoscopic parameter does not allow diagnosis, it only has the potential for assisting in diagnosis. The examples of PAK described in the present article (Figure 2) indicate that the rough surface is not always present. The sign of the surroundings takes into account the fact that other keratotic lesions may be seen in the face with actinic damage, helping in the identification of the suspicious lesion, although malignant lentigines can be found in actinic skin. When the PAK does not have pigmented areas, (Figure 2) the presence of classical aspects of actinic keratosis can be of help (hyperkeratosis, reddened areas and the "strawberry" characteristic), however reddened areas arranged in rhomboidal layout around the follicle should raise suspicion of the LM diagnosis, as it has been described more recently.[4] The pigmentary patterns described for the dermatoscopic diagnosis of LM 1 (Table 1) have been published with diagnostic accuracy,[3-5] and therefore can provide guidance for the choice of the site to be biopsied in case of the suspicion of malignancy, however those patterns can be found in

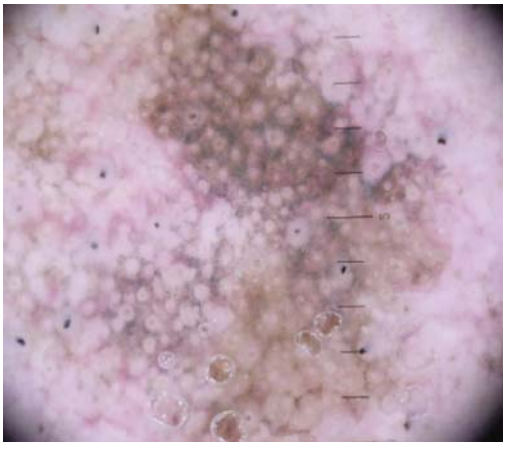
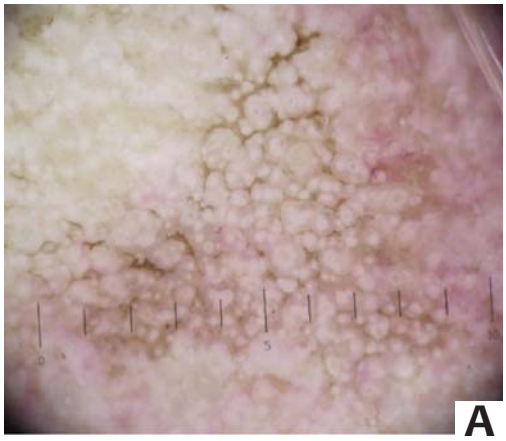
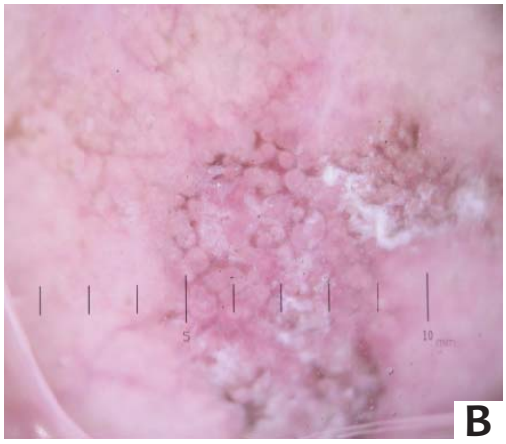
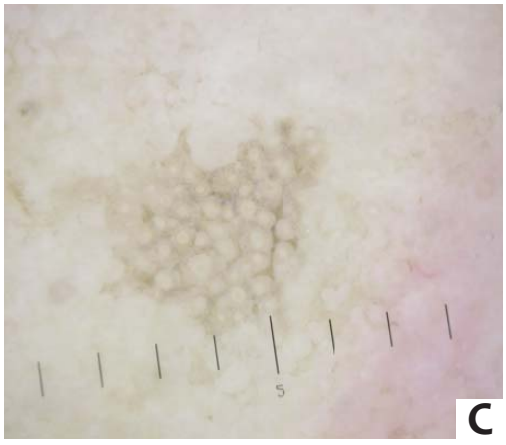


Figure 1: Lentigo maligna: 1 lesion with rhomboidal structures, annular pattern granular, pigmented follicular openings, assimetrical dots and slate-gray-globules







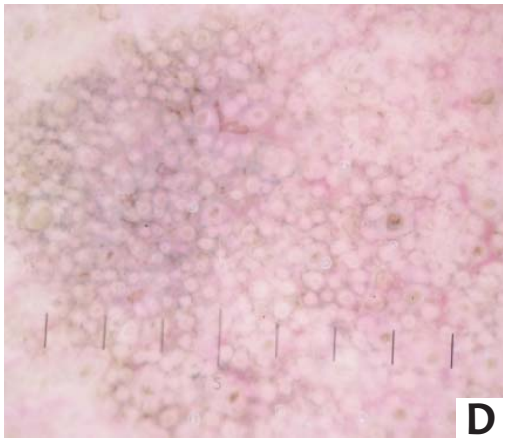


Figure 2: Pigmented actinic keratosis with dermatoscopic patterns similar to those of lentigo maligna: **A.** Rhomboid pattern; **B.** Rhomboid pattern and asymmetrical pigmented follicular openings; **C.** Asymmetrically pigmented follicular openings, annular-granular pattern and slate-gray dots; **D.** Asymmetrically pigmented follicular openings, annular-granular pattern and slate-gray dots.

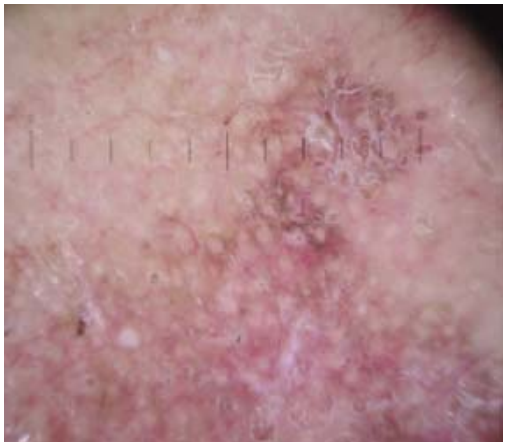


Figure 3: Pigmented actinic keratosis. This lesion shows typical patterns of actinic keratoses, such as the "strawberry" pattern (reddened areas with centers of follicles spared from involvement) as well as a roughsurface,in addition to patterns that resemble lentigo maligna, such as asymmetrically pigmented follicle openings, annular-granular pattern and slate-gray dots.

PAK (Figure 2). The examples presented show that the annular-granular pattern, as well as the slate-gray dots and globules, are possible in PAK (Figures 2 and 3). In this manner, a more regular distribution of dots and the absence of follicular openings asymmetrically pigmented are parameters that aid in the definition of PAK.[5] The presence of asymmetrical openings, however, does not exclude the possibility of PAK, in which case the biopsy will define the diagnosis.

CONCLUSIONS

Pigmented lesions on the face present a diagnostic pitfall when it is necessary to exclude the diagnostic possibility of LM—in particular because this diagnosis has dermoscopic aspects in common with PAK, leading to unnecessary biopsies. Both lesions can be found in all areas of the face, and their distribution is similar.[5] Thus, further studies are needed to validate the parameters for differentiating between PAK and LM. To date, in those cases, a skin biopsy remains the gold standard and is mandatory in order to exclude malignancy. ●

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Reconstrução completa de asa nasal com retalho de Spear após cirurgia micrográfica de Mohs no tratamento de carcinoma basocelular

Complete reconstruction of the nasal ala with a Spear's flap, following Mohs micrographic surgery in the treatment of basal cell carcinoma

Authors:
Frederick Hassin Sanchez[1]
Juliany Lima Estefan[2]
Ivan Diazgranados Fernandez[3]

[1] Head of the Centro de Cirurgia Micrográfica do Rio de Janeiro; Preceptor, Dermatologic Surgery Fellow Program, Hospital Federal de Bonsucesso (UFB)—Rio de Janeiro (RJ); Technical Manager, Clínica Catarinense de Dermatologia—Chapecó (SC), Brazil

[2] MSc in Clinical Medicine from the Universidade Federal do Rio de Janeiro (UFRJ)—Rio de Janeiro (RJ), Brazil

[3] Fellow in Dermatologic Surgery at the Hospital Federal de Bonsucesso (UFB); Fellow in Mohs micrographic surgery, Centro de Cirurgia Micrográfica do Rio de Janeiro—Rio de Janeiro (RJ), Brazil

RESUMO

O carcinoma basocelular é tumor maligno localmente invasivo, com maior incidência em caucasianos. A asa nasal é localização frequente dessa neoplasia. O tratamento de eleição é cirúrgico, sendo a cirurgia micrográfica de Mohs uma das técnicas indicadas, por apresentar grande acurácia no controle histológico das margens e alto índice de cura com baixas taxas de recidiva. Nessa localização se faz necessária não apenas a cura, mas também a tentativa da manutenção da estética facial. Descrevem-se cinco casos de amputação completa da asa nasal após cirurgia micrográfica de Mohs, seguida de reconstrução com retalho de Spear.

Palavras-chave: carcinoma basocelular; cirurgia de Mohs; retalhos cirúrgicos.

ABSTRACT

Basal cell carcinoma is a locally invasive malignant tumor, most frequently affecting Caucasian people. The nasal ala is a frequent site for this neoplasia. The treatment of choice is surgical, and Mohs micrographic surgery is one of the indicated techniques for presenting great accuracy in the histological control of margins and high cure rates with low recurrence rates. In this location, not only is a cure needed, but also the maintenance of facial aesthetics. The authors describe five cases of complete amputation of the nasal ala after Mohs micrographic surgery, with reconstruction using the Spear's flap.

Keywords: *carcinoma, basal cell; Mohs surgery; surgical flaps.*

Correspondence:
Centro de Cirurgia Micrográfica do Rio de Janeiro
Dr. Frederico H. Sanchez
R. da Assembléia, 10 / sala 2.807—Centro
Cep: 20011-000—Rio de Janeiro— RJ, Brazil
E-mail: fredhsanchez@gmail.com

INTRODUCTION

The nasal ala is a complex structure that is part of the nasal vestibule. It has respiratory function: it filters,moistens, and warms the air—allowing it to reach the lungs in addition to assisting in the phonation process.[1] This process is possible thanks to the anatomical structure of the nasal ala, which is composed of dense connective tissue and part of the alar cartilage, which provides support to it and prevents it from collapsing during inspiration (valve movement). The integrity of the nasal ala is crucial for maintaining the contour and aesthetics of the face and nose, the latter constituting one of the most prominent and central structures.

Basal cell carcinoma (BCC) is the most common malignant tumor in the world 2 and has as its main risk factor expo-

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sure to the sun.[3,4] Most cases occur in photo-exposed body sites[5] and its frequency in the face ranges from 27.5-91.1%.[5] Its most common form of occurrence is the nodular-ulcerative type,[5] which presents clinically as an erythematous-pearly papule or nodule with telangiectasias, possibly with a central ulceration.[2] Its occurrence increases in the elderly.[3,4] About 25.0% of BCCs occur on the nose.[6] The nasal ala is exposed to ultraviolet radiation daily, resulting in a high prevalence at that site.

Several therapeutic modalities are described in the literature for the treatment of BCC. Among them, Mohs micrographic surgery (MMS) stands out for allowing a rigorous histological control of surgical margins, with a high cure rate and low recurrence rates.[7]

In most cases the tumors are small or superficial and do not compromise the full thickness of the nasal ala. When tumors are large, infiltrating, or recurring, the compromise can be complete, including the nasal mucosa (Figure 1) and may lead to partial or total amputation of this structure, having a great psychological impact on the patient. Its surgical reconstruction poses a challenge to the surgeon, who should prioritize the oncologic cure, preserving the functionality and aesthetic aspect whenever possible.

METHODS

The present article describes a series of five cases, each involving complete amputation of the nasal ala after treatment of BCC with MMS, and which were reconstructed using the reverse Spear's nasolabial flap, also known as the "somersault" flap. The authors' objective is to describe the technique in detail, demonstrating the surgical applicability of this type of reconstruction, its advantages, difficulties, and results.

A number of techniques are described for the total reconstruction of the nasal ala, most of them including the use of cartilage grafts to allow tissue support and prevent the "valve" movement during inspiration. The flap described by Spear et al. in 1987 [8]—and more recently published in detail by Cook,[8] allows the complete reconstruction of the nasal ala, maintaining its structural integrity without cartilage grafts and providing contour to the structure with satisfactory cosmetic results in a single surgical event. The decision to use the "somersault" flap is made based on the examination of the donor area in the nasogenian fold and cheek. This area should have enough skin for preparing the flap and for the primary closure, with minimal actinic damage. It should be thoroughly evaluated before surgery, for when it is "folded" it will end up occupying a location that is difficult to assess. Therefore, before choosing this technique, the potential for development of cutaneous neoplasms in the nasal vestibule should be considered.

The Spear's flap is prepared based on the detachment of the cutaneous flap from the nasogenian fold ipsilateral to the amputated nasal ala. A subcutaneous pedicle is left in order to take advantage of the vascularity of that region (described by Hebert[8]), which is supplied by the angular artery (Figure 2). The proximal third of the flap is lifted in the alar base and the proximal skin is used to reconstitute the interior area of the nasal ala, with its edges sutured to the remaining tissues of the nose. The distal 2/3 of the flap is folded over itself, reconstituting the free border and the external part of the nasal ala. Intradermal suture is carried out between the two parts of the flap, and the external part is adjusted so as to cover the entire surgical defect. The border of the flap is adjusted and sutured and the primary closure of the donor area is carried out. Nasal packing is recommended for 15 days in order to provide support for the shape of the nasal ala and prevent the retraction of the flap.[8,9]

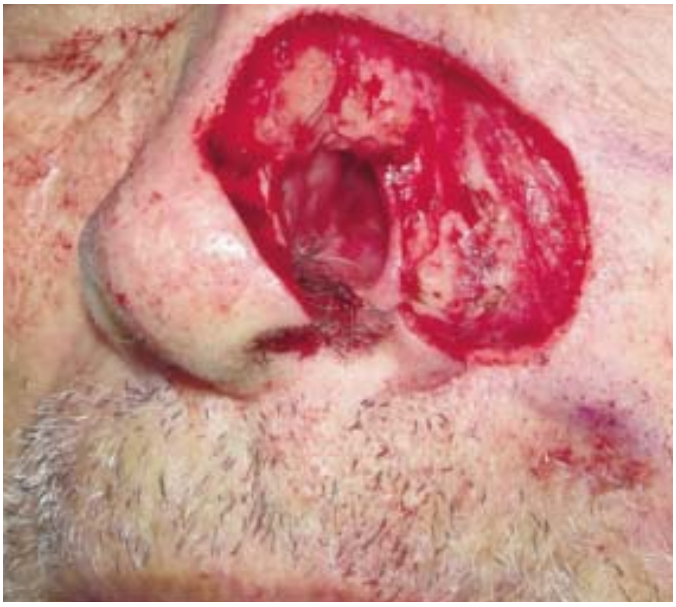

Figure 1: Nasal ala's full-thickness defect

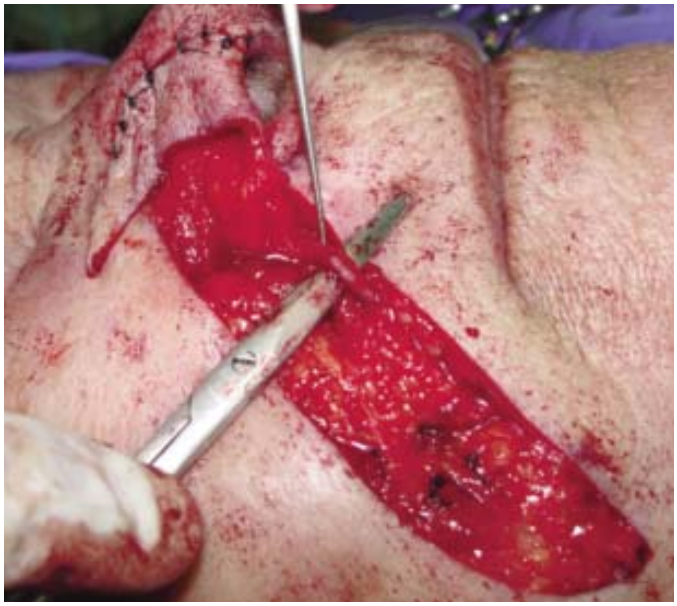

Figure 2: Angular artery and a part of the flap already folded over itself

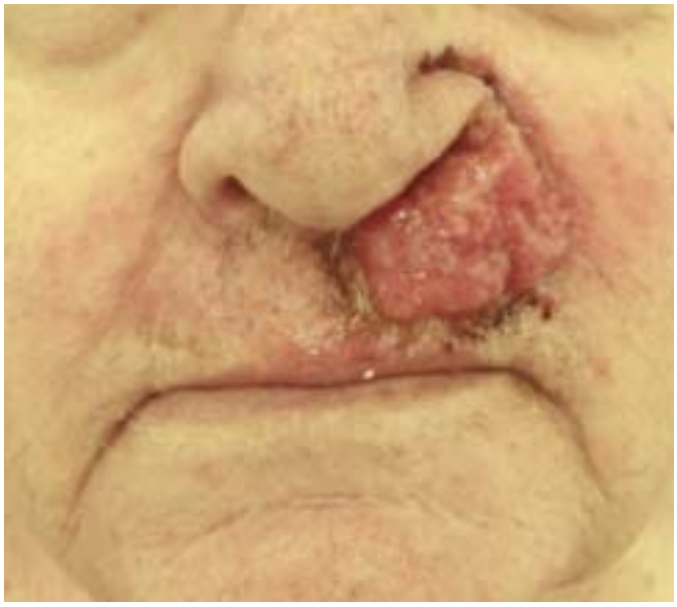

Figure 3: Lesions that extend beyond the nasal ala

All cases selected by the authors involve tumors of the nasal ala that were operated on at a MMS specialist center from July 2010 to April 2012.

RESULTS

During this period, 15 patients who presented with perforation of the mucosa and a transfixing of the entire thickness of the nasal alaunderwent surgery. Of these, 10 presented loss of the distal part (free border), corresponding to a complete amputation; 5 underwent surgical reconstruction with Spear's flap and were therefore selected for the present study.

Two patients had lesions that extended beyond the nasal ala (Figure 3), and therefore underwent other complementary methods for closing the surgical wound. In threecases, the authors recommended subsequent procedures for the refinement of the flap in order to achieve a better cosmetic result (Table 1). One of the patients had beard hairs transferred with the flap and was referred for laser epilation post-operatively.

In cases requiring a second surgical event, the authors aimed at correcting the asymmetry of the nasal alae, caused by the greater thickness of the flap. In one patient,thisthickening was corrected with direct corticosteroid infiltration into the flap.

All patients had their nasal ala function preserved, and none showed the "valve" phenomenon during inspiration (Figure 4).

DISCUSSION

BCC is a common tumor in the nasal ala. MMS is the method of choice for the treatment of invasive or recurrent tumors in this region. Amputation of the nasal ala may be required for the complete excision of the tumor, resulting in a difficult to correct surgical defect.

The Spear's flap allows the complete reconstruction of the nasal ala, maintaining its structural integrity and providing contour to the nasal ala with satisfactory cosmetic results. Although this reconstruction was originally described as a single surgical event, in some cases a second procedure is indicated for refining the flap and improving the aesthetic outcome.

Given the complexity of the surgical defects, the cosme-

Table 1: Description of cases

Diagnosis	Size	Final surgical defect	Reconstruction type	Complication	Procedure for refining the flap in order to improve the cosmetic outcome
1 Recurrent BCC	1.2x1cm	2.4x2cm	Spear's flap + skin graft	Necrosis of the Flap's distal part (smoker)	No
2 Primary sclerodermiform BCC	1.3x1cm	1.8x1,5cm	Spear's flap	No	No
3 Infiltrative BCC	2.3x1,5cm	3x2.2cm	Spear's flap	No	Corticoid injection
4 Recurrent infiltrative BCC	1.1x1cm	2.2x2cm	Spear's flap	No	Refinement surgery and laser hair removal

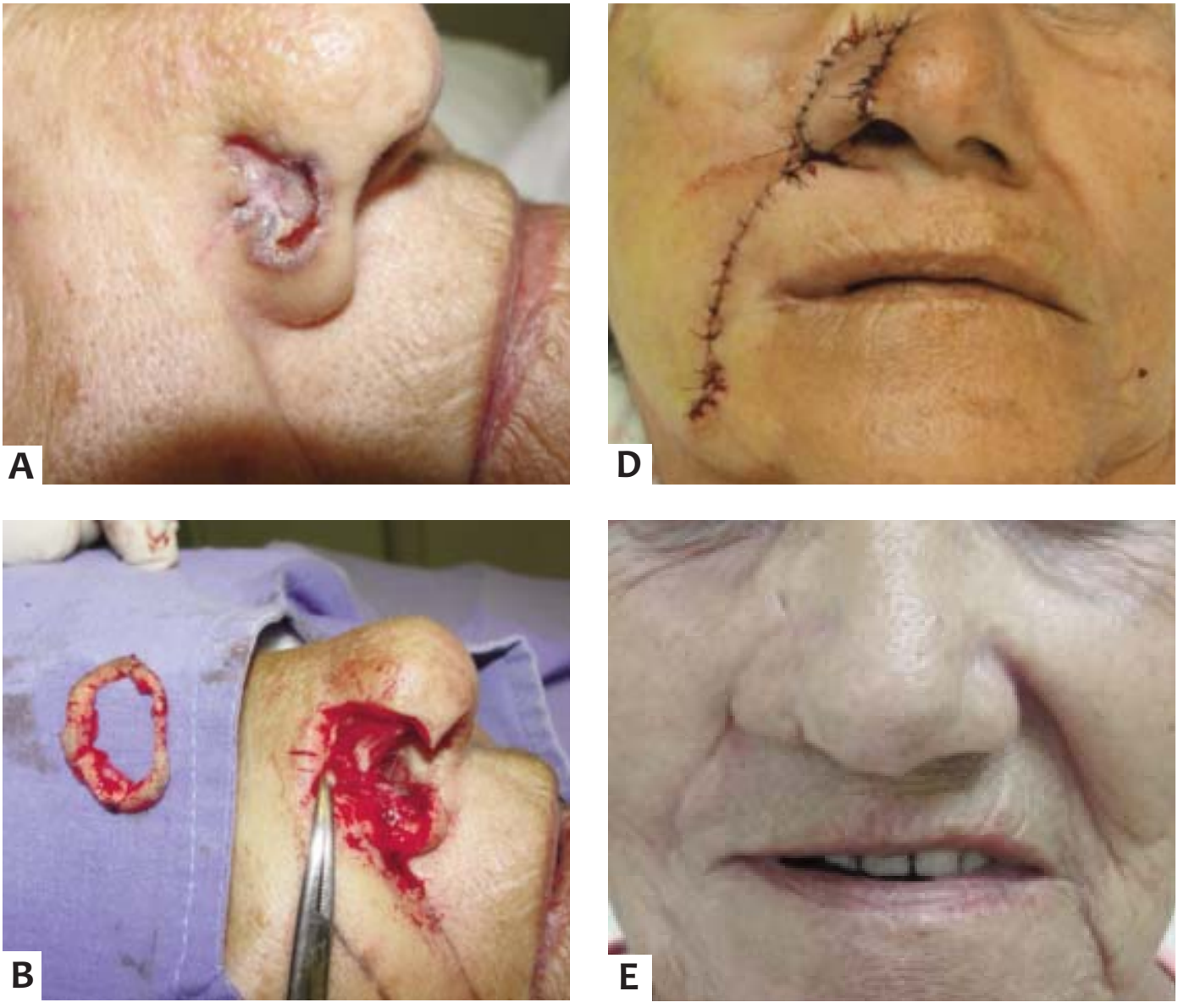

Figure 4: (A to E): A sclerodermiform BCC series, and the results before, during, and after

tic outcome was already deemed satisfactory in the studied patients by the first surgical event—even in the cases that underwent a second procedure for refinement.

CONCLUSION

The complete reconstruction of the nasal ala is a challenge, and the Spear's flap is a good option for ensuring structural integrity to the tissue and for preventing the "valve" movement without need for a cartilage graft, and in addition it confers satisfactory cosmetic resultsaftera single surgical event. ●

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Case Reports

Surgical approach to True Gynecomastia

Abordagem Cirúrgica da Ginecomastia Verdadeira

Authors:
Érico Pampado Di Santis[1]
Leopoldo Duailibe Nogueira Santos[2]
Sheila Martins Di Santis[3]
Yuri Vieira Dair[4]
Marcia Lanzoni Alvarenga Lira[5]

1 Physician collaborator at the Department of Dermatology, Hospital Universitário de Taubaté / Universidade de Taubaté (HUT / UNITAU)—Taubaté (SP), Brazil

2 Specialist Candidate, Department of Dermatology, (HUT / UNITAU)—Taubaté (SP)

3 Physician at private practice—São Paulo (SP), Brazil

4 Physician at private practice—São Paulo (SP), Brazil

5 Assistant Professor I, Special Pathology Discipline, Department of Medicine, Universidade de Taubaté (UNITAU)—Taubaté (SP), Brazil; Dermatopathologist Physician, Department of Dermatology, (HUT / UNITAU)—Taubaté (SP), Brazil

Correspondence:
Dr. Leopoldo Duailibe Nogueira Santos
R. Dr. Neto de Araujo 101/112—Vila Mariana
Cep: 04111-000—São Paulo—SP, Brazil
E-mail: leops8@hotmail.com

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ABSTRACT

True gynecomastia is a benign proliferation of the glandular tissue of the male breast. In general, management is conservative, however if there is development of fibrosis after the inflammatory phase, surgery is recommended. The present article describes a case of true gynecomastia with symmetrical enlargement of the breasts since adolescence. In light of this diagnosis, corrective surgery was performed with tumescent anesthesia and exeresis in block of the mammary gland.

Keywords: gynecomastia; ambulatory surgical procedures; dermatology; anesthesia, local.

RESUMO

A ginecomastia verdadeira é uma proliferação benigna do tecido glandular da mama masculina. Em geral, o manejo é conservador, porem se houver o desenvolvimento de fibrose após a fase inflamatória, preconiza-se a cirurgia. Relata-se um caso de ginecomastia verdadeira, em homem com aumento simétrico das mamas desde a adolescência. Frente a este diagnóstico foi realizada cirurgia corretiva com anestesia tumescente e exérese em bloco da glândula mamária.

Palavras-chave: *ginecomastia; procedimentos cirúrgicos ambulatórios; dermatologia; anestesia local.*

INTRODUCTION

True gynecomastia (TG) is a benign proliferation of glandular tissue in the male breast. There are three peaks of incidence: in newborns, adolescents, and middle-aged adults. Gynecomastia in childhood is transient and subsides after two or three weeks, when the level of maternal estrogen in the newborn decreases. In adolescence, there is a peak between 13 and 14 years, decreasing on average in 18 months. In those cases, persistence of the condition is rare, however it may linger after puberty, continuing into adulthood. The third peak occurs in men between 50 and 80 years old.

Mammary tissue is sensitive to serum levels of free estrogen. The augmentation of the tissue is related to a higher absolute level of free estrogen, or relative to the level of testosterone, resulting in greater stimulating action, which causes its growth.[1-3]

The most common cause of gynecomastia in adolescence is physiological. In adults, the main causes are: persistence of juvenile gynecomastia and the idiopathic form, followed by those resulting from the use of certain drugs—such as spironolactone, nifedipine, estrogen, anti-androgen, and efavirenz. There are other causes of lesser expression, like certain diseases—such as cirrhosis, hypogonadism, and testicular tumor, among others.[1,2]

TG should be differentiated from pseudogynecomastia, which occurs due toan increase in theadipose tissue of the breast. Causes include obesity and lipodystrophy, including that triggered by a patient's treatment with antiretroviral therapy. In these cases, it is not possible during palpation of the breast to verify a subareolar mass—as is the case in TG. Regarding neoplastic lesions, breast cancer is an important differential diagnosis. In general, it arises as a mass eccentric to the nipple, adhered to deep planes and with a hardened consistency.

The diagnosis of TG is primarily carried out through detailed anamnesis and physical examination. In inconclusive cases, there is a need for additional tests, both laboratorial and image based, in order to exclude tumors, among other causes.

The treatment will depend on the cause,the duration of the clinical condition since onset, and the level of disruption the condition presents to the patient. Should it be secondary to the use of any medication, the first measure is to suspend the suspected drug. The time since onset is important due to the fact that, initially, the tissue is in the inflammatory phase. In such cases, it is possible to choose either a conservative approach (given that there is spontaneous regression in most cases) or to introduce medications (such as androgens, selective modulators of estrogen receptors and aromatase inhibitors) to accelerate the involution of the inflamed mammary tissue. Nevertheless, after the initial inflammatory period, the tissue becomes fibrotic, requiring surgical treatment. The excision of mammary tissue is performed as a surgical procedure. If there is excess adipose tissue associated with it, it is possible to administer supplementary liposuction treatment.[5]

CASE REPORT

A 26-year-old male patient complained of a "lump" in the breasts since adolescence. Local symptoms were denied. Dermatological examination evidenced a symmetrical increase in breast volume (Figure 1). On palpation, it was possible to notice dense fibroelastic tissue in the subareolar region. The patient reported worsening of the increase in size after starting the use of injectable medication (was unable to refer the drug type) during training at the gym, as well as dietary supplements aimed at gaining muscle mass (creatine and protein).In addition, the patient used 1 mg finasteride per day for treatment of androgenetic alopecia—the drug was initiated in the presence of an already established gynecomastia picture.

Thus, an evaluation carried out by an endocrinologist was indicated, when supporting tests were requested, including prolactin, serum testosterone, liver biochemistry, renal function, thyroid evaluation, FSH, LH, lipid profile, fasting blood glucose, insulin, and scrotal ultrasonography. All tests came back within normal parameters, with tumoral or secondary causes (such as kidney or liver disease) being excluded. Breast ultrasonography was also requested, revealing a significant increase in fibroglandular tissue. In light of the above, a case of true adolescent gynecomastia with persistence in adulthood, probably exacerbated by the use of injectable drugs, was diagnosed. Due to the aesthetic discomfort experienced by the patient, surgery to decrease the breast size was indicated.

Surgery was performed under local anesthesia with tumescent solution in the proportion of 0.9% saline solution (200ml), 2% lidocaine (20ml), sodium bicarbonate (8 ml) and epinephrine (1ml). A decision was made for a semicircular periareolar incision, followed by the block exeresis of excess mammary gland (Figure 2). Suture was performed with 5.0 monofilament nylon thread. Compressive dressing with elastic mesh was used for 48 hours.There were no post-operative complications. A satisfactory cosmetic result can be noticed three months after the surgery (Figure 3).

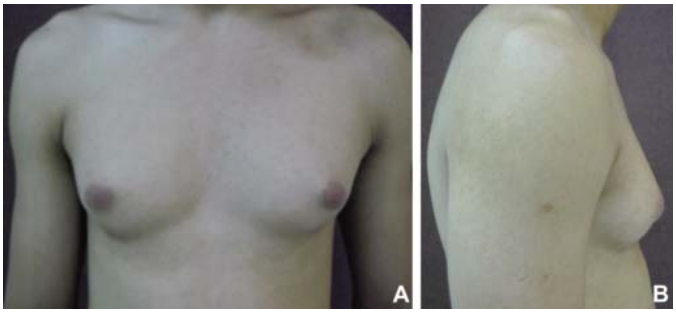

Figure 1: A (anteroposterior) and **B** (profile): symmetrical increase in the volume of the breasts

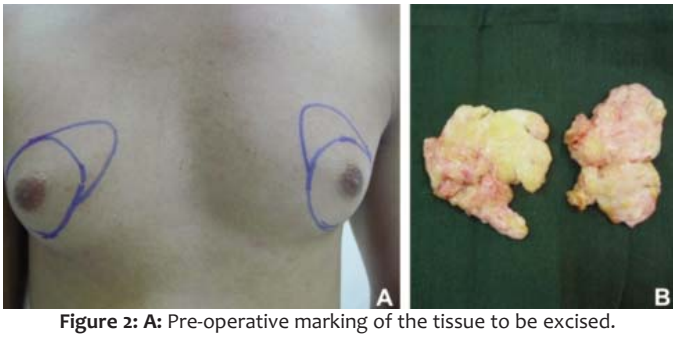

Figure 2: A: Pre-operative marking of the tissue to be excised. **B:** Excised tissue of each breast

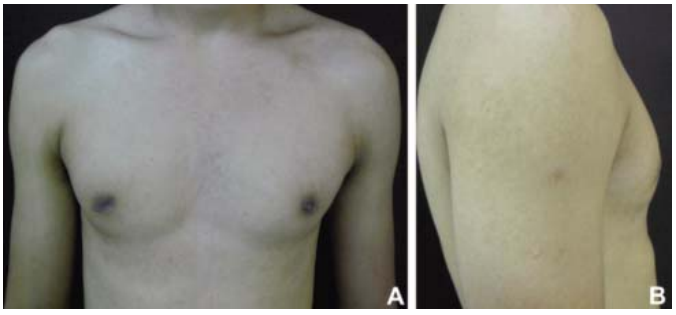

Figure 3: A (anteroposterior) and **B** (profile): three months post-operative; reduction of the breasts

The excised tissue was sent for histological examination, revealing breast parenchyma with dense stromal tissue (and thick collagen fibers), some adipocytes, ducts with ectasia overlaid with simple cuboidal epithelium without atypia, and absence of inflammatory infiltrate (Figure 4)—all confirming the diagnosis of true gynecomastia in the fibrotic phase.

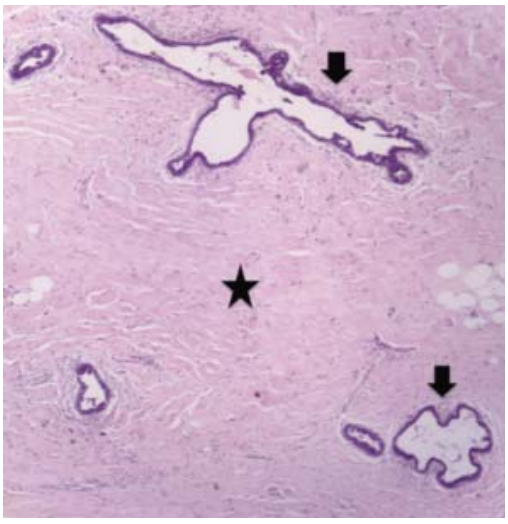

Figure 4: Histological analysis—Arrows: ducts with ectasia. Star: dense stroma with thick collagen fibers

DISCUSSION

The description demonstrates a typical case of true gynecomastia persistent in adulthood. The hypothesis of TG in adolescence is strengthened by the age of onset in the studied patient—i.e. the second peak of incidence of true gynecomastia. Nevertheless, it was not possible to rule out exogenous causes (drugs).

As there was no regression after 18 months, the mammary tissue evolved from the inflammatory to the fibroticphase. In such cases, the only treatment option is surgical. According to the Moschella and Cordova's morphological classification of gynecosmastia, the patient was in Grade II, indicating hypertrophy of all structural components of the breast, with the nipple-areolar complex located above the breast fold. In such cases, surgical treatment may be associated to liposuction and glandular resection. Regarding the options for incision, these are: periareolar semicircular, intra-areolar, the pull-through approach, or endoscopic.[6]

After hormonal investigation and interruption of injectable medication, a decision was made for the excision of glandular tissue, discarding the need for liposuction, once there was only a small amount of adipose tissue. In this way, there was no removal of excess tissue, which could have resulted in the flattening of the chest, local irregularity or even concavity. Finally, a good cosmetic result was obtained. ●

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Case Reports

Uso de hialuronidase em complicações causadas por ácido hialurônico para volumização da face: relato de caso

The use of hyaluronidase in complications caused by hyaluronic acid for volumization of the face: a case report

Authors:
Simone Ramos Nogueira Guerra Neri[1]
Flavia Alvim Sant'Anna Addor[2]
Meire Brasil Parada[3]
Sergio Schalka[4]

[1] Dermatologist Physician, Ambulatory Service, Medcin Instituto da Pele—São Paulo (SP), Brazil

[2] Dermatologist Physician; Technical Director, Clinical Research Laboratory, Medcin Instituto da Pele—São Paulo (SP)

[3] Dermatologist Physician; Collaborator at the Cosmiatry, Surgery, and Oncology Unit, Universidade Federal de São Paulo (UNIFESP)—São Paulo (SP), Brazil

[4] Dermatologist Physician; Clinical Director, Medcin Instituto da Pele—São Paulo (SP)

Correspondence:
Dr. Flavia Alvim Sant'Anna Addor
R. Dr. Carlos de Moraes Barros, 304
Cep: 06544-540—Osasco—SP, Brazil
E-mail: flavia@medcinonline.com.br

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RESUMO

O uso do ácido hialurônico (AH) injetável no preenchimento de rugas e volumização facial está consagrado na prática dermatológica. O manejo de suas complicações, embora raras, deve ser do conhecimento do dermatologista. No uso dos preenchedores de aplicação mais profunda, a formação de nódulos pode ocorrer, e a conduta é similar à utilizada para preenchedores mais superficiais e menos viscosos. O uso da cânula mais fina possivelmente reduz esse risco, sobretudo em áreas de derme mais fina.

Palavras-chave: ácido hialurônico; acidentes; derme.

ABSTRACT

The use of injectable hyaluronic acid (HA) in wrinkle filling and facial volumization is well established in the dermatological practice. While complications are rare, techniques for their management should be known by the dermatologist. Nodules may occur with the use of deeper application fillers, and the treatment is similar to that used for the more superficial and less viscous fillers. The use of a thinner cannula may reduce this risk, especially in areas where the dermis is thinner.

Keywords: *hyaluronic acid; accidents; dermis.*

INTRODUCTION

Hyaluronic acid (HA) based fillers have been the most frequently used filling substances in recent years for the treatment of wrinkles and folds, due to their practical application and good safety margins, in addition to their effects (which are immediately visible after application and have a long-term duration). The biocompatibility of HA and its relatively simple-to-learn technique has helped it become a frequent choice when addressing wrinkles and other alterations of the skin relief, especially on the face, but also in other areas such as the dorsum of the hands.[1]

More recently, HA has been used in facial volumization, for correcting the loss of fat pads due to aging, especially in the malar and mandibular areas. For these indications, the choice of HA has some particularities that differentiate it from its use for simple filling procedures. These include particle size, more vis-

coelasticity, different length of the polymer chain, and the type and density of the crosslinker, all of which play a part in obtaining the best result in the accommodation of the product into the skin, without the risk of migration from the injection site.

The application must be carried out in the supraperiosteal or deep subcutaneous planes; and cannulas—which reduce the risk of bleeding—can be used.[2] Although all commercially available options for HA volumization present good tolerance, there is no filling substance available that is totally devoid of risk and even seasoned professionals can come across immediate reactions, such as erythema and bleeding, or others that manifest later, such as nodulations.[3]

The management of complications must be well known to the specialist physician, for while they may also result from poor technique, accidents in the application and anatomical variations may contribute to their onset.

CASE REPORT

A thirty-five year-old female patient underwent a filling procedure with HA (Juverderm Voluma®, Allergan) aimed at facial volumization through the retroinjection technique in the zygomatic arch region. An 18G, 70mm cannula was used without immediate complications (erythema or echymosis) and no particularities regarding the appearance. The patient was instructed to return within 15 days.

After that period, the patient returned with a pearly nodule 3cm in diameter, which extended from the zygomatic arch to the infraorbital region on the left-hand side, as well as with a deeper nodule1cm in diameteron the right-hand side infraorbital region. The patient reported mild pain on palpation of both nodules; nonetheless there were no phlogistic signs. The diagnostic hypothesis was that of the formation of nodules due to the accumulation of the filler itself, while the left-hand side, more medially, showed signs consistent with the Tyndall effect ("blue bump"). (Figure 1)

The patient was advised to use Prednisone 10mg every 12 hours for three days and apply warm and cold compresses alternately, for 15 days. As after that period there was no improvement seen at the reassessment visit, a decision was made for the application of lyophilized hyalurodinase (HYALOZIMA®/ 2,000UTR) diluted in 5ml, resulting in 400UTR/ml hyaluronidase doses; 0.3 ml and 0.1 ml were applied in the left and in the right-hand side of the patient's face, respectively. The injection was applied exactly within the nodules, pinching and isolating them with the thumb and forefinger. The patient was reevaluated after 15 days, with complete regression of the nodules and a satisfactory appearance, without signs of atrophy or asymmetry (Figure 2).

DISCUSSION

The formation of nodules after injection of HA fillers, due to its accumulation, is described as an early and relatively rare complication, among other observed adverse effects, for the total percentage of complications described with HA fillers is already low (less than 1%). [4]

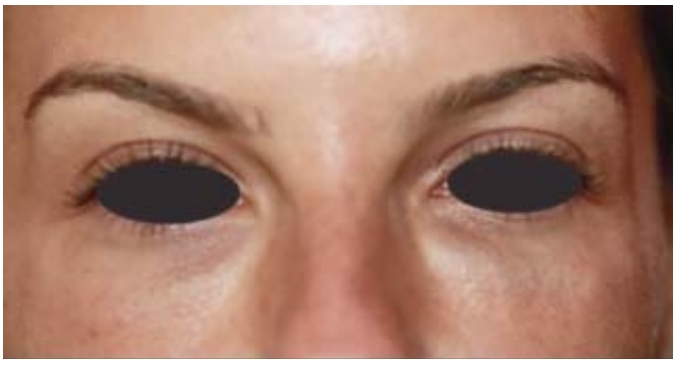

Figure 1: Patient on the 15th day after the filling procedure. Bilateral nodulation; left infraorbital tyndalization can be noted.

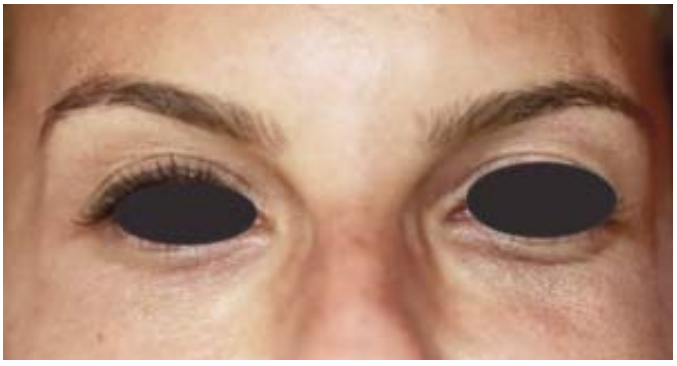

Figure 2: Patient 15 days after the application of hyaluronidase. The complete regression of the nodules without atrophy or asymmetry can be noted.

Although nodules resulting from the accumulation of the product itself do not necessarily constitute a serious complication, they are nonetheless aesthetically undesirable, and treatment must be agile and careful in order to preserve the aesthetic outcome—especially in the presence of the Tyndall effect ("blue bump").

Nodules must be differentiated from granulomatous reactions, which are most often more delayed in onset. This might, however, be clinically difficult, particularly in cases of deep nodules, demanding nodule biopsy with pathological examination in order to differentiate the type of adverse reaction that has occurred. [5,6]

As volumization filling procedures are applied more deeply, in theory there would be reduced risk of superficial nodules, however in areas of very thin dermis—such as in the periorbital and upper malar regions—the risk of nodule formation may increase. The use of thinner cannulas, such as 21G or 22G, can also assist in the homogeneous aspect of the filler, or in the use of less dense fillers, with lower visco-elasticity or smaller particule size. [7]

Tyndalization is described in reference to the Tyndall effect, which occurs when the filler has been applied too superficially, and a bluish hue is observed in the overlying skin, obser-

ved through the thinner skin's transparency. That result is unaesthetic and can be seen even without palpation.

For correcting nodules and granulomas, local application of hyaluronidase is the treatment of choice; its use leads to faster and superior results than those obtained with the use of oral or injectable corticosteroids.

Hyaluronidase acts by reversibly depolymerizing existing HA around the cells of the connective tissue, thus temporarily reducing that tissue's viscosity and making it more permeable to the diffusion of liquids. Based on this mechanism of action, hyaluronidase started to be used in cases of complications and/or adverse reactions as a treatment option to promote the degradation of injected HA, with resulting improvement. In Brazil, there is availability of Hyalozima® 20,000UTR (Apsen), which after diluted in the solvent that accompanies the product, presents 4,000UTR / ml. [8,9] Its use, however, should be administered very carefully in order to avoid excessive acid hydrolysis of HA, clinically entailing a depressed and atrophic appearance. Therefore, all dermatologists who perform filling procedures should master the application technique.[10]

The preparation should be carried out as follows: mix the entire contents of the diluent (5ml) with lyophilisate powder, in the vial. After the dissolution in complete, aspirate the contents and apply the minimum possible dose (0.1 to 0.2 ml per point), in the area where the HA is intended to be degraded. If necessary, repeat the application 10 to 15 days later. The remainder must be totally discarded and should not be stored and applied under any circumstances. This technique is similar to that of Brody, who suggests a five-minute interval between applicationsin order to observe any swelling, due to a rare but possible hypersensitivity to thedrug. In Dermatology, Crocco et al. corroborated this use in a recent article reviewing the complications of filling procedures.[11]

The necessity and usefulness of skin testing are questionable, due to its allergenic power.[12]

There are several brands of hyaluronidase available in the United States, however with different concentrations (Liporase,® Inno,® Hydase.®) In Brazil there is only one (Hyalozima®), and the use as described in the present study is considered off label.

CONCLUSION

The cautious use of hyaluronidase has consolidated itself in clinical practice as an effective drug in the management of nodules and granulomas arising from the application of HA, both in the case of superficial fillers and in the use of volumization substances.

The main focus of the authors in the present article is to highlight the fact that the use of hyaluronidase for degrading HA requires good technique and management by a dermatologist, as well as abiding by best practices and information, since there is no consensus on the use of this enzyme.

The type of complication described in the present article—which seems to happen more frequently in practice than the literature indicates—should be addressed promptly by the dermatologist, with a high probability of having favorable outcomes in most cases. ●

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Frontal advancement flap for the reconstruction of the nasal dorsum in a single surgery event: a study of two cases

Retalho de avanço frontal para reconstrução do dorso nasal – cirurgia em tempo único: estudo de dois casos

Authors:
Rubens Pontello Junior[1]
Roger Nabor Kondo[2]
Paul Muller Ramos[2]
Ricardo Pontello[3]

[1] Dermatologist Physician; Assistant Professor of Dermatology, Hospital Universitário Regional do Norte do Paraná da Universidade Estadual de Londrina (UEL)—Londrina–Paraná (PR), Brazil

[2] Dermatologist Physician in Londrina—Paraná (PR), Brazil

[3] Dermatology resident Physician at the Hospital Federal de Bonsucesso (HFB)—Rio de Janeiro (RJ), Brazil

Correspondence:
Dr. Rubens Pontello Junior
R. Professor João Candido, 1.515, sala 501
Cep: 86010-610—Londrina—PR, Brazil
E-mail: rubensjr@pontello.com.br

ABSTRACT

Skin cancer is the main neoplasia in both men and women. Basal cell carcinoma is the primary type of head and neck tumor, comprising 25% of nasal tumors. The treatment of choice is exeresis, which often presents a challenge to the dermatologic surgeon, who must achieve an oncologic cure along with a good aesthetic result. The options for nasal reconstruction are diverse, and some are high in complexity, preventing their common use. The authors present the reconstruction of the nasal dorsum using a flap from de glabellar area, a safe procedure with low surgical complexity and performed in a single step, making it a good option for large lesions of the nasal dorsum.

Keywords: *surgical flaps; nose; carcinoma, basal cell.*

RESUMO

O câncer cutâneo é a principal neoplasia tanto em homens quanto em mulheres. O carcinoma basocelular é o principal tumor de cabeça e pescoço, perfazendo 25% dos tumores nasais. O tratamento de eleição é a exerese, o que muitas vezes constitui um desafio ao cirurgião dermatológico, devendo associar cura oncológica com bom resultado estético. As opções para reconstrução nasal são variadas, algumas com alta complexidade, inviabilizando sua utilização corriqueira. Apresentamos neste artigo a reconstrução do dorso nasal com retalho da área glabelar, procedimento seguro, de baixa complexidade cirúrgica, realizado em única etapa, constituindo boa opção para grandes lesões do dorso nasal.

Palavras-chave: retalhos cirúrgicos; nariz; carcinoma basocelular.

INTRODUÇÃO

A reconstrução nasal foi um dos primeiros procedimentos cirúrgicos praticados pela humanidade; seus primeiros registros são datados do Papiro Cirúrgico de Edwin Smith, no antigo Egito, em 3000 a.C. Segundo esse papiro,ela já era praticada por sacerdotes 30 séculos antes da era cristã. Em 600 a.C., Sushruta descreve no livro sagrado dos hindus a reconstrução do nariz com retalho frontal e geniano.[1,2]

As principais indicações clinicocirúrgicas das reconstruções nasais são as retiradas de tumores, em especial, carcinoma basocelular (CBC) e carcinoma epidermoide.[2,3] Outras causas menos frequentes podem ser lembradas, como radiodermite crônica, infecção e traumatismo. O tratamento cirúrgico das neoplasias deve ser norteado pela retirada total do tecido acome-

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Conflict of interest: None

tido, prezando a funcionalidade e a estética do nariz, e objetivando a cura do paciente.

Há ampla variedade de retalhos com o propósito da reconstrução nasal. O retalho de avanço glabelar é boa opção após a retirada de tumores que acometem o dorso do nariz sem possibilidade de fechamento primário bordo a bordo.

RELATO DOS CASOS

Paciente 1

Mulher de 84 anos, apresentando CBC confirmado por biópsia prévia, com 1,4cm no maior diâmetro, no dorso do nariz. Após demarcação com margem de 4mm e anestesia local infiltrativa, procedeu-se à exerese em bloco,em formato retangular, e com a incisão acompanhando os limites da subunidade cosmética do dorso do nariz até região glabelar (Figura 1). Foi feito a seguir o descolamento da pele adjacente à ferida, no dorso nasal e na região glabelar (Figura 2), seguindo-se sutura com pontos de ancoragem com fio de náilon 5-0 e pontos simples, utilizando náilon 6-0, no restante da ferida (Figura 3). Em uma semana foi possível a retirada total dos pontos, sem sinais de deiscência. Após seis meses observou-se bom resultado cosmético, (Figura 4) com plena satisfação da paciente.

Paciente 2

Na segunda paciente (79 anos), apresentando CBC no dorso do nariz, com 1,1cm no maior diâmetro, realizou-se a mesma técnica, destacando-se o fato de a incisão acompanhar a curvatura da sobrancelha na região glabelar (Figuras 5 a 8).

DISCUSSÃO

O câncer de pele cutâneo não melanoma, mesmo apresentando altos índices de subnotificação, é o tipo de câncer mais frequente entre os homens brasileiros e o segundo entre as mulheres. Aproximadamente 93% dos CBC ocorrem na cabeça e no pescoço, e deles 25% aparecem na pirâmide nasal, de forma que esse, indubitavelmente, é o câncer mais comum de cabeça e

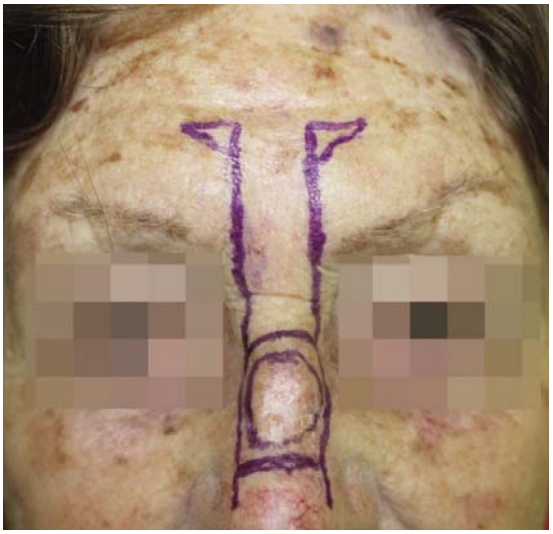

Figure 1: Marking of the tumor with safety margin and incision lines

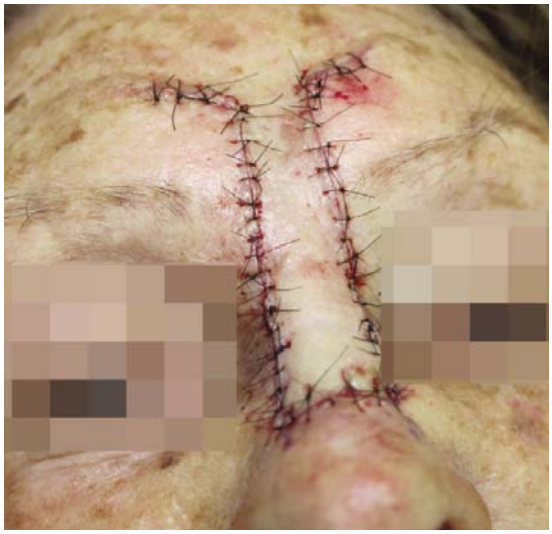

Figure 3: Appearance immediately postoperative

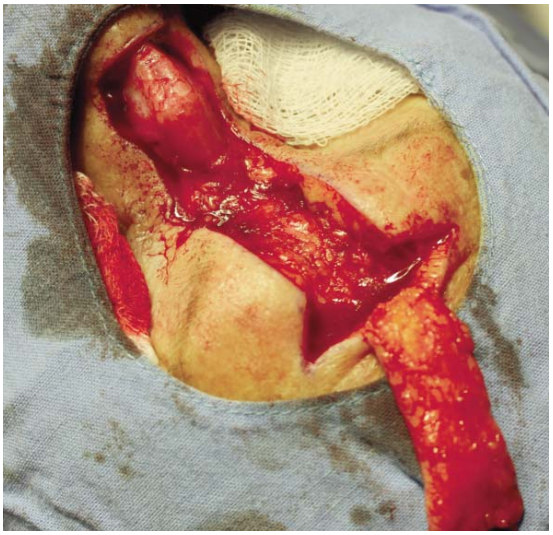

Figure 2: Block excision of the tumor and detachment of the skin surrounding the wound in the nasal dorsum and glabellar region

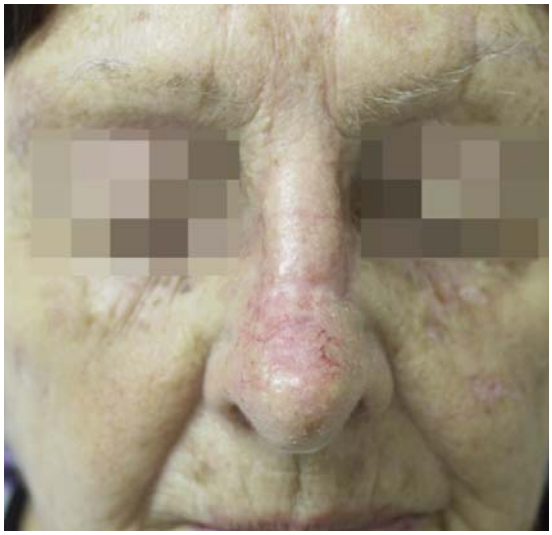

Figure 4: Final result, after six months

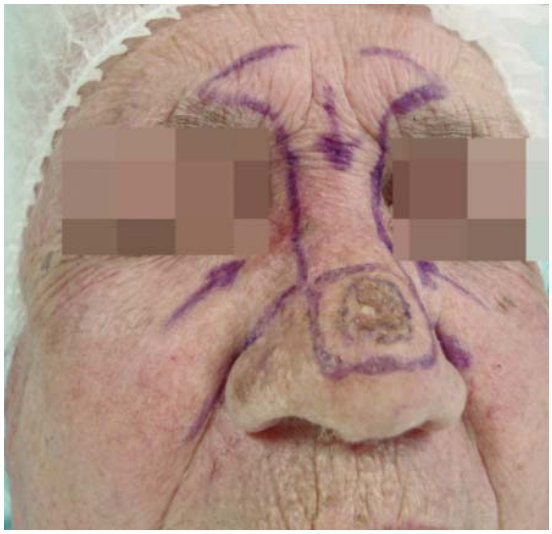

Figure 5: Illustration of the marking of the lesion and flap, in addition to the tension lines

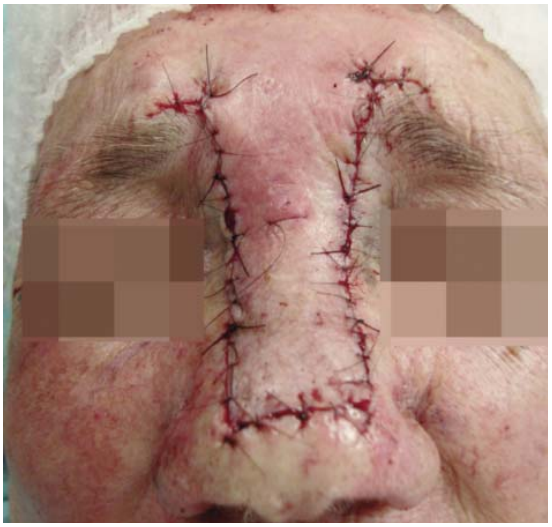

Figure 7: Appearance immediately postoperative

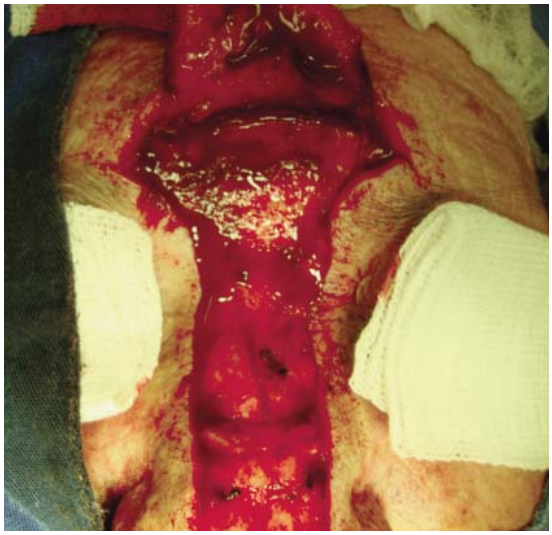

Figure 6: Incision and detachment of the nasal dorsum up to the glabellar region

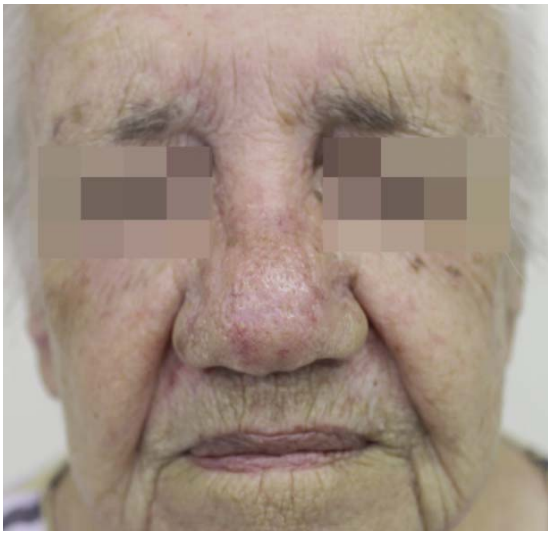

Figure 8: Two months after the procedure; complete accommodation and good aesthetic appearance

pescoço.[2,4] Topograficamente, o acometimento do dorso nasal leva à necessidade de amplas reconstruções, que constituem desafio cotidiano do cirurgião dermatológico.[2,5]

Várias são as opções para fechamento da ferida cirúrgica, incluindo a cicatrização por segunda intenção, enxerto de espessura total e utilização de retalhos cutâneos. Devido à textura e à cor peculiares da pele nasal, é preferível que tecidos semelhantes a substituam. O conhecimento das unidades cosméticas faciais favorece a colocação das incisões em locais em que sua camuflagem ocorre de maneira natural; portanto, a reconstrução nasal deve ser orientada pelas linhas-limite das subunidades cosméticas.[1,4,5]

Retalhos de avanço, também chamados de avançamento, são aqueles nos quais o tecido doador é deslocado num padrão linear em direção ao defeito cirúrgico, o local principal. Procede-se ao descolamento do tecido adjacente, permitindo o deslocamento do tecido com menor tração.[6] Quando ocorrem grandes defeitos primários, uma boa opção é o retalho de avanço glabelar. Nele, há o descolamento do tecido do dorso nasal e região glabelar, obtendo-se largo pedículo que, com tração suave, tende a acomodar-se nas bordas da ferida, tal como observado nos casos descritos. Com o descolamento cuidadoso em planos superficiais, não há acometimento da musculatura da mímica, como o procero, ou dos vasos supratrocleares, o que confere grande segurança ao procedimento. Em ambos os casos não foram observadas áreas de deiscência ou outras complicações, alcançando-se sucesso terapêutico e cosmético.

Por ser procedimento realizado em etapa única, com bom resultado cosmético, configura-se como opção ao fechamento de feridas cirúrgicas amplas no dorso nasal.

CONCLUSÃO

A reconstrução do nariz, em particular do dorso nasal, sempre que possível deve ser realizada com tecido de características semelhantes. Assim, a utilização dos retalhos torna-se imperiosa. No caso de lesões no dorso nasal com acometimento exclusivamente cutâneo, sem atingir cartilagens, com cirurgia em tempo único e bom resultado cosmético, o retalho de avanço glabelar é extremamente atrativo, sendo, portanto, a escolha dos autores para a reconstrução após retirada de lesões amplas de dorso nasal.

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Vulvar extramammary and unilateral Paget's disease: a case report

Doença de Paget extramamária vulvar e unilateral – Relato de Caso

ABSTRACT

Extramammary Paget's disease is a rare cutaneous neoplasm typically occurring in the vulva of Caucasian women after menopause. Clinically, the most common symptom is pruritus, when an erythematous, desquamative and eczematous lesion can be observed. Due to the rarity and nonspecific appearance of the disease, it can be confused with other dermatological conditions, delaying diagnosis. The present case demonstrates a form of vulvar extramammary unilateral Paget's disease confirmed by anatomical pathologic and immunohistochemical study. The standard treatment used for the disease in this case was surgical and the patient underwent complete excision of the lesion, with continued monitoring every six months.

Keywords: genital neoplasms, female; vulgar neoplasms; vulvar diseases; paget disease, extramammary.

RESUMO

A doença de Paget extramamária é neoplasia cutânea rara, ocorrendo tipicamente na vulva de mulheres caucasianas na pós-menopausa. Clinicamente, o sintoma mais comum é o prurido, observando-se lesão eritematosa, descamativa e eczematosa. Devido à raridade da doença e a sua aparência inespecífica, pode ser confundida com outras condições dermatológicas, retardando o diagnóstico. O presente caso demonstra uma forma de doença de Paget extramamária vulvar unilateral confirmada por estudo anatomopatológico e imuno-histoquímico. O tratamento-padrão da doença é cirúrgico, e a paciente foi submetida à exérese completa da lesão, continuando em acompanhamento semestral.

Palavras-chave: *neoplasias dos genitais femininos; neoplasias vulvares; doenças da vulva; doença de Paget extramamária.*

INTRODUCTION

In 1874, Sir James Paget described a breast disease with a very particular histopathology, which was individualized two years later by Butlin. In 1889, Cracker found this very characteristic alteration in a lesion on the scrotum, calling it extramammary Paget's disease.[1]

Extramammary Paget's disease (EMPD) is a rare group of cutaneous neoplasias. It affects both genders, the vulva being the most affected site, followed by the perianal region, perineum, scrotum, and axilae. There are rare reports of the condition in the thighs, buttocks, eyelashes, and external ear.[2,3] It typically occurs in patients 60 to 80 years of age, mainly affecting postmenopausal Caucasian women. In Asian populations, however, men are more affected.[4]

Clinically, the most common symptom is pruritus, and it is evidenced through erythematous, desquamative, and eczematous lesions. It is a slow growing neoplasm in which the appearance of old lesions can be modified by trauma, repeated abrasions, or secondary infection.[5] Due to its nonspecific appearance,

Authors:
Barbara Lima Araújo Melo[1]
Lara Lima Araújo Melo[2]
Igor Santos Costa[3]
Ruana Moura Rocha[4]
Regia Maria Vidal do Socorro Patrocínio[5]

1 Dermatologist Physician at private practice—Fortaleza (CE), Brazil

2 Medical Academician, Centro Universitário Christus (Unichristus)—Fortaleza (CE), Brazil

3 Dermatopathologist Physician, Centro de Dermatologia Dona Libânia—Fortaleza (CE), Brazil

4 Medical Emergency Physician—Fortaleza (CE), Brazil.

5 MSc in Pathology from the Universidade Federal do Ceará (UFC)—Fortaleza (CE), Brazil

Correspondence:
Dr. Barbara Lima Araújo Melo
R. Professor Dias da Rocha, 694 / apt 501—Meireles
Cep: 60170-310—Fortaleza—Ceará, Brazil
E-mail: barbaramelo@yahoo.com

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it can be mistaken for other dermatological conditions—such as psoriasis, contact dermatitis, squamous cell carcinoma, amelanotic melanoma, and mycosis fungoides—delaying diagnosis.[2,3]

The standard treatment for EMPD is local surgical exeresis with a 1 cm margin of normal skin, associated with inguinal lymphadenectomy.[6] Due to high recurrence rates, which range from 16-50%, [7] other therapeutic options, such as Mohs micrographic surgery, photodynamic therapy, radiotherapy, and more recently immunotherapy with imiquimod, have been proposed.[8] Regardless of the treatment option, it is crucial to follow up with the patient to detect possible recurrence of the disease as early as possible.

CASE REPORT

A seventy-two-year-old mulatto female patient sought medical attention in February 2010, reporting a vulvar lesion with pruritus, which onset eight years earlier. She reported the use of various topical corticosteroids without improvement. On physical examination, an erythematous, desquamative, crusted, and poorly delimited plaque could be observed in the vulvar and perineal region, on the right hand side of each. There were no palpable lymph nodes in the inguinal region (Figure 1).

The main diagnostic hypotheses were EMPD and chronic eczema. A biopsy of the vulvar region was then carried out, with the histological (Figure 2) and immunohistochemistry (Figures 3-6) studies confirming EMPD. The thorax radiography, the bilateral mammography, and the abdominal ultrasonography showed no abnormalities.

In September 2010, a vulvectomy was performed on the right hand side, with complete excision of the lesion and superficial inguinal lymphadenectomy. No signs of residual tumor were observed in the post-operative examinations. The patient remains in regular follow up every six months, with no signs of recurrence to date.

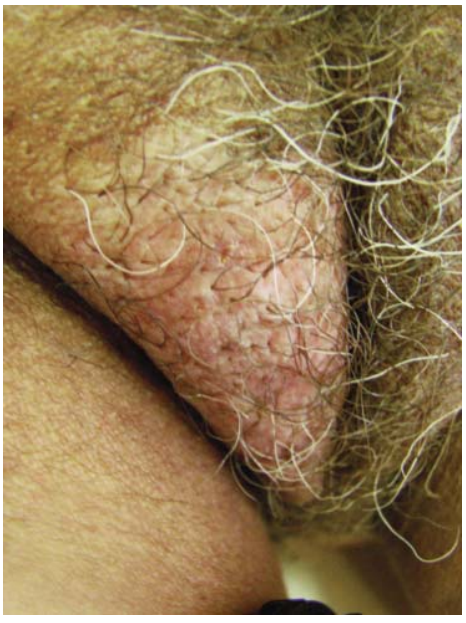

Figure 1: Erythematous,desquamative, crusted plaque in the vulvar region on the right-hand side

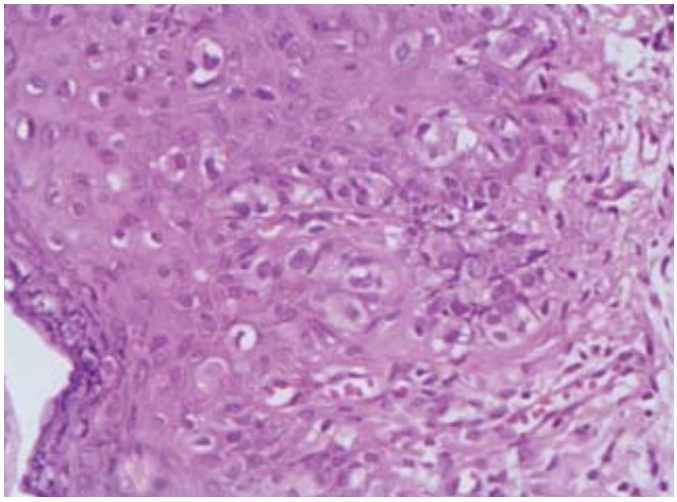

Figure 2: Clinical anatomical pathology: nests of atypical epithelial cells with clear cytoplasm within the epidermis—Paget cells. Staining with hematoxylin-eosin, 40x magnification

DISCUSSION

The occurrence of EMPD corresponds to less than 2% of vulvar neoplasias. 5 The patient's epidemiological characteristics are aligned with the literature's data: female, 72-years-old and postmenopausal. The 8-year clinical history of symptoms confirms the slow progression of the neoplasia, while pointing out the difficulty of diagnosis and appropriate management of the disease.

The present case demonstrated a rare and unilateral form of vulvar EMPD, confirmed through biopsy and followed by histological analysis, which showed numerous foci represented by atypical cells with large, pale cytoplasm containing large nuclei with distinct nucleoli, extending across the mucosal epithelium in a pagetoid pattern.The immunohistochemistry revealed positivity for cytokeratin 7 (CK7), a sensitive marker, however not specific for EMPD. Negativity to that marker is rare, generally occurring in association with malignancy in internal organs.[9] Negativity was also observed for cytokeratin 20 (CK20), Melan-A and CDX-2. Positive CK20 is more commonly present in EMPD associated with carcinoma,[9] therefore the negativity of this marker in the studied case suggests the absence of other neoplasms. In this context, the expression pattern of cytokeratins provides a clue about the presence or absence of internal malignancy. Melan-A is a melanocyte's differentiation marker, and its negativity practically excludes the presence of amelanotic melanoma. CDX-2 is found when there is a colorectal tumor, being relevant in the diagnosis of other associated neoplasias.

EMPD generally remains restricted to the epidermis, rarely spreading via the lymphatic system.[10] Subjacent malignancy ranges from 12-33% of cases, anatomically correlating to the sites of the lesions and neoplasias, with investigation being fundamental to detect internal malignancy.

Being a rare disease, little is known about the most effective treatment, and the standard approach is surgical excision with anatomopathologic evaluation of frozen margins. 6 The

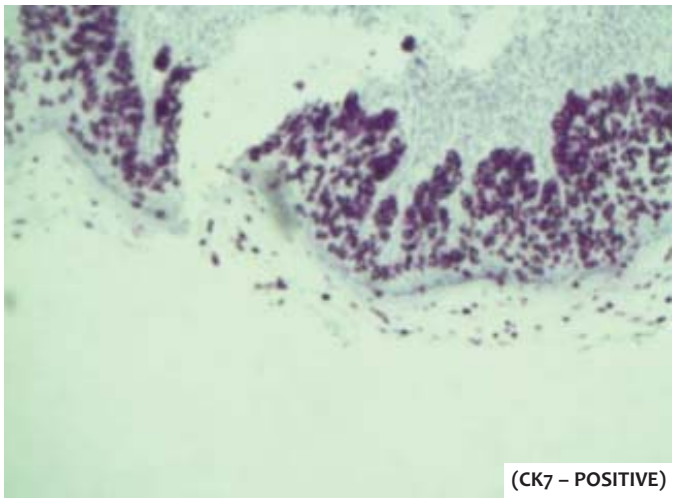

Figure 3: Immunohistochemistry: CK7 positive, 5x magnification

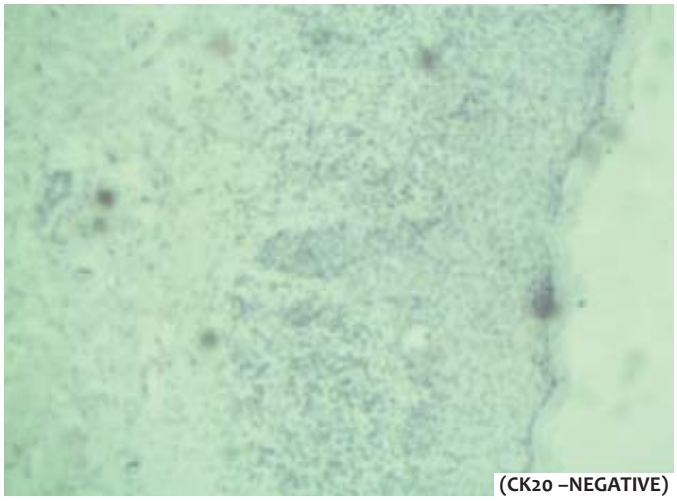

Figure 4: Immunohistochemistry: CK20 negative, 5x magnification

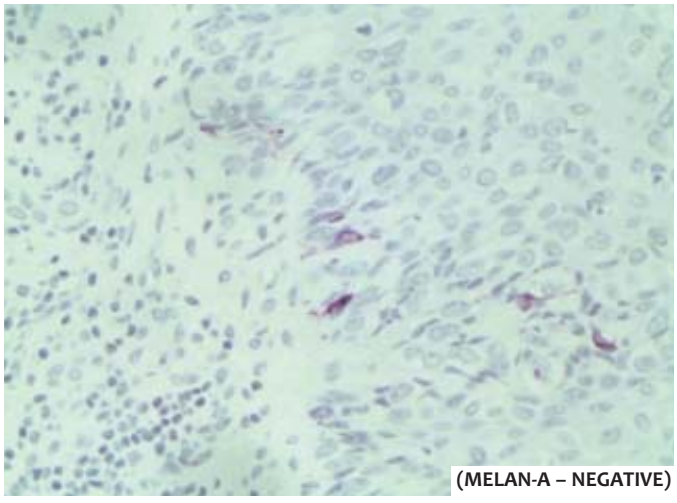

Figure 5: Immunohistochemistry: Melan-A negative ; 40x magnification

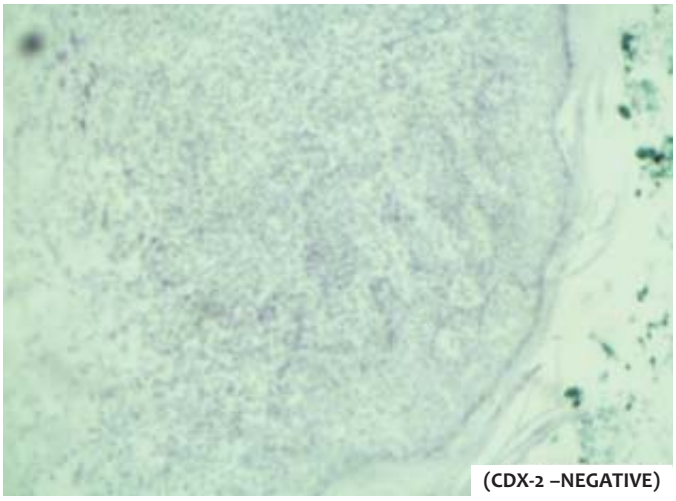

Figure 6: Immunohistochemistry: CDX-2 negative, 5x magnification

recurrence rate after surgery is high, occurring on average after 30 months. The patient continues on a semiannual clinical follow-up, remaining asymptomatic to date. The present case suggests a good prognosis due to the presence of pagetoid cells restricted to the epidermis, and for not presenting lymph node metastases—the two main criteria for prognostic evaluation.

Due to the rarity of the case, dermatological knowledge for early diagnosis, attention to other concomitant neoplasia, and the choice of appropriate treatment—whether medical or surgical—are crucial.

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