

Histological changes of collagen types after different modalities of dermal remodeling treatment: a literature review

Alterações histológicas dos tipos de colágeno após diferentes modalidades de tratamento para remodelamento dérmico: uma revisão bibliográfica

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ABSTRACT

A range of treatment options is available to restore and increase dermal collagen. The purpose of the present review, based on articles selected on PubMed database, is to study the histological effect of four methods for skin rejuvenation: Intense Pulsed Light, non-ablative fractional laser, ablative fractional laser and percutaneous collagen induction. The therapeutic implications of each type of treatment will depend on the induced collagen type and its ability to elicit a regenerative healing response versus a fibrotic scarring response. Intense Pulsed Light and the percutaneous collagen induction produced regenerative healing response with increased collagen type I.

Palavras-chave: intense pulsed light; laser therapy; collagen; rejuvenation; skin aging

RESUMO

Uma série de alternativas de tratamento está disponível para restaurar e aumentar o colágeno dérmico. O objetivo desta revisão, apoiada em artigos selecionados na base de dados PubMed, é estudar o efeito histológico de quatro modalidades para o rejuvenescimento da pele: luz intensa pulsada, laser fracionado não ablativo, laser fracionado ablativo e indução percutânea de colágeno. As implicações terapêuticas de cada tipo de tratamento dependerão do tipo de colágeno induzido e de sua capacidade para provocar uma resposta de cura versus uma resposta regenerativa de cicatriz fibrótica. A luz intensa pulsada e a indução percutânea de colágeno produziram resposta de cura regenerativa com aumento de colágeno tipo I.

Palavras-chave: luz intensa pulsada; terapia a laser; colágeno; rejuvenescimento; envelhecimento da pele

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INTRODUCTION

Due to the rapid increase in the life expectancy of the world population, skin aging has become a field of scientific importance in recent decades, with the emergence of multiple treatment modalities.

Both intrinsic alterations (secondary to the loss of cell regeneration capacity, resulting from chronological action) and extrinsic alterations (mainly caused by the exposure to ultraviolet radiation) have influence in the skin aging process.

There are several treatment options aimed at attempting to restore and increase dermal collagen,^{1,2} though their specific histological responses are not clear and there is lack of understanding regarding the specific effects that each of them has on dermal collagen.

Characteristics of normal and pathological skin

The maintenance of the skin's tissular architecture and physiological properties are attributed to the connective tissue's extracellular matrix, which comprises a large number of components including collagen and elastic fibers, proteoglycans and glycosaminoglycans macromolecules, and several non-collagen glycoproteins. The abilities of resident cells – such as fibroblasts – to synthesize and organize the extracellular matrix are critical for the morphogenesis, angiogenesis and skin healing processes. Collagen is the main responsible for the skin's strength, elasticity and the dermal volume, corresponding to about 80% of its dry weight.

Dermal collagen synthesized by fibroblasts in normal skin contains type I collagen (80% – 85%) and type III collagen (10% – 15%). The anchoring fibrils are composed mainly of type VII collagen and contribute to the dermal-epidermal junction's stability. A reduction in the amount of non-fibrillar collagen (type I and III) seen in the chronologically aged skin and can be aggravated by photoaging.³

In chronological aging, a decrease in the dermal thickness occurs due to biochemical and structural changes in collagen and elastic fibers, and in the ground substance. There is a reduction of collagen synthesis and an increase in its degradation due to increased levels of collagenase. The total collagen amount is reduced by 1% per year throughout adult life, and the remaining collagen fibers become disorganized, more compact and grainy, with a greater number of cross-links. Elastic fibers decrease in number and diameter. The ground substance's amount of the mucopolysaccharides decreases, in special that of the hyaluronic acid (HA). These changes negatively influence the skin's turgor and also have an impact on the deposition, orientation and size of collagen fibers.^{4,5}

In photoaging – a term that refers to skin changes associated with chronic exposure to ultraviolet light – the epidermal and dermal changes affect cellular components and the extracellular matrix with the accumulation of disorganized elastic fibers, loss of collagen fibers, and a reduced proportion of type I : type III collagen^{6,7} (Figure 1). Clinically, it manifests as roughness, loss of elasticity, appearance of fine wrinkles, dyschromias and melanoses. Varani et al.⁶ showed that the reduction of collagen in the photodamaged skin is caused by both the increased collagen degra-

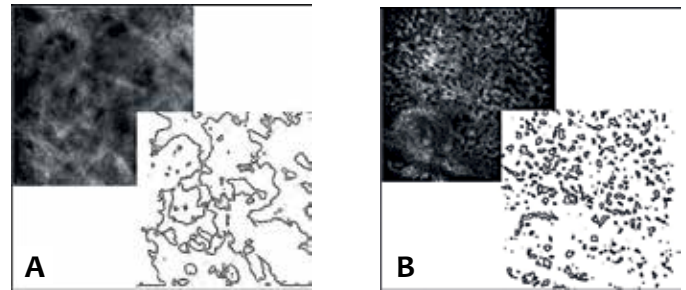


Figure 1: Confocal microscopy shows increased collagen fragmentation with advancing age. A. Image of a 25-year old person. B. Image of a 68-year old person. (<http://www.orion-concept.com>)

ation by the action of metalloproteinases (especially collagenase) and the decrease in the production of collagen by fibroblasts. This interruption in the synthesis of new collagen is caused by the interaction with an altered extracellular matrix, which exerts an inhibitory mechanism on fibroblasts. When isolated, fibroblasts regain their ability to grow and produce collagen.

Facial wrinkles have histologic differences in the photodamaged skin. A recent study compared the static wrinkles of the forehead with the adjacent skin and noticed that the wrinkles show significant reduction of type VII collagen, elastin and tropoelastin. The levels of collagen type I and III are similar to that of the adjacent photoaged skin.⁷ The reduction in type VII collagen in the wrinkles' bottom seems to contribute to the appearance of a thin, flattened dermal-epidermal junction, weakening the connection between the epidermis and dermis, leading to their proliferation.

There are currently many procedures designed to stimulate neocollagenesis in the treatment of the aging skin, aiming at remodeling the dermis and consequently improving the sagging skin and wrinkles. The main issues regarding the collagenesis are linked to its control and stimulus, especially in rejuvenation treatments. Controlling the formation of collagen is critical to maintaining a proper dermal structure and the lack of control contributes for the formation of hypertrophic scars and keloids, for instance.

In the wound repairing process, healing results in a fibrous inflammation with predominance of type III collagen, which is stronger and more resistant, and scars are classified into three types: normotrophic, hypertrophic and keloid. Verhaegen et al.⁸ found differences in the collagen's morphology among the scar types and the normal skin. When compared to the normal skin, hypertrophic scars and keloids have collagen fibers arranged in more parallel pattern. In keloid scars, the collagen bundles are significantly thicker and the distance between them is increased.

In hypertrophic scars and keloids, fibroblasts produce collagen excessively as compared to normal skin fibroblasts. Oliveira et al.⁹ found that this increase is caused by an increase

in type III collagen. They compared hypertrophic with normotrophic scars and showed that hypertrophic scars have greater amounts of type III collagen accumulated in the deep dermis, and that both scars have equal amount of collagen type I. These findings are consistent with those of Syed et al.¹⁰ who have ratified the fact that the ratio collagen type I : collagen type III is altered in keloids and showed that fibroblasts of the growing perilesional skin have a greater collagen production than that of other regions in the same keloid. Moreover, differences are observed in the production of collagen in different locations of the same keloid, with a decrease in the ratio collagen type I : collagen type III. The perilesional region has an increase of collagen type III and a slight decrease in collagen type I as compared to the intralesional area.

OBJECTIVES

The objectives of the present study are to evaluate the evidence published in the literature about different types of collagen in four skin rejuvenation methods (Intense Pulsed Light – IPL), Non-Ablative Fractional Laser – NAFL), Ablative Fractional Laser – AFL) and Collagen Induction Therapy – CIT); and evaluate the therapeutic implications of each procedure and infer which of them can most closely achieve outcomes with characteristics of normal skin.

The hypothesis of the present study is that IPL and ICT, acting through a process of regeneration rather than healing, are the procedures that can most closely achieve outcomes with characteristics similar to those of healthy skin.

METHODOLOGY

The methodology consists of reviewing the scientific literature, based on selected articles on PubMed database, using the keywords *intense pulsed light, ablative fractionated laser, nonablative laser, percutaneous collagen induction, rejuvenation, dermal collagen, scar, fibrosis, photoaging* and *complications*. The English, Spanish and Portuguese languages, as well as publication dates between 1990 and 2015, related to dermatology, were the parameters used in the search filter.

RESULTS

One of the most important modulators of the connective tissue's gene expression is the transforming growth factor - type (TGF-) belonging in the family of the growth factors released by macrophages that stimulates the expression of various extracellular matrix genes, including those encoding collagen I, III, IV and V, apparently by the transformation of TGF- into connective tissue growth factor (CTGF) in the fibroblasts. With the aging process, these factors have their levels reduced.⁸ This would be the proposed mechanism for stimulating collagenesis during the healing process and after treatments that act through the induction of an inflammatory response.^{5,11,12}

Histological effects of IPL

IPL devices emit non-coherent and not collimated diffuse light – or polychromatic light, whose characteristics are

different from those of the laser light. The latter has collimated and coherent rays, and always with a single wavelength.³ In this manner, due to the fact that IPL has various wavelengths (ranging from 500nm to 1,200nm) is capable of treating melanocytic and vascular lesions,¹³ as well as stimulating neocollagenesis.¹⁴

The effectiveness of IPL in the remodeling of the extracellular matrix of skin aging has been proven in several clinical studies.¹⁵ The stimulation of fibroblasts, resulting in neocollagenesis, in addition to the dermal remodeling and decreased in elastosis can be seen histologically for up to six months after the treatment.¹⁵⁻¹⁷ However, its precise mechanism of action in photorejuvenation is not fully elucidated.

Research studies have shown that irradiation with IPL has a stimulating effect on cutaneous fibroblasts *in vitro*, promotes cell viability and increases the expression of collagen types I and III.¹⁸⁻²⁰

Feng et al.²¹ studied the effect of IPL on 58 patients. Cut-off filters of 560nm, 590nm and 640nm, with fluences from 14 to 22 J/cm² and pulse durations of 2 to 4 ms were employed. After 3 sessions, 62% of patients had improvement in their wrinkles and skin texture, 85% had reduction in pigmentary lesions, and 81% had a decrease in telangiectasia. Histological results of four patients showed an increase in collagen fibers types I and III.

Another study performed in six female patients showed increased collagen after six treatment sessions with IPL. The increase in type I collagen was higher than that of type III. These results, however, were not statistically significant.²²

A histological analysis in 14 patients with poikiloderma of Civatte (PC) evidenced an increased number of fibroblasts associated with increased compression, thickness and density of collagen. Three IPL sessions were carried out at monthly intervals with 570 nm and 540 nm cut filters, fluence of 18 J/cm², and pulse duration of 15 ms. In 86% of cases there was more homogeneous redistribution of the melanin pigment in the basal layer of the epidermis, consistent with the improvement in the PC's pigmentary component.²³

Regarding the IPL's beneficial effect on hypertrophic scars and keloids in a series of 109 patients, Erol et al.²⁴ reported an improvement of over 75% in the pigmentation and a 50% reduction in size and thickness of hypertrophic scars. The parameters used were energy at 30 to 40 J/cm², cut filters of 550 nm to 590 nm and pulse duration of 2.1 ms to 10ms. The number of sessions ranged from 1 to 24, depending on the severity of the scar.

More recently, Hultman et al.²⁵ described the efficacy of IPL in the treatment of dyschromias in burn scars in 20 patients using cut filters of 560 nm to 650 nm, and fluence of 10 J/cm² to 22 J/cm². Sarkar et al.²⁶ reported decreased vascularity, flattening and prevention of hypertrophy in recent scars after burns. Four sessions were performed with 590 nm cut filter and fluence at 25 J/cm².

According to the authors,²³⁻²⁵ the beneficial effect of IPL on hypertrophic scars could be explained both by the inhibitory action of IPL on the blood vessels and the inhibition of type III collagen synthesis. So far there is still absence of studies on the

histological effect of IPL in scars, since those found in the literature describe only clinical parameters.

Histological effects of non-ablative laser

Non-ablative lasers (NAL) have arisen in order to enhance the undesirable effects of ablative lasers. Non-ablative resurfacing, performed with 1,064 nm Nd:YAG for instance, has a deeper penetration in the dermis that does not cause dermal ablation.²

In 1997, studies by Golberg²⁷ proved the positive effects with few adverse effects using Q-switched Nd:YAG laser in skin rejuvenation, observing that only 4 of the 6 patients showed a slight increase of collagen in the papillary dermis and concluded that the clinical effects did not correlate to histological effects.²⁸ Studies in animals²⁹⁻³¹ showed increased collagen type I and type III associated with a decrease of metalloproteinases after irradiation with QS Nd:YAG. In the three studies,³⁰⁻³² the expression of type III procollagen protein was greater than that of type I procollagen. Moreover, Nd:YAG leads to increased expression of types I and III procollagen when compared to IPL.³²

The concept of fractional photothermolysis introduced by Manstein et al.³³ was first used for non-ablative fractional lasers (NAFL). It consists of thermal damage inflicted in the shape of dermoepidermal coagulation columns, without ablation of the epidermis, leaving areas of untreated skin between them. Tw2

Orringer, et al. 34 studied molecular mechanisms of the treatment with 1,550 nm Erbium NAFL in 20 patients with cutaneous photoaging. Biopsies were performed once a week, for one month. It was possible to observe early inflammatory response with a significant increase in pro-inflammatory cytokines (interleukin-1 β and tumor necrosis factor α) followed by increasing metalloproteinase. After 24 hours, there was a decrease in the expression of types I and III collagens, which was soon reversed to progressively increase during the course of two weeks. Increased levels of collagen types I and III were proportional to the energy used.

In order to evaluate the result of NAFL on burn scars in their chronic phase, Taurdorf et al.³⁵ performed a randomized controlled study with 20 patients. The treatment was carried out with 1,540 nm Erbium:Glass laser, firstly using a deep, and then a superficial tip. Clinical and histological analyzes were performed at one, three and six months after the treatment. The 15 patients who completed the study showed overall improvement in the appearance of the scars, nonetheless 11 patients had one or more prolonged adverse effects, such as erythema, hyperchromia and hypochromia. It was possible to histologically observe an improvement of the flatness of the dermal-epidermal junction and a reorganization of elastic fibers and collagen.³⁶ Both studies conclude that the flat and atrophic scars respond better to treatment with NAFL; however hypertrophic scars have limited clinical response.^{35,36}

When compared to AFL, NAFL led to similar clinical response in the treatment of post-surgical scars, with a lower rate of adverse effects.³⁷

Histological effects of AFL

Carbon oxide 10,600nm and 2,940nm Erbium:YAG ablative lasers were first used for skin rejuvenation. Results were encouraging, however, due to the fact that they cause complete ablation of the epidermis, both showed all possible complications stemming from the total exposure of the dermis in the postoperative period.

Given that the Erbium:YAG laser emits a wavelength that approximates that of the water absorption's peak (3,000nm), almost all energy is absorbed in the epidermis and the papillary dermis, producing a more superficial ablation with a lower underlying thermal damage than that of the CO₂ laser.³⁸

Ablative fractional laser (AFL) employs an innovative technology that combines the principles of classic ablative techniques with fractional photothermolysis. The beam applied on a fraction of the skin surface produces a microscopic area of treated skin, comprising a central ablative focus encircled by thin necrotic area, which in turn is surrounded by a coagulation band. The areas of untouched skin among the treated areas enable faster tissue proliferation aimed at repairing the damaged zones.³⁹

In the literature, there is a discussion on whether the lifting type tension effect of AFL is caused by the ablation of the abnormal tissue – resulting in the regeneration and contraction of the collagen – or by the stretching resulting from dermal heating.⁴⁰

In order to determine whether there is a difference between the cutaneous stretching caused by collagen contraction mediated by heat, and that occurring secondarily to a regenerative process, Fitzpatrick et al. 41 treated the upper eyelids of 9 patients with two types of AFL: CO₂ and Erbium:YAG. Ultrasonographic measurements and skin biopsies were performed monthly for 6 months. The authors demonstrated that the Erbium:YAG laser acts through a purely ablative mechanism. The stretching effect starts to be noticed after 1 week after the damage has been inflicted and being a result of the transformation of fibroblasts into myofibroblasts. This mechanism of wound contraction leaves a microcicatrical aspect. With the CO₂ laser, the ablative effect is smaller and there is also immediate stretching of the skin through dermal heating. This reaction is the result of a dissociation of intermolecular peptide bonds of the collagen's triple helix, leading to a longer lasting tension effect. The authors concluded that the tissular stretching and thickening produced by the ablative effect results from the stretching of the collagen, which is caused by the wound contraction mechanism, leading in turn to a healing response. The more intense is the laser ablation, the greater the risk of scarring. In this study, 41.43% of patients showed permanent scars, which were treated with blepharoplasty.

In order to objectively evaluate the histological and immunohistochemical effects of the Erbium:YAG laser, El-Do-myati et al. 42 carried out a comparative study of 12 patients treated with the ablative and the fractional modalities of Erbium:YAG laser. With serial biopsies, they demonstrated a quantitative increase of collagens type I, III and VII in both treatment

modalities after 4 sessions. This increase in collagen was maintained for up to 6 months after the last treatment. The same authors described similar findings in 10 patients after 5 sessions with Erbium:YAG AFL in the skin rejuvenating treatment of the upper third of the face.⁴³

Although CO₂ AFL has proven effective in the treatment of atrophic acne scars,⁴⁴ a recent randomized controlled study could not confirm its clinical effectiveness in different types of scars.⁴⁵

Ozog et al.⁴⁶ evidenced a significant increase of collagen type III along with a significant decrease of collagen type I in scars of burns after treatment with CO₂ AFL. Ten patients were included in the study, with 8 dropping out after the first session of treatment due to adverse effects such as pain, infection and ulceration. Two patients reported improvement in thickness and pigmentation of the scar. This finding coincides with what Laubach et al.⁴⁷ described: that ALF produces epidermal microinjuries and damage to the dermal collagen, which, through a regeneration process, is replaced by collagen type III.

Histologic effects of collagen induction therapy

In 1995, Orentreich and Orentreich⁴⁸ described the term “subcision” as a means to stimulate the connective tissue located beneath scars and retracted wrinkles. Based on these ideas, the collagen induction therapy (CIT) was developed. This is a method that uses a device with a variable number of microneedles of different lengths, which cause microtraumas to the skin and formation of microchannels by performing multiple punctures in the skin. These microchannels function as conduits for active principles, facilitating the absorption of substances, and promoting collagen induction.

The CIT was proven effective and promising for the safe treatment of scars and other dermatologic conditions, safely and without the risk of hypopigmentation.⁴⁹ It was also demonstrated to be safe and effective in the treatment of periorbital wrinkles.⁵⁰

The repair process produced by CIT comprises 3 phases.⁵¹ In the first phase (the injury phase), there is release of platelets and neutrophils responsible for the release of growth factors acting on keratinocytes and fibroblasts. In the second phase (the healing phase), there are angiogenesis, epithelialization and fibroblast proliferation, followed by the production of type III collagen, elastin, glycosaminoglycans and proteoglycans.

Concomitantly, fibroblast growth factors (TGF- α and TGF- β) are secreted by monocytes. The TGF plays a crucial role in the formation of fibrotic scars. Research on the TGF molecules' family found that TGF- β 3 induces regenerative response without producing scars, while TGF- β 1 and TGF- β 2 induce fibrotic scarring.⁵² A repair with the presence of scars is histologically characterized by abnormal dermal organization composed of small parallel bands of type III collagen and fibronectin. A regenerative response without scarring has characteristics similar to those of the normal skin.

Studies in animals show that the CIT induces the expression of TGF- β 3, which remains for 2 weeks after the procedure.⁵³ Finally, in the third stage (the maturation phase), type III colla-

gen is replaced by collagen type I.⁵⁴

Aust et al.⁵⁵ demonstrated a significant improvement in wrinkles, flaccidity and appearance of scars in 480 patients. The same authors showed that the device CIT 3mm (Environ® Medical Roll-CITTM) leads to an increase of collagen type I and that the joint application of retinol and vitamin C maximizes these results. Biopsies taken after 6 months and 1 year showed that the histological changes, such as thickening of the stratum spinosum, normalization of the dermal epidermal junction, and increase in collagen have remained during that period.⁵⁵

More recently, Zeitter et al.⁵⁶ demonstrated that the same effects can be obtained using 1mm long microneedles. The study was carried out in rats and found increased epidermal thickness and expression of collagen type I, and decreased expression of collagen type III. These findings were more evident in the group that underwent 4 treatment sessions, and even better in the group that underwent 4 CIT sessions with the topical application of 1% retinol and 10% vitamin C.

DISCUSSION

The healing and regeneration processes take place in different ways. While the regeneration process culminates in the production of collagen type I (stronger and more resistant), the healing process results in a fibrous inflammation with predominance of type III collagen.^{6, 44, 57}

Hypertrophic scars and keloids have increased production and amount of type III collagen.¹³⁻¹⁴ In cutaneous photoaging, there is increased collagen type III along with a reduction in collagen type I.⁷

All methods studied in this paper lead to an improvement in the texture of the skin, wrinkles and surface irregularities through collagenesis; however, the type of collagen produced can be different.

Intense pulsed light leads to increased expression of collagen type I and reduced expression of collagen type III.^{24, 34, 36} It also proved effective in the treatment of various types of scars,²⁷⁻³⁰ however the resulting histologic effect has not yet been sufficiently investigated.

ICT also generates increased expression of collagen type I and a decrease in collagen type III.^{53, 57-59}

Delayed healing and fibrosis are more frequent with the AFL and NAFL.⁵⁸ This can be explained by the type of collagen whose production is triggered by these lasers. Several articles show that NAFL produces a greater increase in type III collagen than in type I collagen.³³⁻³⁶ Regarding the genesis of collagen triggered by different types of lasers, the one that leads to the greatest increase collagen type III is the QS Nd:YAG NAFL.⁵⁹

The treatment of hypertrophic scars with AFL leads to increased collagen type III and decreased collagen type I.⁵⁰⁻⁵¹

CONCLUSION

It can be concluded that regeneration is an integral part of the clinical improvement observed in the IPL and ICT, which is associated, at the histological level, to an increase of type I collagen, which is stronger and more durable. The clinical improvement

observed with AFL and NAFL depends on the triggered healing process and fibrosis, which produces more collagen type III.

Notwithstanding, it is necessary to expand the knowl-

edge with further studies in order to arrive at credible and reliable conclusions. Many of the studies presented in the present paper have a small number of cases, and the methodologies used were limited. ●

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Questions for continuing medical education - CME

1. Regarding the dermal collagen in the normal skin, it is right to state:
 - a. It is synthesized by macrophages and is composed of 85% collagen type I and 15% collagen type III.
 - b. The anchoring fibrils are composed mainly of collagen type VI and contribute to the stabilization of the dermal-epidermal junction.
 - c. It is synthesized by fibroblasts and is mainly composed of collagen type I.
 - d. Collagen is the main responsible for the skin's strength and elasticity, corresponding to about 50% of its dry weight.
 - e. It consists of 85% of type IV collagen and 15% type III collagen.
2. Which of the below are not characteristics of the aging skin:
 - a. Thickening of the dermal thickness.
 - b. Reduction of collagen synthesis and increase in its degradation.
 - c. The ratio collagen type I : collagen type III is increased.
 - d. Alternatives a and c.
 - e. Only alternative c.
3. In a wound repair process:
 - a. Hypertrophic scars produce type I collagen in an excessively way.
 - b. In keloid scars the collagen bundles are thicker and the distance between them is decreased.
 - c. Scarring results in a fibrous inflammation with predominance of type I collagen, which is stronger and more resistant.
 - d. The keloid scar's fibroblasts produce collagen excessively as compared to normal skin's fibroblasts.
 - e. All of the above are correct.
4. Due to the fact that it has multiple wavelengths, intense pulsed light treats different dermatological conditions, except for:
 - a. Vascular lesions.
 - b. Pityriasis versicolor.
 - c. Tattoos.
 - d. Vitiligo.
 - e. Melanocytic lesions.
5. The effectiveness of intense pulsed light for remodeling the extracellular matrix of aging skin is linked to:
 - a. Stimulation of fibroblasts.
 - b. Neocollagenesis.
 - c. Dermal remodeling.
 - d. Decreased elastosis.
 - e. All of the above.
6. Is an example of ablative treatment:
 - a. 1,550nm Erbium laser.
 - b. Collagen Induction Therapy.
 - c. 1,064nm Nd:YAG laser.
 - d. Intense Pulsed Light.
 - e. None of the above.
7. When compared to intense pulsed light, Nd:YAG laser:
 - a. Showed a similar clinical response in the treatment of hypertrophic scars.
 - b. Exerts a greater expression of type III procollagen while intense pulsed light exerts a greater expression of type I procollagen.
 - c. Exerts a greater expression of elastic fibers.
 - d. Exerts a greater expression of procollagen type I while intense pulsed light exerts a greater expression of procollagen type III.
 - e. Both exert the same expression of procollagens type I and type III.
8. Regarding ablative lasers, it is correct to state that:
 - a. The Erbium:YAG laser produces a more superficial ablation with less underlying thermal damage than CO2 laser.
 - b. 10,600nm CO2 laser and 2,940nm Erbium:YAG laser are examples of ablative lasers.
 - c. Ablative fractional lasers employ a technology that combines the principles of classic ablative techniques with fractional photothermolysis.
 - d. The more ablative the laser is, the greater is the risk of scarring.
 - e. All of the above are correct.
9. These are characteristics of the repair process produced by the Collagen Induction Therapy:
 - a. In the third phase, the release of platelet and neutrophils responsible for the release of growth factors acting on keratinocytes and fibroblasts takes place.
 - b. The second phase culminates in the formation of a fibrotic scar.
 - c. The first phase corresponds to the injury phase.
 - d. Angiogenesis, epithelialization and fibroblast proliferation occur in the third phase.
 - e. The first phase corresponds to the healing phase.
10. Regarding the different methods of skin rejuvenation and their action on the different types of collagen, it is possible to state that:
 - a. Intense pulsed light and collagen induction therapy produce an increase of type I collagen, which is stronger and more resistant.
 - b. While the regeneration process culminates in the production of collagen type III, which is stronger and more resistant, the healing process results in a fibrous inflammation with the predominance of collagen type I.
 - c. Regeneration is an integral part of the clinical improvement observed in the treatment with ablative lasers.
 - d. The collagen induction therapy produces an increase in the expression of collagens type III and type IV.
 - e. All of the above are correct.

Key:

Hyaluronidase in cosmiatry: what should we know?
2015;7(3):197-204.

1-B, 2-C, 3-D, 4-E, 5-D, 6-E, 7-C, 8-E, 9-A, 10-A

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 access link to the journal.

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Trichloroacetic acid peeling in the treatment of actinic melanosis in the back of the hands: a comparative randomized study between two vehicles

Peeling de ácido tricloroacético no tratamento de melanosas actínicas no dorso das mãos: estudo comparativo e randomizado entre dois veículos

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ABSTRACT

Introdução: actinic melanosis is a pigmentation disorder caused by the cumulative action of sunlight on the skin and its incidence increases with advancing age.

Objective: Considering the lack of studies comparing agents with the same concentration, however in different vehicles, the authors compared the clinical effects of chemical peelings performed with 20% trichloroacetic acid (ATA) paste or solution in the treatment of actinic melanoses in the back of the hands.

Methods: A prospective, controlled, randomized study was carried out with 15 patients bearers of bilateral actinic melanoses on the back of the hands. Three monthly sessions with 20% ATA peelings were performed with paste in one hand and solution in the other. The degree of whitening was evaluated by 13 blinded dermatologists, and patients were asked about the satisfaction and preferred method.

Results: There was no preference for any of the methods used ($p = 0.41$), however, according to the medical evaluation, there was greater whitening with the paste ($p = 0.01$). Only the paste caused significant adverse effects, affecting 4/15 patients.

Conclusions: Compared to the solution, when applied for two minutes in the treatment of actinic melanosis, the 20% ATA paste had greater whitening capacity, however demonstrated a tendency to cause more local adverse effects.

Keywords: trichloroacetic acid; melanosis; hand; chemexfoliation; skin pigmentation

RESUMO

Introdução: A melnose actínica é transtorno de pigmentação originado pela ação cumulativa da luz solar na pele, e sua incidência aumenta com o avanço da idade.

Objetivo: Considerando a falta de estudos que comparem agentes com igual concentração, porém em veículos diferentes, analisamos os efeitos clínicos de peelings químicos realizados com pasta ou solução de ácido tricloroacético (ATA) 20% no tratamento de melanosas actínicas do dorso das mãos.

Métodos: Estudo prospectivo, controlado, randomizado, com 15 pacientes portadoras de melanosas actínicas bilaterais no dorso de mãos. Foram realizadas três sessões mensais de peelings de ATA 20% em pasta em uma das mãos e em solução na outra. Foram avaliados o grau de clareamento por 13 dermatologistas cegos e a satisfação e preferência de método pelas pacientes.

Resultados: Não houve preferência por qualquer dos métodos utilizados ($p = 0,41$), porém, segundo avaliação médica, houve clareamento mais intenso com a pasta ($p = 0,01$). Apenas a pasta provocou efeitos adversos significativos, afetando quatro das 15 pacientes. **Conclusões:** Em relação à solução, a pasta de ATA a 20%, quando aplicada por dois minutos no tratamento das melanosas actínicas, demonstrou clareamento mais intenso, porém revelou tendência a causar mais efeitos adversos locais.

Palavras-chave: ácido tricloroacético; melnose; mãos; abrasão química; pigmentação da pele

INTRODUCTION

In a study conducted by the Brazilian Society of Dermatology, pigmentation disorders were the most frequent causes of visits to dermatological practices among patients aged 40–64 years.¹ Actinic melanosis (AM), or solar melanosis, is a common skin disorder among these dermatological complaints, originating from the cumulative action of sunlight on the skin after the third or fourth decades of life.^{2,3}

In addition to the effective and regular protection against the sun, treatment of melanoses includes topical medications with lightening effect and ablative procedures such as cryotherapy, laser, intense pulsed light and localized application of caustic liquids such as trichloroacetic acid (TCA) and phenol. The application of caustic agents in the form of chemical peelings on the dorsum of the hands is also reported in the treatment of solar melanosis. A more diffuse application of the caustic agent in the affected region has the additional effect of treating incipient or sub-clinical lesions, as well as other aspects of photoaging often associated with solar melanosis.^{4,5}

Despite the availability of a number of options for the treatment of solar melanosis, there are few studies comparing techniques.

The use of TCA for performing chemical peels have been reported mainly in two vehicles: aqueous solution and water-soluble paste.

In general, the TCA peeling in aqueous solution is carried out in successive applications, interspersed with standardized time intervals after which the level of the inflicted damage (frosting) caused by prior applications is checked.⁶

The TCA paste was created with the purpose of obtaining greater uniformity in the acid's effect. Pastes are semisolid consistency pharmaceutical preparations that contain a significant proportion of insoluble solid particles (~20–50%), and are formulated with excipients of oily or aqueous characteristics.²

The rheological characteristics of the pharmaceutical preparations interfere with the speed of release of the active principle, in speed of evaporation of the solvent and in the amount of the active principle applied per area of skin.

In the present study, the authors compared the efficacy and safety of TCA (paste and solution) in the treatment of solar melanosis in the dorsum of the hands.

METHODS

A prospective, controlled, randomized, clinical trial was performed with 15 selected patients who bore at least five AM lesions on the dorsum of the hands and sought care at the Dermatology Ambulatory of the Hospital Universitário Evangélico de Curitiba (Curitiba, Paraná State, Brazil).

The exclusion criteria were: individuals with previous or current history of warts or recurrent herpes in the dorsum of the hands; pregnant women or nursing mothers; patients with active skin infection in the site of application the peeling; history of hypersensitivity to TCA, sunburn in the previous three days, surgery, cryotherapy, radiation therapy or PUVA in the previous six weeks; patients under systemic use of isotretinoin in the previous

six months; and patients unable to understand the post-peeling care instructions or who were unable to complete the study.

The TCA solution was prepared only in demineralized water, and the base paste for the TCA contained the following components: glycerin, sorbitol, talc, aerosil, Veegum k, blanc covasop, phenonip and water. The concentration of TCA was titled at 20% of solute mass / solution mass for both formulations.

Three peeling sessions were performed with 30-day intervals. Before the application, the dorsa of the hands were degreased with 70% alcohol. In a random manner, the dorsum of one hand was treated with 20% TCAA solution and the other with 20% TCA paste. The preparation type chosen in the first session was applied to the same hand in the following two sessions. The application of the paste was performed with a spatula, leaving the product in contact with the skin for two minutes, with the application site being washed thoroughly with 0.9% saline until complete removal. The solution was applied in layers with a moistened gauze until the appearance of level II frosting (white uniform cover with a bright pink background), without rinsing. The patients were instructed not to wash their hands in the following three hours after the application and to use liquid petrolatum in the application site during the following five days. They were also instructed not to get exposed to the sun and apply sunscreen daily. Both the sunscreen and the liquid petrolatum were standardized and provided.

The degree of lightening of the lesions was evaluated by 13 dermatologists through photographs taken before and 30 days after the end of treatment, without identifying the method used. The level of improvement was evaluated according to a semiquantitative scale ranging from 0 to 3 (0 – Absence of improvement/whitening <25%, 1 – Slight improvement/whitening 25–50%, 2 – Moderate improvement/whitening 50–75%, 3 – Significant improvement/whitening >75%).

Finally, the degree of satisfaction of each patient regarding each treatment was evaluated by using a scale with three choices: unsatisfied, somewhat satisfied and satisfied.

The research project was approved by the Research Ethics Committee of the institution, and all participants read and signed a free and informed term of consent.

The categorical data were represented by proportions and absolute numbers, while the parametric data was represented by mean values \pm standard deviation. The Binomial, Fisher exact and Mann-Whitney tests were used, as well as the intraclass correlation (absolute agreement). The generalized linear mixed model with gamma type curve adjustment was used for the analysis of the scores attributed by the dermatologists. The data were analyzed using the IBM SPSS 20 software, with values being considered significant when $p < 0.05$.

RESULTS

Fifteen (15) female patients were included, of which four (4) had significant adverse effects with the paste, and none had adverse effects with the solution ($p = 0.10$ – Fisher's exact test). One (1) patient did not complete the study due to an intense

irritation in the site of application of TCA paste, with the formation of blisters. Two (2) patients had severe burning sensation during the application of the paste, occasioning a reduction in the time of action to 1.5 minute in the following sessions, with good development. One (1) patient had pustules after the first session on the hand that received paste, with the picture being resolved with systemic antibiotic and topical corticosteroid of medium potency for seven days, without recurrence in the following sessions. In this manner, 14 women completed the study, of which nine (9) had skin phototype II and five (5) phototype III, and a mean age of 58 ± 10.7 years.

Of these 14 women, none was unsatisfied with both treatments, with 12 having been very satisfied with the paste and 11 very satisfied with the solution ($p = 0.99$ – Fisher's exact test). Regarding the preference for the methods, 5 preferred the paste and 8 the solution ($p = 0.41$ – binomial test).

Regarding the assessment of the dermatologists, there was satisfactory intraclass correlation (0.87) among the 13 evaluators, with the mean score of the clinical improvement attributed to the paste being greater than that attributed to the solution (1.28 ± 0.98 x 1.01 ± 0.86 , $p = 0.01$ – Mann-Whitney test) (Figures 1 and 2) (Graph 1). The superiority of the paste was later confirmed by a generalized linear mixed model controlled by the variables *evaluator dermatologist*, *patient* and *treated limb* (p

<0.01 ; Coefficient = 0.11 [IC 95%: 0.04 to 0.18]; Akaike = 361.5; Bayesian = 413.6).

DISCUSSION

TCA has been used in the ablative treatment of solar melanosis with satisfactory results.⁷ It is a chemical cautery that coagulates skin proteins and can be used localized points or in the form of chemical peels.⁸

The depth of the caustic effect is determined by the following factors: thickness and degree of oiliness of the target skin, concentration of the active substance, degree of previous degreasing, friction during application, occlusion and the volume applied.^{1,9,10} Furthermore, there are different preparations that, due to their physico-chemical properties, convey the active principle to the site of action in different ways.

According to literature review performed by the authors, there is absence of studies comparing the application of peelings using different vehicles. On the other hand, some studies compare cryotherapy with 33% to 40% TCA peeling in the treatment of solar melanosis with results favorable to the first method.¹¹⁻¹³

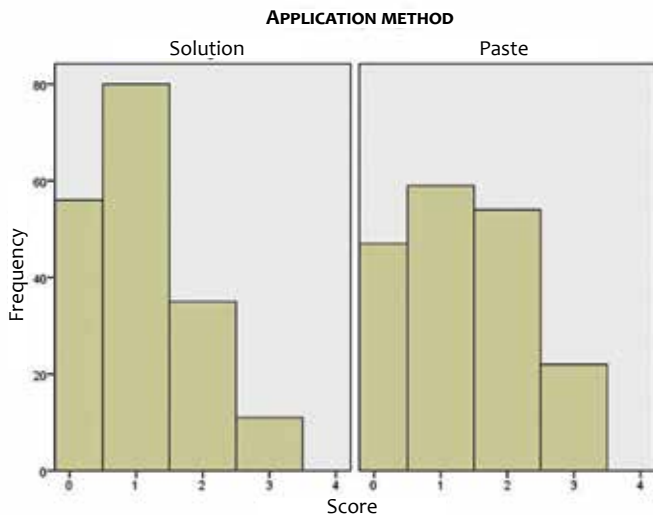
In the present study, from the patients' point of view, none of the methods stood out regarding preference or satisfaction. On the other hand, in the blind evaluation of the aesthetic result carried out by dermatologists, the use of the paste was significantly superior.



FIGURE 1: Results after three peeling sessions using paste (right hand) and solution (left hand) containing 20% TCA



FIGURE 2: Results after three peeling sessions using paste (right hand) and solution (left hand) containing 20% TCA



GRAPH 1: Histogram of the scores from the whitening of the solar melano-sis attributed to each of the methods by dermatologists

Despite the fact that the dermatologists' evaluations have shown a higher degree of whitening with the paste formulation, it is worth to note that the adverse effects with this vehicle tended to be more intense.

The TCA paste's opacity hampers the assessment of the level of damage (or frosting), caused by the active principle, making it difficult to identify the appropriate instant to remove the caustic agent. On the other hand, defining a fixed exposure time to the acid disregards the variability of the response to the product among individuals.

In their study, Goldust M. et al. found hyperpigmentation was the main adverse effect to the use of TCA, however the concentration of the acid used was 40%, the vehicle was the aqueous solution, and it was applied punctually on each of the lesions caused by the sun. Unlike in the present study, where a lower concentration was used and paste applied diffusely, there were no cases of hyperpigmentation or any additional long-term effect.

CONCLUSIONS

Peelings using a solution or paste containing 20% TCA to treat actinic melanosis in the dorsum of the hands were proven efficient. The duration of the exposure to the paste, set at two minutes, seems to provide an effective whitening effect that is superior to that resulting from the use of the solution, the latter limited to a level II frosting. On the other hand, the paste's caustic action intensity is relatively erratic, with one quarter of the patients presenting significant adverse effects.

Setting a standard time of exposure to the TCA paste might prove not to be an adequate approach while objective factors that can predict individual susceptibility to its harmful effects have not been identified by further studies. ●

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Clinical and epidemiological profile of childhood vitiligo: analysis of 113 cases diagnosed at a dermatology referral center from 2004 to 2014

Clinical and epidemiological profile of childhood vitiligo: analysis of 113 cases diagnosed at a dermatology referral center from 2004 to 2014

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ABSTRACT

Introdução: Vitiligo is an acquired autoimmune form of hypopigmentation or depigmentation in which half of the cases begins in childhood.

Objectives: To describe the clinical and epidemiological profile of childhood vitiligo in a referral center for dermatology.

Methods: A cross-sectional, descriptive study was carried out based on the analysis of medical records of patients younger than 13 years diagnosed with vitiligo from 2004 to 2014.

Results: Of the 113 cases identified, 54% were female and 46% male, the age ranged from 0 to 12 years, with most patients in the 4-8 years-old subgroup (54.8%). In 59% of the medical records there was no record of triggering factors of vitiligo; 31% of patients associated the onset of the illness to emotional stress, 3% to physical trauma and 7% did not associate it to any triggering factor.

Conclusions: The discreet prevalence in women has also been reported in other studies. Vitiligo behavior in children is different from that observed in adults. The influence of psychological factors as triggers and potential lasting effects on self-esteem should be considered in the approach of the patient. Although studies on vitiligo in this age group are scarce in the literature, the results of the present study were similar to the reports already available in the literature.

Keywords: child; epidemiology; vitiligo

RESUMO

Introdução: O vitiligo é forma adquirida autoimune de hipopigmentação ou despigmentação, iniciando-se na infância metade de seus casos.

Objetivos: Traçar o perfil clínico e epidemiológico do vitiligo infantil em um centro de referência em dermatologia.

Métodos: Estudo transversal e descritivo com análise dos prontuários de pacientes com menos de 13 anos diagnosticados como portadores de vitiligo entre 2004 e 2014.

Resultados: Dos 113 casos identificados, 54% eram do sexo feminino e 46% do sexo masculino; a idade variou de zero a 12 anos com a maioria dos pacientes (54,8%) no subgrupo de quatro a oito anos. Em 59% dos prontuários não havia registro sobre fatores desencadeantes do vitiligo; 31% dos pacientes associaram o início da doença a estresse emocional, 3% a trauma físico, e 7% não associaram a fator desencadeante.

Conclusões: A discreta prevalência no sexo feminino também foi descrita em outros estudos. O comportamento do vitiligo na criança é diferente daquele observado nos adultos. A influência dos fatores psicológicos como desencadeantes e os potenciais efeitos duradouros na autoestima devem ser levados em consideração na abordagem do paciente. Os resultados deste trabalho foram semelhantes aos relatos existentes sobre o vitiligo nessa faixa etária, que são, aliás, poucos na literatura.

Palavras-chave: criança; epidemiologia; vitiligo

INTRODUCTION

Vitiligo is an acquired autoimmune form of loss of pigment characterized by hypopigmentation or depigmentation.¹ It affects 0.5% to 2.0% of the world’s population, with half of the cases beginning in childhood.¹⁻³ For some authors, the vitiligo’s disfiguring and unsightly potential correlates with depression and other psychosocial disorders at different stages of life, including childhood and preadolescence.⁴⁻⁶ Studies have supported the theory that skin disorders, especially vitiligo, have interference on the individuals’ psychosocial development.^{1, 4, 5, 7, 8} This paper is aimed at outlining the clinical and epidemiological profile of patients under 13 years of age diagnosed with vitiligo in a dermatology referral center in the city of São Paulo - Brazil. In this manner, the authors intend to warn dermatologists of this dermatosis, which can cause harmful effects to the children’s health.

METHODS

This is a cross-sectional descriptive study with retrospective analysis of records of all patients younger than 13 years who were diagnosed with vitiligo in the period July 2004 - July 2014 that used a non-probabilistic sampling method for convenience, in which 113 cases were identified.

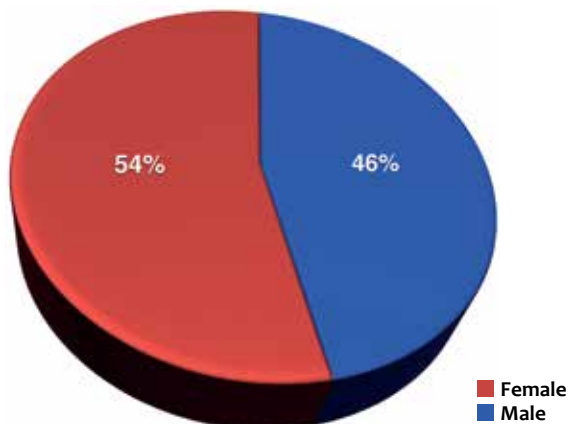
A research clinical and epidemiological data was carried out including gender, age group, lesion topography, elapsed time from the first symptom to diagnosis, presence of triggering factors and treatment used. According to the clinical presentation, the patients’ vitiligo were classified into six types: focal (one or more depigmented spots or patches in some area without distribution by dermatome), segmental (one or more spots or patches in a dermatome or unilateral segment of the body), vulgaris (widely distributed spots or patches), acrofacial (face and acral region, symmetric), universal (affected area of 80% or more), mucosal (one or more mucous membranes).

It is worth to note that due to the study’s design, biases of measurement and information should be taken into consideration.

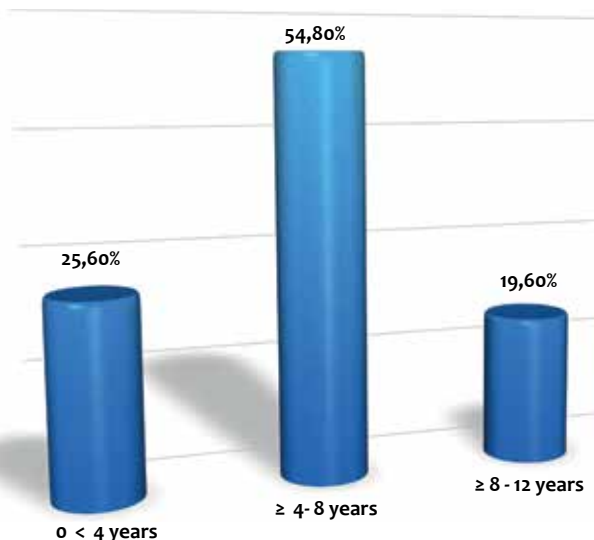
The data obtained were processed in Microsoft Excel®, with frequency and percentage analysis. This software was also used to prepare graphs. The principles of the Declaration of Helsinki were observed during the study.

RESULTS

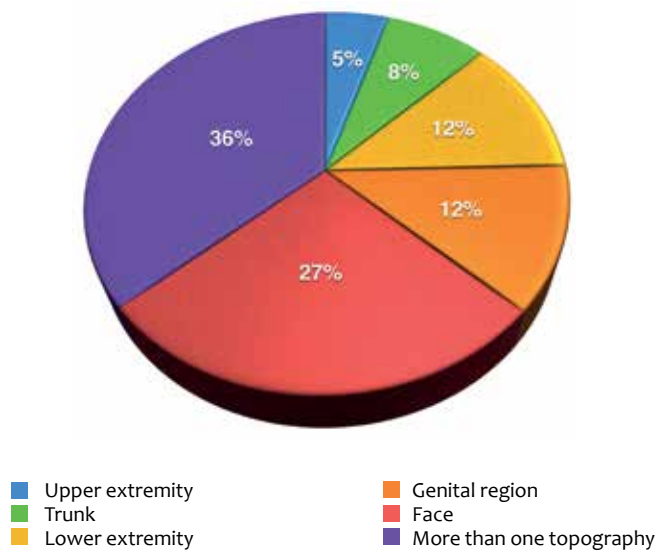
One hundred and thirteen (113) cases of childhood vitiligo were identified. Of these, 54% were female and 46% male patients (Graph 1). Ages ranged from 0 to 12 years, with patients having been grouped according as follows: between zero and four years of age (25.6%), ≥ 4-8 years of age (54.8%) and ≥ 8-12 years of age (19.6%) (Graph 2). The most prevalent location of the first clinical manifestation was the face, affected isolated in 27% of cases and associated to other body segments in 36% of cases. Other body topographies affected were: genital region (12%), lower limbs (12%), trunk (8%) and upper limbs (5%) (Graph 3). The time elapsed between the first symptom and diagnosis was less than one year in 55.7% of cases. Most of



GRAPH 1: Childhood vitiligo prevalence by gender



GRAPH 2: Childhood vitiligo prevalence by age group



GRAPH 3: Topography of the first clinical manifestation

the patients (82.3%) denied family history of vitiligo. In 59% of the records there was no description of triggering factors; 31% of the patients associated the onset to emotional stress, 3% to physical trauma and 7% did not associate the onset to any triggering factor (Graph 4). According to the adopted classification, vitiligo vulgaris accounted for 58.4% of cases; the focal type to 23%, the segmental type for 8.8%, the mucosal type for 6.3%; the universal type to 2.6% and the acrofacial type to 0.9% (Graph 5). Topical treatment was used as monotherapy in 72% of patients. There was association of topical medications with heliotherapy in 5%, and the association with systemic therapy (corticosteroid, vitamins C and E, folic acid) was implemented in 9% of the cases. Phototherapy was used in 11% of patients, and 3% of the total did not undergo treatment in the service where the present

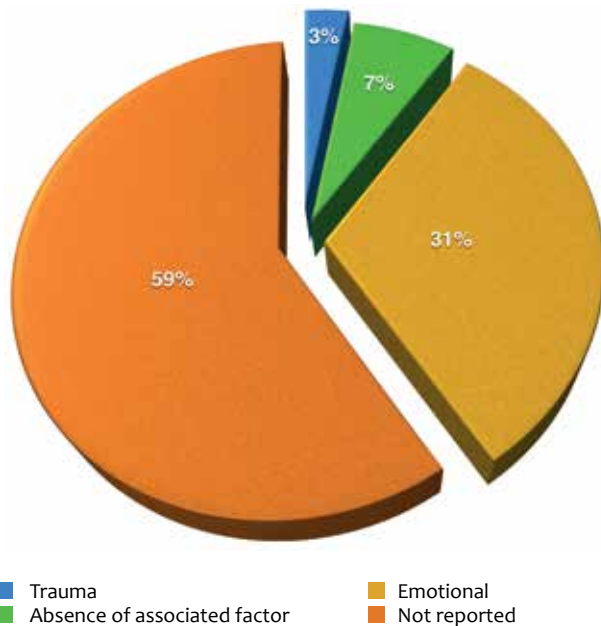
study was performed. Twenty-three percent of the patients were referred for psychotherapy 20.3% of the patients studied.

DISCUSSION

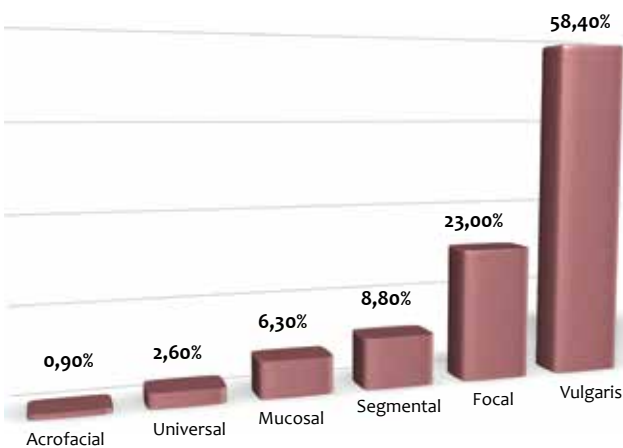
The discreet prevalence in women has also been reported in Brazilian and international studies.^{1-3, 9, 10} This may be associated with the possible greater concern of parents at daughter's aesthetics.^{3, 10} The most affected age group was that ranging from 4 to 8 years of age (54.8%), however there are studies suggesting an older age.^{1, 3, 10} In most patients the diagnosis occurred in less than one year, which can be considered early when compared to a recent Indian study where the average was 18.6 months¹ and the most common vitiligo type in childhood was the acrofacial type (38.1%) – whereas in line with the majority of the studies, the present paper suggested the vulgaris type is the most common (58.4%). The face was the most affected site (27.4%), also in line with most of other authors.^{1, 2} Vitiligo family history was positive in 17.7% of the patients, a lower percentage than that found in a diverse study (28.7%).¹ The psychological consequences of vitiligo during childhood are much described in the literature.^{3-5, 9} Little is known, however, about the influence of possible triggering factors (psychological and physical trauma), frequently observed in the clinical practice. Parents of 34% of the studied children associated an event to the beginning of the lesions, with emotional stress being the most reported. A Brazilian nationwide study showed that in 60% of cases some relevant situation was referred (separation or death of a parent, sexual abuse or death of a pet).³ Only 20.3% of our patients were referred to psychotherapy, evidencing the need to provide more prominence to this treatment modality. Topical monotherapy was the most used treatment due to lower risks of side effects and the benign character of the lesions.

CONCLUSION

Vitiligo behavior in children is different from that observed in adults. The influence of psychological factors as triggers, as well as the lasting effects on the patients' self-esteem should be considered when choosing a treatment. The results obtained in the present study were similar to those described in the few reports on the clinical and epidemiological profile of vitiligo in this age group existing in the literature. ●



GRAPH 4: Triggering factors of childhood vitiligo



GRAPH 5: Vitiligo classification

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Ex vivo study for evaluating the whitening activity of Pycnogenol® after exposure to ultraviolet and infrared radiations, and visible light

Estudo ex vivo para avaliação da atividade clareadora do Pycnogenol® após exposição à radiação ultravioleta, infravermelha e luz visível

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ABSTRACT

Introdução: *Hyperpigmentation is a common dermatological condition, usually associated with exposure to the sun and relative difficulty of treatment. Pycnogenol® is an extract obtained from the French pine tree Pinus pinaster, with known antioxidant and anti-inflammatory activity, having been proven to inhibit melanin synthesis in previous studies.*

Objective: *To evaluate the whitening activity of Pycnogenol® in an ex vivo experimental model after exposure to ultraviolet A and B, infrared-A radiations and visible light.*

Method: *Human skin fragments obtained from elective plastic surgery were treated with Pycnogenol® and then irradiated with ultraviolet A and B, and infrared-A radiations, and visible light, having been sent for histological evaluation of melanin pigmentation by the Fontana-Masson staining technique.*

Results: *The histological evaluation demonstrated an increase in melanin deposition in all irradiated groups. However, fragments pre-incubated with Pycnogenol® showed a reduction in the deposition of this pigment after irradiation.*

Conclusions: *This study demonstrates the reduced melanin deposition in skin culture treated with Pycnogenol® after irradiation with ultraviolet A and B, and infrared-A radiations, and visible light, concluding that this substance may have lightening properties.*

Keywords: *hyperpigmentation; skin lightening preparations; solar radiation*

RESUMO

Introdução: A hiperpigmentação é condição dermatológica frequente, geralmente associada à exposição solar e com relativa dificuldade de tratamento. Pycnogenol® é extrato obtido do pinheiro francês Pinus pinaster, com conhecida atividade antioxidante e anti-inflamatória, tendo demonstrado em estudos prévios capacidade de inibir a síntese de melanina.

Objetivo: Avaliar a atividade clareadora do Pycnogenol® em modelo experimental ex vivo após exposição à radiação ultravioleta A e B, infravermelha-A e luz visível.

Métodos: Fragmentos de pele humana obtidos de cirurgia plástica eletiva foram tratados com Pycnogenol® e posteriormente submetidos à radiação ultravioleta A e B, infravermelha-A e luz visível, para avaliação histológica da pigmentação melânica pela técnica Fontana-Masson.

Resultados: A avaliação histológica demonstrou aumento na deposição de melanina em todos os grupos irradiados. Entretanto, os fragmentos incubados previamente com Pycnogenol® demonstraram redução na deposição desse pigmento após a irradiação.

Conclusões: Este estudo demonstra a redução na deposição de melanina em cultura de pele tratada com Pycnogenol®, depois de submetida à radiação tanto ultravioleta A e B quanto infravermelha-A, bem como à luz visível, e conclui que essa substância pode apresentar propriedades clareadoras.

Palavras-chave: hiperpigmentação; clareadores; radiação solar

Original Articles

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Conflict of interests: None

INTRODUCTION

When it comes to skin care, clinical signs evidenced by chronic exposure to solar radiation, such as the presence of wrinkles and hyperpigmentation, are among the main aesthetic concerns that affect human beings, given the amount of active principles and cosmetic products marketed based on their alleged action in the mitigation of such effects.¹⁻⁶

Cutaneous pigmentation depends both on the number of melanocytes and the activity of melanogenic enzymes, which culminates in the production of melanin. Melanin plays an important role in protecting the skin from the harmful effects of solar radiation, however an excessive amount of this pigment can become an aesthetic problem.⁷

Exposure to sunlight, artificial tanning, the use of medications and other chemical agents, as well as chronic inflammatory processes and hormonal influences, can increase the production of mediators, such as the melanocyte stimulating hormone (α -MSH) and endothelin-1, which trigger a melanization process in the skin.⁷⁻⁹ Studies show that, in addition to the exposure to ultraviolet light, infrared-A radiation and visible light also promote changes in skin pigmentation.¹⁰⁻¹²

The availability of active principles and more effective and lower irritating power products with whitening or depigmenting properties is steadily sought after in the cosmetic marketplace. Aligned with this, the pursuit of substances that promote the homeostasis of the skin and are capable of delaying or reversing the clinical signs of cutaneous photoaging is a research and development tool in the cosmetic and dermatology fields.

Pycnogenol[®] is a standardized extract sourced from the bark of French maritime pine *Pinus pinaster*, which is rich in procyanidins, which in turn has demonstrated antioxidant and anti-inflammatory activity.¹³ Several possible effects of Pycnogenol have been investigated, including its action in reducing pigmentation and melanogenesis, in addition to its anti-edematous and vascularization actions.¹⁴

The present study is aimed at evaluating the whitening activity of Pycnogenol[®] based on the histological evaluation of melanin pigmentation using the Fontana-Masson technique in human skin fragments subjected to ultraviolet A and B (UVA/UVB) and infrared-A (IRA) radiations, visible light (VL), and the association of UVA/UVB, VAT and VL.

METHODS

Fragments of human skin harvested in an elective surgery were incubated in culture medium and treated with Pycnogenol[®] (Flebon[®], *Pinus pinaster*, FQM Farmoquímica S/A, Brazil) at concentrations of 0.0316, 0.0100 and 0.00316 mg/ml, defined after performing a cell viability test for determining non-cytotoxic concentrations for the efficacy trial. After 48 hours of incubation, all fragments were underwent irradiation as described below.

For exposure of the fragments to UVA/UVB radiations (10 J/cm² UVA) the following devices were used: UVA/UVB Cube 400, SOL 500 H2 filter and UV Meter (Hönle UV America Inc., MA, USA). Regarding the infrared-A radiation (360

J/cm² IRA radiation), the Hydrosun 750 and HBM1 devices (Hydrosun Medizintechnik GmbH, Müllheim, Germany) were used. For the irradiation of visible light (480 J/cm²) the devices used were UVA/UVB Cube 400, SOL 500 H1 filter for filtering the UVA radiation; Rosco Cinegel 3114 filter for filtering UVB and VLP-471RAD Radiometric Sensor (Deta Ohm, Caselle di Selvazzano, Italy).

The fragments were maintained for 48 additional hours and fixed in 10% buffered formalin, embedded in paraffin blocks, and subjected to serial sectioning on a microtome to about 5µm thick. The sections were stained with hematoxylin-eosin (H/E) associated with the Fontana-Masson technique. The slides were photographed under an optical microscope (Nikon Eclipse) at 10X magnification with the aid of the Image-Pro software.

The use of human skin fragments harvested in elective surgeries for carrying out the present study was approved by the Research Ethics Committee of the Universidade San Francisco (SP), Brazil.

RESULTS

As can be seen in Figure 1, the histological evaluation showed that cultures of human skin fragments exposed to UVA/UVB, IRA, VL and to the association of the radiations showed higher density of melanin pigmentation by Fontana-Masson technique as compared to the control group (fragments maintained at baseline).

Conversely, all fragments treated with Pycnogenol[®] showed noticeable reductions in melanin density as compared to the fragments that were only photoexposed.

It is important to note that the results observed in this *ex vivo* experiment corroborate the *in vitro* trials obtained in our laboratory using cultured human melanocytes (in progress; unpublished data) in which the radiation promote, isolatedly, increased production of melanin and tyrosinase enzyme activity. An interesting observation obtained from the *in vitro* trials indicates that the increase verified in the production of melanin is significantly higher in cell groups exposed to the association of the radiations than that observed in the groups irradiated isolatedly.

DICUSSÃO

Several studies have attempted to relate the use of anti-oxidants to skin pigmentation disorders and justify its use as a possible therapeutic alternative in these cases.

Procyanidins have demonstrated a significant free radicals sweeping action, promoting anti-edematous and anti-inflammatory action in conditions that occur with capillary fragility. Its topical and oral use in experimental studies with mice has been shown capable to inhibit erythema induced by UV radiation and to increase vascular permeability. Grape seed extract rich in proanthocyanidins, was proven to be able to suppress the formation of melanin in pig skin, as well as to have a whitening effect on hyperpigmentation induced by UV radiation. Later on it was observed in Japanese women that grape seed extract could

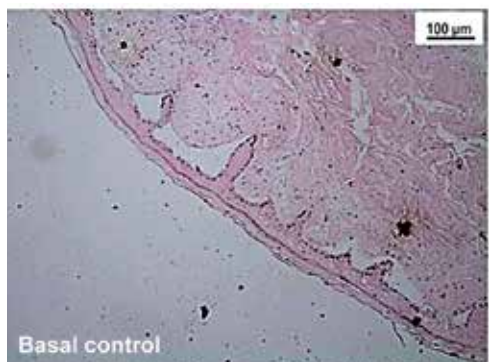
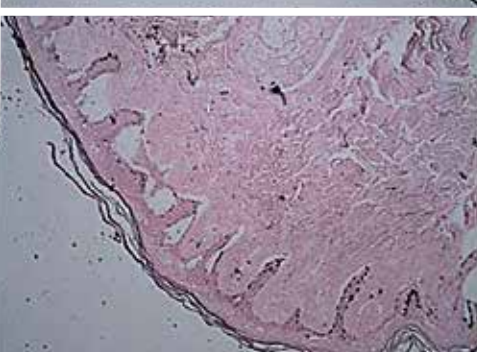
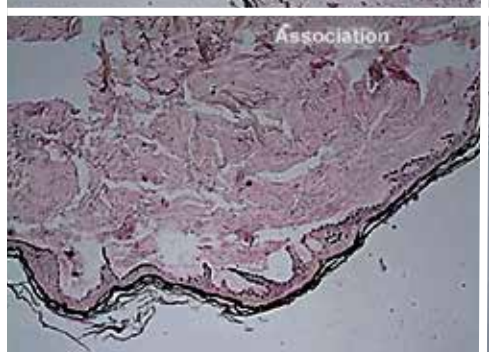
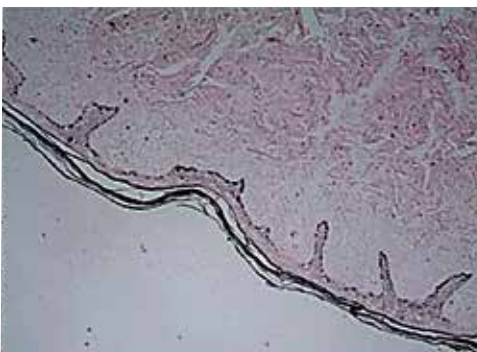
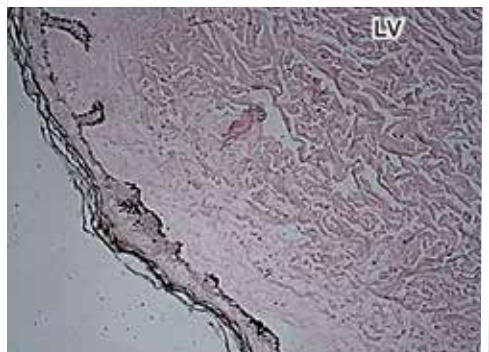
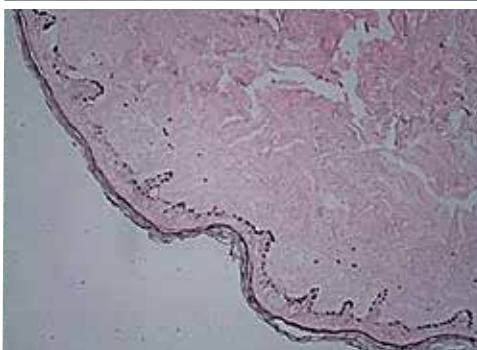
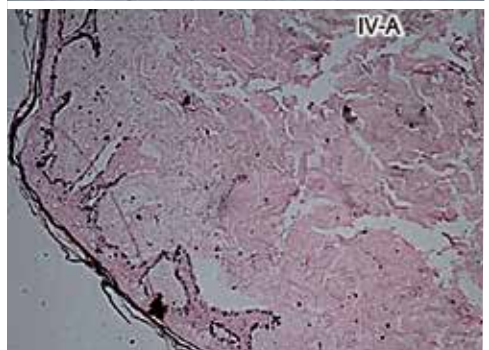
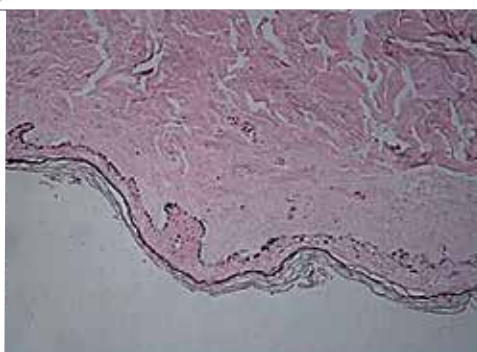


FIGURE 1: Histological evaluation of the deposition of melanin in human skin culture incubated with Pycnogenol® and exposed to UVA/UVB, IVA, VL and their association (UVA / UVB, IVA, LV), compared to the control. Reference bar = 100μm



inhibit melanogenesis or the proliferation of melanocytes in the skin of the face affected by melasma.¹³

Handog et al. have shown that the association of pycnogenins, vitamin A, C and E could be effective as an adjuvant in the clinical treatment of melasma. In this study, the use of 48mg/day Pycnogenol® was combined with 6mg of beta-carotene, 60mg ascorbic acid and 15UI D-alpha-tocopherol, and compared to the administration of placebo for eight weeks. The results evaluated with the assistance of a mexameter showed that there was a decrease in pigmentation and also a significant improvement in the Masi score, leading to the conclusion that this combination is safe and effective in the treatment of melasma.¹⁵

In 2002, a study by Ni et al. investigated the efficacy of Pycnogenol® in the treatment of melasma. Twenty-five milligrams (25mg) were administered three times a day (75mg/day) in 30 women with melasma. At the end of 30-day period there was a decrease in the melasma area, in the intensity of pigmentation, with 80% effectiveness rate, according to the authors.¹⁴

Pycnogenol® is a plant extract obtained from the bark of French maritime pine *Pinus pinaster*, a source of flavonoids. It has attracted attention due to its powerful antioxidant action, with demonstrated ability to modulate melanogenesis, UV radiation induced erythema, and the expression of kappa-B nuclear transcription factor (NFkB).¹³ *In vitro* studies have demonstrated that Pycnogenol® is more potent than vitamins E and C, having the ability to recycle vitamin C, regenerate vitamin E and increase the endogenous antioxidant system.¹⁶

The improvement of techniques for its extraction allowed to obtain extracts with higher antioxidant activity, favoring the chromatographic identification of the main pharmacological components of Pycnogenol®, such as caffeic acid, ferulic acid, catechin and taxifolin.¹⁷

Studies have shown that, in addition to the antioxidant action, Pycnogenol® has anti-inflammatory activity, also being capable to stimulate the synthesis of Enos (endothelial nitric oxide synthase).^{18,19}

The use of this active principle in cardiovascular disorders has also been reported with promising results.²⁰ In the skin, in addition to studies involving the reduction in melanin production, the inhibition of metalloproteinases type 1, 2 and 9 (MMP-1, MMP-2 and MMP-9) has also been observed, recognizing its role in improving skin hydration and elasticity.²¹

In the study by Kim et al. it was possible to demonstrate that Pycnogenol® is able to suppress reactive oxygen species (ROS) and has a strong antityrosinase action, leading to suppression of melanin biosynthesis, corroborating its antimelanogenic potential. Its antioxidant capacity was assessed based on the suppression of the activity of peroxynitrite, superoxide, nitric oxide and hydroxyl radicals, with a positive regulation in the ratio reduced glutathione/oxidized glutathione in B16 cells also taking place. Its inhibitory action on tyrosinase activity was compared to that of other inhibitors; kojic acid was used as the reference inhibitor, with the results showing a significantly greater potency for Pycnogenol®. The treatment with the product promoted a reduction of the melanin content in B16 cells in a concentration-dependent way, ranging from 22.2% (50mg/ml) to 58.9% (5mg/ml) as compared to the control group treated with α -MSH, demonstrating its action in controlling melanin synthesis.^{22,23}

Using human skin fragments incubated with Pycnogenol®, the present study demonstrated that the deposition of melanin pigment was less intense after exposure to UVA/UVB radiation, IVA,VL and their association, as compared with untreated fragments, confirming the literature data, which demonstrate its antimelanogenic activity. However, the treatment of pigmentary disorders remains in the focus of new promising studies. Plant extracts rich in flavonoids have been investigated due to their ability to modulate cutaneous pigmentation, and Pycnogenol® is a substance that is gaining prominence.

CONCLUSION

The present study demonstrates that ultraviolet A and B, IRA radiations and visible light, in addition to the association of all these radiations, are capable of increasing the melanin's pigmentary density. It also demonstrates that cultures that have been previously treated with Pycnogenol® showed a noticeable decrease in the deposition of melanin, leading to the conclusion that this substance may have whitening properties.

Recent studies have shown that due to its antimelanogenic action, Pycnogenol® can be considered an option in the treatment of disorders like melasma and can have great importance in the maintenance and control of recurrences, although further studies may be required. ●

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Extended cervicoplasty: assessment of long-term results

Extended cervicoplasty: assessment of long-term results

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ABSTRACT

Introduction: Extended cervicoplasty is used to treat the aging stigmas of the lower third of the face, especially in cases of severe tissue sagging. However, the maintenance of its long-term results has been little studied in the literature.

Objective: To assess the maintenance of the results of extended cervicoplasty in the long-term.

Methods: Twenty-three patients with severe tissue sagging underwent extended cervicoplasty, having been followed up for five years. The postoperative results in the first and fifth year were evaluated by 8 plastic surgeons. The analysis of the results was performed using the McNemar and paired t-student tests.

Results: In the first year, 12 (52.2%) patients had the outcome rated as very good, 9 (39.1%) as moderate and 2 (8.7%) as poor. In the fifth year, 9 (39.1%) had the outcome classified as very good, 11 (47.8%) as moderate and 3 (13.1%) as poor. None of the patients had the outcome rated as excellent or bad in any of the analyzed periods. There was no significant difference regarding the classification ($p = 0.450$); and the total score ($p = 0.373$) during the study period.

Conclusion: Even in difficult cases, extended cervicoplasty provided good results that were maintained in the long-term.

Keywords: rhytidoplasty; cervicoplasty; neck

RESUMO

Introdução: A cervicoplastia ampliada é utilizada para o tratamento dos estigmas do envelhecimento do terço inferior da face, especialmente para os casos de intensa flacidez tecidual. Porém, a manutenção de seus resultados em longo prazo foi pouco estudada na literatura.

Objetivos: Avaliar a manutenção dos resultados da cervicoplastia ampliada a longo prazo. **MÉTODOS:** Vinte e três pacientes com intensa flacidez tecidual foram submetidos à cervicoplastia ampliada e acompanhados durante cinco anos. Os resultados pós-operatórios no primeiro e no quinto ano foram avaliados por oito cirurgiões plásticos. A análise dos resultados foi realizada por meio dos testes McNemar e t-Student pareado.

Resultados: No primeiro ano, 12 (52,2%) pacientes tiveram o resultado classificado como muito bom, nove (39,1%) como moderado, e dois (8,7%) como fraco. No quinto ano, nove (39,1%) tiveram o resultado classificado como muito bom, 11 (47,8%) como moderado, e três (13,1%) como fraco. Nenhum paciente teve o resultado classificado como excelente ou ruim em nenhum dos períodos analisados. Não houve diferença significativa em relação à classificação ($p = 0,450$); e entre a pontuação total ($p = 0,373$) no período avaliado.

Conclusões: Mesmo em casos difíceis, a cervicoplastia ampliada proporcionou a obtenção de bons resultados mantidos em longo prazo.

Palavras-chave: ritidoplastia; cervicoplastia; pescoço

INTRODUCTION

A recurrent complaint from patients who underwent surgery for cervical rejuvenation is precisely related to the partial loss of the outcome over time, especially when there is pronounced tissue laxity preoperatively.^{1,2} In addition to frustrating and undesirable, the early recurrence of the complaints that led the patient to undergo cervical surgery makes it difficult for him or her to possibly undergo a second procedure.¹⁻³

The development of facial plastic surgery achieved in recent years offered different techniques, strategies and possibilities to surgeons, however it unfortunately did not determine which option to choose for cervical lifting, and the search for the optimal treatment still continues.^{1,3-5} Regarding the search for the maintenance of long-term cervicoplasty results, the current focus of research appears to be in the approach of multiple anatomical structures and in the use of different surgical strategies.^{1,2,4,6,7}

Aligned with this, the authors of the present paper have been using the so-called expanded cervicoplasty for cervical rejuvenation for over 10 years, with safe, reliable and reproducible results.⁸ The technique is nothing more than a combination of classic precepts advocated by surgeons like Millard et al.,⁹ who privileged a wide cervical access and the direct lipectomy through an incision in the submental region; Connell¹⁰ and Feldeman,¹¹ who demonstrated the importance of more aggressive and direct approaches in the platysma muscle; and Pitanguy,¹² who called for the restoration of the natural anatomy of the tissues approached with the *round lifting* technique.

The present study was designed aiming at presenting the authors' experience with the expanded cervicoplasty and evaluate the maintenance or not of its long-term results.

METHODS

The study included all patients who underwent expanded cervicoplasty at the authors' private practices, from January 2008 to August 2010, and were classified as McKinney grade

IV¹³ – presence of pronounced sagging skin in the lower third of the face and of very visible platysmal bands – the so-called difficult neck.⁸

Before undergoing the procedure, the patients were photographed by a same photographer, in pre-established positions (frontally, right and left profiles) at the same location and with the same image parameters (digital camera Nikon Inc., Melville, New York, USA).

The surgery was performed according to the following methodology: with the patient in sitting position, tumescent anesthetic was injected in the region with about 150 ml of solution containing 0.125% lidocaine with 1:200,000 epinephrine. The liposuction of the cervical region was then carried out. The submentonian groove was then incised (variation of 4cm to 6cm), and the anterior region of the neck was dissected with a Metzemaum scissors, exposing the platysma muscles. The platysma muscles were then partially released from the deep structures in the mid-cervical region through blunt divulsion, allowing the preparation of two muscle flaps with roughly 4cm in length. The subplatysmal fat became clearly exposed, with its central part being excised. Next, the platysmal muscle flaps were drawn closer to each other over the midline, forming a single layer of between 5cm and 9cm long (from the submentonian incision to the thyroid cartilage), using continuous suture with 4.0 mononylon thread. The classic Pitanguy's *Round Lifting* sequence¹² was then performed, starting at the retroauricular incision, with extensive dissection of the cervicofacial skin flap. With the superficial system muscle-aponeurotic exposed, the plication in inverted "L" was carried out, starting in the zygomatic-facial region, running up until the lateral cervical region, near the sternocleidomastoid muscle. The tension of skin at the end of the surgery contributed for the further definition of the cervical region.⁸ (Figures 1 and 2)

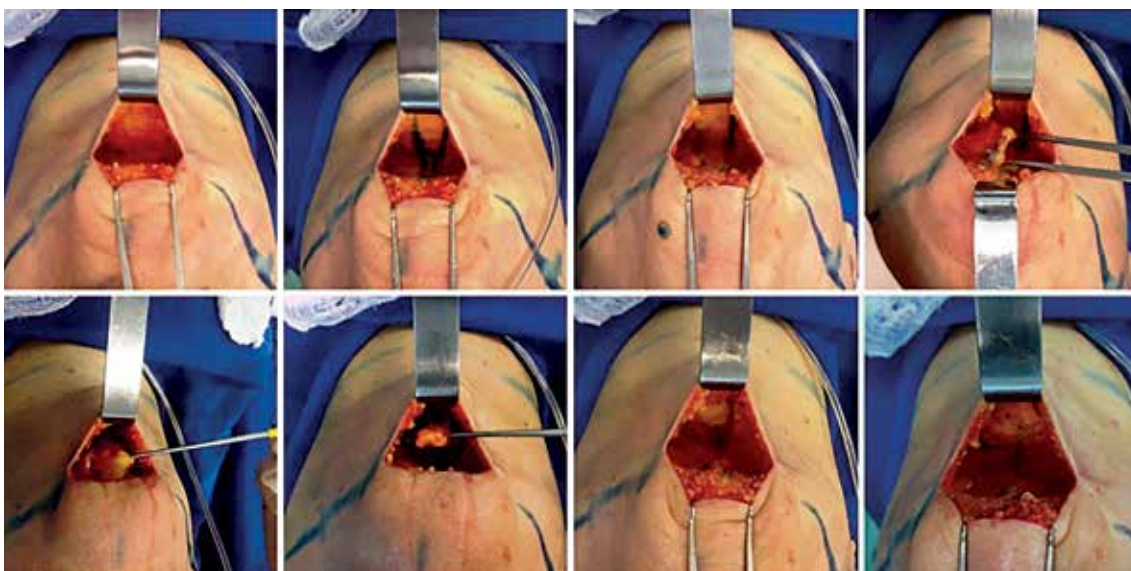
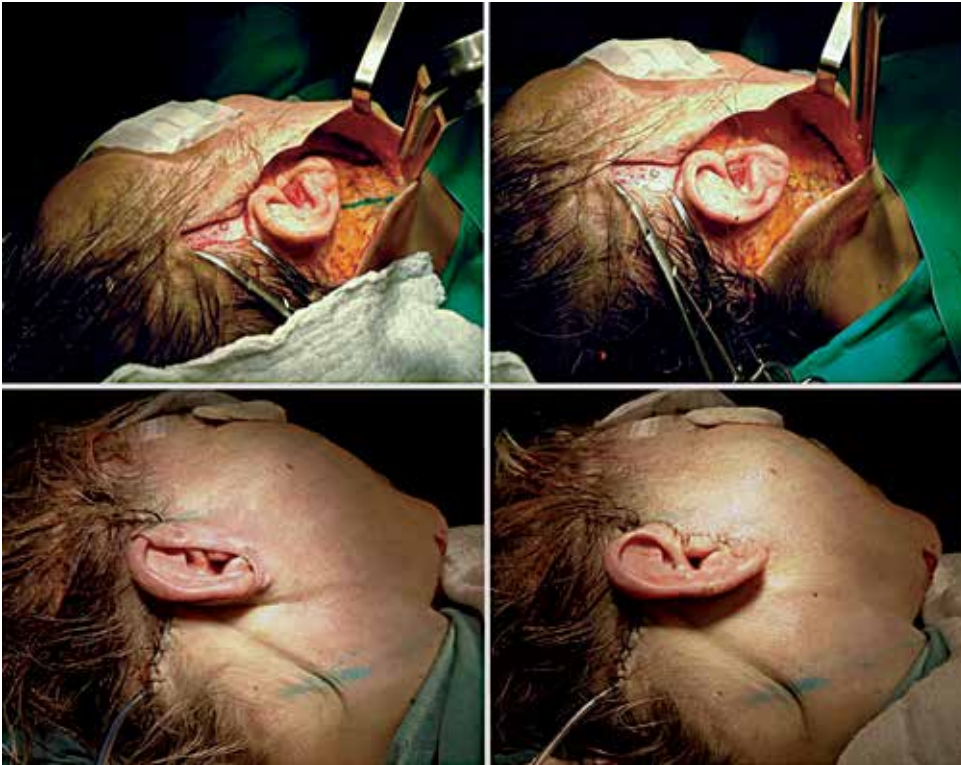


FIGURE 1:

Transoperative aspects of expanded cervicoplasty, mid-cervical approach. Top: broad detachment and visualization of the medial borders of the platysma muscles (marked in blue in the detached area); detachment of the medial borders of the platysma muscle and their elevation. Bottom: visualization and resection of the subplatysmal fat; advancement and suturing of the two muscle flaps in the mid-cervical line

**FIGURE 2:**

Transoperative aspects of the expanded cervicoplasty lateral-cervical approach. Top: broad detachment and visualization of the cervical area to be applied (marked in blue in the detached area); platysmal plication with lateral traction of the tissues. Bottom: traction of the facial flap and resection of excess skin

The patients were monitored weekly during the first month after the surgery, and every two months until the 12th month, when new images (identical to those of the pre-operative) were captured. The patients were contacted in the 5th year after the surgery and invited for a re-evaluation. Those who did not attend the re-evaluation visit were automatically excluded from the study.

In the 5-year postoperative visit, new photographic images were captured (in conditions identical to those of the pre-operative). Patients were also asked whether they had undergone other procedures in the middle or lower third of the face during that period. Those who answered positively were excluded from the study.

The patients had their photos (before the surgery, and one and five years after the procedure) evaluated by eight plastic surgeons, members of the Brazilian Society of Plastic Surgery (SBCP).

The outcome of the expanded cervicoplasty was assessed by the modified method of Antell & Orssek,¹⁴ according to which the eight plastic surgeons carried out two assessments of each patient using subjective criteria (before versus 1 year after; before versus 5 years after).

The evaluator physicians used the following scores for each period analyzed: 0 = worsened, 1 = unchanged, 2 = slight improvement, 3 = moderate improvement, 4 = significant improvement, and 5 = maximum possible improvement.

The scores attributed to each patient were added up in a way that each patient received a final rate classifying the surgery outcome as: unsatisfactory (0-9), poor (10-19), moderate (20-28), very good (29-36), and excellent (37-40).

The analysis of the correlation between the surgery's outcome classification and the instant at which this classification was attributed regarding the preoperative instant was performed using the McNemar test. The comparison between the one-year and five-year instants as compared to the average total score of the surgery's outcome was performed using the paired Student t-test. The statistical analysis was performed using the statistical software SigmaPlot 12.5, using a significance level of 5%.

RESULTS

During the study period, 39 patients classified as McKinney grade IV¹³ underwent extended cervicoplasty. Of these, 16 (41.02%) were excluded from the analysis: 12 of them for not having returned to late post-operative consultations and 4 for having undergone definitive cutaneous filling in the lower third of the face during that period. The 23 patients who completed the study were female Caucasians, with a mean age of 58 ± 13 years.

The surgical procedure had a mean duration of 205 ± 34 minutes. There were no difficulties to perform the platysma muscle flaps or the subplatysmal fat resection. All patients were discharged within about 24 hours of admission. The postoperative recovery was considered satisfactory. Three patients had hematoma, 2 had partial necrosis of the retroauricular skin flap, 1 had temporary paralysis of the submandibular branch of the facial nerve. The remaining patients did not have complications.

The evaluation summary is shown in Table 1, with the classification of outcomes one and five years after the procedure.

None of the patients had her outcome rated as excellent or unsatisfactory in any of the periods. The percentages of the

classification of the surgery's outcomes after one and five years as compared to the preoperative scores are presented in Table 2.

The results are expressed in relative frequency. There was absence of significantly different distributions regarding the classification of results in the assessments one year after and five years after the (McNemar's test, $p = 0.450$).

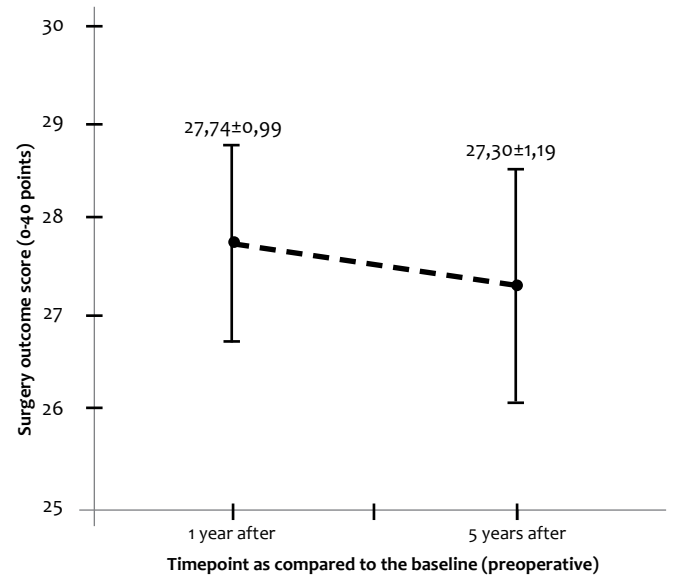
One year after the procedure, 12 patients had the surgery outcomes classified as very good and, of these, 58.3% ($n = 7$) maintained this classification in the 5th year after having undergone the procedure. Eleven (11) patients had a moderate or weak outcomes and, of these, 81.8% ($n = 9$) maintained the outcome in the 5th year after having undergone the procedure. There was not a significantly different distribution regarding the outcomes classification and the period evaluated (McNemar test: $p = 0.450$). In general, the classification of the surgery outcomes in the 1st and 5th years after the procedure were concordant in 69.6% ($n = 16$) of cases.

The average total score of the surgeries outcomes in the 1st year evaluation was 27.74 ± 0.99 points (mean \pm standard error of the mean), while in the 5th year it was 27.30 ± 1.19 points. Likewise, there was not statistical difference in the scores between the evaluation timepoints and the total score evaluating the surgery outcomes (t-Student test, $p = 0.373$) (Graph 1).

In Figures 3 and 4, the operated patients are depicted frontally, and in left and right views, in photographs before the surgery (top), after one year (middle) and after five years (bottom).

DISCUSSION

Several surgical options are available for treating the signs of aging on the lower third of the face.^{5,6} The development of



GRAPH 1: Mean score of the outcome of the surgery, according to the timepoint, as compared to the baseline (before the procedure). Each symbol represents the mean value, and the bars, the standard error of the mean. There was no significant difference between the timepoints one year and five years after the surgery regarding the score attributed to the surgery outcome (paired Student t-test, $p = 0.373$)

techniques has gone through several interesting moments: from the simple initial tractioning of the skin to the most complex cervical muscle flaps.^{3,4} The transient character of the outcomes forced surgeons to seek alternatives to stabilize the tissues of the region and that would maintain the desirable cervicofacial angle obtained in the immediate postoperative period for as long as possible.^{2,5} It seems obvious that the success of the surgery contemplates obtaining a natural result, free from stigmas and, above all, be maintained over time.¹

The expanded cervicoplasty is precisely aimed at offering better long-term results in the cervical rejuvenation surgery. It brings together the three basic factors for obtaining longer lasting results in facial surgery: i) it approaches the structure to be treated in a wide and direct manner, ii) it attenuates the opposing muscle forces accurately and effectively, and iii) it repositions and anchors the detached tissues to stiff and firm structures.² The technique is capable of directly treating the main factors involved in cervical aging: the submentonian lipodystrophy (supra and infraplatysmal), the platysma muscle's sagging, and the face's middle third cutaneous ptosis.^{1,15} Less common deformities, such as prominent submandibular glands and the appearance of the digastric muscles, are also well handled indirectly with the use of the technique, reducing the need for more aggressive procedures with potentially more serious complications.^{1, 2, 15, 16} In general, the technique is used by the authors of the present article in all candidates to cervical rejuvenation. The variation is in the intensity of implementation: in the more pronounced

TABLE 1: Classification of the expanded cervicoplasty outcomes in the assessed timepoints

Outcome classification	1 st year postoperative	5 th year postoperative
Excellent	0 (-)	0 (-)
Very good	12 (52,2%)	9 (39,1%)
Moderate	9 (39,1%)	11 (47,8%)
Poor	2 (8,7%)	3 (13,1%)
Unsatisfactory	0 (-)	0 (-)

TABLE 2: Percentage of patients according to the surgery outcome classification after one year and after five years, as compared to the preoperative timepoint, assessed by eight plastic surgeons

Five years	One year		Concordance
	Very good	Moderate/poor	
Very good	58,3 (7)	18,2 (2)	69,6 (16)
Moderate/poor	41,7 (5)	81,8 (9)	



FIGURE 3:
Top: patient M. preoperative
Middle: 1 year postoperative
Bottom: 5 years postoperative

cases, such as in the previously described McKinney grade IV, the approach and detachment are larger, the markings are wider, and the plications, stronger.⁸ The authors of the present article believe that the technique is particularly recommended for these cases, in which a more conservative treatment would lead to poorer and more ephemeral results for most patients.^{2,4,17} In less exuberant cases, McKinney III for instance, the technique is also used by the authors, with less aggressive detachments, tractions and plications.⁸

Most authors report few complications in cervical rejuvenation surgeries, even in wider approaches, such as in the

preparation of platysmal flaps and in large dissections in the region.¹⁶ The complications described in the present study intensely resembled those published by Montedonio et al.⁵ Fortunately, the authors did not face major bleedings such as those reported by Righesso et al.¹⁷ and Mendelson & Tutino.¹⁶ The authors of the present study believe that the excellent final quality of the submentonian scar undermines the concern reported by some authors who advocate the need to reduce it,¹⁶ and contributes to a broad view of the surgical area, facilitating the cauterization of blood vessels and minimizing the probabilities of hematomas and of the feared nerve lesions.

**FIGURE 4:****Top:** patient H. preoperative**Middle:** 1 year postoperative**Bottom:** 5 years postoperative

The long-term evaluation of outcomes obtained with the expanded cervicoplasty is crucial to define the actual role of technique in the armamentarium of plastic surgeons, especially when its outcome is compared with much less invasive strategies currently advocated by some authors.⁴

Unfortunately, long-term analyses of facial surgeries are scarce in the literature. In general, the late results referred by most authors are to some extent, in fact early.^{4,7,17} Like Crassas³ and Pitta et al.,² the authors of the present study believe that later analysis, such as the one as presented here (5 years after the procedure), are important when the late value of the technique is being questioned. Early assessments can lead to wrong conclusions regarding the procedure's durability.⁶

The methods described in the literature for the evaluation of long-term results also vary considerably and there is no consensus on how to best perform them.⁴ With a view to using an accurate and reproducible assessment technique, the authors of the present article applied the Antell & Orssek modified method.¹⁴ Using subjective criteria, eight plastic surgeons assessed the results, indicating whether or not there was existence and degree of improvement in the postoperative period, in the 1st and 5th year. Authors, such as Rima et al.,⁴ used a very similar method, confirming its effectiveness.

The results reported in the present study demonstrated that expanded cervicoplasty was able to offer satisfactory results that remained stable in the long term, even in difficult cases.

These results qualify the technique as an alternative for the treatment of facial aging, especially when aiming at maintaining the outcomes in the long-term.

CONCLUSION

The balance between the immediate results achieved in the cervical rejuvenation surgery and their durability is an im-

portant aspect to be evaluated when indicating techniques and tactics to be used in cervicoplasty. In this sense, the expanded cervicoplasty is confirmed as an important component in the surgeon's armamentarium, leading to satisfactory outcomes that remain in the long term, even in difficult cases. ●

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Epidemiological study of 740 areas treated with cryolipolysis for localized fat

Estudo epidemiológico de 740 áreas tratadas com criolipólise para gordura localizada

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ABSTRACT

Introdução: A non-invasive alternative for the treatment of localized fat is cryolipolysis that, by freezing adipocytes, reduces fat volume in the region where the procedure was performed.

Objective: To statistically describe the experience of a referral center for this procedure.

Methods: A cross-sectional study with 251 patients undergoing cryolipolysis was carried out with the epidemiological analysis of patient data.

Results: Thirty-eight males and 213 females underwent the procedure, with a total number of 740 treated areas. The anterior abdomen (lower third) was the most popular region, with 45.30% of cases. Eighty-eight percent were satisfied or very satisfied with the result. Nearly all cases required 2 or more sessions to achieve this degree of satisfaction.

Conclusions: Cryolipolysis is a noninvasive method for the selective reduction of fat that has shown efficacy in reducing the subcutaneous tissue, with minimal and reversible side effects in this study.

Keywords: lasers; abdominal fat; lipolysis

RESUMO

Introdução: Uma das alternativas não invasivas para o tratamento da gordura localizada é a criolipólise que, mediante o congelamento dos adipócitos, diminui o volume de gordura na região em que foi realizado o procedimento.

Objetivo: Descrever estatisticamente a experiência de um centro de referência para esse procedimento.

MÉTODOS: Estudo transversal com 251 pacientes submetidos à criolipólise, com análise epidemiológica dos dados dos pacientes.

Resultados: 38 homens e 213 mulheres, com número total de áreas tratadas de 740. O terço inferior do abdômen anterior foi a região mais procurada, com 45,30% dos casos. 88% dos pacientes ficaram satisfeitos ou muito satisfeitos com o resultado. Quase todos os casos necessitaram de duas ou mais sessões para atingir esse grau de satisfação.

Conclusões: É método não invasivo para redução seletiva de gordura que demonstrou eficácia na diminuição do tecido subcutâneo, com efeitos colaterais mínimos e, neste estudo, reversíveis.

Palavras-chave: lasers; gordura abdominal; lipólise

INTRODUCTION

Liposuction used in the removal of excess localized fat is the most frequently performed surgery in the United States of America. Due to the disadvantages inherent to this surgical procedure, such as the possibility of hospitalization and general anesthesia, complications and time of postoperative recovery, there is a growing demand for non-invasive body esthetical procedures.¹⁻⁶

A frequently used non-invasive alternative is the cryolipolysis, that reduces fat volume in the region where the procedure was performed through the freezing of adipocytes. Due to the fact that adipocytes are more sensitive to cold than other histological structures such as the epidermis, dermis, blood vessels, sweat glands, muscles and nerves, their apoptosis occurs before that of the other cells.^{2,7-10}

The adipose tissue is placed in contact with cold plaques using a pressure applicator that thermally “kills” the fat without damaging the skin.¹¹ The dead cells are then removed metabolically, as with the fat found in food.^{1,9}

The present study statistically describes the experience of a referral center for this procedure in the Brazilian Southeast city of São Paulo.

METHODOLOGY

A cross-sectional study was carried out with 251 patients who spontaneously and randomly sought a private dermatologic practice for the treatment of localized fat. All patients in this study underwent only the cryolipolysis procedure with the Coolsculpting® device (Zeltic Aesthetics, Pleasanton (CA), USA). The exclusion criteria for not undergoing this therapy were: cryoglobulinemia, cryofibrinogemia, cold urticaria and obesity grade I, II and III according to the Abeso's (Brazilian Association for the Study of Obesity and Metabolic Syndrome) body mass index.

The present study described the epidemiological profile of patients who underwent this procedure with the percentage analysis of the following variables: *gender, age, number of sessions per area, distribution of body sites treated with the procedure, patient's satisfaction, independent observer evaluation and description and management of adverse events.*

The patient satisfaction rate was determined by the following scale: 0 = unsatisfied, 1 = somewhat satisfied, 2 = satisfied and 3 = very satisfied. The results were compared by an independent observer in the before the treatment and eight months after the treatment based on three dimensions digital photographs (Vectra M3®, Canfield), according to the following scale: 0 = absence of improvement, 1 = little evident improvement and 2 = evident improvement.

RESULTS

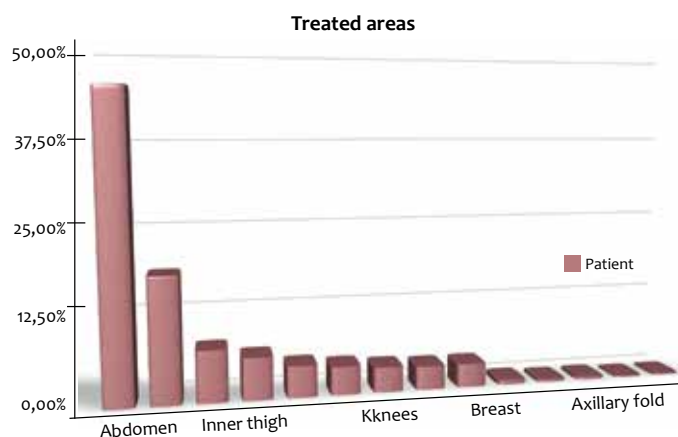
The authors treated 251 patients (38 men and 213 women) who had accumulation of localized fat, with a total of 740 areas treated. Ninety-six (96) patients underwent the procedure in more than one area, with 8 having undergone more than one session in the same area (the most common combination being

flanks and abdomen). The average age of the study participants was 45 years (min = 13, max = 71).

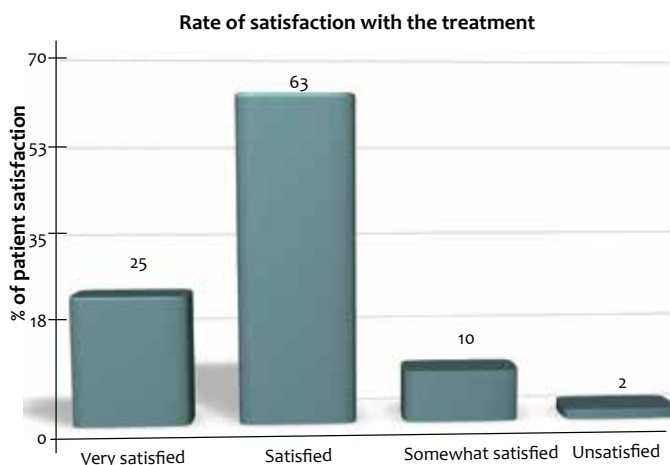
The treated areas showed the following distribution (Graph 1): anterior abdomen – lower third (45.30%), flanks (18.77%), lateral side of the thigh or (7.74%), internal side of the thigh (6.33%), arms (4.69%), infragluteal area (4.22%), knees (3.75%), lateral abdomen (3.52%), accumulation around bra area (3.52%), breast (0.70%), anterior side of the thigh (0.46%), iliac (0.46%), axillary fold (0.23%) and gluteus (0.23%).

The patient satisfaction index seen in Graph 2 depicts the following percentages: 25% were very satisfied, 63% satisfied, 10% somewhat satisfied and 2% were unsatisfied. The 3D photographic analysis carried out by the independent observer presented the following distribution: 17% of cases were rated as 1 and 83% were rated as 2.

The minimum number of sessions required to achieve any level of clinical outcome in the body area can be seen in



GRAPH 1: Distribution of the body areas treated in the study



GRAPH 2: Patient satisfaction index

Table 1. It is worth to note that all areas required two sessions in order to acquire some satisfactory result, except for the anterior region of the abdomen, in which 21% of cases required only one session.

Adverse events observed were: late pain of varying duration within two to three days after the procedure, appearance of hematomas and 5 cases of panniculitis. The events were managed with analgesia, using 30mg codeine associated with 500mg paracetamol, 50U sodium heparin with 2.067mg nicotinate benzyl, and ultrasound sessions (Accent Ultra®, LBT Lasers, São Paulo, Brazil), respectively.

TABLE 1: Distribution of minimum number of sessions required per area for achieving some level of clinical outcome

TREATED REGIONS		N. PATIENTS
Abdomen	1 session	217
	2 sessions	58
FLANK	1 session	12
	2 sessions	96
OUTTER THIGH	1 SESSÃO	5
	2 session	8
BRA AREA	1 SESSÃO	2
	2 session	22
INNER THIGH	1 SESSÃO	0
	2 session	25
LATERAL ABDOMEN	1 SESSÃO	0
	2 session	22
AXILLARY FOLD	1 SESSÃO	0
	2 session	2
ARMS	1 session	0
	2 session	30
ANTERIOR THIGH	1 session	0
	2 session	3
BREAST	1 session	0
	2 session	5
INFRAGLUTEAL	1 session	3
	2 session	22
KNEE	1 session	3
	2 session	21

DISCUSSION

Cryolipolysis targets only the fat cells in the selected region. The physician chooses the region to be treated and areas to place the application device. The device pulls and holds the fat between its two panels, automatically cooling it for one hour. The sensation is that of a firm pull, and the freezing action does not affect the skin or other organs and tissues. The epidermis and dermis are protected by a gel film during the session. For this reason, given that the contraindications for the procedure are observed, it can be performed in patients of any age, which is consistent with the present study, which included patients

between 13 and 69 years of age. The average age of 40 years observed in the present study is consistent with the literature, coinciding with the age when the greatest level of concern with the body takes place.¹¹

The majority of the population in the present study lived in the Brazilian State of São Paulo, and in most of the cases had greater concern with the abdominal region (67.60%). This can be due to the trend to be overweight that is expected to occur in the population of more developed areas and the fact that the abdominal region is the primary body site that develops localized fat.

The rate of patient satisfaction and the independent observer evaluation carried out before treatment and eight months after the last session through 3D digital photographs presented high scores in the present study. The reduction of the treated fat, with some studies finding an average of 22.4% four months after the treatment,^{2, 4, 9, 12} can explain the high effectiveness of the method and the resulting high degree of satisfaction in patients with good indication.

Another point of agreement would be the histological evaluation carried out in some studies, which confirm the gradual selective reduction of adipose tissue in humans and animals after cryolipolysis sessions.^{2, 9, 13, 14} The exclusion of patients with obesity grades I, II and III according to the Abeso's body mass index contributed to the correct selection of the study patients, as well as to the high level of positive results.

All patients had late pain that lasted for two to three days after the procedure, nevertheless having been easily controlled by analgesia using 30mg codeine associated with 500mg paracetamol. The cases presenting hematomas were managed with 50U heparin sodium combined to 2.067mg nicotinate benzyl. The five cases of panniculitis were described as painful subcutaneous nodules, with absence of systemic signs or symptoms. The patients were followed up on weekly sessions with non-focused ultrasound (Accent Ultra®, LBT Lasers, São Paulo, Brazil), with complete clinical improvement of the picture. The authors of the present study did not observe bacterial or mycobacterial infections, or temporary alterations in the peripheral sensory nerves' function.

CONCLUSIONS

Cryolipolysis is a non-invasive method for the selective reduction of fat that has shown efficacy in the reduction of subcutaneous tissue with minimal and reversible side effects in the present study. This technology should be used by dermatologists who have experience with it, always observing the contraindications, in order to achieve good results. ●

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Nasal filling with a new hyaluronic acid: a series of 280 cases

Preenchimento nasal com novo ácido hialurônico: série de 280 casos

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ABSTRACT

Introdução: Nasal filling can be used as an alternative to traditional rhinoplasty aiming at correcting small nasal defects and for complementation or correction after surgical procedures.

Objective: To describe the profile of patients who underwent nasal filling and demonstrate the efficacy and safety of a new hyaluronic acid based filling substance.

Methods: Retrospective analysis with statistical study of nasal filling procedures conducted in 280 patients.

Results: The sample was composed mostly of Caucasian women with a mean age of 43 years. The nasal regions more commonly treated with the filler were the nasal root, tip and septum. Patients showed significant improvement and expressed satisfaction with the results. 17.1% of the patients were re-treated, and 7.2% had easy to resolve complications.

Conclusion: The results were long lasting and natural, especially those related to thinning of the nasal tip.

Keywords: nose; hyaluronic acid; esthetics

RESUMO

Introdução: O preenchimento nasal pode ser empregado como alternativa à rinoplastia tradicional para a correção de pequenos defeitos nasais e como complementação ou correção após procedimentos cirúrgicos.

Objetivo: Descrever o perfil dos pacientes que foram submetidos ao preenchimento nasal e demonstrar a eficácia e segurança de um novo preenchedor de ácido hialurônico.

Métodos: Análise retrospectiva com estudo estatístico, de preenchimento nasal realizado em 280 pacientes.

Resultados: A amostra foi constituída em sua maioria por mulheres caucasianas com média de idade de 43 anos, e as regiões do nariz mais comumente tratadas com o preenchedor foram a raiz, a ponta e o septo nasal. Os pacientes apresentaram melhora significativa e se revelaram satisfeitos com os resultados. Foram tratados novamente 17,1%, e 7,2% apresentaram complicações de fácil resolução.

Conclusão: Os resultados foram duradouros e naturais, principalmente aqueles relacionados ao afinamento da ponta nasal.

Palavras-chave: nariz; ácido hialurônico; estética

INTRODUCTION

Due to the importance of personal appearance, aesthetic corrections of the nose have been of interest since ancient times. In the Middle Ages, Gaspare Tagliacozzi introduced the famous “Italian method” for the reconstruction of nasal traumas and deformities. During the 20th century, various rhinoplasty surgical techniques were created. ¹ However, Broeckaert, who is considered the father of modern rhinoplasty – was the first to perform nasal corrections using liquid paraffin as cutaneous filler in the early twentieth century. Doctors favorable to minimally invasive procedures developed techniques and safer materials for correction of nasal defects henceforth. ²

Although being considered the gold standard, the surgical approach of nasal defects is an invasive procedure that often requires the fracture of the nasal bone. Cutaneous fillers arise as an alternative for the correction of small nasal defects and complementation or post-surgical correction. ^{2,3} Although not definitive, they have gained ground since they are less traumatic and painful, and have minimal complications as compared to the traditional rhinoplasty. ^{4,5}

The search for materials that are safe and long lasting, and have predictable effects is continuous. Hyaluronic acid (HA) based cutaneous fillers are currently the most used due to their ease of application, predictable efficacy, good safety profile and speedy patient recovery. ^{6,7}

In face of the need for further studies on new cutaneous filling substances, the present article aims at profiling patients and demonstrating the effectiveness and safety of a new HA based filler.

METHODS

A retrospective and single-center study was carried out with 280 patients who underwent nasal filling with Juvederm Volift® (Allergan Inc., USA) between October 2012 and May 2015 at a private practice located in the city of Rio de Janeiro, Brazil. All study patients were subjected to standardized photographs and followed up with specific data collection forms.

The sociodemographic variables included were *gender, age, ethnicity, amount of product applied, treated area, application method, retreatment and complications*. The study followed the ethical guidelines established by the Declaration of Helsinki.

The filling substance

Hyaluronic acid is a polysaccharide (glycosaminoglycan composed of alternating and repeating units of D-glucuronic acid and N-acetyl-D-glucosamine) with hydrophilic properties, which causes an increase of the injected tissue. ⁸⁻¹² The initial filling effect is directly related to the volume of injected filling substance. Nevertheless, studies have shown that there is an indirect effect when the dermis is injected due to the activation of fibroblasts. Hyaluronic acid fillers generally last from 6 to 24 months after injection. ^{13,14} When an appropriate volume is placed in the correct plane, the filling material can not be perceived visually or by palpation.

The vycross® technology (Allergan Inc., USA), incorporates short to long chains of HA, which generates more efficient crosslinking than that of previously used HA fillers. The inclusion of short HA chains allows attaching HA to the ends of the molecules, resulting in a product with longer durability than that of the fillers that include only long chains of HA. Furthermore, this technology provides higher viscosity to the gel, resulting in an increased lift capacity against the pressure of the skin.

Its elastic modulus (G') is smaller than those the other fillers, providing a more fluid and soft gel that is easier to extrude from the syringe, resulting in a product with better spreadability during injection.

Due to the optimization of crosslinking, products with the vycross® technology may have greater durability in the tissue using at lower HA concentrations in its formula. This lower concentration of HA makes the gel less hydrophilic, which lends more safety and predictability to the results, causing a natural appearance. ¹⁵ The filling of the nasal deformities of the studied patients was performed with Juvederm® Volift® Allergan Inc., USA (17.5mg/ml of HA).

TECHNIQUE

After asepsis and antisepsis with alcohol chlorhexidine, the needle was introduced directly into the region to be treated, and the product was deposited anterogradely. In most cases topical anesthesia was not used, and only 2% lidocaine with vasoconstrictor was injected at the entry puncture in cases treated with microcannulae.

The amount of HA used in each region varied according to the specificities of the case and application plan. Thus, the following quantities are merely mean parameters: in the upper third of the nose, the needle was inserted into the skin at 90° to the nasal root and the product was deposited in the subcutaneous or juxta-periosteal (Figure 1). The amount used ranged from 0.05 to 0.25 ml of HA in one or more punctures.

In the middle third of the nose, fillers were not in general applied for volumizing the area, but only small amounts (0.05 and 0.15ml) were injected aiming at improving the quality of or for “rounding” the skin at the site. In Asian patients or in those with unsightly concavities resulted from surgical procedures in the nose to improve the projection along the nasal dorsum, larger quantities of product were used (0.1ml to 0.4ml).

Injections at the base of the columella were performed with the needle at 90°, depositing from 0.1ml to 0.3ml of HA in a single bolus injection in the retrocolumellar plane, on the nasal spine (preseptal). The application in the cartilaginous septum was performed through the same inferior orifice, however with the needle angled at 45° toward the nasal tip and with a deposition of 0.1ml to 0.2ml in retroinjection, from the upper portion up until the base of the septum.

In some patients, access to the nasal septum was also obtained superiorly with the needle inserted perpendicularly in the nasal tip toward the columella, with retrograde deposition of the product. The elevation of the nasal tip was also obtained with the deposition of HA in this area, between the alar cartilages. The

application was deep, with the needle inserted at 90° degrees regarding the septum. The elevation occurred immediately when the filler was deposited (from 0.1ml to 0.3ml) on the structures that form the nasal septum. Superficial applications were not performed in this region due to the risk of necrosis of the nasal tip by vascular obstruction.

An aesthetic result was deemed satisfactory when the nasolabial angle measurement was gauged at between 90° and 100° for men (Figure 2), and 95° and 110° for women (Figure 3).

When microcannulas were used, a single entry was made in the nasal tip or in the glabellar region, with the deposition of the product being carried out with the retrograde technique. The nasal septum was reached downwardly through the orifice in the nasal tip. Microcannulas with 22G to 25G were used, with lengths varying from 4cm to 7cm. The cannulas were used to improve the projection of the middle third of the nose. In the treatment of the nasal lateral extensions, 27G microcannulas were used in some instances, due to the thinner skin.

Statistical analysis

The data collected with the specially developed forms allowed to carry out the descriptive statistics analysis.

Ten variables were selected for this analysis: i) *gender*, ii) *age*, iii) *ethnicity*, iv) *amount of product applied*, v) *treated area* vi) *application method* (cannulas, needles or both), vii) *outcome after the application* (aimed at assisting in the decision of whether or not to apply the product to completion), viii) *retreatment*, ix) *complications* (presence and type), and x) *photographic results in 30 and 60 days after*.

Results

One hundred and eighty female (64.3%) and 100 male patients (35.7%) were studied. Their ages ranged from 15 to 88 years (women’s mean age = 43 years, men’s mean age = 37 years).

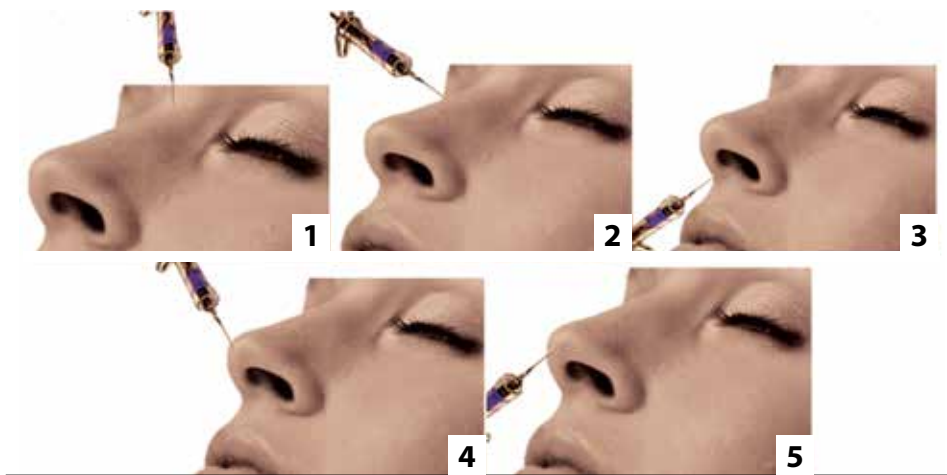


FIGURE 1:
 1 – In the upper third of the nose, the needle is inserted into the skin at 90° to the root and the product is deposited in the subcutaneous or juxta-periosteal.
 2 – Treatment of the dorsum of the nose with a needle.
 3 – The injection at the base of the columella is performed with the needle at 90°, where the bolus is deposited in the retrocolumellar plane on the nasal spine (pre-septa).
 4 – Needle perpendicularly inserted in the nasal tip toward the columella and injection of the product with the retrograde technique.
 5 – In order to lift the nasal tip, the application must be performed deeply between the alar cartilages inserting the needle at 90° to the septum.

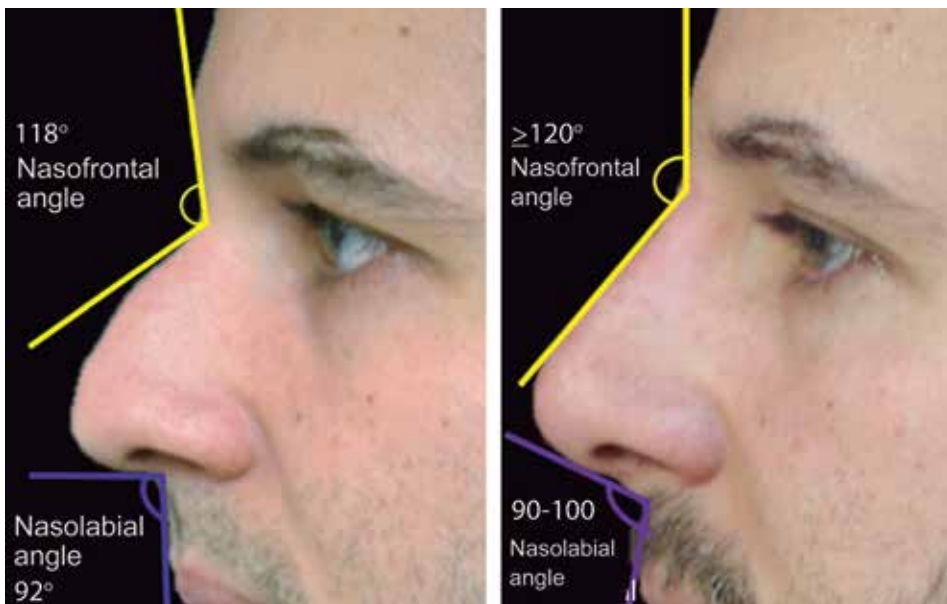


FIGURE 2:
 Male patient before and after nasal filling with optimization of nasofrontal and nasolabial angles

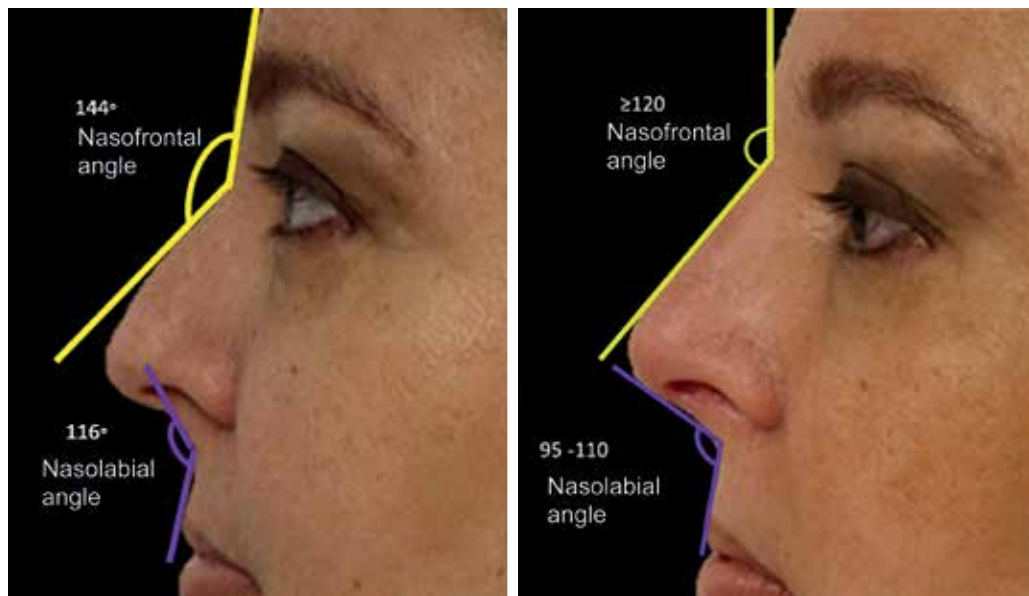


FIGURE 3:
Female patient before and after nasal filling with optimization of nasofrontal and nasolabial angles

Of the treated patients, 248 were of Caucasian origin (88.5%), 20 were negroids (7.1%) and 12 were Asian (4.2%). (Table 1)

The application techniques and amounts of filler used in each region of the nose followed those described above, ranging from 0.3ml to 1.0ml of the product in total per application. One milliliter per treatment (session) was used in 90% of cases.

The treatment was performed in the superior third of the nose (root) in 260 cases (92.9%), in the middle third of the nose in 80 cases (28.6%), in the nasal tip in 230 cases (82.1%), and in the nasal septum in 255 cases (91.1%).

Only needles were used for application in 235 cases (83.9%), only microcannulas were used in 20 cases (7.1%), and a combination of the two methods was used in 25 patients (8.9%).

Between 30 and 60 days after the treatment, 22 patients (8.4% of the 260 patients treated in this region) required complementation in the nasal root, which ranged from 0.1ml to 0.2ml of the product. No complementation was performed in other previously treated regions of the nose.

Eight patients (2.8%) with very pronounced nasal deformities underwent a second application, which took place after 30 to 60 days of the first application. In these cases, the total dose HA dose was 2.0ml in the two applications.

Since the authors started to use this filling material for the correction of nasal defects in their practice, 48 patients (17.1%) have returned for reapplication of the product. The eight patients who underwent the initial treatment in two stages are not included in this statistic. The minimum time elapsed between the two applications was nine months, and the maximum, 24 months. The average interval relating to all patients who underwent reapplications was 14.5 months. The amount of product used in retreatments varied from 0.3ml to 1.0ml and, in general, a lesser amount was necessary as compared to the initial application. Only 60% of these patients used 1.0ml in the reapplication.

Even using needles for application in almost all cases, only eight patients (2.9%) described visible hematoma. All who underwent the application reported pain to the touch and edema in the application site, in special those treated in the nasal tip and columella. These occurrences, however, receded within 2 to 14 days after the treatment. Twelve patients (4.3%) reported important post-procedure erythema in the nasal tip that in general decreased within up to four weeks – only in one patient (Figure 4) it persisted for longer, having receded after four monthly sessions of intense pulsed light (IPL). There were no complications related to the injection or intravascular occlusion.

All patients had evident improvement in the nasal contour and deformities in the photographic assessment performed immediately after the procedure and in the 30 and 60-day follow-ups after the procedure. There was no report of unaesthetic increase or enlargement of the nasal tip in follow-up visits.

DISCUSSION

The nasal cutaneous filling procedure is indicated for the correction of the contour and deformities of the nose, constituting an alternative to plastic surgery or a post-surgical complementation. Despite not being definitive, it brings quick and safe good aesthetic results, provided that the applicator physician has mastery of the anatomy of the region to be treated and of application techniques.

Hyaluronic acid based fillers started to be applied in the nasal region eight years ago, with the use of biphasic and monophasic products, different technologies, good aesthetic results and duration ranging from 6 to 12 months. In turn, the product analyzed in the present study started to be used in the nasal region, with the already described application techniques 32 months ago. Unlike the results outcomes obtained with the previously used products, the new product leads to a greater thinning of the nasal tip, which was observed within 3 and 4 weeks after the application.¹⁶ This effect was reported by most of the patients treated and also observed by the applicator physician.



FIGURE 4: Female patient before and after nasal filling with optimization of nasofrontal and nasolabial angles

Despite the fact that Webster et al. have developed a study on nasal filling with injectable silicone in 347 patients in 1986,¹⁷ it was not possible to find in the literature the description of such a large sample using HA.

The fact that the majority of patients were females can be explained by the interest for aesthetic procedures, which is more frequent among women than among men. Other studies also show a predominance of female patients in the search for that kind of procedures.^{17, 18}

The predominance of Caucasians among the treated patients can be explained by the greater purchasing power of this population in Brazil. The fact that most of the sample consisted of Caucasians may also explain the lower number of applications in the middle third of the nose, since this population in general already has a projected nasal dorsum.¹²

The amount of product used and the parts of the nose that were filled are in line with the literature, despite the fact that the latter have not been conducted with the same product. The reports found in the literature often mention permanent fillers, such as silicone,¹⁷ or semipermanent fillers, such as calcium hydroxyapatite.¹⁹⁻²¹

The amount used in the nasal root varied from 0.05 to 0.25 ml of HA in one or more punctures. An angle greater than 120° is desirable, however excessive deposition of product in this area should be avoided, as this could lead to the widening of the nasal root, and the consequent increase in the distance between the eyes.^{18, 22}

Application in the lateral extensions of the nose can be performed to improve asymmetries or widen the middle third of the nose (0.05 to 0.2 ml).^{18, 22}

TABLE 1: Profile of patients treated with Volift® Juverderm® in the nasal area at a private practice in the city of Rio de Janeiro, Brazil - Jan/2013 – Aug/2015 (n = 280)

Universe characterization	Description	%
Follow-up period	32 months (2013-2015)	
Gender	Female	
Age	Men (average) = 37 y.o. Women (average) = 43 y.o.	
Ethnicity	Caucasian	
Amount applied	1ml	
Treated area (*)	Root Nasal septum Nasal tip Middle third	
Application technique	Needle only	
Outcome after the application	Needed complementation	8.4 of the nasal roots treated
Retreatment (**)	All the nose (average time = 14.5 months)	
Complications after the application	Hematoma Erythema in the nasal tip Injection or intravascular occlusion	

(*) The same patient underwent applications in more than one part of the nose.

(**) Only 2.8% of patients with considerably pronounced nasal deformities were instructed to undergo a second application within 30 to 60 days after the initial application. The second application was not deemed as a retreatment.

The most significant changes caused by the use of fillers in the nose are obtained with the treatment of the lower third of the nose, resulting in the alteration of the position and format of the nasal tip. To lift the nasal tip and consequently increase the nasolabial angle, one or more of the following regions can be treated: the columellar base, nasal septum or nasal tip (between alar cartilages).^{18, 22}

As the study product has lidocaine in its formulation, despite the fact that no topical or injectable anesthetic was used in the applications with needle (anterograde injection), the pain during the procedure is quite tolerable, being described with lower intensity as compared to that verified when using the same product in the nasolabial fold.

Despite the immediate improvement of the nasal contour and angles with the use of HA, it is worth to note edema will occur immediately after the procedure and remain in place for a few days. The final result is obtained in about four weeks, when the need for supplementation will be assessed. Unlike the results obtained in the treatment of the middle and lower thirds of the nose, 8.4% of the treated patients needed complementation in the upper third. The authors believe that this is due to the greater mobility of the skin in that region, making it more susceptible to local edema immediately after the procedure, with the occurrence of small decrease in volume in the following weeks. Moreover, the product's lower volumerization capacity regarding other fillers with higher elasticity moduli may also have contributed to this increased need for reapplication in that location.¹⁴

In general, the results in the middle and lower thirds of the nose remain after the initial procedure. Eight patients with more pronounced nasal deformities were instructed to undergo the treatment in two sessions, entailing that a two-stage treatment was used, which present a lower risk of complications, such as vascular compressions, for example. Furthermore, as the nose is a structure with low mobility, there is a limit on the amount of filler being applied in each session, a threshold beyond which there will be reflux of the product via the entry orifice.¹⁴

The duration of the results varies among patients and is mainly related to the amount of product used, the severity of the nasal deformity and the treated nasal region.^{23,24} In general, results persist for over a year and in some patients have remained almost unchanged after 18 months of application, which suggests the possibility of an even greater permanence. The authors of the present article did not find similar results for the use of HA in the literature.²⁵⁻²⁸

After the assessment of the initial result, 48 patients returned for retreatment 14.5 months (on average) after the first application. It is not possible to state that this would be the average product life in nasal treatments, for patients with longer durations might still have not returned for retreatment, and some other patients might not return for considering that the outcome or duration differed from the expected.

There was a small number of complications linked to the procedure and none of them resulted in permanent problem for patients. Anatomical knowledge and experience in the treatment of this region with fillers can be the main factor related to the low rate of adverse effects found in the present case series.^{14,29,30}

The authors of the present article did not find in the literature a study with a significant sample and/or a follow-up period longer than two years, involving the use of the analyzed product in any site of the face.³¹

Therefore, the present study is a contribution from the Brazilian dermatology to other countries that may use the product and may serve as the basis for future studies.

Conclusion

The use of HA based fillers in the nose is an increasingly common procedure in the medical practice that leads to good aesthetic results when well indicated. The authors described their experience with the use of a new product in the treatment of this body site, with long lasting and even more natural outcomes, mainly related to the thinning of the nasal tip. In general, nasal fillers are safe and effective and are a consistent alternative to rhinoplasty due to their few adverse events and considerable patient satisfaction. Further research with HA is needed for comparison and reproduction of results.

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Association of microneedling with phenol peeling: a new therapeutic approach for sagging, wrinkles and acne scars on the face

Associação do microagulhamento ao peeling de fenol: uma nova proposta terapêutica em flacidez, rugas e cicatrizes de acne da face

DOI: <http://dx.doi.org/10.5935/scd1984-8773.201573693>**ABSTRACT**

Introdução: The beneficial role of medium peelings and microneedling in photoaging and scars yield satisfactory results.

Objective: A retrospective, descriptive, single-center study evaluating the results of the association of 88% phenol and microneedling for treating sagging, wrinkles and acne scars on the face.

Methods: Medical records and standardized photographs, taken before and 3 months after the procedure, of 28 patients diagnosed with wrinkles, sagging or acne scars and treated with 88% phenol peeling followed by microneedling with 2.5 mm needles, were analyzed. Events and complications were recorded 15 days after the procedure. The investigator physician performed clinical and photographic assessments 3 months after the procedure, when patient satisfaction questionnaires were also applied.

Results: Twelve patients had only wrinkles and sagging, 5 had only acne scars and 10 had both pictures, with skin phototypes I to III. Erythema persisted for 30 days and post-inflammatory hyperpigmentation was observed in 7 of 28 patients. Based on the clinic and photographic evaluations, the author considered the results as good and very good. 100% of patients reported satisfaction with the outcomes.

Conclusions: Good results were observed with the association of 88% phenol and microneedling. Few patients experienced adverse effects, allowing the author to suggest that the procedure showed a good safety profile.

Keywords: : therapeutics; rejuvenation; cicatrix s

RESUMO

Introdução: O papel benéfico dos peelings médios e do microagulhamento no fotoenvelhecimento e em cicatrizes revelam resultados satisfatórios.

Objetivo: Estudo retrospectivo, descritivo e unicêntrico, avaliando os resultados da associação do peeling de fenol 88% e microagulhamento no tratamento de flacidez, rugas e cicatrizes de acne na face.

Métodos: Foram considerados registros em prontuários e fotografias padronizadas prévias e três meses após o procedimento, de 28 pacientes com diagnóstico de rugas, flacidez ou cicatrizes de acne, tratados com peeling de fenol 88% seguido de microagulhamento com agulhas de 2,5mm. Quinze dias após o procedimento, foram registrados eventos e complicações. As avaliações clínica e fotográfica, de acordo com escala com as categorias muito bom, bom, razoável e ruim, foram realizadas pelo investigador três meses após o procedimento, quando também foram aplicados questionários de satisfação aos pacientes.

Resultados: 12 paciente apresentaram apenas rugas e flacidez, cinco apenas cicatrizes de acne, e dez apresentaram ambos os quadros, com fototipos de I a III. O eritema persistiu por 30 dias, e a hiperpigmentação pós-inflamatória foi observada em sete dos 28 pacientes. Na avaliação clínica e por meio de fotografias, o autor considerou os resultados bons e muito bons. 100% dos pacientes relataram satisfação com os resultados.

Conclusões: Observam-se bons resultados com a associação de fenol 88% e microagulhamento. Poucos pacientes apresentaram efeitos adversos, o que nos permite sugerir que o procedimento apresentou bom perfil de segurança.

Palavras-chave: terapêutica; rejuvenescimento; cicatrizes

INTRODUCTION

The beneficial role of medium peelings in photoaging and facial scars has been extensively studied.¹ Evidence of the increase in collagen fibers type I and III, and restoration of elastic fibers, followed by dermal remodeling induced by caustic agent are effects already described by some authors.^{2,3} Phenol has an immediate caustic action, with the ability to promote denaturation and coagulation of epidermal keratin proteins, achieving unparalleled clinical results as compared to other ablative techniques.⁴ The microneedling technique, applied to the skin aimed at generating multiple micropunctures, resulting in inflammatory stimulus and collagen production, has been described as being a percutaneous induction of collagen (PIC). Firstly there is loss of integrity of the skin barrier, aimed at dissociating keratinocytes and causing the release of cytokines, resulting in dermal vasodilation and keratinocytes migration in order to restore the epidermal damage.^{5,6} Fibroblasts and keratinocytes are stimulated, causing the production of type III collagen, elastin, glycosaminoglycans and proteoglycans, as well the formation of fibronectin matrix, allowing the deposit of collagen just beneath the basal layer of the epidermis.⁷ The reviewed literature does not contain any description of the association of these two therapies, which, isolated, induce similar responses. The objective of the present retrospective, descriptive, single-center study was to evaluate the results of the association of 88% phenol peeling and microneedling in the treatment of facial sagging, wrinkles and acne scars.

METHODS

Records of 28 patients diagnosed with wrinkles, sagging or acne scars in the genian regions, treated with the combination of 88% phenol peeling followed by microneedling, according to a same protocol performed by the same physician, between January 2011 and January 2015. The study complied with the ethical recommendations of the Helsinki declaration. Patients with skin infections and prone to keloids were excluded.

The following treatment protocol was applied: monitoring of heart rate record, oxygen saturation and arterial blood pressure during the procedure; degreasing of the skin with liquid soap, antiseptis with chlorhexidine and block anesthesia of the infraorbital and mentonian nerves, followed by infiltrative anesthesia with 2% lidocaine and saline (1:3) of the genian region, observing the maximum anesthetic dose according to the patient's weight. The 88% phenol was applied with gauze until obtaining a solid frosting in the skin, being immediately followed by the microneedling procedure with a cylindrical device equipped with one hundred ninety-two (192) 2.5mm long needles arranged in eight rows, sterilized by gamma irradiation (Dr. Roller®, Mooham Enterprise Co., Gyeonggi-do, South Korea, Anvisa n. 80669600001). Back and forth movements were performed up until an uniform bloody dew emerged. The contralateral genian region was treated with the same technique. The procedure was completed with the application of a dressing with sterile gauze, which was removed 24h after at home, during the bath, being followed by the use of a cutaneous barrier regener-

ator three times a day. Fifteen days after having undergone the procedure, all patients were examined and asked to answer a questionnaire about the period following the intervention. The objective was to identify expected effects as erythema and edema, or complications such as post-inflammatory hyperpigmentation or infections. On this visit, all patients were instructed to use an industrialized depigmenting substance (0.05% retinoic acid + 4% hydroquinone + 0.01% fluocinolone acetonide), alternating it with a cutaneous regenerator for 15 days and SPF 50+ industrialized tinted sunscreen. Later on, patients were instructed to use the depigmenting substance every night, which was done with good tolerability.

The clinical evaluations (according to the categories *very good*, *good*, *regular* and *poor*) and photographic assessment (immediately before and three months after the procedure, with the same digital camera) were performed by the investigator physician three months after the procedure, when patient satisfaction questionnaires regarding the results were also applied.

TECHNICAL CHARACTERISTICS OF MICRONEEDLING AND 88% PHENOL PEELING

The device used to perform the microneedling comprises a polyethylene cylinder studded with stainless steel sterile needles symmetrically aligned in rows, totaling 192 units. The length of the needles is constant throughout the instrument's structure. For this needle length, anesthetic blocks complemented by infiltrative anesthesia are recommended. Microneedling is a technician-dependent procedure, and familiarization with the device used and technical mastery are factors that directly influence the final result. It is recommended to position the device between the thumb and index finger, as if holding a *hashi*, controlling the force with the thumb. The back and forth movements must be guided by a uniform pattern of petechiae throughout the treated area, and can be mild to intense. Theoretically, a number of passes between 10 and 15 in the same region yield 250-300 punctures / cm². The time elapsed before the emergence of the petechiae varies according to the thickness of the treated skin and the length of the selected needle. In this manner, a thinner and looser, commonly photodamaged skin will present a uniform petechiae pattern earlier than thicker skins, observed in patients with acne scars, for example. Lima et al.⁸ proposed a classification relating the length of the needles of microneedling devices with the expected damage's depth, terming the severity of the inflicted injury as *mild*, *moderate* and *deep*. The patients evaluated in the present study underwent a *deep* injury degree as they were treated with 2.5mm long needles.

RESULTS

Among the 28 patients treated, 12 had only wrinkles and sagging, 5 had only acne scars, and 10 had wrinkles, sagging and acne scars.

The patients' skin phototypes ranged from I to III, according to the Fitzpatrick classification.



FIGURE 1: Patient before and 3 months after the 88% phenol association with 2.5mm microneedling

In the clinical and photographic evaluation, the author rated the results from *good* to *very good* on a scale that included the categories *very good*, *good*, *regular* and *poor*. (Figure 1)

In the patient satisfaction questionnaire, 100% of patients reported satisfaction with the results. All informed they would undergo the procedure again, if necessary.

The degree of pain and discomfort during the procedure was considered tolerable by the patients. The heart rate, oxygen saturation and arterial blood pressure records presented very little fluctuation during the intervention.

The return to professional activities occurred within seven to ten days. Moderate edema and erythema persisted during a period ranging from 25 to 35 days, having been well camouflaged by the use of tinted sunscreen. Moderate post-inflammatory hyperpigmentation was observed in 7 patients (from a total of 28 patients), having been reversed with the use of the depigmenting substance within 30 to 45 days. It was also found that all 28 patients were responsive to the technique used and would undergo the same procedure in other cases with similar indication. At the time the present article was submitted for approval, 13 of the 28 patients evaluated were already being followed-up for 24 months after the procedure, with satisfactory maintenance of the results. (Figure 1)

DISCUSSION

It is known that the penetration of needles into the epidermis and dermis, resulting in multiple punctures, triggers the stimulus for the activation of fibroblasts and keratinocytes and consequent release of growth factors, collagen proliferation and renewal of the perforated epidermis,^{9, 10} while the effects of medium peelings, particularly those of the 88% phenol, were already well ratified by the literature.¹⁻⁴ In the present retrospective review of 28 patients, it can be assumed that both techniques

would isolatedly yield good results in the studied cases. Nevertheless, the objective of the present study is to present new therapeutic approach that is based on the simultaneous use of these two procedures. Despite being a retrospective investigation, the results allow to present some conclusions:

1. The international literature attests that microneedling with 2.5mm long needles as an isolated technique is able to produce improvement in the quality of the skin, reduction of wrinkles and correction of depressed acne scars.
2. In the author's experience, the recovery time of microneedling as an isolated technique is shorter than that when 88% phenol is associated.
3. Few patients experienced adverse effects; the post-inflammatory hyperpigmentation was reversed in a short time, allowing the author to suggest that the procedure showed a good safety profile in the group assessed.
4. When the author compares his experience with the cases evaluated in the present study with those previously treated only with microneedling, he notices a substantial further improvement in the results of the first, which prompts him to conclude that the addition of 88% phenol before microneedling potentiates the results.
5. Based on the experience presented, the author recommends the association of 88% phenol before surgical microneedling with 2.5mm long needles in the treatment of depressed acne scars, sagging and rhytids as an additional approach in the already existing broad therapeutic armamentarium.

Further studies are needed aimed at assessing a greater number of patients, and checking for the incidence of adverse effects, with a view to obtaining more accurate conclusions about the safety profile of the intervention, as well as evaluating the addition of the results of this association. □

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Review Article

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Radio Frequency: a non-invasive method for treating cutaneous sagging and the body contour

Radiofrequência: método não invasivo para tratamento da flacidez cutânea e contorno corporal

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ABSTRACT

Radiofrequency is considered a safe and non-invasive method for treating cutaneous sagging and for improvement of the body and facial contours. It has proven effectiveness, which is however limited in the more serious cases of ptosis. The effects of radiofrequency are based on the volumetric heating of the deep dermis, heating the collagen and elastic fibers. The heat generated by the radiofrequency leads to the contraction of collagen, improving the skin's firmness and elasticity. Furthermore, the heating induces the activation of fibroblasts, leading to neocollagenization (altered in diameter, thickness and frequency), with subsequent tissue remodeling.

Keywords: *pulsed radiofrequency treatment; collagen; skin aging*

RESUMO

A radiofrequência é considerada método seguro e não invasivo para tratamento da flacidez cutânea e para melhora do contorno corporal e facial. Apresenta eficácia comprovada, porém limitada em casos de ptoses mais graves. Seus efeitos baseiam-se no aquecimento volumétrico da derme profunda, aquecendo o colágeno e as fibras elásticas. O calor gerado pela radiofrequência leva à retração do colágeno, melhorando a firmeza e a elasticidade da pele. Além disso, o aquecimento induz a ativação dos fibroblastos, levando à neocolagenização (alterada em diâmetro, espessura e periodicidade), com subsequente remodelamento do tecido.

Palavras-chave: *tratamento por radiofrequência pulsada; colágeno; envelhecimento da pele*

With the increasing demand of patients for rejuvenation treatments and their intense desire to achieve this aesthetic improvement with minimal risk and a quick recovery, several non-surgical rejuvenation technologies have been developed.¹ A wide variety of high-tech devices are presented as effective, selective and safe therapeutic options.¹

Traditionally, most non-surgical methods destroy the epidermis and cause dermal wounds, leading to the dermal remodeling of collagen, which causes the tightening of the skin, attenuating wrinkles.¹ Radiofrequency (RF) is a non-ablative, non-invasive rejuvenation method.

The electrical current produced by RF can reach deeper tissues, generating energy and strong heat due to the resistance present in the dermis and subcutaneous tissue. While a volumetric heating occurs on the inner layers of the skin, the surface is kept cooled and protected.

When heated, the collagen fibers denature and contract, resulting in the retraction of tissue. As the immediate contraction of the collagen fibers takes place with their shrinking, the formation of new fibers is stimulated (late neocollagenesis), increasing their efficiency in sustaining the skin.²⁻⁵

Of all techniques based on the heating of the tissues, RF appears to be the most established and clinically proven, with the advantage of reaching the skin in its depth, due to the fact that even the hypodermis can be affected.³ Therefore, Dermatology uses RF in a non-ablative way, promoting increased elasticity of tissues rich in collagen.²

This source of energy and heat is defined as a radiation belonging in the electromagnetic spectrum (between 30KHz and 300MHz).² Many devices used in the day-to-day life, such as radios, televisions, wireless Internet, telephones, microwave ovens, satellite communications etc, operate based on RF.² Although the used energy (RF) is the same, different applications make use of different frequencies.² For medical and/or aesthetic purposes, RF frequencies above 10MHz are used.²

Electrical currents have been used in medicine for more than a century, and in medical treatments for over 75 years, usually for minimizing the invasiveness of surgical procedures, while RF is used for ablation and coagulation procedures.³

In aesthetic treatments, RF acts through its high-frequency current, which generates heat by conversion, deeply affecting tissular layers and promoting oxygenation, nutrition and vasodilation of the tissues; it acts by denaturing collagen fibers, resulting in their shortening and leading to the contraction of the redundant conjunctive tissue.^{2,3} When passing through the tissues, the current generates a slight friction (resistance of the tissues to the flow of RF), producing an increase in the local temperature.²

At the cellular level, the energy penetrates in the epidermis, dermis and hypodermis, also reaching muscle cells. It is worth to note that the RF's penetration depth is an inverse function of its frequency (Figure 1).³

In July 2000, the US Food and Drug Administration (FDA) recognized the first RF system as a "non-invasive treatment for the attenuation of wrinkles and temporary improvement in the appearance of cellulite." This pioneering RF device was able to demonstrate its heating action up to the level of the papillary dermis and subcutaneous fat, leading to increased activity of fibroblasts and formation of new collagen (observed in a period that spanned months). With this, it was possible to clinically demonstrate the presence of significant contraction in the treated areas.³ Since then many other RF devices have been developed, based on two main operating system types: unipolar (where the RF current flows through the body) and bipolar (where the RF current flow is limited to the volume located between the two electrodes).³ Due to the fact that the use of the bipolar system is more localized, it usually requires less energy to achieve the same heating effect.³

Several studies suggest RF as the gold standard noninvasive treatment leading to the retraction of the skin, demonstrat-

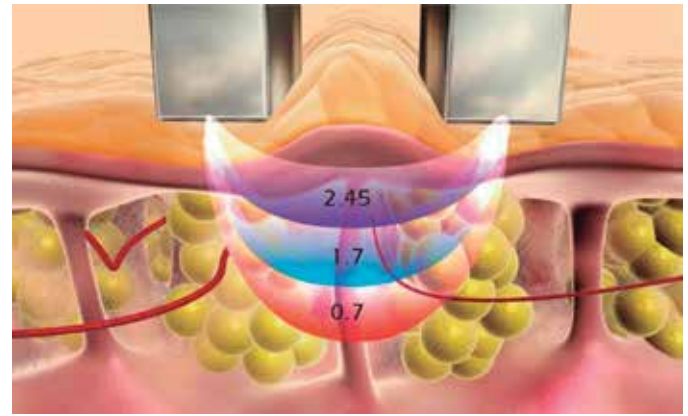


FIGURE 1: Schematic example of different depths reached by RF, according to the frequency (measured in MHz)

ing that the preservation of the skin's integrity minimizes the recovery and the risk of complications.⁶⁻¹¹

Many authors reported a significant attenuation of the sagging located in the neck and face of their patients, using scores to evaluate the clinical improvement and patient satisfaction.⁶⁻¹¹

Other scientific publications attest to the safety of RF for treatments diverse from skin tightening, for instance in acne scars, skin rejuvenation and wrinkle reduction.⁹ Its use in the palpebral area has also been proven safe, though it is deemed more effective when the defect is considered moderate.¹²

Histological studies have evidenced the contraction of collagen fibers after treatment with RF, which led to a contraction in the tissue due to a mediate thermal stimulus, inducing the production of new collagen.¹³ A number of studies monitored the action of the RF generated heat in the induction of collagen contraction, collagenesis and elastogenesis, with the resulting remodeling taking place during the treatment and for months after the application.¹⁴⁻¹⁷

While the effects of RF on the retraction of skin are undisputed, several studies describe limitations of this technology.¹⁴⁻¹⁷ The thermal effects of unipolar and bipolar RF were proven beneficial in skin tightening; nevertheless, they can be partial or unpredictable.¹⁸

Up until a few years ago, the choices for treating sagging skin were strictly surgical. With the introduction of RF and other devices employing different energy sources used for shrinking tissue in a noninvasive manner, new options have emerged. However, these methods are limited by the recognized fact that the improvement of sagging skin can be difficult to achieve without the use of surgical procedures.¹⁹ One hypothesis for the lack or unpredictability of the effectiveness of RF systems is the difficulty to adapt the power delivered to different individual skin impedances.¹⁸

Adequate patient selection and the careful management of expectations are crucial, since the clinical results obtained with RF still have low predictability and reproducibility, and

are not equivalent to those of plastic surgery.^{18,19} In this manner, defining the RF treatment as a rejuvenation, non-ablative technique that has action on the retraction and contour of moderately loose skin in patients without structural ptosis, will most likely lead to patient satisfaction regarding clinical outcomes.^{4,5}

In these patients – and in those where avoiding surgical treatment modalities is desirable – RF offers a non-invasive alternative treatment based on the retraction of the skin and subcutaneous tissue, causing improvement in nasolabial lines and firmness in the jaw region, promoting the definition of the cervicomental angle, with absence of complications or need for recovery time.^{5,20} (Figure 2)

In a clinical trial, almost 100% of patients experienced some degree of attenuation of sagging skin resulting from the treatment with a RF device.²¹ (Figure 3) This study evidenced that patients often obtained visible results rapidly (within a week), however from a clinical point of view they became clinically more noticeable three months after the procedure, in general.²¹ Other later phase studies have proven the presence of

improvement three months after the treatment, with the follow up of patients being able to demonstrate even better results six months after the application of RF.²² Despite the fact that it has been proved that effects of RF remain visible for six months after a single treatment, the longevity of clinical outcomes has yet to be determined.^{22,23}

Other studies are also concerned with the procedure's execution technique, for it can compromise the RF treatment's outcome. A greater increase in the temperature and its maintenance at around 40°C throughout the duration of the application has the effect of reducing the extensibility and increasing the density of the collagen, entailing an improvement in the sagging of the skin. In RF, this effect is termed *lifting*.²

There are many studies demonstrating the need to achieve a skin temperature of between 39°C and 42°C (clinically effective temperature) in order to obtain aesthetic effects with RF.³ Aligned with this, devices and application techniques have been improved aiming at strengthening the RF's action.²⁴

The low frequency/multiple passes technique is an ef-

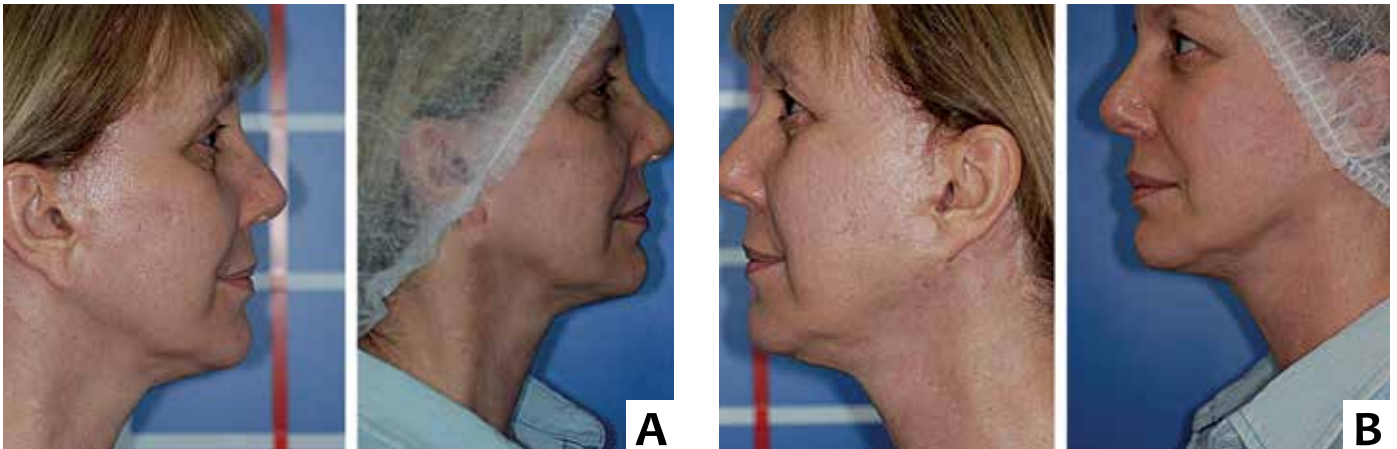


FIGURE 2 A AND 2B : Before and after four RF sessions



FIGURE 3:
Before and after eight RF sessions

fective RF algorithm for skin tightening.²⁴ An evaluation of the multiple passes technique showed that all patients experienced some immediate erythema or edema, most of them completely resolved within 48 hours. There was absence of immediate abrasion or depigmentation in the 6 to 12-week follow up.²⁴ Photographic analyses of images obtained after the application with the multi passes technique confirmed the presence of visible esthetical improvement in facial and neck sagging in 96% of patients treated.²⁴

In another study, the application of monopolar RF on the face and neck using a *vector multipass* proved to be safe and tolerated by patients of all skin phototypes, with the patients' satisfaction being correlated with the images.²⁵

Stacked pulses in the submental region have also led to a reduction of fat.²⁵ The reduction of fat is explained by the fact that, in addition to inducing collagen remodeling, the effects of RF heat also improve blood circulation. As a result, devices that use this source of energy produce electrothermal effects in the skin and subcutaneous tissue, which makes RF also indicated in all degenerative processes involving a reduction or delay of metabolism, irrigation and nutrition.^{2,3}

The method causes vasodilation and increased irrigation beneath the treated area, as well as oxygenation and nutrition of the tissue.² With the increased circulation, a nutritional gain of oxygen, nutrients and trace elements takes place in the tissue. There is also an improvement in the cell residues (toxins and free radicals) drainage system.² These effects provide the opportunity to enhance the quality of adipocytes, causing homeostatic lipolysis and production of better quality elastic fibers.²

When the body detects a temperature higher than the physiological level, capillary vessels open, causing vasodilation. In turn, this improves the tissular trophism and reabsorption of excess intercellular fluid, increasing blood circulation.² The heating effect also leads to an improvement in the microcirculation, resulting in the increase of blood flow to adipose tissues, which in turn causes an increase in the metabolism of the latter, homogenizing the subdermal fat and increasing the elasticity of the skin.³ In theory, therefore, RF technology can be used not only in the reduction of sagging, but also in the reduction of body circumferences.²⁶

Franco et al. demonstrated that a ten-minute thermal exposure to 43°C resulted in adipocyte cell death. In the same line of research, Galitzky et al. described an increase in the strength of fat cells lipolysis due to an increase in the catecholamines and blood flow.³

Clinical studies have also demonstrated the effectiveness of RF in reducing localized fat and body contours, especially when combined with massage mechanisms or other technologies.²⁶

The use of better protocols and the combining RF with other technologies seem to be the future of the use of RF in dermatology.⁵

Various RF based systems with aesthetic purposes (monopolar or bipolar, FDA approved) have emerged – some of

them combining RF with other treatment modalities, such as infrared light, vacuum and mechanical massage – aiming at creating synergism in order to improve blood circulation and, consequently, the action of reducing body circumferences.^{3, 27}

The combination of RF and vacuum has been evaluated as safe and effective in several studies. In general, the vacuum mechanism makes an additional contribution to the penetration of the RF's energy in the skin.^{3, 28}

A histologic study of an area treated with RF associated to vacuum showed a decrease in the atrophy of collagen and an increase in the interstitial edema, indicating an improvement in dermal trophism.³

The first RF device equipped with a vacuum unit has been described by Gold et al.. According to these authors, there was a significant improvement in the skin's appearance during the treatment and in a six-month follow up.³ Montesi et al. reported clinical and histopathologic results using a bipolar device associated with vacuum for treating wrinkles, sagging skin, acne scars and stretch marks.³

In many devices, the mechanical massage technique is used due to its direct effect on the microcirculation, providing improved lymphatic drainage and increased lipolysis.³ Due to its action on the microcirculation, these devices are often used to treat cellulite. Although the therapeutic results of these technologies are apparently long-lasting, periodic applications are required to keep the achieved clinical outcomes.^{26, 29} There are reports in the literature on the use of non-invasive methods combining bipolar RF with other technologies, such as infrared light and massage mechanisms, for the treatment of cellulite, demonstrating that it can be significantly and safely reduced.^{26, 29}

Isolated or associated with other methods, RF has few complications and has the additional advantage of allowing a prompt recover, with the patient returning to his or her daily routine immediately after the application^{4, 21} (Figure 4).

In the literature, reports of side effects were limited to transient erythema, edema and rare dysesthesias.²³ Studies performed with laboratory assessments of patients demonstrated that there were no alterations in the liver and/or lipid function indicators.³⁰ Ulcerations or pigmentation were not observed when the correct technique was applied, leading to the conclusion that RF heats the dermis and can achieve safe and effective tissue retraction.^{21, 23}

Even being considered a safe procedure, RF should be performed with moderate energy and without immediate overlapping in order to avoid overheating, leading to undesirable side effects.³¹ Narins et al. described a rare case of over treatment of the tissue, leading to contour irregularities for more than six months that were later corrected with subincision and autologous fat. This side effect can be avoided asking for the patient's feedback on the feeling of warmth during the procedure.³

There are few contraindications for the use of RF: pregnancy, use of electronic or metallic implant device, collagen or vascular disorders, active or recent malign disease, heat-stimulated disease, use of isotretinoin (controversial) and coagulopathy. It should not be applied over tattoos or permanent makeup.³



FIGURE 4:
Before and immediately after
the application of RF in the
cervical region

It is important to note that, although it cannot be used during pregnancy, RF is a safe and effective method for reducing body circumferences and attenuate sagging skin in the immediate postpartum period.^{32,33}

Radiofrequency is also safe when associated with other rejuvenation methods, such as a dermal implants. A study conducted with the application of RF two weeks after patients had undergone hyaluronic acid or calcium hydroxyapatite implants in the same area did not show any morphological alteration in the implanted material or surrounding skin.³⁴

In another study, patients were evaluated after having undergone dermal implants of hyaluronic acid in both sides of the face, followed by the application of RF in the same location, in only one of the sides. The side that received the dermal implant and the RF was compared to the contralateral side, which received only the hyaluronic acid implant. It was possible to observe that there were not histological changes after using the device over the area with the hyaluronic acid implant, leading to the conclusion that RF applied immediately and safely after the implantation of hyaluronic acid did not cause the reduction of the clinical effect or of other side effects.³⁵

A research conducted with pigs that were injected with different dermal fillers – human collagen (Cosmoplast), polylactic acid (Sculptra), liquid silicone (Silikon 1000), calcium hydroxyapatite (Radiesse) and hyaluronic acid (Restylane) – and subsequently treated with RF levels typically used in the daily practice, was designed to clinically and histologically evaluate changes occurred in the tissue. The filling substances injected

were histologically analyzed five days, two weeks and one month after the treatment. Each of the fillers produced a specific inflammatory response, with no immediate thermal effect arising from the application of RF having been observed. On the other hand, the RF based treatment produced a statistically significant increase in inflammation, foreign body formation and fibrotic response associated with the fillers, which may be considered a positive effect of the combination of the two procedures.³⁶

Another association of methods evaluated was that of the use of RF technology after liposuction or laserlipolysis, aiming at increasing the skin's firmness and eliminating any irregularities after the removal of fat³ (Figures 5 and 6).

In addition, devices that associate liposuction and RF on the same equipment have been positively evaluated for the reduction of significant amounts of fat, as well as for improving contours and effecting skin tightening.³⁷

CONCLUSION

In conclusion, RF is a method for the aesthetic treatment of the skin that has been developing rapidly since its inception, nearly two decades ago.

Both the application technique and the devices themselves have been going through advances, with other methods, such as massage and other technologies, having been incorporated in order to maximize outcomes in the treatment of sagging skin and body contours.

In practical terms, RF was proven effective for patients with good indication, bearing mild or moderate sagging. It has



FIGURE 5: Photographs demonstrating the association of RF in the pre-laserlipolysis (before and after four RF sessions)



FIGURA 6: Photographs demonstrating the association of RF in the pre-laserlipolysis (before and after eight RF sessions).

also showed action in the treatment of body contours and cellulite.

Some additional advantages of the method include a high level of safety, with few side effects having been reported, and the patient's ability to resume his or her routine immediately after undergoing the procedure. Its versatility should also be highlighted, for it can be used after other treatments, such as facial dermal implants or liposuction and its variations, in other body sites.

Despite the fact that its use can be limited in more severe cases, RF is, therefore, a widely used therapeutic method for the treatment of facial and corporeal skin sagging, as well as for improving body contours, with proven efficacy and a great level of safety. ●

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Intraoperative dermoscopy as a tool in the diagnosis of melanonychia

Dermatoscopia intraoperatória como ferramenta no diagnóstico de melanoníquia

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ABSTRACT

The term melanonychia refers to a brownish pigmentation produced by melanocytes in matrix, which extends from the proximal region up until the distal margin of the nail plate. This condition occurs due to the activation or hyperplasia of melanocytes, which presents benign lesions, such as nevi and lentigo or malignant lesions, such as melanoma of the nail unit. The intraoperative dermoscopic analysis of the nail matrix improves the diagnostic accuracy and guides on the best biopsy method for melanonychia. A proper biopsy technique is aimed at obtaining a good quality sample for the histological diagnosis – the gold standard – associated with a lower risk of permanent dystrophy.

Keywords: nails; lentigo; dermoscopy

RESUMO

O termo melanoníquia se refere à pigmentação marrom-acastanhada produzida pelos melanócitos da matriz, que se estende da região proximal até a margem distal da placa ungueal. Essa condição ocorre por ativação ou hiperplasia de melanócitos, que representam lesões benignas como o nevo e lentigo ou lesão maligna como o melanoma do aparelho ungueal. A análise dermatoscópica intraoperatória da matriz ungueal aumenta a acurácia diagnóstica e orienta quanto ao melhor método de biópsia da melanoníquia. Uma técnica adequada de biópsia visa obter uma boa qualidade de amostra para o diagnóstico histopatológico, padrão ouro, associado a menor risco de distrofia permanente.

Palavras-chave: unhas; lentigo; dermoscopia

INTRODUCTION

Longitudinal melanonychia is a term used to describe a brown band that runs from the proximal to the distal region of the nail plate. It occurs more frequently in non-Caucasians aged 50–70 years, with a higher incidence in the thumb, followed by the hallux and the forefinger, being observed in only 1.4% of the population.¹ It can be classified according to two activation conditions: activation of melanocytes (racial melanonychia, inflammatory diseases, drugs) or melanocytic hyperplasia (benign, such as nevus and lentigo or malignant, like nail melanoma). Due to the possibility of the diagnosis of melanoma, biopsy of the melanonychia is necessary, since melanoma in the acral region has a reserved prognosis given the greater possibility of invasion. Intraoperative dermoscopy of the matrix, where the melanocytes responsible for the pigmentation of the nail plate are located, is

Diagnostic Imaging

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seen as one of the main methods in the approach of these lesions. Regular lines with uniform pattern lend benignity to the lesion, while irregular lines with variation in color suggest malignancy.² Based on dermoscopic features, the surgeon can decide with greater certainty on the best biopsy technique to be adopted.³ When performing a biopsy on the nail matrix, the proper technique is aimed at obtaining a good quality sample containing information necessary for histological analysis, associated with a lower risk of permanent dystrophy. There are 4 main surgical alternatives for biopsy of longitudinal melanonychia:⁴

1. tangential excision of the matrix (shaving of the matrix), which is aimed at obtaining a sample of the upper region of the matrix when dermoscopic characteristics suggest the presence of a benign lesion;
2. the use of a 3mm punch, indicated in cases where the lesion has less than 3mm;
3. longitudinal excision of the matrix, indicated for longitudinal melanonychia with medial location, aimed at removing the entire lesion;
4. lateral longitudinal excision, indicated when the melanonychia is located on the lateral part of the nail.

Above all, it is important to obtain a sample that contains the information necessary for the correct diagnosis of melanonychia. The authors present a case of simple nail benign lentigo, the adopted approach, clinical dermoscopic findings, the decision process regarding the surgical biopsy technique and the histologic aspect found.

CASE REPORT

A 31 year-old female patient described the appearance of brown longitudinal, asymptomatic band, in the second left thumb two years before. She described a progressive increase in the width of the band. There was absence of history of trauma or previous use of medications. She did not made reference to family history (Figure 1A). The dermoscopy of the dorsum of the nail plate showed benign characteristics (Figures 1B and 1C). A pattern of regular brown bands, with an absence of globular structures, was observed in the intraoperative dermoscopy of the nail matrix. Due to the benign dermoscopic features, the surgical option for the biopsy was the shaving of the nail matrix. The objective was to obtain a good quality sample for the diagnosis, with the functional preservation of the nail matrix (Figure 2). Histology characterized a picture of unguial benign lentigo (Fig-

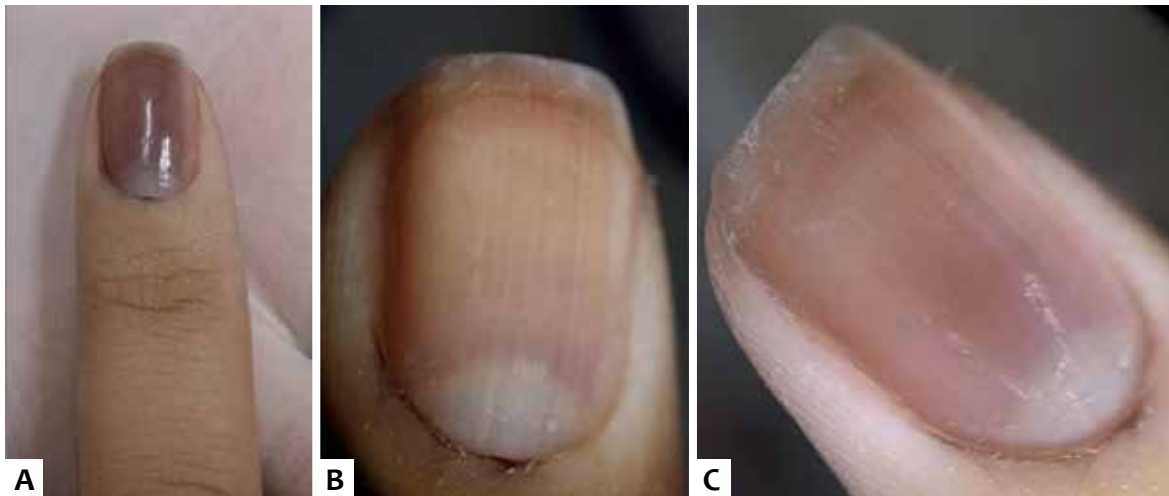


FIGURE 1:
A: Clinical aspect: longitudinal melanonychia occupying 70% of the dorsum of the nail plate, cuticle involvement in the proximal fold.
B and C: Dermoscopy of the dorsum of the nail plate: micro-Hutchinson sign, homogeneous regular brown bands and preserved parallelism

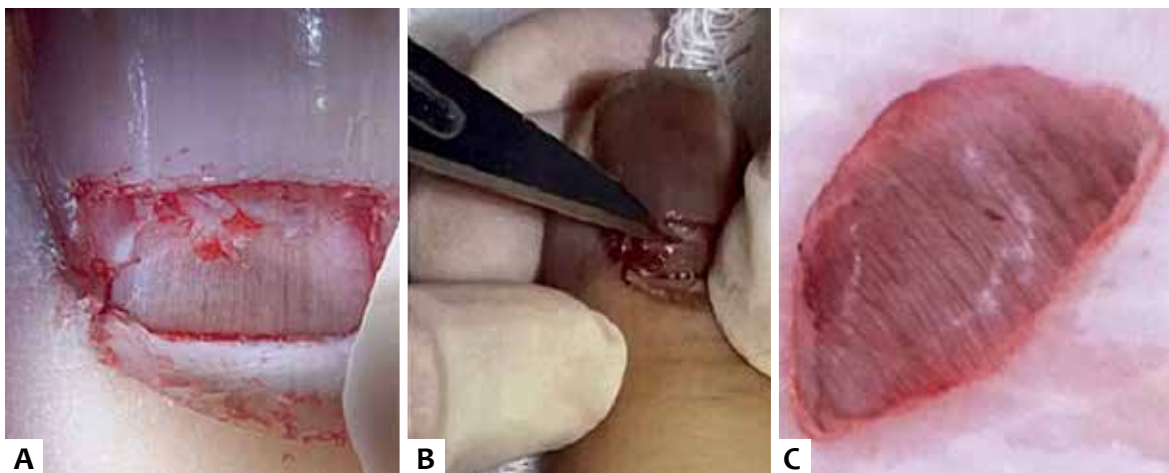


FIGURE 2:
 Dermoscopy of the nail matrix during surgical time, with benign characteristics:
A: Brown homogeneous, regular bands, preserved parallelism and absence of globular structures.
B: Shaving biopsy method.
C: Good quality sample for histological analysis

ure 3). The postoperative course with absence of permanent scar, such as pterygium or onychotrophy, with the nail plate returning to its physiological growth in the 30 and 60 days follow ups (Figure 4).

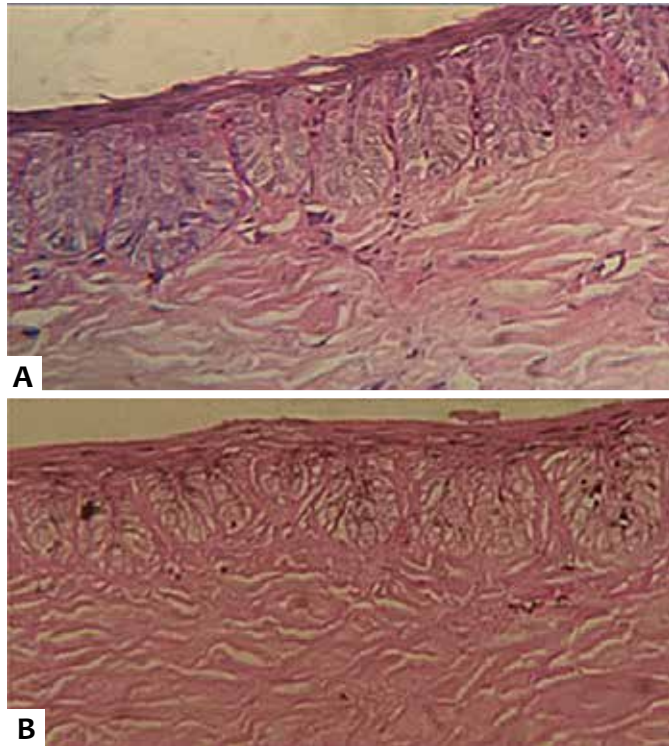


FIGURE 3: Histological analysis using optical microscopy.
A: 100X HE: individually arranged melanocytes among onychocytes in the nail matrix, characterizing a benign lentigo picture.
B: 100X Fontana Masson: Using the same fragment, dendritic melanocytes are more clearly observed in a sparse layout among onychocytes

DISCUSSION

In that case, the patient had indication for biopsy for it was an acquired lesion, in the index finger, with progression in width for two years.⁵ The clinical and dermoscopic analysis of the nail plate is a widely used, simple to perform and cost effective method that provides a better diagnostic accuracy of longitudinal melanonychia. Using this method in the present case, it was possible to verify the melanonychia’s benign pattern – regularity and parallelism of brown lines and homogeneous color. The intraoperative dermoscopy of the matrix allows direct examination of the pigmentation’s origin and, according to the characteristics found, assists in the choice of the best biopsy technique to be adopted. In the present clinical case, the intraoperative analysis of the matrix, which yielded benign characteristics, pointed towards the adoption of the shaving biopsy technique. The good quality of the sample allowed the histological diagnosis of simple lentigo type melanocytic hyperplasia. The choice of biopsy technique depends on factors such as location, origin (proximal or distal matrix) and width of the melanocytic band, as well as on the presence of periungual pigmentation (Hutchinson’s sign).⁶⁻⁹ The tangential excision of the matrix captures a sample of less than 1mm¹⁰ in depth with good quality length. This technique was chosen due to the location of the pigmentation (distal matrix) and the absence of malignant features. It is important to note that the shaving of the matrix is indicated for lesions with more than 3mm, especially those located in the distal matrix. One disadvantage of this method is that the precision degree of the evaluation of the dermal layer may be limited.



FIGURE 4: Postoperative follow up.
A: Immediate postoperative.
B: Thirty-days postoperative: displacement of the surgical wound with proximal hematoma
C: Sixty-days postoperative: displacement of the surgical wound and hematoma, whitening of the nail plate in its most proximal part.

CONCLUSION

The present case illustrates the importance of using varied and relevant tools available for the approach of melanonychia. It is important to track cases suggestive of malignancy. The choice of the appropriate biopsy technique aims at obtaining a good quality sample for histological study, preserving the matrix's functionality, with decreased possibility of onychodystrophy.

The present case demonstrates the use of dermoscopy of the nail matrix during surgical time, assisting in the semiotic and management of melanonychia. Although the clinical and dermoscopic aspects are of great propaedeutic assistance in a great number of cases, anatomical pathological examination is crucial to confirm the diagnosis. ●

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Foreign body reaction with severe infection resulting from facial filling procedure performed by a non-medical professional

Reação de corpo estranho com infecção grave decorrente de preenchimento facial realizado por profissional não médico

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ABSTRACT

In search of a perfect aesthetic, facial filling procedures have been widely used. The presence of animal proteins or synthetic substances in some cutaneous fillers can cause serious allergic reactions, especially when performed by untrained professionals. There are not ideal, pure and free of side effects substances available in the marketplace. The present article is aimed at reporting a case where a facial filling was performed by a non-medical professional, resulting in foreign body reaction and severe skin infection, leading to deformities caused by the procedure carried out. The complications entailed invasive procedures for removal of the material used, and treatment with corticosteroids.

Keywords: Mohs surgery; carcinoma, basal cell; nose neoplasms; surgical flaps; nasal cartilages

RESUMO

Reconstrução de defeitos cirúrgicos nasais, especialmente quando há comprometimento simultâneo, de espessura total de asa nasal bilateral, ponta e dorso nasal, é complexa. Várias opções cirúrgicas são descritas, e a maioria dos autores recomenda enxerto de cartilagem de orelha ou retalho condromucoso de septo nasal, em associação ao retalho médio frontal, para conferir rigidez estrutural à asa nasal e impedir que se colapse durante a inspiração. Os autores descrevem uma alternativa de reconstrução, livre de cartilagem, por meio da combinação de retalhos em dobradiça a partir do sulco nasogeniano, associado ao retalho paramediano frontal.

Palavras-chave: cirurgia de Mohs; carcinoma basocelular; neoplasias nasais; retalhos cirúrgicos; cartilagens nasais

INTRODUCTION

The use of cutaneous filling techniques has been growing, and the procedure's success is closely related to the chosen substance and the application method.¹ The cutaneous filling technique is included among the most commonly performed non-surgical procedures. Currently there is no commercially available ideal substance, pure and free of side effects.² There are several reports of complications with the use of fillers, such as inflammatory reactions, edema, hematoma, formation of nodules due to uneven distribution of the product or hypersensitivity and infection.³ From an aesthetics standpoint, both the training of the applicator professional and the product's origin should be carefully verified. The establishments where the procedures will be per-

Case Reports

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formed must have sound conditions and be properly equipped.⁴ The professional responsible for the procedure should have experience with the selection of the appropriate product and use of application techniques for each specific anatomical site, a capability that also requires extensive knowledge of facial anatomy.⁵ The present study is aimed at describing a case of facial filling carried out by a non-medical professional that resulted in severe foreign body reaction and skin infection, leading to permanent deformities in the patient.

CASE REPORT

A 47-year-old male, was admitted to hospital complaining of allergic reaction to a bee sting occurred 20 days before the appearance of the symptoms. On examination the patient was febrile, tachycardic, with bilateral upper and lower eyelid edema, and erythematous-violet nodules with floating appearance in the nasogenian fold and forehead (Figure 1). Initial tests revealed leukocytosis (24,900 thousand/mm³) and the introduction of clindamycin and oxacillin based antibiotic therapy. On the second day of hospitalization, the oxacillin was replaced by ciprofloxacin, as recommended by the Infectious Diseases Clinic. In addition, the aspiration of the facial lesions was performed with a needle, yielding a purulent secretion, which was sent for culture. The culture for fungi and bacteria and Anti-HIV test came out negative. On the sixth day of hospitalization, with absence of improvement and after persistent questioning, the patient admitted to have undergone a procedure with polymethylmethacrylate injection (PMMA) in the face 20 days before, carried out by a non-medical professional.



FIGURE 1: Initial appearance of the patient

The histopathology of the facial nodule's biopsy showed granulomatous infiltrate throughout the dermis, observing microcysts amid the infiltrate, besides pseudoepitheliomatous acanthosis associated with micro-abscesses, corroborating the clinical proposition of foreign body granuloma. The patient was then referred to the plastic surgery department, where the surgical removal of the product was performed, as well as a monthly treatment with injectable corticosteroids for one year. There was partial improvement, nevertheless the patient remained with sequelae resulting from the procedure (Figure 2).

DISCUSSION

Currently there are different types of cutaneous fillers that are classified into temporary, semi-permanent (which should remain at least 18 months in the tissue) and permanent. Among the latter, are the PMMA and silicone.^{6,2} PMMA is composed of microspheres suspended in bovine collagen solution, carboxymethylcellulose or hydroxyethylcellulose.^{7,8} The silicone based filler is constituted by silicon derived polymers, and may be presented in the form of a gel, foam or liquid, depending on the degree of polymerization.⁹ The use of permanent fillers implies medical responsibility and requires precise injections. Mastering how to manage possible complications, the careful planning of the injection plans, as well as having the knowledge of the most indicated areas are imperative. The application of these substances can cause some undesirable side effects including local edema, inflammation, telangiectasia, hypertrophic scars, allergic reactions and granuloma formation. The latter generally arise between 6 and 24 months after the treatment, with a rate of



FIGURE 2: Appearance after surgical correction and infiltration of corticosteroids

occurrence of 0.6%, however they may also occur several years after the injections.¹⁰

The possibility of the formation of biofilms, with the use of materials foreign to the host for implantation in soft tissues, is also noteworthy. Biofilms consist of gram-positive and gram-negative bacterial communities; nevertheless they may contain fungi, algae and protozoa. It is important to note that the biofilm hampers the action of antimicrobials, as it provides protection mechanisms for the bacteria against these agents. This may justify the infection observed in the site where the procedure was performed in the studied patient, entailing difficulty for the therapeutic response. Rosa and Macedo¹ offer some important and prudent recommendations on the use of filling substances: a) avoid carrying out these procedures on under-age patients, b) start performing filling procedures with absorbable substances before applying permanent substances, c) individually select patients and the correct indication of the procedure, since the substances are difficult to remove, d) adopt a judicious stance regarding the product manufacturer's recommendations, e) provide sterile conditions and limit the number of needle penetrations, thereby minimizing the risk of bacterial contamination, f) monitor patients scheduling return visits for the week following the application, since most bacterial infections occur within 8 to 10 days after the procedure, g) perform antiviral prophylaxis in patients with history of herpes labialis, h) pay attention to the amount injected into the corners of the mouth due to the fact that filling substances migrate easily, i) avoid performing the procedure close to the location where the supratrochlear arteries surface, during the correction of supratrochlear wrinkles.

In the present case, the patient underwent the application of the permanent filler PMMA in the face by a professional who was not qualified in the field of health sciences. Studies of the analysis of the histopathological reactions caused by PMMA revealed the presence of inflammatory infiltrates and a reduction in the quantity of the product according to the time elapsed after the performance of the procedure. In a proportion inverse to the amount of PMMA, the fibrosis and inflammatory reaction were increased with the passing of time, leading to the formation of foreign body granuloma, as evidenced in the studied patient's pathology. Contrary to the literature, which quotes granulomas as a delayed reaction,^{3,10} the patient reported the symptoms 20 days after the procedure, linked to secondary infection of the lesions caused by inadequate asepsis techniques in the product application sites.

CONCLUSION

According to the researched literature, the isolated use of the substance could already cause adverse reactions.³ In the present case, where the procedure was performed by a non-medical professional, there were signs of exacerbation of the reactions, leading to sequelae resulting from the flaws in the technique employed and the lack of knowledge of the facial anatomy, in addition to the absence of minimum conditions of hygiene. The indiscriminate use of certain substances by unqualified professionals can lead to important consequences, resulting in social and aesthetic damage to the patient. ●

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Case Reports

Unipedicled advancement flap from the lower cheek for the reconstruction of a large nasal surgical defect after the excision of a basal cell carcinoma

Retalho de avanço unipediculado da bochecha inferior para reconstrução de grande defeito cirúrgico nasal após exérese de carcinoma basocelular

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ABSTRACT

The basal cell and squamous cell carcinomas are known as non-melanoma skin cancers, having amounted to 98,420 new cases in men and 83,710 in women in Brazil in 2014. The reconstruction of surgical defects in the nose is a challenge for dermatologic surgeons regarding good functional and aesthetic results, since its structure is rigid and of little mobility. The authors introduce an interesting reconstruction method of a large nasal defect after excision of a basal cell carcinoma, using auricular cartilage graft and unipedicled advancement flap from the lower cheek.

Keywords: carcinoma, basal cell; nose neoplasms; nasal surgical procedures; ear cartilage; surgical flaps

RESUMO

Os carcinomas basocelular e espinocelular são conhecidos como câncer de pele não melanoma perfazendo 98.420 casos novos nos homens e 83.710 nas mulheres no Brasil, em 2014. A reconstrução dos defeitos cirúrgicos no nariz é um desafio para os cirurgiões dermatológicos, no que diz respeito a bons resultados nos aspectos funcional e estético, posto que sua estrutura é rígida e de pouca mobilidade. Apresentamos um interessante método de reconstrução de um grande defeito nasal após exérese de CBC, utilizando enxerto de cartilagem auricular e retalho de avanço unipediculado da bochecha.

Palavras-chave: carcinoma basocelular; neoplasias nasais; cartilagem articular; retalhos cirúrgicos

INTRODUCTION

Skin cancer has worldwide distribution and is the most common neoplasia in human beings. Its three main forms and frequencies are: basal cell carcinoma (BCC) (75%), squamous cell carcinoma (15%) and melanoma (4%). The basal cell and squamous cell carcinomas are known as non-melanoma skin cancers and amounted to 98,420 new cases in men and 83,710 women in Brazil in 2014. These figures correspond to an estimated risk of 100.75 new cases per 100,000 men and 82.24 per 100,000 women.¹

BCCs are most commonly located on the face, with 70% of cases in the nose and forehead. In the nose, most are located in the distal two thirds,² particularly in the nasal wings (33% of cases) and in the dorsum (30%).³

Gonzalez-Ulloa et al. observed that the face had different anatomical units, with transition lines separating them, and postulated that these units could be determined by differences in

histologic characteristics, including thickness, amount of subcutaneous fat, color, texture, and presence of hair.⁴ Based on these concepts, Burget and Menick divided the nose in the following aesthetic sub-units: dorsum, tip, columella, nasal wings, lateral walls and soft triangles. In the nasal tip and wings, the skin is thick and sebaceous, while in the dorsum and lateral walls the skin is thin. In addition, the skin has greater mobility in the upper two thirds.⁵

The reconstruction of surgical defects generated by the excision of tumors in the nose is a challenge for dermatologic surgeons regarding good functional and aesthetic results, since its structure is rigid and has low mobility. The patient's age, size and location of the surgical defect according to the aesthetic sub-units are the parameters that serve as guidelines in the choice of the best reconstruction method. Numerous techniques, such as primary synthesis, advancement flaps, transposition flaps, bilobed flaps, grafts or combination of techniques can be used.^{6,7}

CASE REPORT

A 78 year-old, phototype IV female patient, born in the city of São Bernardo (in the Brazilian State of São Paulo) described the appearance of a painless and progressive lesion in the nose five years before. The patient presented arterial hypertension and dyslipidemia, denying prior history of skin cancer. Dermatological examination revealed an erythematous and translucent nodule measuring 2.2 x 1.7cm, with well-defined borders and a crust in its lower portion and arboriform telangiectasias across its surface, located on the nose, covering part of its three aesthetic subunits (left nasal wing, left nasal wall and nasal tip) (Figure 1). It was clinically diagnosed as a BCC and an incisional biopsy was performed, confirming this clinical suspicion. The tumor showed nodular and micronodular histologic subtypes.

The tumor was excised with a 6.0 mm margin after tumescent anesthesia. Also, a decision was made for removing the nasal cartilage which was just beneath the tumor, due to the possibility of invasion of that structure. The surgical specimen and cartilage were sent for histological evaluation. The patient remained with a large nasal defect comprising the left nasal wing, left nasal wall, tip and dorsum (Figure 2). Initially, a cartilage graft from the anti-helix of the left ear was transposed to the left alar base aimed at supporting the rim of the nostril, preventing its upward migration during the healing of the wound, and trying to keep its contours and air passage untouched (Figures 3

and 4). Next, a unipedicled advancement flap was prepared from the cheek, with a superior base, with transfer of skin from the lower cheek towards the medial/superior direction (Figures 5 and 6). The flap was widely dissected in the subcutaneous plane, with internal sutures having been performed with 5.0 monocryl thread in order to fit it in the primary defect. Subsequently, a



FIGURE 2: Large nasal defect after exeresis of BCC



FIGURE 3: Cartilage graft donor area. Removal of cartilage from the anti-helix of the left ear

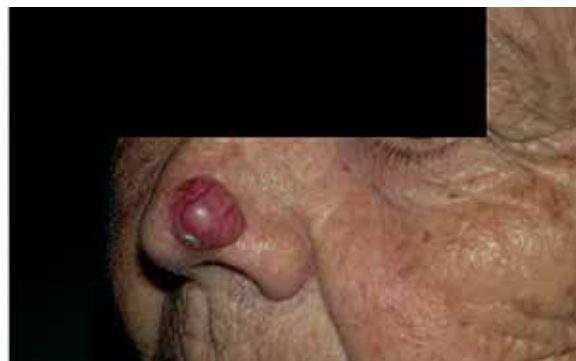


FIGURE 1: Nasal BCC. Erythematous and translucent, well-defined nodule, with a crust in its lower portion and arboriform telangiectasias across its surface



FIGURE 4: Cartilage graft receiving area. Cartilage graft transposed to the left alar base

compensation triangle was removed from the flap aimed at rebuilding the left nasal wing, and anchoring stitches were carried out in the periosteum with 4.0 nylon thread in order to recreate the alar facial groove. Next, a small dog-ear that was formed at the superior part of the wound was corrected and the skin was sutured with 5.0 nylon thread. A compressive dressing was applied, and cephalexin and analgesic were prescribed for seven days. The patient recovered well postoperatively, with good aesthetic and functional results (Figures 7 and 8). The histology of the surgical specimen showed nodular and micronodular histologic subtypes of BCC with free lateral and deep margins. There was no evidence of tumor in the cartilage. The patient had been followed-up for a year and four months by the time the present article was approved, with no signs of recurrence.



FIGURE 5: Unipedicled advancement flap of the cheek, based superiorly. Transfer of skin from the lower cheek towards the medial/superior direction



FIGURE 7: Immediate postoperative. A compensation triangle was removed aimed at rebuilding the left nasal wing



FIGURE 6: Unipedicled advancement cheek flap. Flap widely dissected in the subcutaneous plane



FIGURE 8: Late postoperative. Good aesthetic and functional results after six months

DISCUSSION

Nasal reconstruction has seen great progress in the last 50 years. In the early days, the main objective was to provide tissular cover for the defect without significant concern about the cosmetic appearance. This concept began to change in 1950, when surgeons began to advocate the use of “similar tissue” to replace “similar tissue, according to the aesthetic units of the face.”^{6,7}

In this manner, firstly the functional and breathing capacity of the nose should be restored, maintaining or recovering the structural integrity of the site of the defect. Secondly, an effort should be made aimed at achieving aesthetically pleasing results that are in harmony with the remaining of the face in terms of texture, color and shape.⁷ Understanding of the stratigraphy of the nasal tissues is necessary for this, considering that, when analyzing the defect to be repaired, the surgeon must evaluate and determine the layers of the nose that are involved in the defect and those that are missing. In line with this, Manson et al. described the nasal reconstruction as a three-plane approach: cover (skin, subcutaneous tissue and muscles), structural framework (cartilage, nasal septum and bones) and lining (buccal skin and nasal mucosa), which should be individually assessed before the final decisions related to the repair are taken.^{6,7}

The patient had a large defect in the cover – involving the nasal tip, wing, dorsum and lateral wall – and also in the structural framework, requiring an anti-helix cartilage graft in the left nasal wing base, aimed at maintaining the natural curvature (without flattening it), the respiratory function and the

balance with the opposite side. The auricular cartilage provides good support, is readily available and can be harvested easily with minimal cosmetic deformity. The grafts can be harvested from the different areas of the ear (for example from the helical border, the upper or lower concha, the anti-helix and the triangular fossa), with the specific location depending on the defect's size and location, as well as the surgeon's preference.⁸

Cutaneous flaps originary only from the nose are unfeasible due to the large dimensions of the surgical defect. The reconstruction options available for the authors of the present article were the interposition paramedian frontal flap, the interposition nasogenian flap with cutaneous pedicle, the full-thickness cutaneous graft and the unipedicled advancement cheek flap based superiorly. They chose the latter due to the facts that it could be performed in a single surgical time and the patient had a great volume of sagging and excess skin in the lower cheek. A single and long incision was carried out along the defect, running on the nasogenian fold up until the inferolateral cheek. After extensive dissection in the subcutaneous plane, the skin was advanced medially and superiorly towards the defect, with a small additional pivoting movement.^{7,9,10}

The dermatologic surgeon should recognize the different types of skin flaps since the incidence of nasal tumors has been increasing. In this manner, the authors present an interesting method for the reconstruction of a large nasal defect, with excellent functional and aesthetic results. ●

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Case Reports

Thioglycolic acid peeling as a therapy for post-inflammatory hyperchromia

Peeling de ácido tioglicólico como terapêutica para hiperchromia pós-inflamatória

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ABSTRACT

Post-inflammatory hyperchromia is an important sequel of inflammatory dermatoses. In addition to depigmenting topical treatments, chemical peels can be effective in treating it. The present report describes a case of post-inflammatory hyperchromia after treatment of Lichen Planus handled with thioglycolic acid peels. Thirty percent thioglycolic acid applied in the form of a peel is described as a therapeutic option with discrete results and can be considered an ally in managing this dermatologic condition.

Keywords: *Chemexfoliation; hyperpigmentation; thioglycolates*

RESUMO

A hiperchromia pós-inflamatória é sequela importante de dermatoses inflamatórias. Além dos tratamentos tópicos despigmentantes, os peelings químicos podem ser efetivos em seu tratamento. O presente relato descreve um caso de hiperchromia pós-inflamatória após tratamento de líquen plano manejado com peelings de ácido tioglicólico. O ácido tioglicólico a 30% aplicado na forma de peeling é descrito como opção terapêutica com resultados discretos, podendo ser considerado um aliado no manejo dessa afecção dermatológica.

Palavras-chave: *abrasão química; tioglicolatos; hiperpigmentação*

INTRODUCTION

Post-inflammatory hyperpigmentation (PIH) is an important sequel of inflammatory dermatoses.¹ It can ensue several skin diseases, and its treatment is challenging.¹ The authors describe a case of PIH that ensued a picture of extensive lichen planus treated with thioglycolic acid peels (TA).

CASE REPORT

A 54 year-old female patient sought treatment due to asymptomatic oral lesions, and pruriginous cutaneous lesions with seven months of development. Physical examination revealed lichenoid purplish papules on the upper limbs, trunk and neck, with absence of oral lesions. Biopsy of one of the lesions was consistent with lichen planus, and treatment with 20mg/day prednisone was instituted. Three months after the end of the treatment, the patient presented PIH in the lower limbs and wanted to treat it (Figure 1). She began using 4% hydroquinone and 10% glycolic acid cream for four months without success. A triple formulation (4% hydroquinone + 0.05% tretinoin + 0.1% fluocinolone) was then introduced with little response after three months of use. Due to the ineffectiveness of the treatments, the authors decided to perform 30% TA gel peelings with fortnightly intervals. The peelings were performed starting with the application of 30% TA gel for two minutes. The time of exposure of the skin to TA was increased by three minutes on each session, up until a maximum of 15 minutes was reached. In each session, once the time of exposure to the peeling was reached, neutralization of the TA was carried out by cleansing with gauze moistened with distilled water and saline solution. A total of 6 sessions were conducted. The daily use of a depigmentation formula (1.5% TA + 3% tranexamic acid) at night was associated in order to enhance the peeling treatment. The patient was instructed about the importance of applying daily photoprotection, using SPF 50 sunscreen, as well as physical protection.



FIGURE 1: Post-inflammatory hyperchromia in the lower limbs ensuing the picture of extensive lichen planus

RESULTS

There was partial improvement of the PIH with the whitening of the lesions, as seen in the progression picture (Figure 2).

DISCUSSION

Post-inflammatory hyperpigmentation (PIH) is an important sequel of inflammatory dermatoses, and its management is a challenge for dermatologists.¹

PIH may result from a number of dermatoses, including lichen planus.^{1, 2} The pathogenesis is not completely understood, however it is known that it results from increased production of melanin or from its irregular deposit after dispersion caused by the action of mediators of the inflammatory process.¹ The intensity of the PIH is greater in dermatoses in which inflammation is chronic, recurrent, and when there is damage to the basal layer.²

When PIH is confined to the epidermis, it is possible to observe a brownish hue and there is an increase in the production and transfer of melanin to keratinocytes. The presence of hemosiderotic component in lesions is also described. If not treated, it tends to resolve spontaneously after months or years.¹ In the dermis, it is possible to observe a blue-grayish color and damage to the basal layer, with deposition of melanin in the upper layers of the dermis. These deposits are phagocytized, forming melanophages.^{1, 2} The removal of melanin deposited in the dermis is a very slow process.¹

The treatment of PIH begins with the approach of the underlying condition, however caution is needed for the management of the basic dermatosis can exacerbate PIH.¹ After controlling the underlying dermatosis, the PIH is treated with topical depigmenting agents and procedures, such as chemical peels and laser applications.¹ Photoprotection is essential in any therapeutic modality and should not be underestimated.¹ It must be carried out through the daily use of sunscreen contain-



FIGURE 2: Partial improvement of post-inflammatory hyperpigmentation after 30% thioglycolic acid peels

ing a combination of physical and chemical agents, in addition to physical external protection against ultraviolet radiation.¹

It is crucial to perform photographic records of the PIH before and during the procedure aimed at assessing the results.

The first choice therapy in PIH is the topical application of 4% hydroquinone associated with photoprotection, being more effective and well tolerated if associated with tretinoin and topical corticosteroids, as in triple whitening formulations (4% hydroquinone + 0.05% tretinoin + 0.1% fluocinolone acetonide), for the combination allows greater penetration by reducing the irritation potential.¹ In the present case, the patient had no therapeutic response with the use of the Kligman formula. Hydroquinone has limited effect when the pigment is deposited in the skin.² In resistant cases, other topical depigmenting agents (azelaic or kojic acid, tretinoin, licorice extract, soybean derived depigmenting) can be associated after 8 to 12 weeks of treatment, and the therapy with chemical peels is also indicated (isolated or associated with topical treatments, as was done in the present case). Therapies with light/laser (photodynamic therapy with blue light, selective laser photothermolysis, and Nd:YAG laser) can also be employed.^{1, 2}

Dyschromias – among them PIH – are indications for peeling.¹ Superficial chemical peels tend to be effective in the treatment of PIH when properly applied, with 20–70% glycolic acid, 20–30% salicylic acid, 10–25% trichloroacetic acid or the Jessner's solution being possible options. Preparing the skin with a formula containing 4% hydroquinone for 15 days enhances the results.

Thioglycolic acid (TA) – or mercaptoacetic acid – belongs to the class of thioglycolates, which are substances that solubilize hemosiderotic deposits.³ Thioglycolic acid has sulfur in its composition, is highly soluble in water, alcohol and ether, and is easily oxidizable.⁴ The use of this substance as a depigmenting agent in concentrations ranging between 0.5 and 30% was reported by Izzo and Verzella in 1998.³ Its topical use in the form of peels usually does not cause erythema or pain.⁵ Sensitization occurs rarely, and the resulting desquamation is mild and transient.⁵ In the literature, the weekly or biweekly application in gel vehicle is recommended, with a total of five to six sessions.

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^{4, 5} The treatment begins with the application of TA gel for two minutes, with three minutes being added on each session, until a maximum of 15 minutes of application is reached.⁴

In the present case, as the PIH did not showed satisfactory response to common whitening treatments, the authors decided to carry out 30% TA peelings with sessions at fortnightly intervals, associated with topical depigmenting substance, thus enabling the synergism between the adopted techniques, with good results.

For periocular hyperchromia, the literature mentions a concentration of 10% in gel.⁴ The same concentration was used to treat Schamberg disease in the lower limbs.⁵ As the authors did not find data in the literature describing the use of 30% TA in PIH, they chose to use this concentration and observe the patient's tolerance to each application, with special attention to any signs of local irritation that required the suspension of the treatment.

Some considerations are relevant in the discussion of this case. First, as the patient used association of the depigmenting topical treatment with TA peelings, it was not possible to define the extent of the improvement achieved resulted from the isolated action of the peelings, as compared with that caused by the use of topical depigmenting substances. Further studies evaluating the isolated action of TA peelings, and even comparing them to the isolated use of topical depigmenters may elucidate this issue. Furthermore, the slight improvement observed may have been spontaneous, since this occurs during the natural development of PIH.

CONCLUSION

In light of the present study's findings, the authors believe that the TA peeling can be considered a therapeutically in the treatment of resistant PIH that does not show improvement with first-line treatments, and can be used in combination with topical depigmenting treatments for improving results. Moreover, since the results obtained were discrete and obtained from only one patient, the authors deem that studies reproducing this technique in isolation and with more patients are necessary. ●

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Facial lipoatrophy secondary to Lupus Panniculitis corrected with hyaluronic acid – a case report

Lipoatrofia facial secundária a paniculite lúpica corrigida com ácido hialurônico - Relato de caso

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ABSTRACT

The present paper describes the case of a 47 year-old patient with facial Lupus Panniculitis, with absence of disease activity in excess of one year. The large malar and temporomandibular atrophy caused by the pathology has become a great problem for the patient, with impacts on her quality of life. A cutaneous filling procedure was carried out with hyaluronic acid using microcannulas, compensating the defect and with aesthetically appropriate results.

Keywords: chyaluronic acid; panniculitis, lupus erythematosus; quality of life

RESUMO

Paciente do sexo feminino, de 47 anos, com paniculite lúpica facial, sem atividade da doença há mais de um ano. A grande atrofia malar e temporomandibular provocada pela patologia transformou-se em grande problema para a paciente produzindo impacto em sua qualidade de vida. Procedeu-se a preenchimento com ácido hialurônico através de microcannulas, compensando o defeito com resultados esteticamente adequados.

Palavras-chave: ácido hialurônico; paniculite de lúpus eritematoso; qualidade de vida

INTRODUCTION

Chronic cutaneous lupus is an autoimmune disease with an incidence of 4.3/100,000 per year in the population and prevalence of 73/100,000. Of these cases, a percentage that varies from 2% to 18% can develop into systemic lupus within a period of 8.2 years.¹

Lupus panniculitis is an unusual manifestation, comprising less than 3% of chronic cutaneous lupus cases.² When not diagnosed and treated early, it can lead to large deformations that compromise the facial appearance and cause an important impact on the patient's quality of life.³

Case Reports

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FIGURE 1: Facial lupus panniculitis, oblique view. **A.** Before the filling procedure. **B.** Immediately after. **C.** Six months later



FIGURE 2: Lupus panniculitis, frontal view. **A.** Before the filling procedure. **B.** Immediately after. It is possible to observe the subcutaneous compensation, which evidences the epidermal atrophy in the area. **C.** Immediately after the application of hyaluronic acid with lower density in a more superficial plan.

CASE REPORT

The authors present the case of a 47 year-old female patient with history of lupus panniculitis. She sought care at the service aiming at aesthetically improving the lupus-induced facial defect she had.

The physical examination revealed well-defined areas of skin atrophy in the malar and temporomandibular areas, with histology compatible with lupus panniculitis.

The patient reported a history of clinical stability of existing lesions, with no new lesions arising for more than 18 months, with normal blood count and biochemical profile, negative ANA, normal C2 and C3, negative double helix anti-DNA and ENA profile, having been under clinical control with 200mg/day hydroxychloroquine.

After stabilization of the clinical picture, the facial lesions have become an actual cosmetic problem for the patient, causing

great impact on her quality of life.^{3,4} Deep lupus is an uncommon presentation, with absence of reports in the literature that absolutely contraindicate cutaneous filling with hyaluronic acid in collagenopathies once the picture is deemed stable.⁵

DISCUSSION

It is worth to note that the use of volumizers in collagenopathies is reported in the literature, having been described in several studies, in special related to lupus panniculitis and Parry-Romberg syndrome.^{6,7} Bearing in mind that hyaluronic acid is an innocuous filler, the authors planned the restoration of the volume lost due to the disease using 3ml of hyaluronic acid (Emverl® Volume, Galderma, Santiago, Chile) in the malar and temporal regions with a n. 21G microcannula in the supraperiosteal plan using the retroinjection technique.⁸⁻¹⁰ (Figure 1).

In face of the improvement in the subcutaneous volume, the epidermal atrophy caused by lupus became evident and was treated with 1ml of hyaluronic acid (Emervel® Touch, Galderma, Santiago, Chile) using a 30G cannula and very superficial fanlike retroinjections, compensating the defect in an aesthetically adequate manner (Figure 2).

CONCLUSION

The authors present a lupus panniculitis case, which is a rare form of cutaneous lupus that, when located on the face, has great psychological and cosmetic relevance to the patient. Treating the resulting defect greatly improves the patient's quality of life and, after considering the evident stability of the base clinical picture, cutaneous filling with hyaluronic acid was chosen, due to its excellent biocompatibility and versatility regarding its viscosity.

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Case Reports

Melanonychia striata secondary to pigmented nail matrix fibroma simulating nodular melanoma

Melanoníquia estriada secundária a fibroma da matriz ungueal pigmentado simulando melanoma nodular

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ABSTRACT

Melanonychia corresponds to color patterns in the nail plate, ranging from brown to black. It is a diagnostic challenge due to the fact it has several differential diagnoses, including benign and malignant entities. There are no reports of pigmented fibroma of the nail matrix causing striata (or longitudinal) melanonychia. In light of this fact, the authors report a case of melanonychia striata secondary to pigmented fibroma of the nail, with clinical examination and dermoscopic findings suggestive of nodular melanoma.

Keywords: nails; malformed nails; neoplasms; fibroma

RESUMO

Melanoníquia é a coloração da lâmina ungueal variando do marrom ao negro. Representa um desafio diagnóstico, pois há diversos diagnósticos diferenciais incluindo entidades benignas e malignas. Não há relatos de fibroma da matriz ungueal pigmentado causando melanoníquia longitudinal. Diante disso, os autores relatam um caso de melanoníquia estriada secundária a fibroma ungueal pigmentado, com achados do exame clínico e dermatoscópico sugestivos de melanoma nodular.

Palavras-chave: unhas; unhas malformadas; neoplasias; fibroma

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INTRODUCTION

Melanonychia is the color, ranging from brown to black, of the hands' or feet' nail plates. It may be secondary to exogenous pigments including tobacco, dirt and tar; fungal infections; bacterial infections such as *Pseudomonas aeruginosa* and *Proteus spp*; and subungual hematoma caused by trauma. Clinical findings are variable according to the etiology. Anamnesis, dermoscopy of the nail plate, direct mycological examination and culture for fungi and bacteria are crucial for the diagnosis.^{1,2}

The production of melanin in the nail matrix – in most cases in the form of a longitudinal band – also manifests clinically as melanonychia, and can be called longitudinal melanonychia or melanonychia striata. It occurs in benign diseases, such as nevi and lentiginos of the nail matrix, and in various inflammatory, traumatic and iatrogenic disorders responsible for the activation of the matrix's melanocytes (hypermelanosis). Melanonychia striata can still be secondary to melanoma, and its diagnosis remains a challenge for dermatologists.^{1,3}

Ungual fibroma is a benign tumor of the connective tissue that arises as an asymptomatic, skin color nodule. It usually originates in the proximal border of the nail, with rare cases arising in the matrix region. Trauma is the most important factor associated with the lesion's etiology.^{4,5} There are no reports in the international literature of pigmented ungual matrix fibroma causing longitudinal melanonychia. In light of this fact, the authors of the present study describe a unique case of melanonychia striata secondary to a fibroma associated with epithelial hyperpigmentation, with clinical and dermoscopic findings suggestive of nodular melanoma.

CASE REPORT

A 68 year-old, dark skinned female patient complained of the darkening of the nails of the feet and hands, that had taken place more than ten years before. Examination revealed the presence of melanonychia striata in several nails of the toes and fingers, compatible with racial melanonychia. However, the hyperpigmentation of the fourth toe of the right foot was more exuberant, with involvement of 75% of the nail plate. In addition, it had ungual hyperkeratosis and transverse hypercurvature of the nail (Figure 1). Dermoscopy allowed visualizing uneven pigmentation in the nail plate, with color ranging from brown to black, besides micro-Hutchinson sign (Figure 2).

The nail plate was avulsed, evidencing a papular pigmented lesion in the nail matrix region. Intraoperative dermoscopy revealed a blackened lesion with gray areas simulating blue-whitish veil and microinvasion signs in the proximal ungual fold. In light of these findings, the hypothesis of nodular melanoma was formulated and an excisional biopsy was carried out (Figures 3 and 4).

The pathological examination evidenced a fibrous proliferation in the dermis with hyperpigmentation of the basal layer, compatible with pigmented fibroma, leading to the exclusion of the hypothesis of melanocytic origin for the lesion (Figure 5).



FIGURE 1 : Longitudinal melanonychia in the fourth toes of the right foot

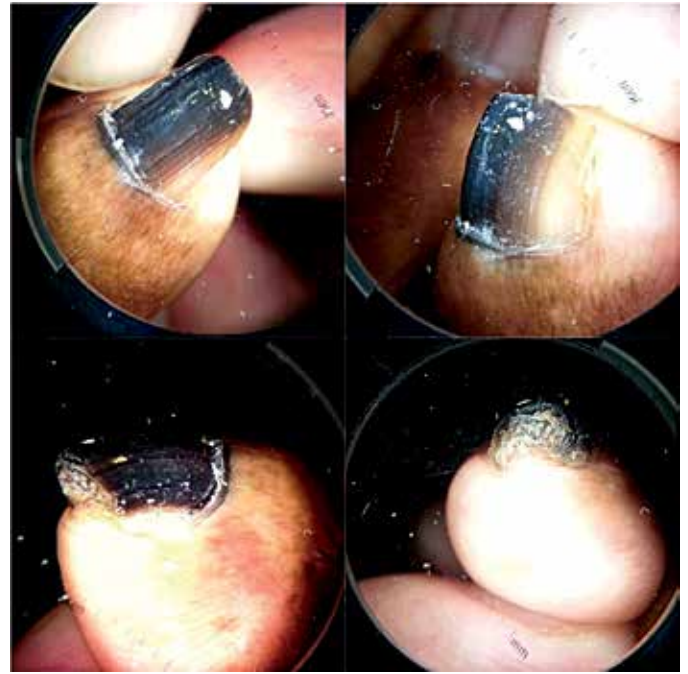


FIGURE 2 : Dermoscopy of the nail plate: irregular pigmentation of the nail plate, with color ranging from brown to blackish and micro-Hutchinson sign

DISCUSSION

Melanonychia can have various etiologies, from physiological causes to malign neoplasia – hence the importance of the early etiologic diagnosis. In this context, dermoscopy of the nail plate is highlighted as a useful test for differentiating benign and malignant lesions.⁶

According to the Consensus on nail plate dermoscopy in melanonychia, a brown background associated with parallel lines of regular spacing and width, in the same color, suggests the presence of a benign lesion (nevus or lentigo), while a brown background associated with longitudinal lines irregular in color, width, spacing, and parallelism suggests the existence of melanoma. Nonetheless, the decision to excise the lesion should be based on the clinical criteria rather than on the patterns observed in the dermoscopy of the nail plate.^{7,8}

In the present case, the patient had melanonychia in several toenails, characterized by longitudinal homogeneous parallel lines, gray in color and regular in their spacing, thickness and color, characterizing a typical presentation of racial melanonychia. However, the nail plate of the fourth toes of the right feet stood out once it had longitudinal lines with irregular spacing and thickness, and color ranging from brown to black and a blue-grayish area in its central portion, which are findings suggestive of melanoma. Corroborating with this hypothesis, the pigmentation extended over the proximal nail fold (micro-Hutchinson sign).

These facts led the authors to decide for avulsing the nail plate and performing an excisional biopsy. During the surgery, dermoscopy of the blackened lesion evidenced in the nail ma-

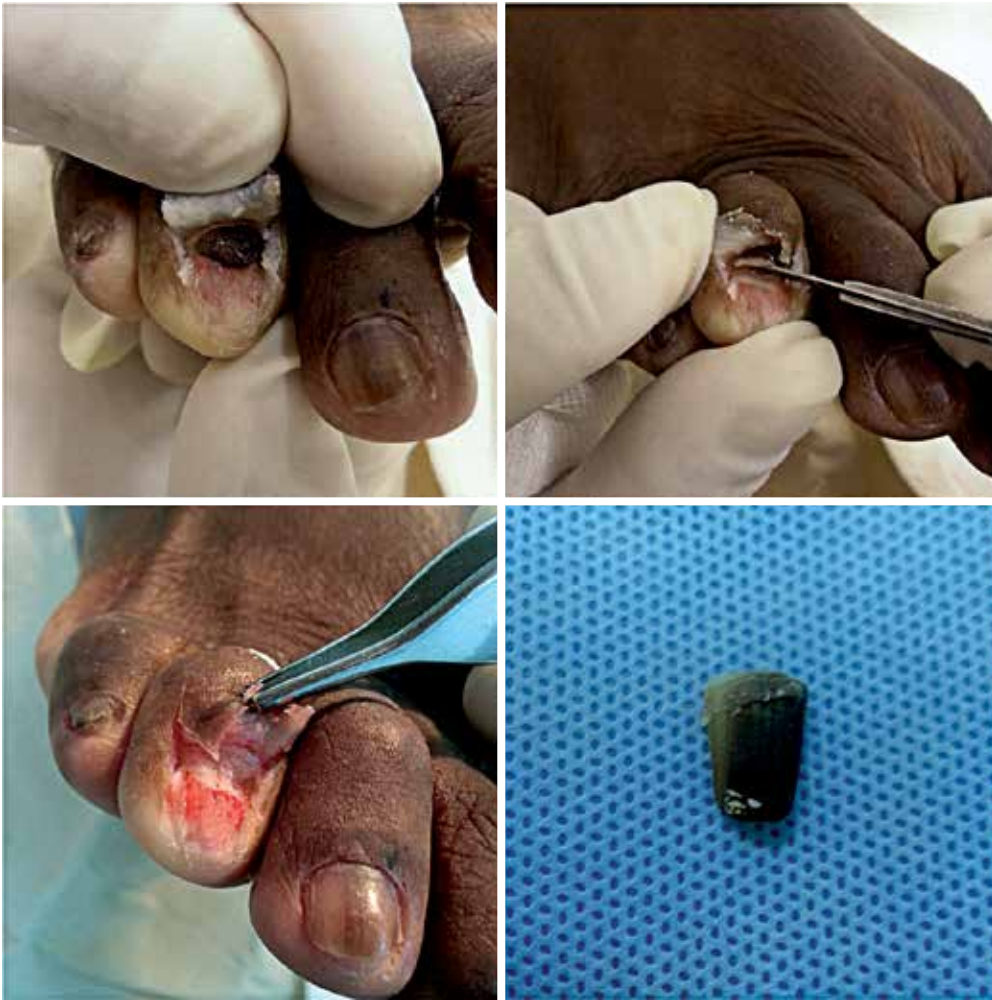


FIGURE 3: Avulsion of the nail plate showing a pigmented nodular lesion in the nail matrix region

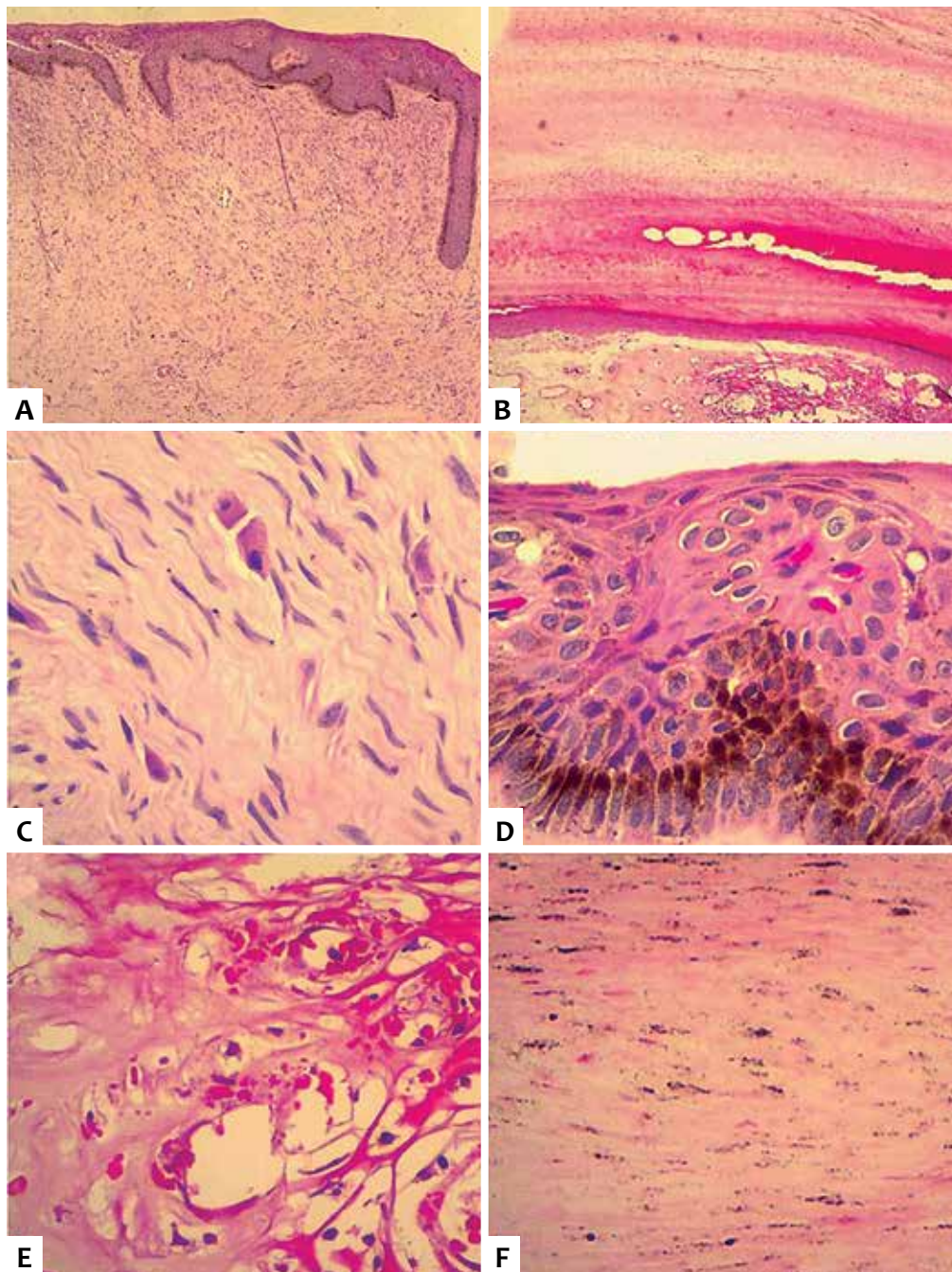


FIGURE 4: Intraoperative dermoscopy: blackened lesion with gray areas simulating blue-whitish veil and microinvasion signs in the distal third of the lesion

trix region revealed multiple colors with irregular longitudinal lines, favoring the initial hypothesis of nodular melanoma. The lesion was then complete excised with 1mm deep shaving.

The material was sent for histological examination, which evidenced fibrous proliferation of the dermis, consisting of spindle-shaped fibroblasts amid dense collagen fibers and acanthotic epidermis with hyperpigmentation in the basal layer, without melanocytic proliferation. The nail plate showed epidermis with hyperkeratosis and melanin hyperpigmentation, and underlying dermis with edema and vascular proliferation. These findings ruled out the melanocytic origin of the lesion, while being consistent with the diagnosis of pigmented fibroma. The presence of edema, vasodilation and extravasation of red blood cells in the dermis suggests local trauma, the main etiological factor for the development of unguis fibromas.

Unguis fibromas are uncommon benign tumors of the fibrous tissue. Solitary lesions are denominated acquired nail fibrokeratomas while multiple lesions are associated with tuberous sclerosis, in this circumstance being called Koenen tumors. There is no histological difference between the two variants. The lesions are usually asymptomatic and arise as pinkish or skin color nodules with globoid morphology. They are most often located

**FIGURE 5:**

Histopathological examination (HE):
A) Fibroblast proliferation amid collagen associated with acanthosis and hyperpigmentation of the basal layer of the epidermis.
B) Hyperkeratotic nail plate with extensive pigmentation covering its entire length. Areas of edema, vasodilation and extravasation of red blood cells in the dermis suggesting local trauma;
C) Detail of fibroblasts (dermal fibrous proliferation).
D) Detail of the acanthotic epidermis with hyperpigmentation of the basal layer.
E) Detail of the nail plate's dermis with edema, vasodilation and extravasation of red blood cells.
F) Details of the extensive melanin pigmentation in the cells of the horny layer in the nail plate

periungually, but rarely are subungual, originating from the nail matrix. The treatment is surgical, with the complete removal of the lesion.^{5,9}

The fibroma of the nail matrix cases described in the literature manifested with thinning of the nail plate, transverse hypercurvature or exophytic growth of the proximal nail border. However, the authors have not found in the literature cases of fibroblast proliferation in nail matrix with characteristics similar to those of fibroma associated with epithelial hyperpigmenta-

tion, resulting in melanonychia striata – hence the relevance of the present report. In addition, the clinical examination and dermoscopy findings led to the hypothesis of nodular melanoma, which can only be discarded after histological analysis. The authors emphasize the need for examining the dermoscopic characteristics of the nail plate and of the lesion itself, after avulsion of the nail plate in light of to all cases of melanonychia, although the definitive diagnosis is established only by pathological examination.

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