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Superficial application technique with cohesive polydensified matrix hyaluronic acid for the treatment of lines and wrinkles

Técnica de aplicação superficial com ácido hialurônico de matriz coesiva polidensificada para o tratamento de linhas e rugas

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ABSTRACT

Introduction: During aging, the skin undergoes structural, cellular, and molecular changes that alter its mechanical properties as well as its biological and physiological functions. These changes manifest as loss of elasticity, and turgor, with consequent appearance of fine wrinkles, lines, and creases that are difficult to resolve, being considered a therapeutic challenge.

Objective: To describe the technique of applying cohesive polydensified matrix hyaluronic acid for the treatment of superficial wrinkles.

Materials and methods: In this retrospective and observational study, the technique of superficial and transverse application to superficial wrinkles with cohesive polydensified matrix hyaluronic acid was performed in women with this type of wrinkles in the perioral, periorbicular and lateral regions of the face, which did not disappear after treatment with botulinum toxin, facial volumization with fillers and technology. The study was conducted over 22 months between 2016 and 2018. The degree of improvement was assessed by a questionnaire applied to the patients who observed paired standardized photographs taken in the previous period and one month after the treatment.

Results: The technique was performed on 40 women aged 55 to 80 years, whose response to the evaluation questionnaire was improved between 90% and 100% after one month of treatment.

Conclusions: The technique of superficial and transverse application to wrinkles with cohesive polydensified matrix hyaluronic acid proved to be an excellent option for the treatment of affected areas, without significant adverse events and/or Tyndall effect, with a high degree of patient satisfaction.

Keywords: Hyaluronic acid; Skin aging; Skin care

RESUMO

Introdução: Durante o envelhecimento, a pele sofre modificações estruturais, celulares e moleculares que alteram as suas propriedades mecânicas e também as suas funções biológica e fisiológica. Estas se manifestam por perda de elasticidade e turgor, com consequente aparecimento de rugas finas, linhas e vincos de difícil resolução, sendo consideradas um desafio terapêutico.

Objetivo: Descrever a técnica de aplicação de ácido hialurônico de matriz coesiva polidensificada para o tratamento de rugas superficiais.

Materiais e métodos: Neste estudo retrospectivo e observacional, a técnica de aplicação superficial e transversal às rugas superficiais com o ácido hialurônico de matriz coesiva polidensificada foi realizada em mulheres portadoras deste tipo de rugas nas regiões perioral, periorbiculares e laterais da face, que não desapareceram após tratamentos com toxina botulínica, volumização facial com preenchedores e aplicações com tecnologias. O estudo ocorreu durante 22 meses entre os anos de 2016 e 2018. O grau de melhora foi avaliado por meio de questionário aplicado às próprias pacientes que observaram fotografias padronizadas pareadas feitas no período prévio e um mês após o tratamento.

Resultados: A técnica foi realizada em 40 mulheres com idade entre 55 e 80 anos, cuja resposta ao questionário de avaliação foi melhora entre 90 e 100% após um mês de tratamento.

Conclusões: A técnica de aplicação superficial e transversal às rugas com o ácido hialurônico de matriz coesiva polidensificada mostrou-se uma excelente opção para o tratamento das áreas afetadas, sem descrição de efeitos adversos importantes e/ou efeito Tyndall, com alto grau de satisfação das pacientes.

Palavras-chave: Ácido hialurônico; Envelhecimento da pele; Higiene da pele

Original Article

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INTRODUCTION

Extracellular matrix (ECM) remodeling is a continuous multistep process involving localized degradation of matrix components, followed by cytoskeleton rearrangement, cell translocation, and deposition of new constituents. Evidence shows that TGF- β plays a central role in ECM biosynthesis, either by controlling collagen synthesis and degradation by binding to fibroblast cell membrane receptors and activating their genes or by inhibiting the action of metalloproteinases (MMPs). Although a variety of molecular mechanisms regulates each of these steps, the presence of proteinases controls the initial stage – especially MMPs such as collagenase, gelatinase, and metalloelastase, capable of initiating the fragmentation process of ECM native macromolecules, predominantly collagen I and III.¹

During aging, all skin undergoes structural, cellular, and molecular changes that alter not only its mechanical properties but also its biological and physiological functions.^{1,2,3} The changes caused by skin aging are the result of a normal physiological process aggravated by photoaging, which is also responsible for the appearance of stains, fine wrinkles, and dilated vessels, as well as surface roughness and skin cancer.⁴

Structurally, during chronological aging, the epidermis becomes thinner, dehydrated, and at the dermal-epidermal junction, the villi become flattened. The papillary dermis is the most affected, with fibroblast activity compromised by changes in cell morphology and metabolism, reduced proliferative potential, loss of response to growth factors, decline in ECM protein production, and increased expression of proteases involved in ECM degradation. Thus, the elastic fibers decrease in number and diameter; collagen synthesis reduces and its degradation increases due to elevated levels of metalloproteinase type I (collagenase), impacting the deposition, orientation, and size of fibers, which appear disorganized, more compact and granular. As a result, fibroblasts slowly lose their adhesion points with collagen fibers, changing their shape from fusiform to rounded. It affects its metabolic functions, creating a vicious circle. The reticular dermis becomes disorganized and degraded, with fragmented fibers.^{5,6} Photodamage tends to aggravate this process, especially in the papillary dermis, reducing the synthesis of type I procollagen and increasing collagenase levels, which generates more collagen

degradation products and inhibits the synthesis of new collagen.

Chronological aging and photodamage also affect the ground substance, reducing the number of mucopolysaccharides, glycosaminoglycans, and proteoglycans, especially hyaluronic acid, altering dermal hydration, negatively influencing skin turgor, and modifying its biomechanical properties.³ Clinically, it is observed dry skin with loss of elasticity and consequent appearance of fine wrinkles, lines, and creases that are difficult to solve. These are considered a therapeutic challenge since they do not always disappear with botulinum toxin applications, facial volumization, and/or use of technologies (Figures 1A-C).

OBJECTIVE

This was a retrospective and observational study to describe the technique of superficial application of cohesive polydensified matrix hyaluronic acid and to evaluate the degree of satisfaction of the treated patients.

MATERIALS AND METHODS

Patient care was conducted in a private clinic for 22 months between 2016 and 2018, according to ethical guidelines indicated by the Declaration of Helsinki. The applications were performed in female patients with medium depth wrinkles and/or superficial creases in the perioral, periorbital, and lateral areas of the face that had not been resolved by previous botulinum toxin treatments for expression wrinkles, facial volumization by fillers, or by treatments with technologies. The product of choice was Belotero Soft® (Merz Brasil, São Paulo, SP) because of its indication for subepidermal applications. The degree of improvement was assessed by a questionnaire administered to patients after observing their own paired standardized facial photographs taken before and one month after the treatment.

TECHNICAL DESCRIPTION

We performed the applications under topical anesthesia at the site to be treated, according to the manufacturer's specifications and after the application of cold compresses for a few minutes to minimize pain and bruising.

The applications were in all regions of the face affected by

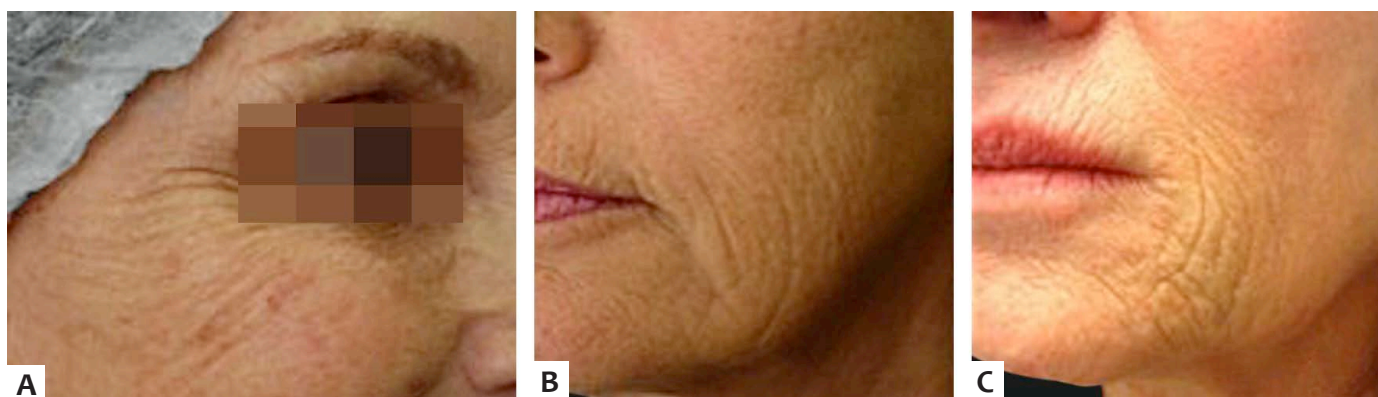


FIGURE 1: Creases and lines caused by dermal thinning and dehydration, which didn't disappear with botulinum toxin (A), face volumization (B), or technologies (C)

wrinkles and creases, perpendicular to the lines for the treatment of the entire affected area. They were applied to the superficial dermis in retro-injection, with the entrance of the full length of the 13mm 30G 1/2 needle at an angle of 10 to 12 degrees, that is, practically parallel to the skin surface, allowing the needle to be visualized (Figure 2). The needle bevel was normally upward, especially in thin skins, as downward placement could limit the application to the superficial dermis. The multiple implant placement lines were made about 5mm apart, with a small amount of product deposition (approximately 0.03mL), creating a slight elevation until the entire affected area was treated. All patients received 2mL of the product, 1mL in each hemiface, with distribution in all affected areas. After application, the treated areas were gently massaged to facilitate the horizontal spreading of the product, allowing the disappearance of any undulations on the skin surface, for better final correction. At the first sign of hematoma formation, digital compression was performed to prevent its progression.

RESULTS

Applications were performed on 40 women, aged 55 to 80 years (mean age 70.4 years). Improvement in facial lines was immediate in all cases (Figures 3-6). In some patients, two applications were necessary (Figure 7), according to the degree of skin atrophy, depth of lines and creases, or if the increase of the treated area volume was the desired objective that could be achieved uniformly and gradually, resulting in a very natural look. The treated patients were very satisfied with the results, assessing the degree of improvement. The achieved effects lasted for at least one year (Figure 7C).

DISCUSSION

The contribution of the dermis to the structure and function of the skin is crucial as it nourishes and shapes the epidermis, gives elasticity, resistance, tensile strength, protects the body from mechanical injuries, collaborates in thermoregulation

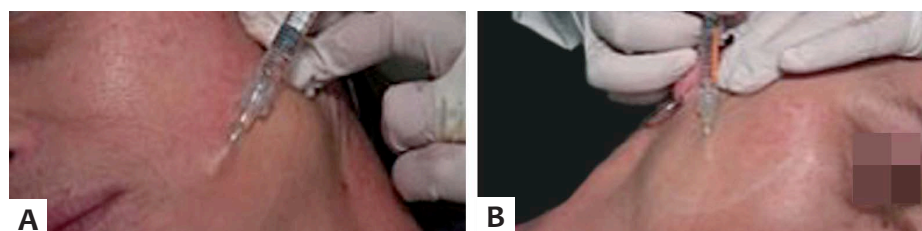


FIGURE 2:
Retro-injection application with full needle insertion at 10-degree angle



FIGURE 3.
Pre-application (A) and immediately after (B) application for the treatment of lines on the side of the face

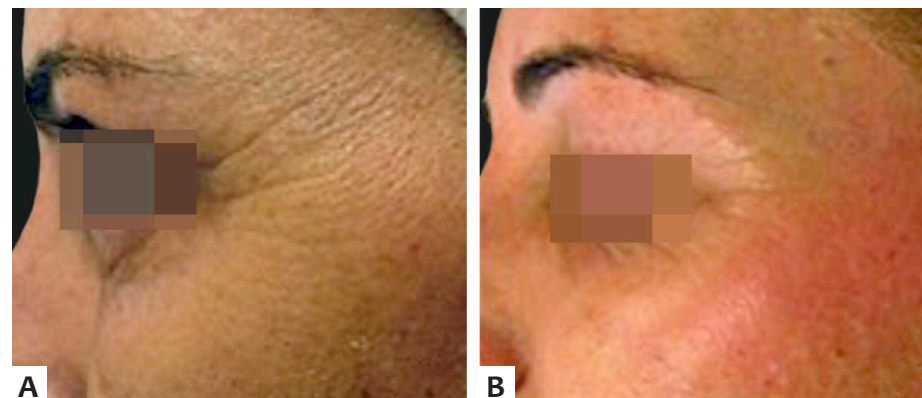


FIGURE 4.
Pre-application (A) and immediately after (B) application for the treatment of periorbital lines, 15 days after botulinum toxin

and contains sensory receptors, besides regulating the healing process.⁵

The amorphous or ground substance is mainly responsible for maintaining the dermal structure because it retains hydration; confers elasticity; helps the skin return to its original shape by facilitating the movement of fibers; protects and surrounds the fibers and cells; and promotes nutrient distribution.^{5,6}

During aging, the dermis undergoes significant changes in the composition, thickness, and biomechanical properties of the extracellular matrix, thus reducing its turgidity and elasticity. Consequently, lines, wrinkles, and grooves appear.⁷ Hyaluronic acid gels implant directly into the dermis may be a strategy to re-

plenish the ground substance and increase the dermal thickness, thus restoring the mechanical properties of the skin.

Filling techniques with deep or intradermal injections or subdermal injections are especially pertinent for less cross-linked gels and/or hyaluronic acid at low concentrations, which are indicated to treat fine wrinkles directly in areas such as the periorbital or perioral region. Applications should be made at depths indicated by the risk for the Tyndall effect or visualization of the injected material.

However, recent technological advances have introduced new dermal fillers with unique characteristics, such as cohesive polydensified matrix hyaluronic acid used in the group of



FIGURE 5.
Pre-application (A) and immediately after (B)
application with immediate improvement of
periorbital lines and lateral face



FIGURE 6.
Pre-application (A) and one month after (B)
a single application for the treatment of the
perioral and lateral lines at the corners of the
mouth

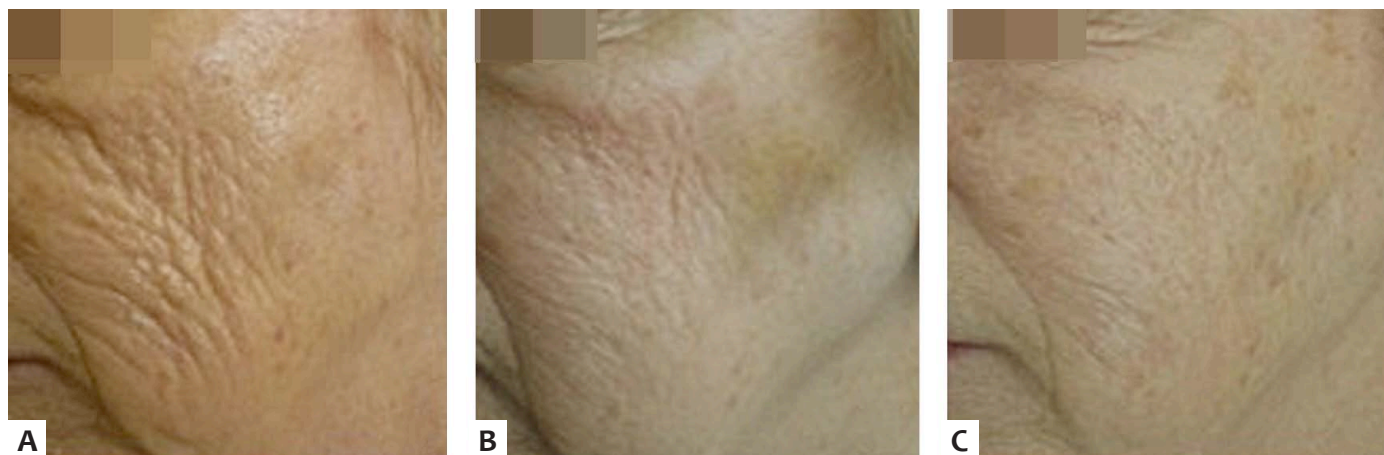


FIGURE 7. Pre-application (A), seven days after the first application (B) and one year after second application (C)

patients included in the present study. It presents particles of varying sizes and is produced by two cross-linking cycles with butanediol diglycidyl ether (BDDE), which results in a dermal filler gel with higher and lower density zones, giving the product the following characteristics: low viscosity, low elasticity (G'), high tan and high cohesiveness, which maintain affinity between gel molecules and allow tissue expansion in the superficial dermis with a predominant horizontal vector, resulting in high dermal integration and dermal volumization without changing its architecture.^{2,8,9} Therefore, these rheological properties determine the distribution evenly within the dermis without the risk for the Tyndall effect.⁹ Histological images with various stains and an ultrasound scan of the treated skin demonstrate a cohesive and homogeneous appearance that confirms the high degree of dermal integration and isoechogenicity regarding the adjacent dermis.^{2,8} These product properties allow its application in the superficial reticular dermis with natural results and without risk of skin undulation.

Thus, we chose to apply the Belotero Soft cohesive polydensified cohesive matrix hyaluronic acid (Merz Farmacutica Comercial Ltda, São Paulo, SP, Brazil), due to its rheological characteristics, using the superficial transverse retro-injection technique, to wrinkles in the periorbital and perioral regions, in addition to those located on the lateral regions of the face, which did not disappear after botulinum toxin, filling or technologies.

The retro-injection application technique allows the homogeneous distribution of the product throughout the affected area, presenting improvement of the skin thickness and not only of the lines, keeping the mobility of the treated area, and the natural appearance, without the visualization of the material due to its high tissue integration.

The applications were practically painless and with little bruising, probably due to their depth in the dermis. We should highlight the fact that there was no description of the Tyndall effect in the treated patients, in agreement with the data obtained by Kuhne (2012) and Micheels (2013).^{10,2}

There was a high degree of patient satisfaction with the treatment, with significant improvement of lines and wrinkles, as well as improvement of turgor and overall skin appearance with a single application. Still, some patients requested a second application due the thin skin thickness, the depth of the lines and wrinkles, and the extent of the affected areas.

The long-term cosmetic benefits on aging skin can be attributed not only to gel application (immediate response) but to fibroblast elongation promoted by cross-linked hyaluronic acid injection and concomitant release of TGF- β , which stimulates the synthesis of dense bands of mature collagen markedly, partially restoring the extracellular matrix components.^{6,11}

It should be noted that patients under the effect of muscle relaxation promoted by botulinum toxin were informed about the possibility of relapsing of some facial lines, in the case of expression, after the return of the movements.

CONCLUSION

The cohesive polydensified matrix hyaluronic acid proved to be the ideal filler for the treatment with the technique of superficial and transverse application of wrinkles and superficial creases, located in the periorbital, perioral and lateral regions of the face, caused by skin aging, which did not disappear after the treatment with botulinum toxin and/or face volumization and/or technology treatments, and no Tyndall effect or other adverse events were observed.●


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Study design and planning; effective participation in research orientation; active participation in research orientation; intellectual participation in propaedeutical and/or therapeutic conduct of studied cases.

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Data collection, analysis and interpretation; active participation in research orientation.

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Critical literature review; critical revision of the manuscript.

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Approval of the final version of the manuscript; critical revision of the manuscript.