Use of botulinum toxin type A associated with nonthermal microneedling for treating erythematoustelangiectatic rosacea: A case report

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Abstract
Treatments for rosacea control the pathology for a short period, requiring daily maintenance with topical and oral cosmetics. This research aimed to report the result of treatment of microneedling associated with botulinum toxin type A in a 37-years old female affected by erythematoustelangiectatic rosacea. The procedure consisted in applying botulinum toxin type A (100 UI diluted in 4 ml of saline, via drug delivery), with the electric nonthermal microneedling device. It was performed in 2 sessions, with an interval of 15 days. The evaluation was done 45 days after the first session through the Evaluation Formfacial, photographs, quality of life questionnaire – RosaQol, and evaluation by CEA (Clinician Erythema Assessment). As a result, improvements were observed in skin texture, flushing, and the participant’s quality of life. It was concluded that the technique improved the appearance of rosacea flushing, as well as decreased telangiectasias. Still, more studies and practical research are needed to determine the number of sessions and the adjusted amount of A botulinum toxin used in the therapeutic correlated to the rosacea severity.

Keywords: Aesthetic procedure; Botulinum toxin type A; Microneedling; Rosacea.

Introduction
Rosacea is an inflammatory disease of sebaceous glands affecting the cheeks, nose, chin, and forehead which present persistent facial erythema, papules, pustules, telangiectasia, recurrent flushing, among other symptoms [1]. There is no standard protocol for its treatment, albeit several treatment methods have been suggested. One of them is microneedling, a popular treatment associated with the application of topical agents, it can enhance outcomes [2,3]. According to the systematic review done by Zhang et al. [4], botulinum toxin type A showed satisfactory efficacy and safety in the treatment of rosacea.

Therefore, the present study aimed to describe for the first time the result of the association of these two procedures for treating erythematoustelangiectatic rosacea.

Case presentation
A 37-year-old woman was referred to the study with complaints of active rosacea with no previous treatment. She did not present any type of injury or inflammation, burns at the site, poor healing, diabetes, presence of skin cancers, warts, herpes, skin infection, pregnancy, the habit of using sun screen daily, or treatment with acute or chronic corticotherapy.
The patient presented Fitzpatrick skin phototype I, mixed lubrication, opened pores in the nasal region, normal (smooth) keratinization, presence of erythematous telangiectatic rosacea with telangiectasias on the cheeks, cheekbones, and nose under undefined erythema, reporting a burning sensation during episodes of facial flushing. Clinical Erythema Assessment (CEA) determined a score of 2, which means rosacea with mild erythema and a defined redness. Besides, the quality of life of patients with rosacea by the Rosa Qol [5] indicated a total score of 81 (the minimum value of the questionnaire score is 21 and the maximum is 105, being the higher the score, the worse the quality of life).

The patient received 2 sessions (one-hour duration each) of the treatment at fifteen days of intervals. The skin cleaning was done with chlorhexidine 0.12%. 100 UI of botulinum toxin type A (incobotulinum toxinA, Xeomin®, Merz Pharmaceuticals, Frankfurt, Germany) was diluted in 4 ml of saline solution 0.9% and applied topically directly to the skin, only in the area affected by rosacea [6]. In sequence, the nonthermal microneedling procedure was performed by sliding over the face regions (Figure 1). The gliding microneedling machine (Smart Derma pen®, Smart GR, Lisbon, Portugal) was adjusted to the third vibration speed, with a 36-needle cartridge and punctured 0.5 mm of the skin, performing rectilinear and circular directions four times in each quadrant of the affected area. After the procedure, 2 ml of serum was applied. After 2 sessions, no side effects were seen. Forty-five days after the first sessions of treatment, the telangiectasias in the malar region became less apparent and there was a reduction in erythema in the same place (Figures 2a and 2b). The same also occurred in the nasal region. The participant reported less burning sensation during episodes of facial redness (flushing). In general, the aspect of the skin showed a more uniform tone (Figure 2). The RosaQol score was 35 and the CEA indicated a score of 1 (almost clear skin; slight redness). Written consent was obtained from the patient for publication of this case report and any accompanying images.

**Discussion**

It is the first time that a study investigated the effects of the association in the treatment of rosacea. Analysis of post-treatment photographs showed visible improvement in telangiectasias and erythema even after 45 days from the first treatment session. Therefore, microneedling associated with botulinum toxin type A triggered a positive cost-effective result.

Microneedling is a very simple, safe, effective, and minimally invasive therapeutic technique that allows drug delivery without the risk of post-inflammatory pigmentation [2]. The uptake of drugs and biologic agents is enhanced when microchannels are created in the dermis through microneedling [3]. In this study, botulinum toxin type A was chosen to be used in the drug
delivery with a needle size of 0.5 mm, because approximately only 50 to 70% of its length penetrates and reaches the minor capillaries facilitating the absorption of the drug [7,8]. Thus, the damage would be limited to the superficial dermis, and consequently, the inflammatory response would be lesser intense than that provoked by longer needle length, which could favor an exacerbate inflammatory process in the case of rosacea.

There is now increasing evidence that rosacea is an inflammatory disease characterized by an abnormal innate immune response, major vascular changes, and increased colonization by Demodex mites, along with a genetic predisposition and multiple external aggravating factors [1]. Overall, erythematotelangiectatic rosacea is characterized mainly by vascular components, then, the findings of the present work are in line with the botulinum toxin type A mechanisms of action described in the review by Rho, Gil [9]:

- An anti-inflammatory role by lowering the arachidonic acid level, inhibiting the expression of cyclooxygenase-2 and mast cell activity;
- Vasconstriction due to the suppression of the release of acetylcholine at cholinergic nerve terminals;
- Regulation in the human sebocyte activities through the inhibition of signaling of the Transient Receptor Potential Vanilloid Subtype 1 (TRPV1).

As seen, botulinum toxin type A can be a potential tool to treat abnormal sebaceous gland activities such as erythematotelangiectatic rosacea [9,10]. Meanwhile, at the current data, there are no studies reporting effects of nonthermal microneedling for treating rosacea or associating it with drug delivery. Therefore, although the current work was limited by short follow-up visits or lack of histologic or dermoscopic analysis, it showed promising results to the clinical practice being a cost-effective option in aesthetics. Still, more studies are needed to determine the number of sessions and the adjusted amount of A botulinum toxin used in the therapeutic correlated to the rosacea severity.

Statements and declarations

Competing interests: The authors declare that they have no conflict of interest.

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Author contribution: All authors contributed to the study’s conception and design. Material preparation, data collection, and analysis were performed by Andressa Dall’agnol Soares and Marcia Gerhardt Martins. The first draft of the manuscript was written by Andressa Dall’agnol Soares, Flavia Tasmin Techera Antunes, and Marcia Gerhardt Martins. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval: All procedures performed in the present study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of the Lutheran University of Brazil (No.3.774.026).

Informed consent for publication: Written informed consent was obtained from the patient.

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