



Research Article

Therapeutic Effects of Ozone in the Treatment of Stretch Marks

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Abstract

Introduction: Stretch marks are atrophic scars resulting from excessive stretching of the skin. Ozone has therapeutic properties can promote various cellular interactions including cell proliferation and renewal.

Objectives: To evaluate the therapeutic effects of applying two different concentrations of ozone in the treatment of striae alba in the abdominal region.

Methods: The study included 30 participants, divided into two groups: Group 5 received ozone at a concentration of 5 μ g/mL and Group 15, with 15 μ g/mL, both applied in a volume of 2 mL per point, totaling four treatment sessions. The initial assessment, before treatment, was used as a control. Morphology analysis was assessed using Antera 3D® (Miravex). The diameter of the stretch marks was measured with a digital caliper and skin elasticity was analyzed with the Cutometer®. **Results:** The results indicated that the group treated with 15 μ g/mL showed a significant reduction in the diameter of the stretch marks, with an average of 0.86 mm (+0.56), as well as a significant improvement in skin elasticity.

Conclusion: Ozone therapy at a concentration of 15 μ g/mL proved to be effective in the treatment of abdominal striae alba, promoting an improvement in the diameter and texture of the stretch marks.

Keywords: Adults; Stretch Distensae; Ozone Therapy; Guided Tissue Regeneration; Oxidative Stress

Introduction

Stretch marks are an aesthetic dysfunction of the integumentary system capable of having a high psychological impact, since they affect the quality of life of the individual suffering from them, causing a tendency to develop syndromes such as anxiety, depression, social isolation, altered self-esteem and body image [1,2]. Although both sexes can be affected by them, the highest incidence and prevalence occurs in females with around 55% to 65% of cases [1,3].

They are characterized as atrophic scars of the skin, which occur due to changes in the integumentary tissue. Its pathophysiology is related to excessive stretching of the skin tissue, which leads to the tearing and separation of elastic and collagen fibers. In the initial period, the stretch marks are ruddy, reddish and raised, indicating a local inflammatory process; later they become alba, pale and flattened, indicating that the inflammatory process has ceased [4,5]. However, the main etiological factor remains unclear, but it is believed to be related to factors that alter the elasticity of the tissue, possibly triggered by hormonal changes; excessive stretching of the tissue and factors potentially related to toxic substances. Thus, the formation of stretch marks is usually directly associated with pregnancy, puberty, Cushing's syndrome, the use of corticosteroids and rapid changes in body weight [6,7].

Among the approaches described in the literature for the treatment of stretch marks are low-power laser, radiofrequency, electro lifting, intense pulsed light, chemical peeling, carboxytherapy and microdermabrasion and their applications always depend on the period of formation in which they are found [8]. Although there are various therapeutic interventions, no record has been found of a significant improvement in the appearance of stretch marks, therefore there is no protocol considered to be the gold standard for treating this type of condition [9]. In view of this, the search for new therapeutic resources is growing.

Ozone (O_3) is a gas characterized by a cyclic structure, composed of 3 atoms of Oxygen (O_2) [10]. In nature, its production occurs in the Atmosphere or from an electrical discharge produced by lightning, in both situations it has a combination of O_2 atoms, giving rise to O_3 . The use of ozone was introduced into medicine in the 19th century during the First World War, with the aim of treating gangrenous conditions in German soldiers. After that, reports of the use of medical Ozone in cases such as gangrenous pulpitis, colitis and rectal fistulas made the application a safe and advantageous practice, carried out for decades in Germany. However, the lack of scientific evidence about its benefits has resulted in an underestimated resource, leading to skepticism about the method to this day [11]. The generation of medical and industrial ozone is produced through an electrical discharge known as a corona discharge and can also occur through electrochemical processes or with the use of UV radiation. Industrial O_3 is produced from atmospheric air, but Ozone for medical use is only produced using medical Oxygen, otherwise the formation of Nitric Oxide (NO_2) can lead to cases of high toxicity. In this way, medical ozone generators control the electrical discharge at high voltages, promoting the breakdown of O_2 molecules to subsequently form O_3 . The final concentration of the gas is defined as ozone-oxygen, consisting of a maximum of only 5% ozone, guaranteeing the safety and effectiveness of the application [11].

In addition to its application in gas form, ozone can also be prepared for therapeutic purposes in the form of water or oil and can be used in ozonated hydrotherapy, ozonated oil, ozonated oil-based emulsions and ozonated autohaemotherapy [12,13]. Ozone administration routes include intramuscular, subcutaneous, intra-articular, intradiscal, myofascial, auricular, rectal, dental, vaginal, oral and cutaneous application. However, caution should be exercised with regard to the use of O_3 , since its intravenous application in gas form is unsafe due to the risk of pulmonary embolism [10,11].

Considered to be a procedure that triggers minimal adverse events, ozone's mechanisms of action promote a counterbalance between the oxidizing and antioxidant systems, depending directly on the dosage to be used, its immunomodulatory and antimicrobial action and its interaction with the skin epithelium [12,14]. Thus, when in contact with the human body, ozone interacts with the polyunsaturated fatty acids present in cell membranes and promotes the formation of by-products such as Reactive Oxygen Species (ROS) and Lipid Peroxidation Products (LPP), thus activating biochemical pathways concomitantly, including nuclear factor kappa kappa-light-chain-enhancer of activated B cells (NF- κ B) and Nuclear factor erythroid-derived 2 (Nrf2) pathways, triggering multiple cellular interactions [10,12]. The Nuclear Kappa Factor B pathway is responsible for promoting the start of an inflammatory process, while Nrf2 promotes a reduction in the inflammatory response, suppressing NF- κ B. Thus, the activation of different biochemical pathways depends on the intensity of the oxidative stress generated, which, when controlled, may be able to promote a state of reaction and inflammatory balance [12-14].

Thus, when used in the wound healing process, it is expected the ozone, by forming ROS and PPL, will be able to trigger an increase in different growth factors through platelet aggregation, including beta Transforming Growth Factor (TGF- β), Fibroblast Growth Factor (FGF), Vascular Endothelial Growth Factor (VEGF) and platelet-derived growth factor (PDGF), which are essential for tissue repair. A process of cell proliferation would then begin, with an increase in the deposition of collagen matrix, the number of macrophages, fibroblasts and the development of angiogenesis [12,14].

The immunomodulatory action of ozone is capable of triggering the release of factors involved in modulating the inflammatory response, including Tumor Necrosis Factor and Interleukin 2 (IL-2). As a result, when ozone interacts with the exudate present in the lesion, the release of peroxides should be sufficient to increase local oxygenation, stimulating tissue repair [14]. By promoting vascularization, O_3 directly aids the supply of oxygen to the tissue, stimulating fibroblast migration and collagen synthesis, making it potentially beneficial and efficient for the healing treatment of wound, ulcers and burns, making it possible to infer the ozone therapy is possibly effective for the treatment of striae alba [12,14]. In this context, the aim of this study was to evaluate the therapeutic effects of applying two different concentrations of ozone in the treatment of stretch marks on the abdomen.

Materials and Methods

Randomized controlled clinical trial with experimental arm, carried out from December 2023 to November 2024. The pre-procedure assessment of each patient was considered the control and randomization was carried out equally in two groups. This research was approved by the research ethics committee under CAAE: 73847423.8. 0000.5382 carried out at IPECLIN - Instituto de Pesquisa Clínica do Centro Universitário das Faculdades Associadas de Ensino - UNIFAE, São João da Boa Vista - SP, Brazil. We recruited 30 female volunteers with stretch marks on the abdomen, diagnosed through a visual inspection carried out by a physiotherapist specializing in dermatofunctional medicine. Group 5 (G5) consisted of 15 participants who received an ozone concentration of 5 μ g/mL and a volume of 2 mL per application point and Group 15 (G15) consisted of 15 participants who received an ozone concentration of 15 μ g/mL and a volume of 2 mL per application point, maintaining 2 cm between each point, until the entire length of the streak is completed.

The inclusion criteria were healthy females between the ages of 19 and 50 who had striae alba in the abdominal region. Participants under the age of 18 and over the age of 50, who had vitiligo, psoriasis, keloids, nickel allergy, Cushing's syndrome, diabetes, polycystic ovary syndrome, continuous use of corticoids or other steroids, pregnant and breastfeeding women were excluded from the study.

The Ozone therapy treatment was carried out once a week, with a total of four applications. The patients were instructed to return 30 days after the end of the procedure to evaluate the results obtained. For the procedure, the abdomen was first aseptically cleaned with 70% alcohol. Ozone was applied intradermally using a disposable 30G1/2 needle. To do this, a 45° puncture was made in the center of each stretch mark, so that the gas emission (2 mL per point) filled the entire interior. A distance of 2 cm was maintained between each puncture, treating the entire length of each stretch mark. The equipment used was the Ozion® manufactured by Indústria Brasileira de Equipamentos Médicos - IBRAMED Ltda with ANVISA registration number 10360319022.

During the evaluations, the patient filled out an anamnesis form prepared exclusively for the study, which reported age, lifestyle habits, medication, information related to inspection of the treatment area, skin phototype, history of therapeutic procedures in the abdominal region, pain assessment and a questionnaire on patient satisfaction with the treated area.

The treatment site was photographed before and after each procedure using a digital camera. To standardize the area to be assessed, an acrylic template was used in a specific area on the fabric measuring 5x5 cm. In addition, for the specific analysis of morphological changes such as depressions, elevations, wrinkles and skin texture, the Antera 3D® photographic device (Miravex) was used, limiting the evaluation area to a specific area in the tissue with a medium filter.

The quantitative analysis was carried out by measuring the diameter of the stretch mark using a Digimess model 100.178BL digital caliper, programmed to measure in millimeters. An assessment of skin elasticity was carried out using the Cutometer® device, which through the mechanical suction method is able to provide values in relation to the viscoelastic variables of the skin; according to the operating manual, the following variables were measured in MODE 1: R0 = Passive behavior of the skin in relation to force; R2 = Gross elasticity, the value closer to 1 is the most elastic curve; R5 = Net elasticity, the closer to 1 the more elastic it has. R6 = Visco-elasticity, the lower the value the greater the elasticity; R8 = The closer to 0, the greater the skin's ability to return to its original state.

In order to classify the number of stretch marks in the treatment area, the evaluator visually inspected a scale where 1 = No stretch marks, 2 = 1 to 4 stretch marks in the area, 3 = 5-10 stretch marks in the area, 4 = More than 10 stretch marks in the area. The skin phototype classification according to Fitzpatrick was used, where 1 White = Always burns, never tans, very sensitive to the sun [15]. 2 White= Always burns, tans very little, sensitive to the sun, 3 Light brunette= Burns (moderately), tans (moderately), normal sensitivity to the sun, 4 Moderate brunette= Burns (little), always tans, normal sensitivity to the sun, 5 Dark brunette= Burns (rarely), always tans, little sensitive to the sun, 6 Black= Never burns, fully pigmented, insensitive to the sun. As a way of assessing safety, after the protocols were applied and during the period of application of the techniques and the post-application follow-up, the tissue was assessed in relation to its condition. This assessment was graded as 1= Erythema, 2= Edema, 3= Dryness, 4= Desquamation, 5= Crusts, 6= Burns, 7= Presence of blisters, 8= Hyperpigmentation, 9= Hypopigmentation, 10= Tingling, 11= Itching.

A 0-10 subjective visual analog scale was used to assess pain in the application area, where 0 = No sensation of pain or discomfort, 1-4 = Mild pain or discomfort, 5-7 = Moderate pain or discomfort, 8-10 = Severe pain or discomfort [16]. Treatment progress was assessed qualitatively using the adapted GAIS (Global Aesthetic Improvement Scale), where 1 Exceptional improvement = Excellent results, 2 Significant improvement = Improvement in skin appearance, but not completely restored, 3 Relative improvement = Improvement in appearance compared to the initial condition, but still requires intervention, 4 Unchanged = Skin appearance remains the same compared to the condition before treatment, 5 Worsening skin appearance = Skin appearance has worsened compared to the initial condition [17]. Statistical analysis was carried out using the Student's t-test and descriptive statistics.

Results

The study was carried out with two different concentrations of O3, G5 (5 μ g/mL) with 15 women with an average age of 33 (± 9.52) years and G15 (15 μ g/mL) made up of 15 women with an average age of 36 (± 5.00) years. As for the number of stretch marks, 73% of the volunteers had more than 10 stretch marks in the abdominal region and 27% had between 5 and 10 stretch marks in the region evaluated. In terms of phototype assessment, the volunteers in both groups had phototype 3. The results showed differences between the concentrations used, as evidenced by the comparison between the two groups, G5 and G15. Significant differences were also observed in the intra-group evaluation when comparing the data before and after treatment, especially in the group that received the 15 μ g/mL concentration.

Photos were taken with a digital camera and an ANTERA 3D camera. No changes were observed in relation to the appearance of the skin, reduction of the depression and thickness of the stretch mark in the recording made via digital camera photo (Fig. 1) for the treatment concentration of 5 μ g/mL. However, when looking at the photos recorded by the ANTERA 3D equipment (Fig. 2), it was possible to identify a slight difference in the depression of the stretch mark, which was smaller after treatment.

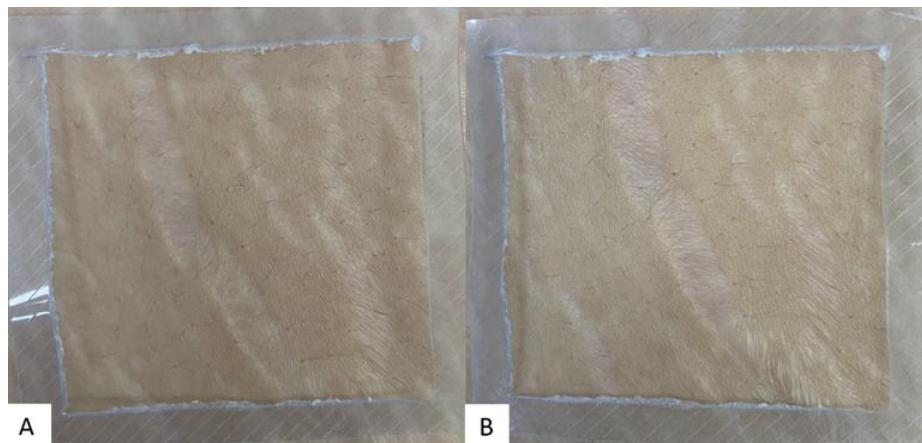


Figure 1: G5- Image with digital camera. A- Image before the procedure, B- Image 30 days after completion of the procedure.

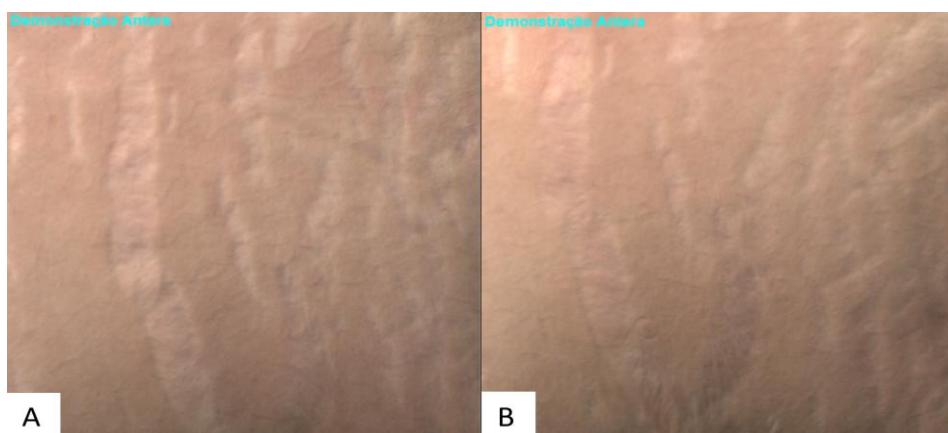


Figure 2: G5- Image with Antera 3D® (Miravex). A- Image before the procedure, B- Image 30 days after completion of the procedure.

In the evaluation of the group that received the 15 μ g/mL concentration, differences were observed in both photographic recording methods. The digital photograph (Fig. 3) shows an improvement in the appearance and vitality of the skin in the treatment area and a reduction in the thickness and depression of the stretch mark. The photo taken by the ANTERA 3D equipment (Fig. 4) shows these changes. It is possible to observe the surface of the stretch mark, due to the reduction in its depth and a reduction in its thickness, which should be related to the improvement in the tissue matrix.

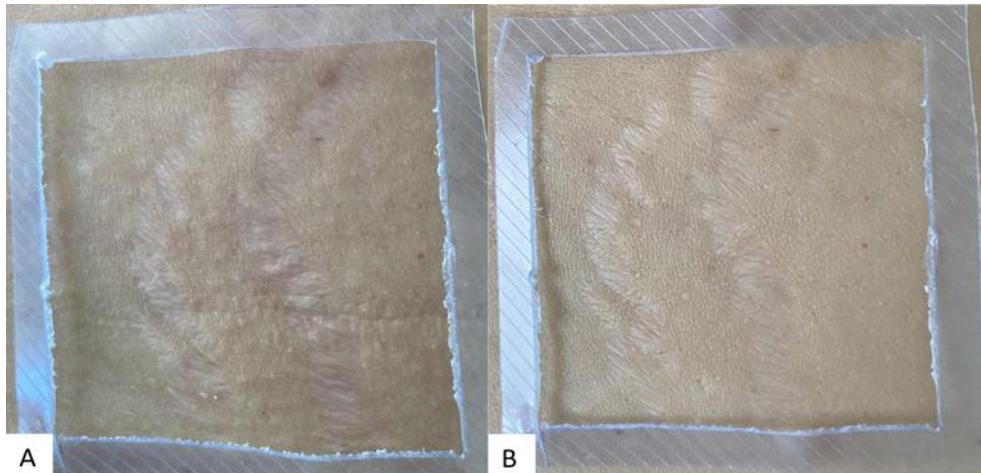


Figure 3: G15- Image with digital camera. A- Image before the procedure, B- Image 30 days after completion of the procedure.

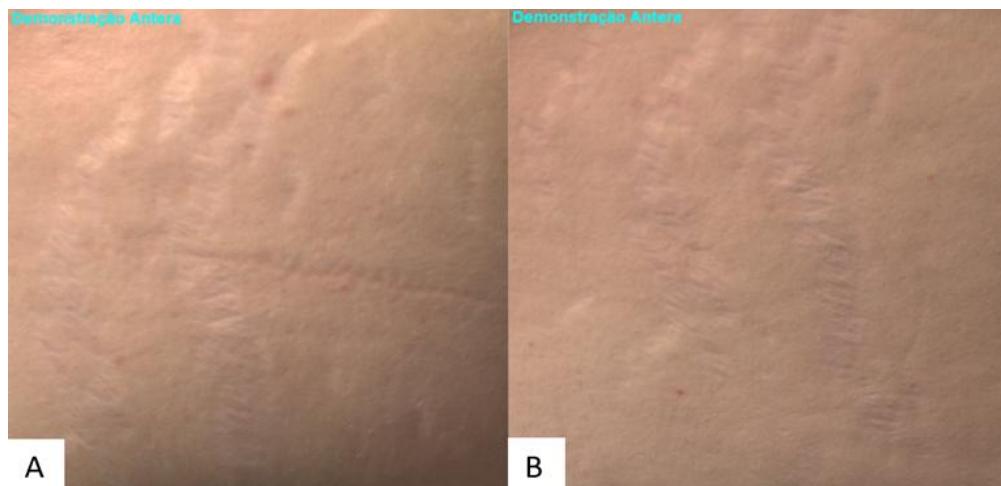


Figure 4: G15- Image with Antera 3D® (Miravex). A- Image before the procedure, B- Image 30 days after completion of the procedure.

The thickness of the stretch mark was assessed using a digital caliper. Table 1 shows that there was a reduction in stretch mark thickness in both groups, although G15 showed a more significant reduction.

	Beginning	Final	Delta	P-value	
G5	3.32	2.89**	0.43	0.004828	
G15	4.89	4.03**	0.86*		
*p-value = 0.01: statistically significant difference between groups.					
**p-value = 0.05: statistically significant difference between time points (baseline vs. final assessment).					

Table 1: Stretch mark thickness analysis in millimeters.

A correlation analysis between age and reduction in stretch mark thickness (Fig. 5) showed that G5 had a minimal but consistent reduction in stretch mark thickness in all age groups. On the other hand, G15 showed a significant reduction in the thickness of stretch marks in younger individuals, while in older participants this reduction was not as significant.

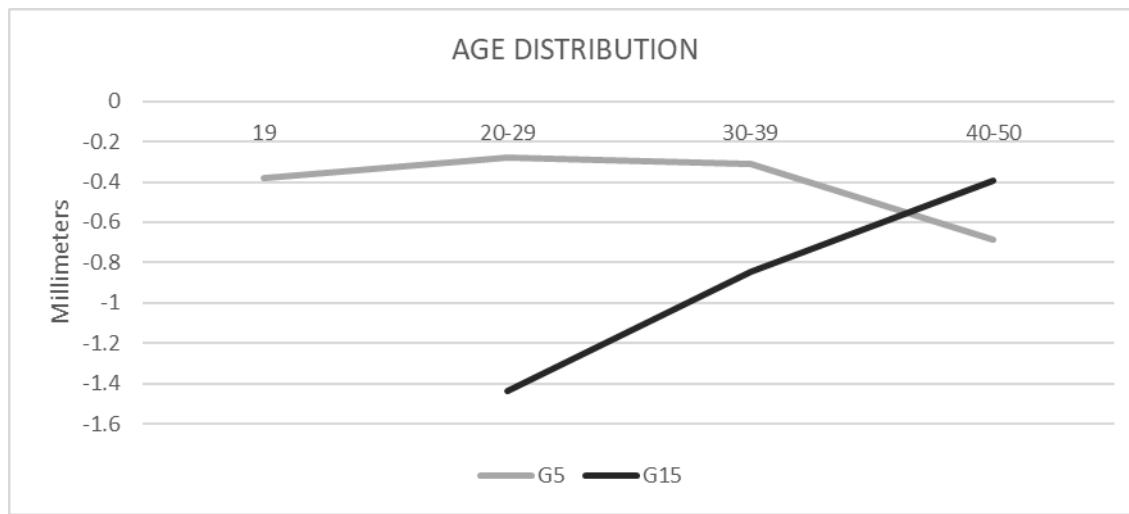


Figure 5: Correlation chart between age and thickness reduction in mm in groups G5 and G15.

The evaluation of skin elasticity, carried out using the Cutometer (Fig. 6), in relation to the R0, R2, R5, R6 and R8 variables, showed the 5 μ g/mL concentration had no differences in the variables analyzed when comparing the initial and final evaluations. On the other hand, the 15 μ g/mL concentration showed promising results in the R5 variable, suggesting an improvement in the net elasticity of the skin of the G15 patients.

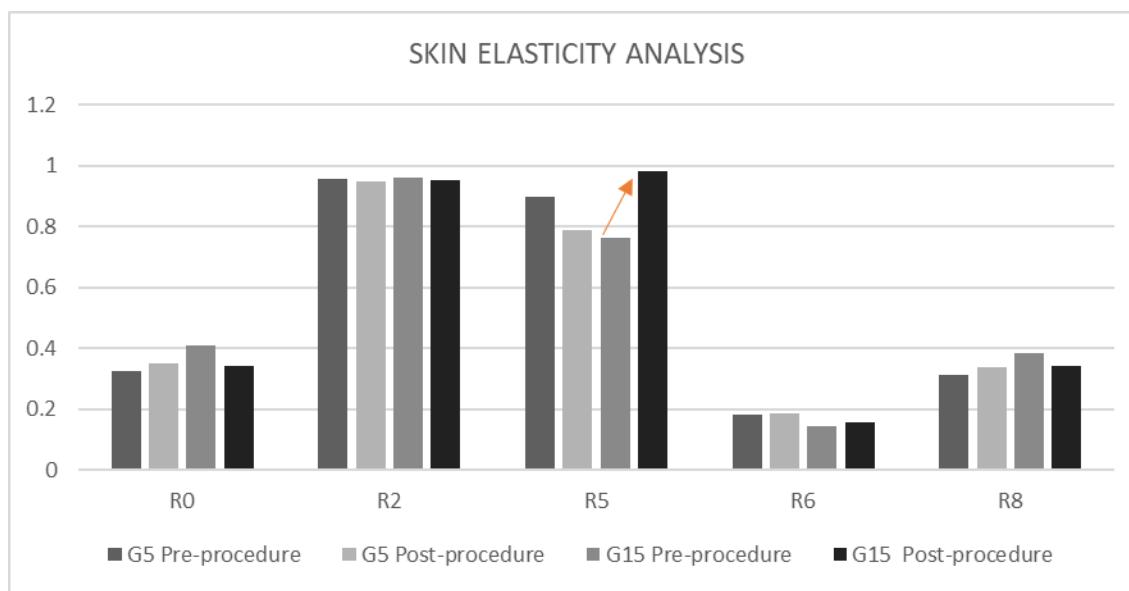


Figure 6: Chart analyzing the elasticity of G5 and G15 skin, before and 30 days after the procedure.

After the four ozone applications, some adverse effects were observed. Erythema and edema occurred in 100% of the volunteers, regardless of the concentration of ozone used, an expected effect. In addition, 10% of the participants in G5 and 5% in G15 reported the presence of itching. No other adverse effects were observed or reported by the volunteers.

With regard to the visual analog scale for G5, an average of 6 was obtained in 4 sessions, while G15 had an average of 7, both classified as moderate pain or discomfort during the application of O₃.

Satisfaction was assessed using the adapted GAIS (Global Aesthetic Improvement Scale), which showed that G5 had an average satisfaction score of 3, classified as relative improvement = improvement in appearance compared to the initial condition, but still requiring intervention, while G15 had an average score of 2, classified as significant improvement = improvement in skin appearance, but not completely restored.

Discussion

The purpose of this study was to evaluate the effects of ozone therapy with two different concentrations for the treatment of stretch marks. The results showed a clinical improvement with the 15 μ g/mL concentration evidenced by photographic methods, including a possible improvement in skin vitality and the appearance of stretch marks, associated with a reduction in signs of depression. In addition, the statistical analysis indicated a significant reduction in the thickness of the stretch mark, while the evaluation with the Cutometer showed relevant results on the net elasticity of the skin.

The findings of Min P, et al. and Akhtar N, et al., indicate the net elasticity is defined as the ratio between the immediate retraction and deformation properties of the skin and is related to changes in collagen fibers, elastin and fibroblasts. Thus, corroborating the findings of this study, it is believed that a possible synthesis of these cells should have been stimulated by ozone therapy [18,19].

The dermal administration of ozone can be considered both safe and effective, as it avoids the need for venipuncture and is carried out superficially to the tissue [10,11]. When choosing the dose of O₃ to be used, the application site and treatment purpose must be taken into account. The literature shows the dosages of between 15 and 50 μ g/mL are safe for humans, promoting beneficial effects and without toxicity, with protocols ranging from weeks to months [14]. Studies using ozone by submerging the lower limb in ozonized water under wounds used concentrations of approximately 50 μ g/mL; while its oil form applied in topical therapies for wound treatment suggest a concentration of 40 μ g/mL on average [14]. These findings partially corroborate this study, as concentrations were selected within the therapeutic range previously established as safe, in addition to the choice of the dermal application route. It should be emphasized, as reported in the literature, no serious adverse events were recorded throughout the course of this study, thus reinforcing the safety of this treatment protocol.

Zhang J, et al., report the ozone (O₃) therapy is capable of positively regulating the levels of Vascular Endothelial Growth Factor (VEGF), Fibroblast Growth Factor (FGF), Transforming Growth Factor Beta (TGF β) and Platelet-Derived Growth Factor (PDGF), as well as promoting an increase in collagen fibers, triggering beneficial effects on the tissue repair process in cases of ulcers [20]. Considering that stretch marks are atrophied lesions, a possible reversal of their state of tissue hypoxia could trigger a process of tissue repair. The findings of Liu L, et al. and Zeng J, et al., point to such hypotheses, in which the induction of moderate and controlled oxidative stress can lead to the activation of the Hypoxia Inducible Factor (HIF), which can promote the activation of the VECF and the PDCF, factors responsible for reversing tissue hypoxia through the process of angiogenesis [12,13].

In addition, the results of this study showed the induction of oxidative stress is directly related to the concentration used, since higher concentrations are capable of inducing more significant cellular changes. A correlation between concentration and age showed the group exposed to a concentration of 5 μ g/mL showed a low reduction at all ages, while the group treated with 15 μ g/mL showed more promising results, possibly related to the induction of a more significant oxidative stress. Therefore, even in more active cells, i.e. younger individuals, to induce a greater oxidative stress of at least 15 μ g/mL is considered necessary. On the other hand, older individuals showed a smaller reduction, possibly due to a decrease in cellular activity in relation to collagen and elastin synthesis. We can therefore hypothesize for this age group, oxidative stress should be stimulated with even higher concentrations, i.e. above 15 μ g/mL, in order to achieve more expressive clinical results. Thus, when the results obtained in this study are associated with the therapeutic effects of O₃ described by Pivotto, et al., its ability to reverse tissue hypoxia should be considered by improving local oxygenation associated with increased levels of growth factors, and collagen matrix deposition and the number of myofibroblasts is sufficient to improve the condition of striae alba, when applied within the ideal therapeutic window for this condition [14].

A limitation of this study is the absence of a pilot study and a control or placebo group. After collecting a number of patients, it became clear there was a need to take a wide photograph of the entire treatment region so that the evaluation after 30 days would encompass all the stretch marks treated, not just a specific region. Another limitation was the impossibility of collecting biological material from the integumentary tissue before and 30 days after the ozone procedure, to assess the synthesis of collagen, elastin, fibroblasts and the release of growth factors, so it is only possible to hypothesize, from the tissue aspect found, there was a possible difference in the expression of these cells and markers. In addition, a more objective measurement of the thickness of the stretch mark is essential in order to determine more reliable values, so we recommend using the ImageJ image processor in future work, as well as increasing the number of samples in order to obtain more significant statistical results.

This research can be considered pioneering in relation to the use of ozone therapy in the treatment of stretch marks, demonstrating it is a safe and effective resource, with promising clinical results and no significant adverse events. It should also be emphasized the advantage of applying this technology is that it is a minimally invasive, low-cost and easily accessible method, which facilitates its inclusion in treatments for the proposal studied.

Conclusion

Ozone therapy at a concentration of 15µg/ml was able to improve the appearance of stretch marks, associated with a reduction in diameter and depth. This ability demonstrates the use of ozone can be considered a possibly effective resource for the treatment of abdominal striae alba in this target group, thus contributing to the physical and mental well-being of the patients. However, as this study is the first to present promising results on the use of this technology for the treatment of stretch marks, there is a need for more detailed future studies to add scientific knowledge related to this clinical approach.

Conflicts of Interest

The authors declare no conflict of interest in this paper.

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