

Potential applications of topical oxygen therapy in dermatology

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ABSTRACT **Background:** Topical oxygen therapy is a cosmetic procedure that is becoming more and more popular in dermatology; however, only a few articles on this topic are present in the literature. In this work we report our group experience with oxygen therapy as an adjuvant treatment in various dermatological conditions.

Methods: Four studies were conducted. In the first study we used vehiculated oxygen therapy for diseases that cause hair loss. In the second study oxygen was used in the treatment of mild acne. In the third study moderate acne was treated with topical oxygen. In the fourth study chronic dermatological conditions such as psoriasis and atopic dermatitis were treated with this procedure.

Results: In studies 1 and 2 the outcomes in groups who used topical oxygen therapy as an adjuvant treatment were better than in the groups that did not use it. Studies 3 and 4 also showed very good results, but no control groups were present in the study.

Conclusion: Topical oxygen therapy was useful in the treatment of hair loss conditions, mild and moderate acne, and in chronic cutaneous diseases, showing effectiveness as a support therapy in all of these conditions. Further and larger studies should be conducted to better evaluate its effectiveness in dermatological conditions.

Introduction

Topical oxygen therapy is a cosmetic procedure that is becoming more and more popular in dermatology. Oxygen infusions provided by devices such as the X2 Exea (Exea, Castello d'Argile, Italy) allow flows of pure oxygen (up to 96% purity)

to reach the superficial layer of the skin and to be absorbed by the dermis and the epidermis.

Oxygen therapy is not a recent innovation in the dermatologic field [1]. Other techniques of oxygen therapy, such as hyperbaric oxygen treatments, are widely used in the treatment of other skin diseases, including wound healing, pyo-

derma gangrenosum, hidradenitis suppurativa, burns, skin grafts, and others [2]. Hyperbaric oxygen therapy was also proposed as a skin rejuvenation and antiaging treatment [3].

Oxygen has various beneficial effects on the skin. It is capable of improving cellular metabolism, of accelerating the healing processes, of reducing skin irritations, and of producing an anti-inflammatory effect [4]. Oxygen is also able to produce a neoangiogenic effect [5]. In fact, it promotes the release of vascular endothelial growth factor (VEGF) and other factors involved in neoangiogenesis [4]. Oxygen also has an antibacterial effect thanks to its ability to release reactive oxygen species (ROS), compounds that are extremely toxic, as they degrade cellular membranes and cause death of the pathogenic microorganisms [6].

However, the use of oxygen infusion therapy is not readily found in the medical literature. Few, if any, articles describe the use of oxygen infusion therapy in dermatologic diseases and their effectiveness, although these kinds of infusions are widely used.

Our group attempted to evaluate the effectiveness of oxygen infusion therapy in association with traditional drugs in the treatment of diseases that cause hair loss (androgenetic alopecia and telogen effluvium), mild acne, moderate acne, and chronic inflammatory dermatologic diseases. Four studies were conducted. In the first, the objective of the study was to evaluate the greater therapeutic efficacy of 5% minoxidil carried by an oxygen dispenser compared to the traditional method of topical application. A second comparison was made between minoxidil and a phytotherapeutic agent consisting of capsicum A, ginseng, sage and *Cathamus tinctorius* carried by an oxygen dispenser. In the second study the objective was to evaluate the effectiveness of topical oxygen therapy in mild acne and to compare the local administration of 96% pure oxygen to the use of a phytotherapeutic drug and a local oxygen administration therapy. In the third study patients with moderate acne were treated with topical clindamycin and oxygen infusion therapy. In the fourth study patients with psoriasis or atopic dermatitis were treated with topical medication (vitamin D derivatives for psoriasis and corticosteroid for atopic dermatitis) and local oxygen therapy.

Methods

Topical Oxygen Therapy and Diseases that Cause Hair Loss

Androgenetic male or female alopecia (AAG) and telogen effluvium (TE) are the most common forms of non-scarring alopecia. They affect men and women of all ages and remain an unresolved therapeutic problem.

Telogen effluvium is a very intense hair loss that causes thinning of the hair without the appearance of glabrous patches. The causes can be multiple, the most frequent being

nutritional protein deficiencies, sideropenic anemia, intense psychophysical stress, trauma, chemotherapy, deficiencies or excess of thyroid hormones (hypothyroidism or hyperthyroidism), hypervitaminosis from vitamin A, and celiac disease [7].

AAG is a hereditary thinning of the hair induced by the effects of androgenetic hormones on the follicles of hair in genetically susceptible men and women. Hair follicles become smaller, producing shorter and thinner hair. Currently no definitive therapies are available for the treatment of AAG and TE [8]. These pathologies affect about 70% of men and 40% of women at a certain stage of their lives. Men typically present with a recession of the attachment of hair at the temples and hair loss at the crown, while the women normally have a widespread thinning on all the top of the scalp. Both genetic and environmental issues play a role, and definitive etiologies remain unknown [9]. The treatment methods currently available vary from the use of non-pharmacological therapies such as the use of supplements, amino acids, and other essential elements [10]. Pharmacological therapies include minoxidil, finasteride, phytosterols, low doses of corticosteroids, estrogenic therapy, and anti-androgenic drugs [11]. Vehiculated oxygen therapy has been used in medicine to improve cellular metabolism, accelerate the healing process, and reduce irritation. Additionally, it has anti-inflammatory and antibacterial effects.

Thirty patients with AAG and telogen effluvium were enrolled and randomized into 3 treatment groups:

- Group A was treated daily with 5% minoxidil 3 times per week in monotherapy for 16 weeks with follow-up at 8 weeks after finishing the therapy.
- Group B was treated with 5% minoxidil administered every other day (topical) and oxygen delivery with the X2 Exea device) in sessions lasting 30 minutes for 16 weeks with follow-up at 8 weeks after finishing treatment.
- Group C started treatment with a phytotherapeutic agent (composed of *Zingiber officinale*, *Salvia officinalis*, *Cuscuta epithimum*, *Carum petroselinum*, and *Capsicum annuum*) administered with the traditional topical application alternating with oxygen infusion with the X2 Exea device in sessions lasting 30 minutes for 16 weeks with follow-up at 8 weeks after stopping treatment. The rationale for the phytotherapeutic drug's components was to intervene in several targets of the pilosebaceous unit: to increase blood flow, decrease local inflammatory state, decrease local PH, check for excessive bacterial growth, and to have moisturizing, emollient action on the hair.

The study parameters were:

- Objective and dermatoscopic examination of the hair
- Hair count
- Evaluation of the stage of AAG classified according to the scale of Norwood and Ludwig

All 30 patients completed the study. No dropouts or adverse events occurred.

Group A showed an increase in the number of hairs of 1.5% after 8 weeks, 8% after 12 weeks, with a maximum result of 10.7% at 16 weeks.

Group B showed an increase in the number of hairs of 3.9% after 8 weeks, 11.8% after 12 weeks, arriving to a maximum result of 15.9% at 16 weeks.

Group C showed an increase in the number of hair of 1.1% after 8 weeks, 2.1% at 12 weeks, arriving at 3.6% at 16 weeks.

As expected, at the 8-week follow-up the increase in number of hair reached by all groups during treatment was maintained.

The results obtained show a statistically significant improvement in group B, treated with minoxidil 5% in combination with oxygen therapy, compared to Group A treated with minoxidil only. Furthermore, treatment with a phytotherapeutic drug (Group C) showed less effectiveness than pharmacological treatment, but it has proven not to have a rebound effect at follow-up. The delivery of minoxidil with 96% pure oxygen seemed to increase the performance of the drug. The results obtained in our study allow us to consider oxygen therapy as a valid support in medical therapy for hair loss. The use of herbal remedies composed of *Zingiber officinale*, *Salvia officinalis*, *Cuscuta epithimum*, *Carum petroselinum*, and *Capsicum annum*, although not as effective as drug therapy, is a valid alternative not burdened by complications of traditional therapies.

Topical Oxygen Therapy and Mild Acne

A second study was conducted to evaluate the effectiveness of oxygen therapy in the treatment of mild acne vulgaris and effectiveness of the same treatment in conjunction with a sebo-regulating phytotherapeutic drug.

Acne is an inflammatory chronic dermatosis [12] with a multifactorial etiology [13] that mainly affects teenagers and young adults [14]. It is characterized by a remarkable lesional polymorphism due to the presence of both noninflammatory (open and closed comedones) and inflammatory cutaneous elements (papules, pustules and nodules), located in the seborrheic areas of the face and trunk. Acne is one of the dermatologic conditions with the greater impact on social life [15]. The main goal of the treatment is to prevent the extension of the inflammation to the deep tissue structures and the consequent appearance of scars [16]. Topical treatments currently available for the treatment of mild acne are topical retinoids and their derivatives are benzoyl peroxide, topical antibiotics, and azelaic acid [17].

Twenty subjects were enrolled, 9 males and 11 females, aged between 19 and 66 years old (median age 32.3) affected by acne vulgaris of mild degree, randomized into 2 treatment

groups. The diagnostic dermoscopic tool used to evaluate acne was the DL4 Dermlite (3Gen, San Juan Capistrano, CA) dermatoscope. The degree of acne was determined by evaluation of the inflammatory state and the count of active lesions. The technology used to dispense oxygen was the compact device, X2 Exea, composed of one base unit, a compressor unit and the hand sprayer/vaporizer. The base unit was equipped with an onboard computer and touch screen. Delivery was done with the use of a special airbrush (hand piece) able to modulate the flow of oxygen and combine vaporization of specific active substances. Every therapeutic session was 30 minutes.

Clinical evaluation and investigation occurred at: TO (at the beginning of treatment), T8 (after 8 weeks of treatment), T12 (after 12 weeks of treatment), T16 (after 16 weeks of treatment), and follow-up (8 weeks after the suspension of treatment), for a total of 6 months.

Group A was treated with oxygen therapy by X2 Exea 3 times per week for 16 weeks in 30-minute sessions, followed by clinical follow-up 8 weeks after stopping the therapy.

Group B underwent treatment with a combination of a phytotherapeutic drug (consisting of on *Paeonia suffruticosa* flower water, propylene glycol, chlorhexidine digluconate, sodium usnate, *Arctium lappa*, *Echinacea angustifolia*, sodium chloride, and lauramidopropyl betaine) administered via the oxygen dispenser and oxygen treatment in 30-minute sessions for 16 weeks followed by clinical follow-up 8 weeks after completing treatment.

To be judged suitable for enrollment in the study, each patient aged between 18 and 60 was asked to not to treat acne with topical or systemic therapy during the 6 months prior to the study. All women had to have a pregnancy test before the beginning the study. Patients not willing to provide consent, pregnant women or lactating women, subjects treated with topical or systemic therapy for acne in the 6 months prior to the study, patients allergic or intolerant to any of the components of the drugs, and patients with medical conditions that could interfere with the safety and effectiveness of the treatment were excluded.

All 20 patients completed the study, and no dropouts or adverse events occurred. Patients showed different therapeutic responses to treatments.

Group A was treated with oxygen therapy 3 times per week in monotherapy and at T16 showed a reduction of inflammatory and non-inflammatory lesions. There was a significant reduction in the number of all types of lesions. After 16 weeks of treatment the comedogenic component was diminished by 20.7%; the papulopustular component decreased by 67.7%; and the cystic was reduced by 40.0%. The results were partially maintained at the clinical follow-up 2 months after the suspension of therapy. At the

clinical follow-up the comedogenic component was reduced by 17.2% compared to T0, the papulopustular as well as the cystic components maintained a 40.0% reduction.

Group B was treated with oxygen and a phytotherapeutic drug, administered 3 times per week in 30-minute sessions and showed a reduction of inflammatory and noninflammatory lesions. All kinds of lesions examined diminished significantly. After 16 weeks of treatment, the comedogenic component diminished by 44.4%; the papulopustular component decreased by 84.9%; and the cystic component by 75.0%. The results were partially maintained at the clinical follow-up 2 months after the suspension of therapy. At the clinical follow-up the comedogenic component was reduced by 45.3% compared to T0, the papulopustular component maintained a 62.4% reduction; and the cystic component was reduced by 50.0%.

In conclusion, oxygen therapy is a valid therapeutic aid in the treatment of mild acne and oxygen therapy when combined with a phytotherapeutic drug and demonstrated results significantly more effective in the treatment of inflammatory and noninflammatory lesions than with oxygen treatment alone.

Vehiculated Oxygen Therapy and Moderate Acne

Eighteen patients suffering from acne on the face of moderate degree were selected for this study (10 females and 8 males; mean age 23 years). The patients showed typical papulopustular lesions; the average number of lesions on the face before treatment was 21.9. All the patients had suspended previous acne treatments for at least 4 weeks prior to the study. Liquid formulations were applied during oxygen delivery. The session consisted of the application of clindamycin 1% lotion 3 times per week for about 30 minutes, followed by oxygen infusion therapy.

In between treatments, the patients applied a moisturizing base cream without active ingredients (Cetaphil, Galderma Laboratories, Fort Worth, TX) after washing morning and evening.

In our study, the patients participated 3 sessions of oxygen therapy per week for a total of 12 sessions, and progress, safety, and effectiveness were evaluated before, during (6 sessions, 2 weeks) and after treatment (12 sessions, 4 weeks). All patients showed an improvement in terms of number of typical papulopustular lesions. The initial average number of lesions was 21.9. After 1 week it was reduced to 8.7, after 2 weeks it was 3.7 and at the end of treatment was 3.1. The lesions were also evaluated at a follow-up 1 and 3 months after treatment (the average number of lesions being 3.2 and 3.9 respectively), showing maintenance of total or partial results.

The combination of oxygen therapy with clindamycin, in our opinion, enhances the effect of topical antibiotic therapy

and favors its penetration. Sessions performed 3 times per week also considerably reduced the quantity of drugs that would otherwise be applied daily for months, risking drug resistance of *Propionibacterium*.

Topical Oxygen Therapy and Inflammatory Dermatological Lesions

The patients who participated in this study had suspended previous treatments of their respective dermatological diseases for at least 4 weeks to the study. They participated in treatments with safe and effective topical therapies in liquid formulation, which were applied during oxygen delivery. A derivative of vitamin D was used for psoriasis (calcipotriol lotion 50 µg per 1 mL) and a low-potency steroid (hydrocortisone butyrate 0.1% lotion) was used for atopic dermatitis.

Twenty-four (16 females, 8 males) patients with psoriasis were selected with an average age of 45.5 years. The PASI score was between 4 and 13, so the pathology could be defined as mild-to-moderate. Lesions were distributed on different parts of the body, in particular, the elbows, knees, trunk, hands and feet. All patients received the same cycle of oxygen therapy with the application of active ingredients suitable for treating the underlying disease. A follow-up was performed at 1 and 3 months after the last session to evaluate the maintenance of results. In between treatments, the patients applied a moisturizing base cream without active ingredients (Cetaphil) once a day.

Twenty-four patients with atopic dermatitis (10 males and 13 females, mean age 34 years) had an initial SCORAD disease severity index between 2 and 6. The oxygen therapy cycle involved 12 sessions (3 times a week for 1 month) combined with a lotion of butyrate hydrocortisone 0.1%.

In our study, all patients received 3 sessions of oxygen therapy per week for a total of 12 sessions, and progress, safety, and effectiveness were evaluated before, during (6 sessions, 2 weeks) and after treatment (12 sessions, 4 weeks). PASI improved during the study from 6.2 (T0) to 1.8 (4 weeks, 12 sessions).

The SCORAD disease severity index for patients with eczema and atopic dermatitis showed a decline (the mean score dropped from 3.6 to 2.1 after 12 sessions). During the 1- and 3-month follow-up visits, these indices were also evaluated, with maintenance of the result,

At follow-up all patients highlighted maintenance of the total or partial results. The adverse effects were practically nonexistent, and the treatment was well tolerated. This is the first time that topical oxygen therapy to chronic inflammatory dermatologic disorders such as psoriasis and atopic dermatitis has been used, accelerating the healing processes as compared to traditional therapies. This treatment can therefore be proposed as a safe alternative to traditional therapies or in combination with them.

In the future, more studies will certainly be needed to support the results obtained and to extend this technology to other dermatological indications.

Conclusions

Topical oxygen therapy was useful in the treatment of hair loss conditions (such as androgenetic alopecia or telogen effluvium), in the treatment of mild and moderate acne, and in the treatment of chronic cutaneous diseases. Topical oxygen therapy showed its effectiveness as a support therapy in all the diseases and therefore should be offered as a possible therapeutic treatment to the patient. Infusions of phytotherapeutic drugs and minoxidil via the X2 Exea oxygen dispenser, according to our studies, seem to improve the effectiveness of the drugs in both hair loss conditions and mild acne. Topical oxygen therapy should be proposed as an adjuvant therapy in the treatment of these conditions. Other studies should be done to evaluate the effectiveness of topical oxygen therapy as an adjuvant therapy in larger study groups.

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