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Vaginal Natural Oxygenation Device (VNOD) and Lichen: A Pilot Study on the Assessment of Effectiveness of the Simultaneous and Local Administration of High Concentration Oxygen and Hyaluronic Acid to treat Vulvar Lichen Scleroatrophicus

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Abstract

Background

This is a pilot study to assess the effectiveness of simultaneous and local administration of high concentration oxygen and hyaluronic acid by a specific medical device (VNOD) to improve vulvar lichen symptoms healing vulvar lesions.

Methods

17 women with histological diagnosis of vulvar lichen were included. Five weekly administrations of concomitant oxygen-hyaluronic acid therapy with VNOD were performed. The severity of the pathology was evaluated using the Vaginal Health Index (VHI). Patients' symptoms were evaluated with two questionnaires: VAS and FSFI. VAS, FSFI and VHI were evaluated at the start and at the end of the therapy. The statistical analysis was performed according to the Kruskal-Wallis method and using the t-test calculator.

Results

The study has showed that each subsequent treatment determined a significant increase in all parameters, especially for VHI hydration index, VAS fluidity index and FSFI lubrication index, however all the patients reported a recovery of their sexuality at the end of the five treatment sessions. All the parameters maintain their value at six weeks of follow-up. No adverse effects were observed.

Conclusions

Combined topical oxygen therapy with hyaluronic acid by VNOD seems to be a valid and totally painless treatment for vulvar lichen scleroatrophicus, improving symptomatology, and sexual wellbeing.

Keywords: Vulvar Lichen Scleroatrophicus, Topical Oxygen Therapy, Hyaluronic Acid, Sexual Wellbeing

Introduction

Lichen Scleroatrophicus is a cutaneous-mucosal dermatosis characterized by chronic changes in the trophism of epithelial maturation together with connective tissue alterations. According to others, it is a chronic inflammatory disease manifested by sclerosis, atrophy and ulceration of the involved tissues and leading to the formation of scarring outcomes of varying degrees accompanied by more or less disabling symptoms.

In 80% of cases, it is localized in the ano-genital region with a higher incidence in the female sex (ratio 6 to 1). [1-2].

In the ano-genital area, the clitoris and labia minora are mainly affected by the disease; this is followed by the labia majora and the perineal area. Lichen Sclerosus can occur at any age although it prefers the peri- and post-menopausal period [3].

The causes are not entirely clear to date, but correlations have been noted with hormonal trends, especially in women, especially after menopause and with hyperactivity of the immune system [4].

Lichen is part of unobligated precancerous, meaning that not all patients with the disease will develop a neoplastic form,

however, statistics show that 6-10% of untreated severe forms evolve into vulvar cancer. The predominantly reported symptom is itching; this is followed by burning, spontaneous pain, dyspareunia (painful or impossible intercourse), dysuria (difficulty urinating) and skin-mucosal dryness with recurrent fissures [5].

The vulva is pearly white in colour with an atrophic surface; the labia minora may show varying degrees of atrophy up to total fusion with hooding of the clitoris. The vestibule is rigid and sclerotic; the vaginal introitus appears reduced to the point of sometimes not allowing vaginal exploration. Fibrosis can involve the periurethral region with dislocation of the urethra and cause so-called vaginal urination. Tissues so sclerotic go into ulceration causing intense pain and burning to the point of difficulty with even simple intimate hygiene manoeuvres or contact of the mucosa with clothing [6].

Materials and methods

17 women with histological vulvar diagnosis of Lichen were considered. The mean age at diagnosis of the 17 included cases was 56.5 years (range 48 - 65).

Patients were identified and recruited from investigators clinics and referring physicians, with privacy protection and avoiding undue influence. Each included patient provided an informed consent that allowed treatments, that certified the comprehension of the information provided, with voluntary agreement of the subject, free from coercion. The treatments were administered at Antonio Cardarelli Hospital in Napoli (AORN "A. Cardarelli").

Every patient was submitted to a colposcopy and histological biopsy to confirm lichen diagnosis. Topical corticosteroid therapy performed in the previous 30 days was considered as an exclusion criteria from the study.

The clinical study was approved by the local institutional review board (Comitato Etico Campania 3 Prot. N. 00014304-14/06/2024) and conducted in accordance with the ethical standards of the Declaration of Helsinki.

Five weekly administrations of concomitant oxygen-hyaluronic acid therapy with VNOD were performed.

The severity of the pathology was evaluated using the Vaginal Health Index (VHI) which includes three parameters: Vaginal elasticity, vaginal secretions, and vaginal hydration. The degree of the health of the vagina was defined by the final score obtained after the evaluation of each parameter based on a five-point scale: Score 1 = absence of elasticity, secretions, hydration, score 2 = weak elasticity, secretions, hydration intensity, score 3 = mild elasticity, secretions, hydration intensity, score 4 = good elasticity, secretions, hydration intensity, score 5 = excellent elasticity, secretions, hydration intensity.

Patients' symptoms were evaluated with two questionnaires: VAS and FSFI.

VAS studies the intensity of the four following symptoms: (I) well-being such as absence of dyspareunia, (II) vaginal dryness, vaginal lubrication and presence of fluid, (III) vaginal burning, (IV) vulvar or vaginal itching. Symptoms were collected from patients based on a six-point scale: Score 1 = maximum intensity, score 2 = strong intensity, score 3 = average intensity, score 4 = mild intensity, score 5 = weak intensity and score 6 = absence of symptom).

The Female Sexual Function Index (FSFI) based on clinical interpretations of a principal components analysis, included desire, subjective arousal, lubrication, orgasm, satisfaction and pain and were evaluated based on a six point score scale: Score 0 = absence of symptoms, scores 1 = weakness of symptoms, score 2 = mild symptoms intensity, score 3 = medium symptoms intensity, score 4 good symptoms intensity; score 5 =excellent symptoms intensity.

VHI, VAS and FSFI were evaluated at the start and at the end of the therapy. The final administration was performed after 5 weeks. The vaginal well-being and symptoms were determined and recorded by the clinician with a numerical score according to the scales described above.

The statistical significance of the trend of variation in values between treatment sessions was analysed using the one-way variance analysis according to the Kruskal-Wallis method. The significance of couples' comparisons between treatment sessions was analysed using the t-test calculator for two independent means. A $p < 0.05$ was considered statistically significant. Statistical Analysis was performed using SOCS statistics. After 6 weeks since the last treatment a follow up was performed, and the three most statistically relevant parameters maintained their value.

For the treatment, the self-cooling Caress Flow (Caress Flow- srl, Casette di Funo, Bologna, Italy) device was used composed of a compressor-base unit (generator) able to deliver up to 2+/- 0,2 L/minute of 93% +/- 3% pure oxygen provided at a pression of 1+/- 0,1 bar.

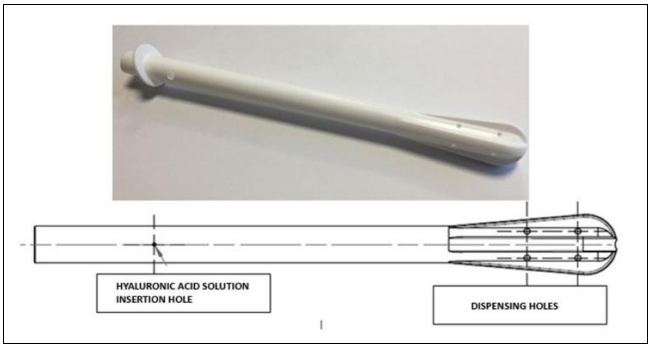

Fig 1: ↓ *Cannula*

Two dispensers were used, the first consisting of a vaginal cannula, connected to the machine body. The cannula is equipped with outlet holes for the delivery of oxygen and hyaluronic acid, which is inserted through a special insertion hole located in the upper part of the cannula (Fig 1). The vaginal cannula is used for treatment inside the vaginal canal.

Fig 2: ↓ *Airbrush*

In addition to the cannula, an airbrush was used (Fig 2), always connected to the machine body, capable of delivering oxygen in combination or not with the hyaluronic

acid solution. The airbrush is used for the treatment of external genitalia, nebulizing the combination of oxygen and hyaluronic acid.

The full treatment cycle includes five weekly sessions, during which the treatment was performed for 20 minutes, and the high purity oxygen and the hyaluronic acid were administered in a contemporary way. The treatment began with the delivery of the solution through an airbrush for vulvar therapy. 3ml hyaluronic acid was delivered with oxygen at a flow of 2 L/ minute for 15 minutes; for 5 minutes 12ml of low molecular weight sodium hyaluronate and high purity oxygen, at a concentration of 0.2%, was administered through a cannula specifically designed for vaginal therapy. At visit 0, an accurate collection of patient history and a complete clinical examination was performed to evaluate eligibility criteria.

Results

The analysis of the comparisons between the first and last treatment have showed that each subsequent treatment determined a significant increase in all parameters, especially for VHI hydration index, VAS fluidity index and FSFI lubrication index, however all the patients reported a recovery of their sexuality at the end of the five treatment sessions.

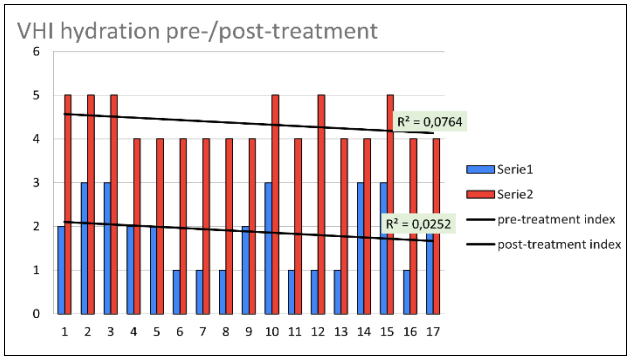

Fig 3: ↓ Diagram - VHI hydration pre-/post-treatment

VHI: The intensity of the three symptoms reported according to the 5-point VHI scale showed an average increase of the elasticity index from 1.8 to 4.2 - p<0,00001, an average increase of the secretion index 1,7 to 4,1 and average increase of the hydration index from 1.9 to 4.9 (Fig 3). The analysis of the comparisons between the start and the end of the therapy have shown that each subsequent treatment determined a significant increase in all parameters, including the vulvovaginal elasticity and the vulvovaginal wall epithelium hydration.

Fig 4: ↓ Photos of the patient's genitals pre-/post treatment

Fig 5: ↓ Photos of the patient's genitals pre-/post treatment

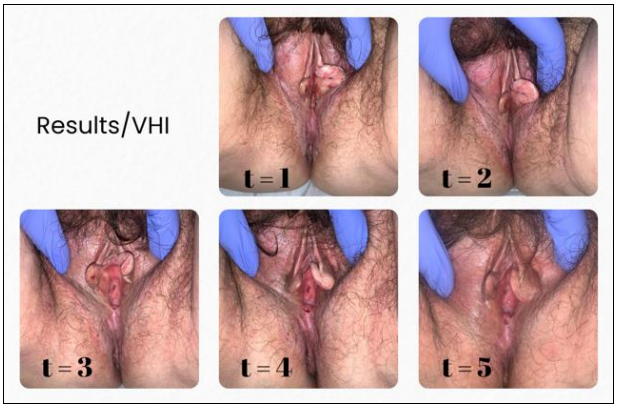

Fig 6: ↓ Photos of the patient's genitals during the 5 weekly therapy session

Below are shown as an example the photographic images of three of the patients in which it is possible to appreciate the differences between the appearance of the genitals before and after the treatment (Figures 4, 5) and also the five stages of the treatment (Fig 6): All initially show an absent or poor overall elasticity and an absent hydration with the mucosa vulvar predominantly white and ulcerated, while at the end good or excellent elasticity with modest/normal hydration with many islands of pink mucosa.

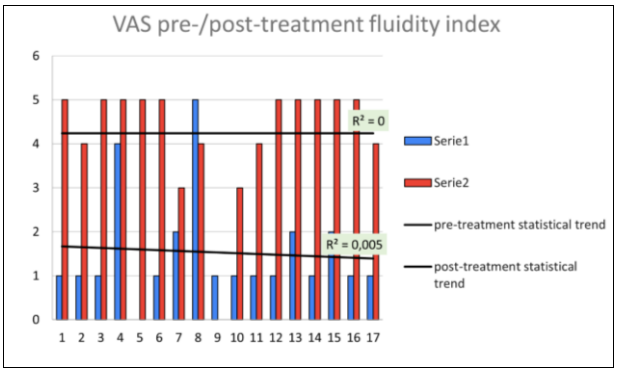

Fig 7: ↓ Diagram - VAS fluidity index pre-/post-treatment

VAS: The results shown a significative improvement of all the mean scores analysed: Well-being such as absence of dyspareunia, vaginal dryness, vulvar and/or vaginal itching, vaginal burning. The intensity of the symptoms reported according to the 6-point VAS scale showed an average increase of the well-being index from 2.1 to 4.7, an average increase of the burning index 1.9 to 5.3, an average increase of the fluidity index from 1.6 to 4.5 (Fig 7) and an average increase of the itching index 2.2 to 5.4.

FSFI: The results shown a significative improvement of all the mean scores analysed: Increasing sexual desire, excitement, satisfaction, raised vaginal lubrication and ability to join the orgasm and decreased vulvar or vaginal pain.

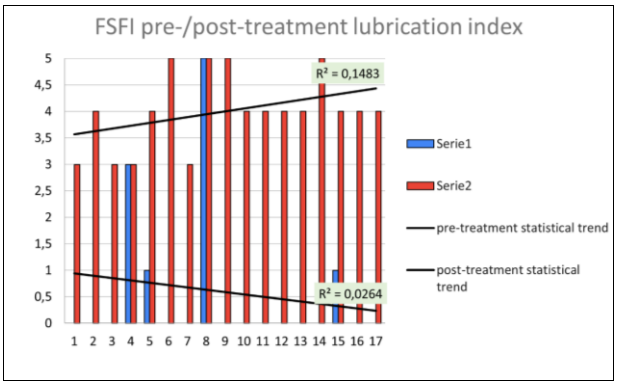

Fig 8: ↓ Diagram - FSFI lubrication index pre-/post-treatment.

The intensity of the symptoms reported according to the 6-point FSFI scale showed the following average improvements: Sexual desire index from 1.5 to 3.5, excitement index from 1.3 to 3.7, satisfaction index from 1.2 to 3.8, vaginal lubrication index from 0.6 to 4 (Fig 8), ability to join the orgasm index from 1.8 to 3.6 and decreased vulvar or vaginal pain index from 4.1 to 1.

Discussion

In this pilot study we found that the combined topical oxygen therapy with hyaluronic acid by VNOD is a valid and totally painless treatment for vulvar lichen scleroatrophicus, improving symptomatology and sexual wellbeing.

Lichen sclerosus is a chronic disorder of the skin and mucosal surfaces, and is most commonly seen on the female genital skin. It also occurs in other areas of the body. Any age group may be affected, although it is seen more often in elderly women [1, 2, 3, 4, 7].

The exact cause of lichen sclerosus is unknown. There have been reports of family members with lichen sclerosus; thus, it may have a genetic link [8]. There is also the possibility of an autoimmune connection [9].

Currently ultra-potent topical corticosteroids (TCS) are the medical treatment of choice: Clobetasol propionate and mometasone furoato [10, 11, 12].

The risk of developing squamous cell carcinoma of the vulva approaches 5% in women with vulvar lichen sclerosus, and therefore close surveillance by the healthcare provider and patient is needed [14, 15, 16].

Long-term TCS has a protective effect from malignant evolution: Carcinoma developed only in nontreated or irregularly treated vulvar lichen sclerosus lesions [17]. It could be interesting to evaluate the efficacy of simultaneous and local administration of high and hyaluronic acid on the malignant evolution of the vulvar lichen in vulvar carcinoma. A long-term monitoring is necessary to set the timing for another session with VNOD therapy and to monitor the evolution of patients' symptomatology and the state of vaginal elasticity and hydration.

Oxygen therapy determines the increase of the reparative processes of the tissues and increases the synthesis of collagen allowing a normal hydroxylation of this protein [18]. In fact, at oxygen tensions lower than normal, the collagen is not correctly synthesised, delaying the healing of the wounds. Furthermore, oxygen induces a neo-angiogenic stimulation trough the release of VEGF [19]. This function is essential for the restoration of the microcirculation in compromised vascular tissues, re-establishing a vascular flow in the hypoxic areas [20]. Hyaluronic acid is a natural polysaccharide and that can bind a large quantity of water molecules contributing to the maintenance of water balance, proper hydration and structure of skin and mucus membranes [21].

VNOD therapy increases the elasticity of the tissues and improves the VVA(Vulvo-Vaginal Atrophy) and the genitourinary symptoms. The therapy has been well tolerated without side effects [22, 23, 24].

Our findings must be confirmed in a well-designed randomised controlled trial.

Conclusions

Combined topical oxygen therapy with hyaluronic acid is a fast, repeatable, and totally painless treatment with no side effects for the patients. It proved to be a valid method for healing vulvar lesions and improving lichen symptoms with excellent compliance by patients.

The results of the study demonstrate that this therapy increases the vulvovaginal mucosa hydration, fluidity and lubrification improving women's sexual health and wellbeing also after 6 weeks from the last treatment.

Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Authors' contributions

Raffaella De Simone, Maria Di Pietro and Rosa Elena Frulio have given substantial contributions to the conception and the design of the manuscript and acquisition of the data, Eleonora Russo to analysis and interpretation of the data. All authors have participated to drafting the manuscript, author Gianpaolo Mainini, Flavio Garoia and Claudio Santangelo revised it critically. All authors read and approved the final version of the manuscript.

All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

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