

Treatment With Vaginal Oxygen Therapy in Patients With Genitourinary Syndrome of Menopause Symptoms: An Observational Trial

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Abstract

Genitourinary Syndrome of Menopause (GSM) GSM is a chronic and progressive condition that can have many medical consequences (vaginal dryness, vulvar pain, dyspareunia, and dysuria) that may affect quality of life. The objective of our study was to evaluate the efficacy of vaginal hyperbaric oxygen treatment on GSM. Thirty patients received six weekly sessions of 95% pure oxygen that was delivered at a flow of 2 lt/minute for 15 minutes using a cannula designed for vaginal therapy, with a subsequent follow-up after two months. There was a significant improvement in vaginal dryness (before treatment VAS 7.52 versus 3.52 after treatment $-p = 0.05$). The same improvement was observed for vulvar burning/pain and dyspareunia, but these were not statistically significant. VHI before treatment was 15.1 versus 19.59 after treatment ($p = 0.05$). All the parameters maintain their value at 2 months of follow-up. No adverse effects were observed.

Introduction

The International Society for the Study of Women's Sexual Health (ISSWSH) and the North American Menopause Society (NAMS) defined the Genitourinary Syndrome of Menopause (GSM) in May 2013 as the clinical and functional consequences of vulvovaginal and lower urinary tract changes associated with menopause [1]. The definition includes cellular, histological, anatomical, and functional changes due to estrogen deficiency [1–3]. GSM is a chronic and progressive condition that can have many medical consequences that may affect relationships, daily activities, quality of life and enjoyment of sex [4]. Despite being highly prevalent it is frequently underdiagnosed, and thus remains untreated [5]. Women with GSM are often managed with hormonal treatments by the systemic (menopausal hormone therapy (MHT)) or local (local estrogen) routes: MHT improves vaginal lubrication, blood flow and trophicity of genital tissues [5, 6], and small doses of intravaginal estrogen increase vaginal pH and the epithelial maturation index and restore vaginal flora with minimal systemic effect [7, 8]. The Women's EMPOWER Survey conducted in 2017 to evaluate women's perception of the different therapeutic alternatives of GSM showed that approximately 35% of women refuse hormonal treatments, whether systemic or local, for fear of adverse effects [9]. Non-hormonal

alternatives in this context are therefore essential and currently include lubricants, moisturizers, hyaluronic acid, and physical methods such as perineal rehabilitation. Furthermore, due to contraindications to hormonal treatments (hormone-dependent cancer) and the constraints of use and variable effectiveness of local treatments, other therapeutic options have been developed such as vaginal therapy with hyperbaric oxygen. The application of oxygen therapy determines the increase of the reparative processes of the tissues and increases the synthesis of collagen which is defective in GSM [10]. The objective of our study was to evaluate the efficacy of vaginal hyperbaric oxygen treatment on GSM in a prospective approach based on quality of life related to symptoms and signs in treated patients..

Methods

Women included in the study were postmenopausal with at least 1 year of amenorrhoea and at least one moderate or severe symptom of GSM (vaginal dryness, burning, and dyspareunia). Key exclusion criteria included the presence of clinically significant abnormal gynecological findings

other than signs of vaginal atrophy; use of concomitant hormonal medications, SERMs, or products expected to have estrogenic and/or antiestrogenic effects or use of hormone therapy (unless a sufficient washout period preceded any procedure). Review Board

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approval for the study was obtained and all participating individuals gave written informed consent. At the first assessment, symptoms of dryness, burning, and dyspareunia were evaluated on a 10 cm visual analog scale (VAS), and vaginal trophism through Vaginal Health Index was also collected. For the treatment, the Caressflow® device (Caress Flow srl - Via dei Giudei 39 Funo di Argelato 40050 -BO-Italy) was used composed of a compressor unit and a base unit (generator) able to deliver up to 6 l/minute of 95% pure oxygen. The 95% pure oxygen was delivered at a flow of 3 lt/ minute for 15 minutes using a single use 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. The full treatment cycle included six weekly sessions, with a subsequent follow up after 60 days. The statistical significance of the trend of variation in values between treatment sessions was analyzed using the one-way variance analysis according to the Kruskal-Wallis method. The significance of couples' comparisons between treatment sessions was analyzed using the Wilcoxon test for non-parametric data. A $p < 0.05$ was considered statistically significant.

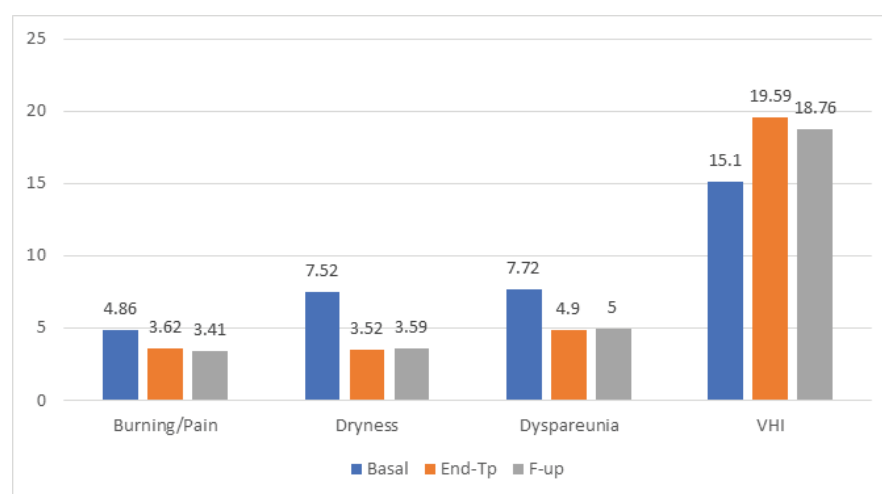
Results

Thirty patients enrolled in the study completed the full treatment protocol and attended the follow up consultation at 2 months. The patients had a mean age of 57.3 years (± 11.1 years). There was a significant improvement in vaginal dryness; the mean VAS before treatment was 7.52 (± 3.14) versus 3.52 (± 3.12) after treatment ($p = 0.05$). The same improvement was observed for vulvar burning/pain and dyspareunia, but these were not statistically significant. Instead, there was an improvement with a significant difference for vaginal trophism; the mean VHI before treatment was 15.1 versus 19.59 after treatment ($p = 0.05$). All the parameters maintain their value at 2 months of follow-up (Fig.1). No adverse effects were observed.

Discussion and Conclusion

Vaginal hyperbaric oxygen treatment appears to have a beneficial impact on the quality of life and management of patients with GSM. In our study, all symptoms and signs

improved, and a significant change was demonstrated in vaginal dryness, one of the main symptoms of GSM. One study demonstrated the efficacy of vaginal hyperbaric oxygen plus hyaluronic acid in patients with GSM, in which a significant improvement in well-being, vaginal burning, presence of fluid, vaginal epithelium appearance, and vaginal elasticity was observed between the first and the last therapy session [11]. We also confirmed the efficacy of vaginal hyperbaric oxygen treatment, but it was used alone without the adjunct of hyaluronic acid, proven the "strength" of vaginal oxygen in GSM. We can say that vaginal oxygen could be a valuable alternative or adjunct to others GSM treatments. Such device is particularly interesting for patients being treated for cancer and who suffer the long-term consequences of the treatments received or who present a contraindication to hormonal treatments. Oxygen therapy has a powerful regenerative and bio stimulating effect, promotes the increase in tissue repair processes and increases the synthesis of collagen allowing normal hydroxylation of this protein [10]. In addition, oxygen induces a neo-angiogenic stimulus by releasing factors such as the Vascular Endothelial Growth Factor (VEGF) [11]. Our results were good but not-so-bright on vulvar pain and dyspareunia. It is our experience that many menopausal women with complaints of dyspareunia have vestibular tenderness with more pronounced atrophic changes in this region rather than the vagina. Furthermore, it is likely, as Kao et al. suggest, that vulvovaginal atrophy alone does not adequately explain the findings of vestibular pain [12]. In 95% of her postmenopausal cohort with vestibular pain and dyspareunia, women used a variety of estrogen supplements, and atrophy varied but vestibular pain persisted. A rich nerve plexus within the vaginal submucosa was identified, but it is composed only of sympathetic and parasympathetic axons with smaller contributions by sensory fibers; in the vulvar vestibule, the sensory nerve endings are dense and shallow, making this region physiologically more sensitive [13]. We can therefore hypothesize that vaginal oxygen is not enough to re-establish a normal vestibular trophism. However, the results are encouraging and should stimulate the research regarding this innovative therapy, using the device also in vestibular area.



Data are expressed as mean

Figure 1. Results before and after vaginal oxygen therapy

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