



CASE SERIES

Adjuvant Treatment with a Non-Hormonal *Centella asiatica*, Hyaluronic Acid and Prebiotic-Based Vaginal Gel in Women with Recurrent Dysbiosis: Case Series

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Abstract

Vaginal dysbiosis (VD) is characterized by the loss of *Lactobacillus* dominance that includes several conditions such as bacterial vaginosis, the most common one. Also, VD can foster the development of sexually transmitted diseases and pelvic inflammatory disease, among others. In this series of case reports we show that the adjuvant treatment with a non-hormonal *Centella asiatica*, hyaluronic acid and prebiotic-based vaginal gel (Palomacare®) can be a useful coadjuvant treatment tool for the management of VD, as symptoms resolved, and no relapse occurred in women with recurrent VD receiving this gel as an adjuvant treatment.

Keywords

Vaginal dysbiosis, Bacterial vaginosis, Non-hormonal *Centella asiatica*, Hyaluronic acid and prebiotic-based vaginal gel, Prebiotic, Adjuvant treatment

Abbreviations

BV: Bacterial Vaginosis; HIV: Human Immunodeficiency Virus; PID: Pelvic Inflammatory Disease; SI: Sexual Intercourse; STDs: Sexually Transmitted Diseases; STIs: Sexually Transmitted Infections; VD: Vaginal Dysbiosis; VMB: Vaginal Microbiome

Introduction

Microbiota is essential for human physiology, contributing to multiple mechanisms including

immunity. It acts as a frontline defense, preventing colonization and consequently infection by foreign micro-organisms [1]. Vaginal microbiome (VMB) normally evolves with age and is influenced by hormonal changes during the different phases of women's reproductive cycle, as well as by ethnic background, vaginal douching or unprotected sexual intercourse (SI) [1-3]. Although it can also transitionally contain a small number of fungi and parasites, healthy VMB during reproductive age is mainly composed of *Lactobacillus*, and vaginal dysbiosis (VD) is characterized by the loss of *Lactobacillus* dominance and increased microbial diversity [4-6]. This change in VMB composition can lead to bacterial vaginosis (BV), vulvovaginal candidiasis, and aerobic vaginitis, among others [7]. The most common clinical condition characterized by VD is BV, which is due to the overgrowth of anaerobic bacteria [5]. The estimated overall prevalence of VD among women aged 18-30 years was 35.8%, of which 32.2% presented BV [4]. VD has been associated with sexually transmitted infections (STIs), including human immunodeficiency virus (HIV), pelvic inflammatory disease (PID), as well as adverse pregnancy outcomes such as preterm birth and maternal and neonatal infections [4]. Currently, VD treatment is mainly based on antibiotics and/or probiotics. Despite showing favorable therapeutic effects, such therapy presents important problems



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like a high recurrence rate or the development of drug resistance [5]. In fact, approximately 30-60% of patients with vulvovaginal candidiasis experience relapse after one year [8], and around 39% of women who initially respond to BV treatment present symptom recurrence within three months, the number being greater than 50% within the following year [9]. Therefore, there is scope for improvement in the therapeutic management of recurrent VD. Recovering and maintaining optimal vaginal conditions with the use of concomitant moisturizers, repairers, and prebiotics might be a strategy to optimize VD therapy. In this context, Palomacare® is a non-hormonal vaginal gel containing *Centella asiatica* phytosomes, hyaluronic acid and β -glucan niosomes, Aloe vera extract and BioEcolia®, which is an α -glucan oligosaccharide with prebiotic properties [10]. Hyaluronic acid is known as a moisturizer [11-14], β -glucan niosomes has got antioxidant properties, as well as immunomodulator [12]. Moreover, an active component of *Centella asiatica*, asiaticoside, and Aloe vera are reepitelising and wound healing facilitators [15-18]. We present a case series of three women treated with this antibiotic-free non-hormonal *Centella asiatica*, hyaluronic acid and prebiotic-based vaginal gel as an adjuvant treatment for VD. As patient-specific information was deidentified to ensure anonymity, patient consent was not necessary.

Case 1

A 32-year-old woman, nulliparous without any relevant clinical background. Who presented malodorous leukorrhea for four months that was affecting her personal life? Two other doctors had previously diagnosed the patient with BV. She followed multiple treatments with oral and vaginal probiotics, dequalinium chloride, metronidazole, and several vaginal gels. However, the improvement was partial, occasional, and intermittent in all cases. The vulva, vagina, and cervix were normal upon examination, presenting slight erythema with a notable greyish and malodorous leukorrhea. Sexually transmitted diseases (STDs) were ruled out via serology, and cervix cytology and pelvic ultrasound examination were normal. Vaginal discharge culture demonstrated the presence of *Gardnerella vaginalis*. Treatment with Palomacare® vaginal gel was prescribed once a day for 14 days in a row followed by every other day application, together with vaginal 10 mg dequalinium chloride daily for 6 days and single strain vaginal probiotics containing 10⁸ CFU of *Lactobacillus crispatus* once a day for 14 days. Two weeks after the end of treatment, the patient reported improvement of symptoms from the second day until their complete vanishing, as well as good tolerance. The patient kept using the vaginal gel every other day combined with the vaginal probiotics intermittently with no recurrence.

Case 2

A 25-year-old woman previously diagnosed with

BV who experienced relapse three times during the last year. Previous treatment with probiotics and metronidazole was initially effective, but symptoms reappeared two to three months later after all three treatments. She attended the medical consultation in March 2021 showing vaginosis-like symptoms. Upon examination, the patient's external genitalia and vagina were mildly hyperemic, a yellowish-brownish discharge was observed together with a well-epithelized cervix, and an amine-like odor was noted. She experienced discomfort during speculoscopy but felt no pain upon mobilization, and bimanual examination was normal. An ultrasound scan showed an anteverted uterus, a 3 mm endometrium, normal ovaries, and no free fluid. A vaginal culture performed two months earlier was positive for *Gardnerella vaginalis*. The patient was prescribed 500 mg vaginal metronidazole (Flagyl®), oral probiotics (*Lactobacillus plantarum* and *Lactobacillus paracasei*) and Palomacare® vaginal gel. Resolution of symptoms was achieved, and no new vaginosis episodes occurred. In November 2021, the patient was reexamined: external genitalia, vagina, and discharge were normal, and no bleeding was observed.

Case 3

A 21-year-old with no toxic habits came to consultation reporting malodorous leukorrhea with itching and an increase in vaginal discharge for the past three weeks. She claimed to have experienced the same symptoms on four occasions during different months of the present year. The patient had surgery one month ago due to a hemorrhagic cyst, without any other relevant clinical history. Physical examination showed a normal vulva and vagina, together with the aforementioned malodorous leukorrhea (Figure 1a). All symptoms are considered compatible with VD, given the risk of recurrence based on her clinical history, an empirical treatment with a three-day 100 mg clindamycin vaginal ovule daily therapy and coadjuvant treatment with Palomacare® once daily for 6 days followed by the same regimen after menstruation. Three weeks later, the symptoms had vanished, the patient did not refer any recurrence of the symptoms during her last consultation 6 months after the initial one (Figure 1b).

Conclusions

VD is a condition with a non-negligible prevalence and high recurrence rates despite current management guidelines [4,5,19], which poses the need for adjuvant therapies. In the three cases presented here, Palomacare® vaginal gel was used as an adjuvant for the treatment of VD. In all cases, patients presented previous VD recent episodes i.e., exhibited recurrence. The patient from case 1 followed several therapeutic strategies that failed to prevent recurrences and the patient from case 2 received an also unsuccessful 500 mg vaginal metronidazole plus probiotics treatment. After treatment with Palomacare®, in all cases, VD

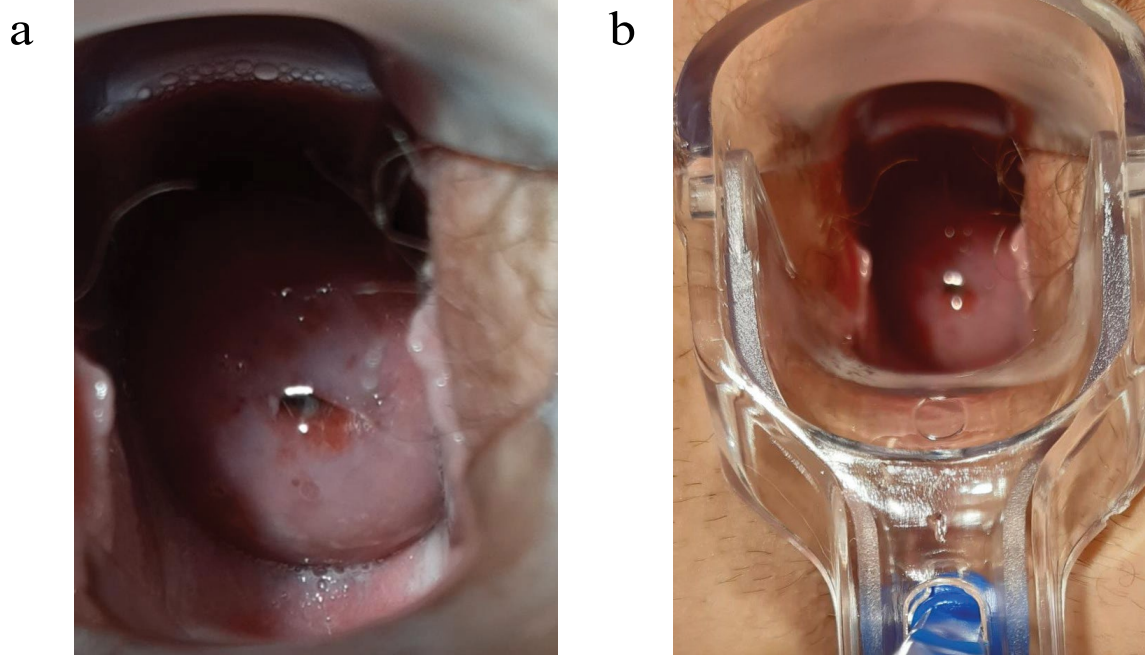


Figure 1: Macroscopical appearance of vaginal tissue during speculoscopy from case 3 patient (A) before and (B) after adjuvant treatment with the non-hormonal *Centella asiatica*, hyaluronic acid and prebiotic-based vaginal gel.

symptoms resolved completely. Importantly, the patient from case 1 stated good tolerance to the vaginal gel and kept using it after the prescribed treatment, as maintenance therapy. Therefore, the non-hormonal *Centella asiatica*, hyaluronic acid and prebiotic-based vaginal gel prescribed as a VD adjuvant treatment was effective in all the reported cases, precluding from recurrence, regardless of the number of previous episodes or management strategies used, and the main treatment prescribed.

Prebiotics have proven beneficial to equilibrate the healthy microbiota, including in cases of VMB [20-23]. As it has been shown in the Epicervix study, the application a vaginal gel containing the same prebiotic (α -oligosaccharide prebiotic) to the same concentration as Palomacare® in HPV-positive women significantly reduced the microbial richness, evenness and diversity measured with Chao, Pielous's and Shannon indexes. It is well-described that on the contrary to what it happens in the gut, the healthy vaginal microbiota is characterized by being highly homogeneous and a complete dominance in Lactobacilli. In this study, after 21-days treatment there was a significant increase in the *Firmicutes phylum* (44.6% vs. 2.1%), which includes de *Lactobacillus spp.* genus. In fact, *Lactobacillus iners* and *Lactobacillus crispatus* were measured independently and were significantly increased at the end of the study. This was accompanied with a reduction in *Proteobacteria phylum* was reduced (38.5% vs. 93.6% at baseline) [24]. In a randomized double-blind study conducted in women previously treated for BV, an intravaginal prebiotic gel improved the recovery of normal VMB [25]. After 8 days of treatment, all subjects who received the prebiotic had a normal Nugent score, whereas 33% of

the subjects treated with placebo had an intermediate or positive Nugent score [25]. Also, a systematic review concluded that pre/probiotic regimens are considered safe and can exhibit benefits for treating BV in both the long- and the short-term [26].

In summary, the case series presented conclude that the use of Palomacare® vaginal gel as adjuvant therapy helped resolve the symptoms and avoid VD recurrence in women of reproductive age prone to relapses. This efficacy might be due to the vaginal gel's prebiotic, moisturizing, and reepithelizing properties that restore optimal vaginal conditions.

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Conflict of Interest

The authors declare that there is no conflict of interest.

Statement of Equal Authors' Contribution

All authors contributed equally to the research, writing, and revision of this manuscript. Each author has reviewed and approved the final version and agree it is accountable for all aspects of the work.

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