# Monotherapy With a Non-Hormonal Centella Asiatica, Hyaluronic Acid, and Prebiotic-Based Vaginal Gel in Women With Bacterial Vaginosis: Case Series

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**ABSTRACT:** Bacterial vaginosis (BV) affects nearly one-third of women worldwide and may predispose patients to sexually transmitted infections or pelvic inflammatory disease. Currently recommended treatment is based on antibiotic use, which poses problems such as antibiotic resistance and the development of secondary vaginal candidiasis. Palomacare® is a non-hormonal vaginal gel containing hyaluronic acid, *Centella asiatica* and prebiotics, with repairing and moisturizing properties used for dysbiosis healing as an adjuvant treatment. A series of 3 cases using the vaginal gel as a monotherapy showed that symptoms improved and even disappeared in women with initial or recurrent BV, suggesting that this vaginal gel is effective for BV monotherapy in women of reproductive age.

**KEYWORDS:** Bacterial vaginosis, non-hormonal *Centella asiatica*, hyaluronic acid and prebiotic-based gel, prebiotic, monotherapy

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## Introduction

Bacterial vaginosis (BV) is characterized by an abnormal vaginal microbiome that results from an overgrowth of opportunistic bacteria in addition to a decrease in the levels of hydrogen peroxide and lactic-acid-producing *Lactobacilli*.[1-3] It is the leading cause of vaginal dysbiosis in women of reproductive age.[4] In general, the major microorganisms in cases of BV are anaerobic like gram-positive cocci and gram-negative bacilli such as *Gardnerella vaginalis, Prevotella* species, *Mobiluncus* species, and *Atopobium vaginae*.[1,2] BV usually presents with altered vaginal fluid discharge, odor, and sometimes irritation.[3,5] However, approximately 50% to 75% of women with BV are asymptomatic.[6] The overall prevalence of BV is around 29%, although it varies depending on the country, ranging from 20% to 60%.[2,5] Nevertheless, bacteria that are present in the normal urinary tract microbiota may cause urogenital tract (UGT) infections making it difficult to estimate the real status of such infections among populations without an updated microbiota pattern. Although there is a variation of microbial patterns of UGTs at different ages, similarities have been found within certain age ranges. Moreover, *Lactobacilli* have been linked to the prevention of sexually transmitted-UGT infections in women.[7] BV is associated with several risk factors such as having female sex partners, multiple male sex partners, a new sex partner, sexual relationships with more than one person, douching regularly, herpes simplex virus type 2 (HSV-2) seropositivity, black or Hispanic ethnicity, and smoking.[1,5] In fact, the microbial patterns of UGTs in people with frequent sexual intercourse with various partners are more variable than in individuals with monogamous sexual activities, and usually sex partners share their UGT microbiota between them. Moreover, the use of sex toys might result in a decrease of the *Lactobacillus* spp. population in women, as well as an increase in *G. vaginalis*.[7] Also, the use of an intrauterine device may be associated with BV due to irregular vaginal bleeding.[8] BV can be clinically diagnosed by Amsel criteria when at least 3 of the following are present: thin homogeneous discharge, presence of clue cells on microscopic examination, pH of vaginal fluid $>4.5$, and fishy odor before or after application of 10% potassium solution to vaginal smear.[1] Untreated BV can lead to several consequences such as an increased probability of preterm delivery in pregnant women and a higher risk of sexually transmitted infections (STIs) acquisition, including human immunodeficiency virus (HIV), HSV, gonorrhea, chlamydia, or *Trichomonas*.[6] Furthermore, BV has been associated with the development of pelvic inflammatory disease (PID) and human papillomavirus (HPV) infection.[5]

Currently recommended BV treatment consists of antibiotics: oral or topical metronidazole, or topical clindamycin, for 5 to 7 days.[1] Also, vaginal dequalinium chloride, an antiseptic agent, is an effective treatment for BV.[9] It is estimated that around 39% of women who initially respond to BV treatment present symptom recurrence within 3 months and more than half within the subsequent 12 months.[6] These high recurrence rates might be the result of the inability of antibiotics to eliminate the vaginal biofilm, since researchers have demonstrated the persistence and recovery of biofilm following antimicrobial treatment, and/or their negative impact on healthy vaginal

microbiome.[6] Moreover, the use of metronidazole and clindamycin has been linked to the development of secondary vaginal candidiasis and antibiotic resistance, respectively.[10,11] Recurrence and resistance linked to the current treatment of BV impose a need for new therapies. Palomacare® is an antibiotic-free vaginal gel containing hyaluronic acid, beta-glucan, *Aloe vera*, *Centella asiatica*, and prebiotic (BioEcolia®), mainly used for treating nonspecific vulvovaginitis, cervicitis, vulvovaginal atrophy, genitourinary syndrome, during peripartum, and post-chemotherapy/radiotherapy.[12-17] Moreover, most gynecologists surveyed perceived it as an effective adjuvant treatment for vaginal dysbiosis that reduces relapses.[12] We present a case series of 3 women with BV treated with this non-hormonal *Centella asiatica*, hyaluronic acid and prebiotic-based vaginal gel as a monotherapy instead of as an adjuvant. Patient consent was not required since patient-specific information was deidentified to guarantee anonymity.

## Case 1

A 42-year-old woman complained about an increased grayish-whiteish vaginal discharge that started 2 days earlier which was accompanied by a "fish-like" odor and dyspareunia. The patient had been previously treated with a single-dose 600 mg fenticonazole vaginal ovule with no improvement. Of interest, she had 2 children, both full-term births with eutocic delivery. Also, she was currently on a progesterone-only-based contraceptive therapy with 4 mg drospirenone daily, she had a stable partner, was sexually active, and smoked 5 to 6 cigarettes per day. Moreover, cytology showed no malignant cells, a coccobacilli predominance, and hypotrophy. Speculoscopy revealed a generalized vaginal edema, very fluid and increased grayish-whiteish vaginal discharge, and erythematous cervix (Figure 1A). Furthermore, the patient reported pain during vaginal exploration. pH value was higher than 5 and clue cells were found in the microscopical discharge examination. Monotherapy with Palomacare® vaginal gel was prescribed twice a day for 14 days. After the treatment, the patient had no signs of irritation or dyspareunia together with a normalized vaginal discharge both in quantity, appearance, and odor (Figure 1B). Also, the new cytology performed showed no presence of clue cells.

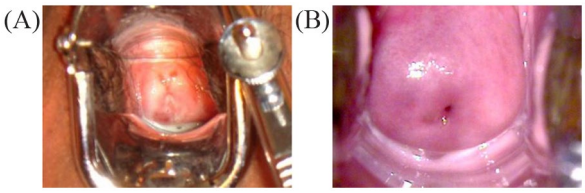


**Figure 1.** Macroscopical appearance of vaginal tissue during speculoscopy from case 1 patient (A) before and (B) after treatment with the non-hormonal *Centella asiatica*, hyaluronic acid and prebiotic-based vaginal gel.

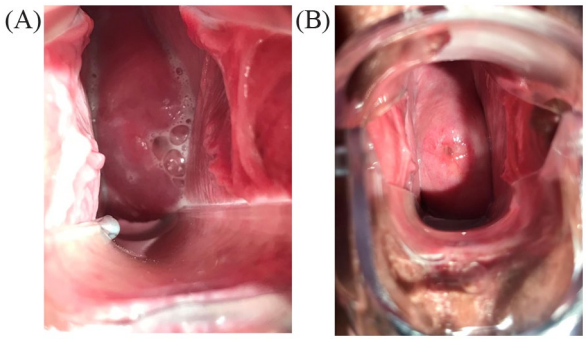


**Figure 2.** Macroscopical appearance of vaginal tissue during speculoscopy from case 2 patient (A) before and (B) after treatment with the non-hormonal *Centella asiatica*, hyaluronic acid, and prebiotic-based vaginal gel.

## Case 2

A 40-year-old woman presented increased vaginal discharge together with vulvar discomfort for several days. After treatment with 100 mg clindamycin vaginal ovuli for 3 days for the suspicion of BV, she felt a partial improvement. Anamnesis included no previous disease of interest or drug allergy, and the patient reported no changes in dietary or sexual habits, no other recent drug intake, or changes in intimate hygiene. The gynecological exam showed slight erythema in the labia minora. Speculoscopy revealed vaginal mucosa and cervical erythema accompanied by whiteish foamy leukorrhea (Figure 2A). Vaginal discharge presented bacterial growth. A complete vaginal discharge culture was performed, and the patient was prescribed the non-hormonal *Centella asiatica*, hyaluronic acid and prebiotic-based vaginal gel once daily for 10 days. Once the treatment was completed, the patient reported a clear improvement in symptoms: vulvar itching disappeared, and vaginal discharge amount decreased. Physical examination found no vulvar erythema and a lower amount of leukorrhea (Figure 2B). The vaginal culture was positive for *Gardnerella vaginalis* so a specific treatment was prescribed with dequalinium chloride vaginal ovuli.

## Case 3

The 40-year-old woman depicted in this case presented postcoital bleeding a week earlier, together with vaginal discomfort and pruritus. Three previous BV episodes during the past year were treated with dequalinium chloride. Her mother had uterus cancer and her maternal aunt had cervix cancer. She regularly took levothyroxine to treat her hypothyroidism and in 2020 she had Covid-19. The patient was nulliparous, had regular menstruation cycles, and had a silver intrauterine device withdrawn 15 days earlier. Also, she presented metrorrhagia and hypermenorrhea since 2020. External genitalia and vagina were normal, and no blood remains were found during examination. Palpation was normal, there was abundant leukorrhea with a fish-like smell, and the cervix, which was painless upon mobilization, presented slight erythroplakia (Figure 3A). Colposcopy

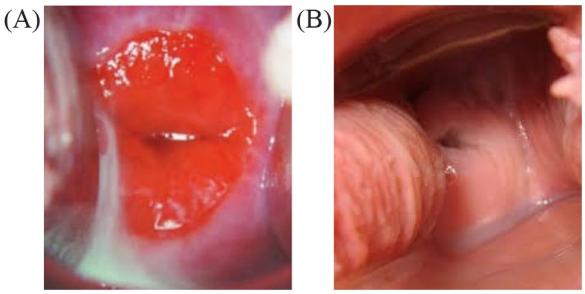


**Figure 3.** Macroscopical appearance of vaginal tissue during speculoscopy from case 3 patient (A) before and (B) after treatment with the non-hormonal *Centella asiatica*, hyaluronic acid, and prebiotic-based vaginal gel.

revealed a transformation zone type 1 without acetowhite or iodine-negative lesions. Cytology showed inflammation-associated changes and examination of vaginal discharge yielded BV. The patient was prescribed Palomacare® vaginal gel once a day for 3 months. After completion of the treatment, she reported no further episodes of post-coital bleeding, nor vaginal discomfort or pruritus. Treatment compliance was good, without application trouble. Physical examination showed no leukorrhea, blood remains or erythroplakia (Figure 3B). Cytology and vaginal discharge were normal.

## Clinical Overview

Despite treatment with antibiotics, a high recurrence rate, together with the development of antibiotic resistance and secondary vaginal candidiasis, pose a problem that merits finding alternative therapy options.[1,6,10,11] Adjuvant therapy with probiotics has proven to be helpful for BV without adverse outcomes.[18] Although more clinical evidence is needed, prebiotics are also prescribed together with the pharmacological treatment.[19] Palomacare® has prebiotic, moisturizing, and repairing properties that make it an effective adjuvant treatment for vaginal dysbiosis by improving healing and reducing relapses.[12]

The cases reported here show that the non-hormonal *Centella asiatica*, hyaluronic acid and prebiotic-based vaginal gel has a beneficial effect on BV as a monotherapy. The treatment was effective both in initial BV, such as in cases 1 and 2, and in recurrent BV in patient from case 3 who had experienced 3 previous BV episodes that were treated with dequalinium chloride. In case 3, therapy with Palomacare® was effective, including good compliance, despite the long 3-month treatment duration. Importantly, this patient exhibited no recurrences during the treatment with the non-hormonal *Centella asiatica*, hyaluronic acid and prebiotic-based gel, despite being prone to their emergence. In case 2, a 10-day therapy was satisfactory to improve symptoms while waiting for the results of the complete vaginal discharge culture. With the aim of reducing antibiotic resistance development, Palomacare® monotherapy arises as a potential immediate treatment while identifying the opportunistic microorganism causing BV to carefully select the proper antimicrobial treatment. A slightly longer treatment used in case 1, for 14 days, was sufficient to treat the condition. Furthermore, although the 3 patients had similar age, the clinical history, and BV presentation was unique to each of them (eg, pain, post-coital bleeding, pruritus, vulvar discomfort), and still the vaginal gel was effective in all cases. Accordingly, Palomacare® may be an alternative to antibiotic use for BV, especially when, despite all efforts, it is still difficult in the regular practice to identify BV etiology and therefore to choose an adequate and specific treatment for BV.[7]

## Conclusion

In the cases reported here, Palomacare® monotherapy exhibited effectiveness for treating BV in women of reproductive age. Its dysbiosis-solving properties were capable of healing BV even without the concomitant use of antibiotics, in both initial and recurrent cases. After treatment with the non-hormonal *Centella asiatica*, hyaluronic acid and prebiotic-based vaginal gel, women had their vaginal health restored or at least markedly improved. Currently, Palomacare® emerges as a potential treatment for BV while there is still a lack of accuracy in the detection of BV etiology. However, case series are not enough to justify a change in clinical practice mainly due to the reduced number of patients and the treatment and patients' characteristics variability. Therefore, more evidence is needed, ideally in the form of randomized controlled clinical trials.

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