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The Effect of Micosin Vaginal Cream and Metronidazole Vaginal Gel on Bacterial Vaginosis.

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ABSTRACT

Bacterial vaginosis is one of the most common complaints among the women who refer to private and maternity clinics. Although most cases are asymptomatic, 50-70% of the patients complain about fishy odor vaginal discharges. Unpleasant side effects and antibiotic resistance have been reported following antibiotics therapy. Thus, use of non-pharmacological therapies and complementary and alternative medicine is essential in treatment of bacterial vaginosis. The present study aimed to evaluate and review alternative therapies. In doing so, more than 70 papers in the field of non-pharmacological therapies for bacterial vaginosis were investigated in PubMed, Elsevier, and Google scholar databases. At the end, complementary therapies were divided into four categories of: probiotics, antiseptics, acidic treatment, and medicinal plants, and advantages and disadvantages of each technique were described. Yet, further laboratory and clinical studies are necessary to be conducted in this area.

Keywords: micosin, vaginal cream, metronidazole, vaginosis.

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INTRODUCTION

Bacterial vaginosis (BV) is a complex polymicrobial disease in which primarily hydrogen peroxide-producing lactobacilli in the vagina are replaced with anaerobic bacteria (e.g. Prevotella and Mobiluncus spp.), Gardnerella vaginalis, Ureaplasma, Mycoplasma, and a number of other anaerobes (1). At the beginning, this syndrome, as non-specific vaginitis, was separated from the specific vaginitis created by Trichomonas vaginalis and other fungi. Later, Gardner introduced a new vaginalis syndrome caused by Haemophilus vaginalis that shortly became known as Corynebacterium vaginalis (2).

Main causes that disrupt the normal vaginal flora are unknown. It has been assumed that alkaline conditions resulting from frequent sexual intercourse or vaginal douching may have roles in disruption of normal vaginal flora. After disappearance of hydrogen peroxide-producing lactobacilli, it is difficult to re-establish normal vaginal flora and BV is common (3,4).

Douching, lack of vaginal lactobacilli, lack of condom use, frequent vaginal douche, new sex partner, and multiple sex partners are the risk factors of BV. However, women who have never been sexually active may also suffer from BV (5).

BV is often asymptomatic, but it is considered as the most common cause of vaginitis (6). Patients with BV may have a variety of symptoms or be completely asymptomatic. In fact, 50% of such patients are asymptomatic, but 50-70% complain about unpleasant vaginal odor (fishy or mold smell). Increased vaginal discharge is another important sign of bacterial vaginosis. Also, Unpleasant vaginal odor and vaginal discharge uniformly occur among the menstrual cycles are another important signs of BV. Yet, localized discomfort rarely becomes a problem in these patients (7).

Since the risk of other Sexually Transmitted Diseases (STD), such as herpes simplex virus, papilloma virus, and immunodeficiency virus (HIV), increase in the patients with bacterial vaginosis, this disease has become a global issue in the recent years (8,9). Furthermore, this disease is associated with other problems, such as infection after surgery, Pelvic Inflammatory Disease (PID), endometriosis, cervicitis, Urinary Tract Infection (UTI), and intraepithelial cervical neoplasia (10). Moreover, it can lead to spontaneous abortion, premature rupture of the fetal membrane, premature delivery, amniotic infection, low birth weight, postpartum endometritis, and cesarean stitched infection in pregnant women (11,12).

Obviously, easy, inexpensive, practical treatments which have fewer side effects are more acceptable to patients. The Centers for Disease Control and Prevention (CDC) recommended oral or vaginal metronidazole or clindamycin for BV treatment (13). Although these drugs can treat the disease temporarily, they are incapable of long-term treatment and prevention (14). Besides, consumption of antibiotics can lead to resistance in microorganisms responsible for vaginosis and also affect normal vaginal flora and lactobacilli (15). A previous study reported a recurrence rate of 70% within a few weeks after treatment with antibiotic therapy (16). In general, changes in natural acidic vaginal PH boosting from 4 to 4.5 could lead to BV (1). Evidence has indicated that the rate of bacterial resistance to metronidazole increased from 20% to 29% from 1993 to 2003 (17, 18). Resistances of gram-negative anaerobic bacteria to clindamycin have been proven, as well (19).

Beigi and colleagues also showed that treatment of BV with clindamycin increased resistant anaerobic microorganisms in the vagina (20).

The common side effects of metronidazole include diarrhea, vomiting, mouth or tongue irritation, dry mouth, metallic taste, vaginal discharge that did not exist before treatment, white plaques in the mouth or on the tongue, sore throat, fever, rash, dizziness, headache, loss of physical skills, lack of coordination, numbness, weakness or tingling in the fingers and toes, and darkening of the urine. Nonetheless, taking the drug with food reduces the gastrointestinal side effects. On the other hand, pancreatitis and severe central nervous system disorders (seizures, ataxia, and encephalopathy) are rare. The concomitant use of alcohol with metronidazole can cause nausea and vomiting. In general, medication should be prescribed with caution for the patients with central nervous system diseases. In addition, the drug should be adjusted for the patients using hepatic and renal medications. Metronidazole can exacerbate the anticoagulants effects of coumarin. Metronidazole and its metabolites are mutagenic in bacteria. Long-term and high dose administration of metronidazole in rats induced tumor formation. Thus, administration of metronidazole should be avoided in

pregnant and lactating women. Although metronidazole is not carcinogenic and does not cause fetal abnormalities in humans, some researchers believe that it is better to be used after the first trimester of pregnancy. It has also been recommended that after administration of 2 g metronidazole, breastfeeding should be discontinued for 12 to 24 hours (21). Moreover, vaginal application of metronidazole may be accompanied by complications, such as many vaginal discharges, yeast infection, and vulvovaginitis (22).

Clindamycin also can lead to the following side effects: dryness, redness and irritation of skin, scaling, tingling, and irritation of vagina (23). Considering the side effects and microbial resistance of antibiotic therapies, use of non-pharmacological therapies, such as alternatives methods, can be beneficial. Overall, non-pharmacological treatments of BV can be allocated into one of the following four categories:

- Probiotic therapy (such as treatment with lactobacilli capsules or probiotic yogurt): The goal of this method is restoration of normal vaginal flora and lactobacilli.
- Acidification treatments, such as buffered gels or creams and lactic acid gels, result in acidification of the vaginal environment and can cause re-growth of lactobacilli.
- Antiseptic treatments
- Complementary and alternative medicine (CAM), such as use of herbal remedies, having antibiotic properties. For example, tea tree oil has been used frequently in treatment of BV.
- The present study aims to review non-pharmacological methods for treatment and prevention of BV.

METHODS

In this study, more than 40 papers in the field of non-pharmacological treatments for BV were investigated. The articles were available in PubMed, Elsevier, and Google scholar databases. Persian literature was also studied. The keywords were searched from 2000 to 2014 and the relevant articles (which evaluated non-pharmacological therapies) were selected to be reviewed. The main searched keywords were BV treatment, alternative and complementary medicine, probiotic treatment, and antiseptic treatment.

RESULTS

In this study, various non-pharmacological treatment methods for BV were categorized into four groups.

Probiotic therapy

According to the the U.S. Food and Drug Administration (FDA) and World Health Organization (WHO), probiotics are microorganisms that with fixed-dose and therapeutic target enter the host's body (24). Treatment with probiotics can lead to mucosal modulation and increase the host's immune responses (25-27). The use of probiotics containing lactobacillus plays an important role in restoring the normal vaginal flora as well as in treatment and prevention of bacterial vaginosis. Two previous reviews confirmed the positive effects of probiotics on treatment of BV (28, 29).

Barrons and Tassone also investigated the effects of probiotics in their review studies. In these two studies, probiotics (lactobacilli) therapy for a period of 30 days was effective in 60% ($P=0.004$) and 88% ($P<0.005$) of the patients, respectively. Prevention of relapse was also reported in 35% ($P=0.004$) and 73% ($P=0.001$) of the patients, respectively. However, no association was found between probiotics and treatment of BV in 7 other studies (30).

In another study, Senok and colleagues examined the impact of treatment with probiotics. They emphasized that studies and trials with large standard probiotic administration were necessary (31).

Acidification

Researchers have indicated that BV results from the alkaline condition in the vaginal environment. Therefore, acidification of the vaginal environment could be a treatment approach. Nevertheless, the results of two clinical trials showed that administration of 5 ml acetic acid gel twice daily for 7 days or 5 g buffering acid once daily for 5 days failed to treat BV (32, 33).

On the other hand, the results of one other study showed that consumption of 500 mg oral metronidazole twice daily and 5 g lactic acid gel once daily for 7 days had better treatment effects and reduced the bad odor in comparison to treatment with oral metronidazole alone. Furthermore, lactic acid had no side effects and reduced the recurrence of BV (34).

Antiseptic treatment

Antiseptics have been used for more than half a century as a therapeutic method for treatment of bacterial vaginosis. In 2004, the effects of metronidazole and chlorhexidine were investigated in 458 women with BVin Italy. Chlorhexidine gel (2.5 g at any dose) and 500 mg vaginal tablets of metronidazole once daily for seven days were used by two different groups. Four weeks after the treatments, the success rates were 93% in the first group and 74% in the second group (35).

Another study investigated the effect of octadine hydrochloride and phenoxyethanol used in form of topical spray. According to the results, topical spray could lead to 58%-71% improvement after 7-14 days, while use of metronidazole alone resulted in a 61% improvement (36).

Verstraelen and colleagues (37) in a review article in 2012 investigated the effects of antiseptics on treatment of BV. They found that most studies in this field were either too old or their error rates were high. For example, major indices such as Amsel or Nugent were not used in diagnosis of the disease. Besides, control groups did not receive placebo or antibiotics in some studies. Moreover, none of the studies examined the side effects of antiseptics. The side effects of antiseptics are very serious and critical, because povidone-iodine may damage to the epithelium of the vagina, thus, the vaginal environment prepare for entrance of harmful elements such as HIV virus (36).

CAM

Nowadays, CAM is a suitable treatment method for various health problems because of being safe, effective, affordable, and less aggressive compared to conventional therapy. These treatment methods are based on the use of natural materials (38). More than 80% of people in developing countries prefer to use traditional medicine and medicinal herbs (39).

Numerous studies have investigated herbal therapies for the treatment of BV (41). A previous study evaluated the use of CAM in 481 women with chronic BV in 2011. The results demonstrated that 64.9% of the women used CAM, and yogurt and acidophilic tablets were the most common treatments used by the women. In that study, most of the women were young and vaginitis had negative effects on their working and social life. Before using CAM, they had visited doctors for two or more times. Diagnosis of BV, itching, and irritation were the factors that led the patients to use CAM (42).

Ahmad et al. conducted a research entitled "In vitro effects of aqueous extracts of garlic (Allium sativum) and onion (Allium cepa) on Trichomonas vaginalis" and showed the inhibiting effects of garlic and onion on proliferation of parasites. In that study, the minimum times for parasitic elimination effects of the extract at 75, 62.5, 50, and 37.5 mg/ml concentrations were 24, 48, 72, and 96 hours, respectively. However, 25 mg/ml concentration of the extract could not inhibit parasitic proliferation. In the end, they concluded that compared to metronidazole, onion and garlic had considerable inhibitory effects on T. vaginalis (43).

Another study investigated the effect of clotrimazol vaginal cream compared to garlic extract vaginal douche on treatment of vaginal candida infection in 100 non-pregnant women. The results revealed no significant difference between the percentages of successful responses in the users of vaginal garlic extract douche and vaginal clotrimazole cream(44). Similarly, bahadoran et al. came to the conclusion that vaginal cream containing garlic and thyme was as effective as clotrimazole vaginal cream in treatment of candida vaginitis, and there were no differences between the responses to treatment by these two drugs(45). Garlic contains certain types of phytochemicals, such as saponins, flavonoids, and sulfur-containing compounds, which act against infectious agents (46).

CJ Watson and his colleagues in 2014 evaluated the effect of oral garlic on reducing the number of candida during the second half of the menstrual cycle in clinically asymptomatic women. The participants

included 63 women with candida-positive cultures without the clinical symptoms of vaginal infection. These women were randomly divided into two groups using garlic or placebo tablets 2 times a day for 14 days. The results showed no evidence of anti-fungal effect of oral garlic consumption on candida infection. (47)

In another study in 2010, the antimicrobial effects of garlic and ginger extract tablets on oropharyngeal microbial flora were assessed in vitro.. In the intervals between the screenings, agar diffusion method was used for investigation of antimicrobial activity against Escherichia coli, Staphylococcus aureus, and Candida albicans. In that study, oral nystatin tablets were used as the standard treatment which inhibited the growth of all these organisms, but the garlic and ginger complex only inhibited the growth of C. albicans. Therefore, it was concluded that garlic and ginger could be used as a tablet formulation for treatment of non-resistant oral thrush (48).

CONCLUSION

In this study, over 40 articles on treatment of BV were reviewed. Accordingly, non-pharmacological treatments for BV were classified into four categories: probiotic, antiseptic treatment, acidification, and CAM, the fourth of which being the most important and having a particular status in these researches.

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