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ORIGINAL ARTICLE/ARTICLE ORIGINAL

Comparison of vaginal ointment of honey and clotrimazole for treatment of vulvovaginal candidiasis: A random clinical trial

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KEYWORDS
Honey;
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Summary
Background and objective. — Vulvovaginal candidiasis (VVC) is the most prevalent vaginitis in women, accounting for 10 million medical referrals a year. Vaginal clotrimazole is a drug of choice for VVC treatment. However, increased drug resistance to this microorganism has led to an interest in naturally derived antifungal drugs. This study was conducted to compare honey vaginal ointment and clotrimazole vaginal ointment for VVC treatment.
Methods. — Eighty women diagnosed with VVC were assigned to two groups for honey ointment and clotrimazole ointment treatment using a simple randomization rule. The ointments were applied at night for seven days. The disease symptoms including inflammation, vaginal discharge, and irritation at baseline in the fourth and eighth days of treatment were examined and compared between the two groups. The data was analyzed by SPSS version 20 with the Friedman test, Chi-square test, and independent *t*-test. $P < 0.05$ was considered as the significance.
Results. — The two groups were similar for inflammation severity, irritation, and discharge at baseline. In both the groups, the symptoms disappeared after treatment. On the eighth day of treatment, there was a significant difference in inflammation and vaginal discharge between the

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two groups. Inflammation ($P = 0.002$) and vaginal discharge ($P = 0.003$) recovered better in the clotrimazole group. But there was no significant difference in irritation severity and satisfaction with treatment between the two groups. In the two groups, no side effects were reported.
Conclusion. — Honey contributes to treating VVC. Thanks to the popular positive attitudes of honey, its availability, no need for sterility, and its cost-effectiveness, it is a choice of treatment for VVC.

Introduction

Vulvovaginal candidiasis (VVC) is one of the most prevalent infections and the second-most common reason for vaginitis in women [1]. On an average, 75% of women are estimated to probably acquire VVC at least once throughout their lifetime. About 40—50% of women report VVC recurrence and approximately 5% suffer from repeated recurrence during their lifetime [2,3]. In 80—92% of the cases, the reason for VVC is *Candida albicans* (*C. albicans*), and in the rest, the reason is other species of *Candida* spp [4]. *C. albicans* is the most common fungus found in human mucous membranes including the oral cavity, esophagus, gastrointestinal tract, bladder, and genital tract [5,6]. When the vaginal ecosystem is disturbed, *C. albicans* appears to be an opportunistic pathogen and causes infection. Lactobacillus is a gram-positive anaerobic bacteria that acts as an important regulator of normal vaginal flora and is able to regulate the growth of other natural flora of the vagina [7]. The prevalence of VVC has been reported in different communities. For example, the prevalence has been obtained as 19.6% in 1100 women from four randomly selected cities in Iran. However, in women who suffer from vaginitis, VVC accounted for 46.4% of infections [8].

The most significant and prevalent symptoms of VVC are itching and severe irritation of the genitals and urinary tract, vaginal inflammation, and dysuria [9]. The diagnosis of VVC is made by a wet smear in saline or potassium hydroxide 1%, and then by detection of filamentous structures, mycelium, and pseudophilus under the microscope [10].

The symptoms of and complications due to VVC and their treatment lead to developing complications, wasting time, and imposing stupendous costs on patients. This disease, particularly if recurrent, is a physical and mental disease causing stress in patients [11]. Vaginal clotrimazole is a drug of choice for treatment of candidiasis but repeated recurrence and the side effects of azole antifungals have caused considerable interest in the use of natural remedies in women. In addition, increased resistance of *C. albicans* to antifungal drugs has caused researchers to study naturally derived antifungal drugs extensively [12].

Today, detection of antibacterial agents or natural products working for highly resistant pathogens is pressing [13] and one of which is honey.

Honey is a natural sweet substance that is produced by bees from the nectar of plant blooms [14,15].

Human beings have long used honey as not only valuable food but also medication. In the Middle East and among Muslims, honey is valued greatly. The Holy Quran says, ''From the bee abdomen a nectar with various colors comes out which is medication and healing for people'' (Surah Nahl, Verses 68—69). The Prophet of Islam (PBUH) said: ''God put blessings in honey in which there is medication for pains'' [16] In addition, honey is known as a disinfectant of the womb in Iran's traditional medicine [17].

Honey is a substance that does not perish, does not need to be kept refrigerated, and can be stored at room temperature. Pure honey acts as a sterilizing substance and prevents any microbial growth in culture medium [18,19]. Honey is an antibacterial and anti-*C. albicans* compound. Studies have demonstrated the bactericide, bacteriostatic, antiviral, antioxidant, antifungal, anti-salmonella, and anti-coliform effects of honey [15,18,20—22].

Gavanji and Larki's study (2015) showed that honey propolis exerted better effects on antibiotic compared to some plant species such as thyme and cinnamon [23]. The studies of Mousavi and Tabatabaei Chehr also confirmed the efficacy of intra-vaginal honey propolis on the symptoms due to *C. albicans* [11,24].

In vitro and clinical finding of studies on the growth inhibition of various fungal species, including *C. albicans* for honey, have been promising, and attributed to high acidity and osmolarity as well as high hydrogen peroxide and low levels of diastase, invertase, glucose oxidase, catalase, phosphatase, and amylase in honey [1].

The medication that is used for vaginitis treatment should be prescribed in such a way that useful bacteria (for example, lactobacillus), which contributes importantly to preserving the ecosystem, is not eliminated. In an in vitro study, honey caused the inhibition of *C. albicans* growth without affecting the growth of lactobacillus [25].

Despite the in vitro study of honey's effect on *C. albicans*, little research has so far been conducted to investigate and compare the effects of the vaginal application of honey and clotrimazole on *C. albicans*. Therefore, a comparative study on the effects of honey cream and clotrimazole cream on VVC symptoms seems necessary.

Materials and methods

This double-blinded clinical trial study was conducted in the Gynecology Clinic of Hajar Hospital, Shahrekord, Iran, from May 2014 to February 2015. The study population consisted of women with the following inclusion criteria: 1. having VVC symptoms (including clumpy, white, cottage cheese-looking discharge as well as inflammation and irritation of the vulva and vagina); 2. confirming *C. albicans* infection by vaginal smear and directly observing *C. albicans* under microscope; and 3. agreeing to participate in the study. The exclusion criteria consisted of the following: 1. being pregnant; 2.

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