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Original Article

Investigating the therapeutic effect of vaginal cream containing garlic and thyme compared to clotrimazole cream for the treatment of mycotic vaginitis

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Abstract

BACKGROUND: Vaginitis is the most prevalent gynecological problem for which women look for treatment and is responsible for 10 million physician visits annually. Use of herbal treatments has been recorded in many of patient groups as well as in general populations to increase health level. The present study was conducted with the purpose of determination and comparison of the effect of vaginal cream containing garlic and thyme compared to clotrimazole cream for the treatment of mycotic vaginitis.

METHODS: This clinical trial is a prospective, multivariate, single-blind, two-stage, two-group study with randomized assignment of samples into the two groups. From the clinics in Isfahan in 2010, 64 cases (32 individuals in each group) entered the study. Data collection was accomplished by demographic information questionnaire and clinical performance checklist, and data analysis was performed by SPSS 16.0 software.

RESULTS: Abundance distributions of clinical symptoms (vaginal discharge; vulval erythema and edema), patients' complaints (secretions, itching, dyspareunia, painful urination, and vaginal irritation) and clinical symptoms (existence of germinating hypha, acidity under 4.5, and culture of vaginal secretions) were different in each group prior to and after the intervention; these factors however were not different between the two groups before and after the intervention.

CONCLUSIONS: The vaginal cream containing garlic and thyme is effective as much as clotrimazole vaginal cream for the treatment of candida vaginitis and there is no difference between responses to treatment by these two drugs.

KEY WORDS: Mycotic vaginitis, clotrimazole, garlic, thyme.

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Gynecological infections are among women's common diseases. Vaginitis is the most prevalent gynecological problem for which women seek for treatment and is annually responsible for 10 million physician visits.[1] Valiani et al quoted from Gor in their paper in 2006 reported the prevalence of vaginitis in American women's clinics as 5-15% and in STD clinics as 32-64%. They also stated that the global prevalence of vaginitis is not obvious, but it is probably similar to that estimated in USA.[2]

In the recent century, prevalence of vaginal candidiasis has increased noticeably. This infection is the highest prevalent infection in Europe. Also in the United States the mycotic vaginitis has experienced a remarkable increase. This disease is the most common cause that female patients refer to gynecologists and midwives, and is the first cause for consulting with physicians.[3,4] In total, candidiasis is the second most common vaginal infection. In the United States, annually 13 million cases of mycotic vulvovaginitis occur.[5] Approximately 70% of all women experience a mycotic vulvovaginitis at least once during their life. In addition, roughly 40-50% of women may experience a secondary episode of candidiasis vulvovaginitis in their life

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whereas 5% of women report the recurrence of candidiasis vulvovaginitis.[4] The number of patients suffering from candida vaginitis in Iran is unknown. In the United States, three out of each 4 women are infected with candidiasis vulvovaginitis at least once during their life.[2] In a study by Jamilian and coworkers, prevalence of candida vaginitis was reported in patients without vaginitis history as 58.33% and in patients with recurred vaginitis as 33.3%.[6] In their study, Ahmad et al reported candidiasis vulvovaginitis in 20.47% of women.[4] Slight invasion of *Candida* to epithelial cells of genitals causes itching and inflammation in a wide extent. This is due to interference of a toxin or mycotic enzyme in disease pathogenesis. Overgrowth of *candida* may be the result of the inhibition of vagina's natural flora bacteria, decrease in local cellular immunity, change in metabolic and trophic environment of vagina, and unknown mechanisms.[7] Though this disease rarely threatens the life, its consequences include serious pathogenesis, loss of work force, and costs.[3] Currently, antifungal drugs are increasingly used both as preventive and treating agents, which in turn causes species resistant to drug. The increase in number of drug-resistant species and observation of numerous cases of treatment failure encourage researchers to seek for novel drugs and study the therapeutic effect of combining different drugs with extracts of medicinal plants in order to reach better results.[8] Annually 500 million dollars of antifungal drugs are sold which makes them a group of best-selling drugs against vaginitis.[7] It seems that the number of *Candida* infections other than *Candida albicans* infections is increasing. These infections do not respond well to treatment by azoles such as fluconazole.[9] One of the common drugs for the treatment of candidiasis vaginitis is the vaginal cream clotrimazole 1%; its side effects include increase of hepatic enzymes, painful urination, and depression, which may occur by drug systematic absorption. Side effects such as irritation or contact dermatitis may also be observed. It is prescribed with caution for patients suffering from hepatic or kidney disorders. Systemic administration of this drug during pregnancy has not been teratogenic for small animals under study, but it has been embryotoxic. Therefore, this drug should be used with caution during pregnancy and even breast-feeding, since it is not obvious whether it enters into mother's breast milk.[10] Bacterial vaginitis and candidiasis vulvovaginitis are the most prevalent causes of marked vaginitis. Due to high recurrence of vaginitis, many women quit antimicrobial treatments and use complementary treatments.[11] These treatments have higher admissibility because of different advantages including their fewer side effects, patient's easier tolerance, lower cost, and high acceptability by the patients during administration. Many medicinal plants are available regionally, especially in developing and less-developed countries. Furthermore, herbal medicines are less encountered with drug resistance. Considering all these advantages, herbal medicines are increasingly become the leading compounds.[12]

Garlic is one of the oldest cultivated plants whose origin is Middle East. It has been used as flavor, food, and regional medicine for more than 4000 years, and it is a herbal medicine on which a wide range of studies has been conducted.[13] Garlic's allyl sulfide compounds have been introduced as antimicrobial agents. Effect of garlic extract has been established in decreasing and preventing the fungal enzymatic activities.[14] Scientists have concluded that not only garlic kills bacteria, but also it enhances body immunity against different diseases. In addition to its fewer side effects compared to antibiotics, garlic has positive side effects. It destroys both viruses and bacteria. Also, garlic destroys bacterial yeasts and increases the immune system of body.[15] It causes nitrite oxide produced by macrophages which in turn enhances body's resistance against fungi, especially *Candida albicans*.[16]

Thyme is another medicinal herb with antibacterial which has been studied extensively. Its essence is among the 10 well-known essences with antibacterial, antifungal, and antioxidant characteristics; it also naturally maintains food and delays senescence in mammals, and has a special position in world trade. Red thyme oil

has been officially presented as microbicide since 16th century. Its antimicrobial property is due to thymol and carvacrol and is extensively used in mouth rinse products, toothpastes, soaps, detergents, and different antiseptic products.[17] This research aims to determine and compare the therapeutic effect of vaginal cream containing garlic and thyme with that of clotrimazole cream for the treatment of mycotic vaginitis.

Methods

This single-blind clinical trial is a prospective, multivariate, two-stage, and two-group study, such that patients did not know whether the drug was clotrimazole or herbal vaginal cream. All married women at reproductive age referring to women's clinics of Alzahra Hospital and Shahid Beheshti Hospital in Isfahan during 2010 who complained for genital infections were considered as the population under study. Simple sampling as a non-probabilistic sampling method was used to choose the samples, while simple random sampling was employed to assign the samples to the two groups, such that those patients visiting the clinics who met the essential criteria were chosen. The codes 1 and 2 (representing the treatment with clotrimazole vaginal cream and the treatment with vaginal cream containing garlic and thyme, respectively) were written down on small pieces of paper, whose number was equal to that of the patients, and put into a pocket. The samples were subsequently put into the two groups through choosing a paper from the pocket. 40 samples were assigned to the group with garlic and thyme treatment, whereas 38 samples were assigned to clotrimazole group. Finally, 32 individuals remained in each group.

The criteria to be met were as follows:

- Women were 18-49 years old and were married;
- They had a single sexual partner and they themselves were the only sexual partner of their respective spouse;
- They had not used antibiotics, immunosuppressive drugs, or vaginal drugs 14 days before the study;
- They did not suffer from trichomonal vaginitis, bacterial vaginitis, or cervicitis based on direct smear, which was controlled by examining the patient's discharge;
- They were not at pregnancy or breast-feeding stage and did not consume alcohol;
- They were not menopause (priority of not being menopause was higher than age criterion, i.e. they must have been non-menopause even if they were younger than 49 years old);
- They had not previously suffered from known medical diseases such as diabetes, immune system attenuating diseases (such as AIDS) or use of immunosuppressive drugs, auto-immune diseases, coagulation disorders, and epilepsy;
- They were not menstruated, and had no bleeding or breakthrough bleeding when they visited the clinics;
- Candidiasis culture was in agreement with clinical symptoms and patient's complaints.

The research was explained for those patients who met the study criteria and sampling was performed after getting their written consent. These patients were in lithotomy posture for checkup and sampling. After administering sterilized speculum and examining vagina and cervix regarding inflammation and unusual findings, the discharge was controlled concerning color and properties. Discharge specimen from upper part of the lateral vagina wall was put on two glass slides by sterilized swap. One glass slide was wet with a drop of KOH solution 10% and light microscopy with magnification of 40x was utilized for Whiff test and observing candida hypha. The second glass slide was wet with a drop of normal saline and put under microscope with magnification of 40x (Microse Co., Australia) to see cue cells and examine the existence of trichomonal vaginitis. The pH value of vaginal discharge specimen was determined by pH paper. The specimens were transferred to laboratory of Alzahra Hospital for fungal culture. The test results were available at most 48 hours later.

In case of positive Whiff test or not observing candida hypha in the first glass slide or the existence of either clue cell or trichomonal vaginitis in the second glass slide, the specimen was re-

moved from study. The disease recognition criterion was based upon a collection of symptoms, including the existence of clinical symptoms, patient's complaint, and positiveness of all laboratory indicators. If clinical symptoms and patient's complaint indicated mycotic vaginitis and all laboratory indicators were positive except that candida hypha was not observed by microscope, it was recognized as mycotic vaginitis, since candida hypha cannot be seen under microscope in 25-30% of the cases when there is certainty of the disease occurrence. To confirm the diagnosis, culture in agar sabouraud was used. For treatment, vaginal cream containing garlic and thyme was prescribed for 7 nights in the test group, and clotrimazole vaginal cream was prescribed in the control group for 7 nights. For their next visit, all activities of the first visit were repeated and the patients were asked for drug side effects. Successful therapeutic response was considered as the absence of candida hypha under microscope together with negative culture of candida. Furthermore, if the group treated with the cream containing garlic and thyme did not show an improvement in the second visit, they were treated with clotrimazole vaginal cream.

The obtained data were analyzed using the statistical software SPSS 16.0 as well as McNemar and Chi-square statistical tests.

Results

Mean age of the population under study was 30-37 years. Also, their weight was 65-70 kg. Mean married life of the samples was 15-20 years (Table 1). Mean number of previous pregnancies was 2.7. Education level of most of the samples was under diploma (60-75%) and most of them were housewives (93.8%); their husbands were mostly self-employed (30-50%).

Comparison of abundance distribution of clinical symptoms, which included the existence of vaginal discharge, vulva erythema, and vulval edema, indicated that there was no significant difference ($p > 0.05$) between the two groups before and subsequent to the treatment according to Chi-square test. However, vulva erythema was different between the groups after treatment ($p = 0.02$), which was decreased more in the group who consumed the vaginal cream containing garlic and thyme (9.4 compared to 34.4). According to McNemar test, significant differences were observed in both groups prior to and after the treatment ($p < 0.05$) and clinical symptoms were improved after the treatment. The clinical symptoms did not get more serious in the two groups.

Abundance distribution of therapeutic side effects (Table 2) in the two groups showed that both drugs caused side effects in the patients. Most side effects were as "other side effects" with percentage of 9.38% in clotrimazole group and 34.4% in garlic and thyme group.

Discussion

The Considering the mean age in the present study, it should be noted that Haghighi et al in their study stated that prevalence of candidiasis vaginitis with clinical diagnosis in the three age groups 21-35 years old, older than 35 years, and 20 years old or younger was 64.4%, 3.8%, and 3.8%, respectively.[7] Their results are in agreement with those of the present study. Like similar studies, the reproductive age was considered

Table 1. Comparison of mean individual characteristics in the test and control groups

Groups	Clotrimazole group				Garlic and thyme group				Independent *t*-test	
Variable	Max	Min	S.D.	Mean	Max	Min	S.D.	Mean	p-value	t
Age	49	19	9.4	35.3	49	20	8.7	36.3	0.65	0.45
Weight	104	45	13.8	68.3	95	45	11	66	0.47	0.73
Married life	33	0	11.4	16.3	32	2	9.3	18.3	0.42	0.8

Table 2. Abundance distribution of therapeutic side effects during and after treatment with the drugs

Groups	Clotrimazole group		Garlic and thyme group		Total	
Side effects	**Number**	**Percentage**	**Number**	**Percentage**	**Number**	**Percentage**
Nausea	1	3.12	3	9.38	4	12.5
Vomit	1	3.12	3	9.38	4	12.5
Vaginal dryness	1	3.12	1	3.12	2	6.24
Vaginal irritation	2	6.25	1	3.12	3	9.37
Other side effects	3	9.38	11	34.4	14	43.78
Total	8	24.99	19	59.4	27	84.39

in this study. Regarding mean married life, Simbar and coworkers obtained mean and standard deviation of married life in the two groups of *Zataria multiflora* and metronidazole as 12.02 (5.95) and 12.3 (6.45), respectively.[18] Concerning the number of previous pregnancies in the current study, Walling [19] in a study in the United States reported that most candidiasis vaginitis samples belonged to patients which had no previous pregnancies, which does not agree with the present study. The difference may be due to point that pregnancy age in Iranian society is probably lower than that in Western countries; in Iranian women, vaginitis is usually observed after beginning of sexual activity, marriage, and pregnancy, whereas in other countries many of women who have sexual relationship without marriage complain about vaginitis while they usually do not get pregnant. Regarding the patients' education level which was often under diploma, Simbar et al in their study obtained the mean education years of test group as 9.05 ± 4.37 and for control group as 9.52 ± 3.61, showing that education of the majority of the samples under study was lower than diploma.[18] Most husbands in this study were self-employed, Haghighi and colleagues in their study reported that the prevalence of *candida* in women whose husbands were laborer, employee, self-employed, or had other occupations was 29.5%, 24.2%, 34.8%, and 10.6%, respectively.[7]

In the current study, decrease of all clinical symptoms was the same in the two groups and both treatments identically improved the clinical symptoms, except in vulva erythema which was significantly better improved in the group who consumed vaginal cream containing garlic and thyme, compared to clotrimazole group. This may be attributed to the fact that clotrimazole has side effects such as skin irritation, redness, and edema, and on the other hand being anti-inflammatory is one of the properties of thyme.[20,21] It should also be mentioned that concerning clinical symptoms and patients' complaints, since Yes/No questions were used, the symptoms were recorded as positive even if the symptoms were decreased but not resolved completely. In their study, Kordi et al indicated that regarding the decrease in clinical symptoms (50% or more decrease in total value of clinical symptoms) during 1-2 weeks after the end of the treatment, the two groups (one group consumed garlic and the other group consumed clotrimazole) were not significantly different ($p>0.05$), such that the clinical symptoms were decreased 50% or more in 83% of garlic group and in 92% of clotrimazole group.[22]

The results provided in Table 2 show that both groups experienced side effects. Most

side effects in test and control groups were as "other side effects" (including itching, vertigo, hives, faint, headache, ectopic beats, and xerostomia) and the fewest side effects belonged to vaginal dryness. Also, most of the complaints in the "other side effects" belonged to itching.

Finally, considering the findings of this research, this medication can be used with higher confidence for treatment of candidiasis vaginitis in patients who tend to consume herbal compounds and medications. Furthermore, as a novel treatment, this medication can be employed to patients who have gained resistance to clotrimazole.

The authors declare no conflict of interest in this study.

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