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Comparing the effects of Mycozin and Clotrimazole 1% creams on vaginal candidiasis: a triple-blinded randomized controlled trial

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Clotrimazole 1% and Mycozin vaginal cream have been reported to be effective in relieving the symptoms of vulvovaginitis caused by Candida. The resistance to azole compounds, and the side effects of chemical drugs have been reported following azole therapy. It was hypothesized that Mycozin is at least as effective as Clotrimazole in treating vaginal candidiasis. This equivalent, triple-blinded, randomized clinical trial was conducted on 126 patients who complained of vaginal itching referred to Al-Zahra Teaching Hospital, Tabriz, Iran between September 2023 and May 2024. Participants were divided into two groups, i.e., Mycozin (n = 64) and Clotrimazole 1% (n = 62), using the block randomization method. The patient's complaints, clinical signs, the pH and culture of the secretions was recorded before and after treatment. The patient's improvement, level of satisfaction, and side effects were recorded. The data were analyzed using Pearson chi-square test, ANCOVA, and Mann–Whitney U test. There was no statistically significant difference between the two groups regarding the mean pH (Adjusted mean difference: 0.01; 95% Confidence Interval (CI): −0.20 to 0.21, P = 0.965), and microscopic evaluation (Odds Ratio (OR): 0.61; 95% CI; 0.28 to 1.36, P = 0.230). After the treatment the frequency of itching in the Clotrimazole group (N = 13; 22.0%) was lower than that of the Mycozin group (N = 26; 43.3%) (OR: 0.37; 95% CI: 0.17 to 0.82; P = 0.013). There was no statistically significant difference in other symptoms and signs before and after the treatment (P > 0.05). Also, there was no statistically significant difference between the two groups in the level of satisfaction (P = 0.056) and patient improvement (P = 0.074). The side effects of treatment with Mycozin and Clotrimazole were observed in eleven and five patients, respectively. Considering the efficacy of Mycozin vaginal cream in eliminating most of the symptoms and signs associated with vaginal candidiasis and its positive effect in negating the results of culture, it can be used as a suitable alternative in the treatment of vaginal candidiasis in patients interested in herbal medicines and resistant to azole compounds.

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Keywords Mycozin, Clotrimazole, Vaginal candidiasis

Abbreviations

ANCOVA	Analysis of covariance
IRCT	Iranian Registry of Clinical Trials
SDA	Sabouraud dextrose agar

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ITT	Intention-to-treat
SD	Standard deviation
CI	Confidence interval

As far as infections of the female genital tract are concerned, vaginitis is the most common and one of the most frequent reasons why women visit a clinic[1]. They account for about 80% of non-routine visits in non-pregnant individuals[1,2]. Candida albicans, Trichomonas vaginalis, and Gardnerella vaginalis are the three most common factors causing vaginitis[3,4], and infection with Candida albicans is the second most common cause of vaginitis[1]. On average, 75% of women suffer from vulvovaginal candidiasis at least once in their lifetime[5,6]. In Iran, in one study the prevalence of vaginitis was reported to be 41.3%. Of the three infectious agents mentioned, Candida was the most common pathogen with an incidence of 47.4%[7]. Predisposing factors for this type of vaginitis include uncontrolled diabetes, obesity, use of birth control pills and antibiotics, use of intrauterine devices for contraception, pregnancy, and a weak immune system[1,8–10].

Vulvovaginal candidiasis is accompanied by cheesy secretions, inflammation and redness, severe itching, and sometimes ulcers or abscesses, and in severe cases, it also affects the perineum and the inner parts of the groin area. It can even cause dysuria or dyspareunia[1,11–13]. All these complications can affect the quality of life of those affected, especially their sexual life. As sexual relationships play an important role in mental health, the treatment of vaginal candidiasis is of particular importance[14]. Various studies have used different drugs such as nystatin, antifungal agents with azole compounds such as Clotrimazole, Miconazole, Ketoconazole, and herbal remedies such as Mycozin, Zataria multiflora, etc.[1,15,16].

Clotrimazole 1% vaginal cream is one of the most effective drugs in the treatment of vaginal candidiasis. However, like most chemical medications, it has side effects such as burning, itching, redness, and skin dryness[17]. In addition to treatment with chemical antifungals, the possibility of developing microbial resistance due to their repeated use is high. Candida species are especially concerning because they are a leading cause of systemic fungal infections with mortality rates reaching 50%. Most Candida infections are caused by Candida albicans and in a study 49.2–100% of isolates of this species that collected from vaginal swab samples are reportedly resistant to some azoles[18,19]. Also, in taking medication, patients may complain of side effects such as changes in the taste in the mouth, nausea, and diarrhea[17].

Garlic, scientifically known as "allium sativum", from the tulip family (Liliaceae), has long been used in the treatment of infections[20,21]. It is a powerful antifungal herb with antimicrobial properties[22]. Thyme, from the mint family, also is another herb known to treat bacterial and fungal infections[23]. Meanwhile, Mycozin vaginal cream has been reported to be effective in relieving the symptoms of vulvovaginitis caused by Candida[15]. The ingredients of this cream are garlic and thyme. Thyme extract was added to the cream to neutralize the smell of garlic. It has an antifungal effect and synergistically enhances the therapeutic effect of garlic[24].

In a single blind study with 64 participants, the results showed that a vaginal cream containing garlic and thyme was as effective as a Clotrimazole vaginal cream in the treatment of vaginal candidiasis, and there was no difference in the responses to treatment with these two drugs[25]. Farshbaf-Khalili et al.[16] showed that the effect of the three vaginal creams of garlic, Zataria multiflora and Clotrimazol was the same in the treatment of vaginal candidiasis, prevention of recurrence and improvement of clinical symptoms and signs. Khosravi et al[26] reported that the use of thyme vaginal cream was effective in reducing discharge and itching caused by vulvovaginal candidiasis.

The use of medicinal herbs is the oldest human approach to treat disease and it is used in many parts of the world, especially in regions with limited access to chemical medicines[27]. Considering the microbial resistance to azole compounds, especially Clotrimazole, the side effects of chemical drugs, the high prevalence of vaginal candidiasis, the tendency of people to use herbal medicines, the present study was conducted to compare the effects of Mycozin vaginal cream and 1% Clotrimazole vaginal cream in treating vaginal candidiasis. This decision is further supported by a previous study[25] that compared the two therapies; however, that study had limitations, including a single-blind design and a smaller sample size.

Study hypothesis

a. Mycozin vaginal cream is as effective as Clotrimazol 1% vaginal cream in eliminating laboratory-confirmed cases of vaginal candidiasis.
b. Mycozin vaginal cream is as effective as Clotrimazol 1% vaginal cream in eliminating symptoms of vaginal candidiasis.
c. Mycozin vaginal cream is as effective as Clotrimazol 1% vaginal cream in eliminating signs of vaginal candidiasis.
d. The mean pH of vaginal secretions is similar in both groups.
e. The treatment satisfaction is similar in both groups.

Methods

Study design and participants

This study is the result of a project approved by the Vice Chancellor for Research of Tabriz University of Medical Sciences under the ethical code (IR.TBZMED.REC.1402.112) and registration code (IRCT20120718010324N77) on the Iranian Registry of Clinical Trials website. This equivalent, triple-blinded, randomized clinical trial was conducted on 126 patients referred to Al-Zahra Teaching Hospital, Tabriz, Iran between September 2023 and May 2024.

The inclusion criteria were as follows: married women aged 18–45 years who had symptoms of vaginal candidiasis and were literate. The exclusion criteria were as follows: Suffering from chronic diseases such as

diabetes, acquired immune deficiency syndrome (AIDS), immune system disorders, depression, use of antibiotics and corticosteroids in the last two weeks, the presence of severe psychological distress in the last three months, such as the death of a first-degree relative. The other exclusion criteria were as follows: menstruation at the time of the study, use of oral contraceptives, presence of a sore or lump in the cervix when viewed with a speculum, the presence of a known pregnancy or breastfeeding at the time of the study, the use of other medications to treat vaginitis, recurrent vulvovaginitis (more than four times per year), abnormal uterine bleeding, allergy to herbal medicines and allergy to azole-containing agents.

Based on the study by Saffari et al.[28] regarding the incidence of negative cultures after treatment and using G-Power software, considering $P_1 = 0.77$, $P_2 = 0.52$ (assuming a non-inferiority margin of 25%, two-sided $\alpha = 0.05$), and power = 80%, the sample size was calculated to be 57 individuals in each group. With considering 10% attrition, the final sample size was 63 in each group.

Sampling

The convenience sampling method was used in this study. The researcher attended in Al-Zahra Teaching Hospital, Tabriz, Iran and after introducing and explaining the objectives of the study, obtained written informed consent from those who complained of vulvovaginal itching and discharge and were willing to participate in the study; A questionnaire on demographic characteristics and history of illness and complaints was completed.

The participants were examined in full compliance with ethical principles. After vaginal examination and direct observation with the speculum without the use of lubricant, clinical signs were checked and the pH of the secretions was recorded with a paper pH meter in the clinical observation checklist.

To diagnose vulvovaginal candidiasis, a sterile swab was taken from the posterior fornix of the vagina of the symptomatic women. The sample was placed in a tube containing sterile physiologic serum and cultured in Sabouraud Dextrose Agar (SDA; Merck, Germany) containing 0.05% chloramphenicol (Sigma Aldrich, USA) and incubated at 37 °C for 24–48 h; colonies were then streaked onto a slide and assessed microscopically after adding 1–2 drops of 10% potassium hydroxide (KOH 10%) to the slides. Light microscopy with magnification of 40× was utilized for observing candida hyphae and, in the case of growth of the fungus in the dextrose agar plate, the culture was considered positive.

In the case of a definitive diagnosis of vaginal candidiasis based on the secretion culture and the presence of yeasts on microscopic examination, participants were invited to visit the selected center to start treatment if they wished and were informed of the confidentiality of their information and the possibility of leaving the study at any time.

Randomization

Participants were divided into two groups, i.e., Mycozin (N = 64) and Clotrimazole 1% (N = 62), using the block randomization method, using Random Allocation Software (RAS) with a block size of 4 and 6. The researcher, all participants and outcome assessor were blinded.

Mycozin and Clotrimazole creams, in similar packaging, were labeled and numbered from 1 to 126 according to the allocation order by a person not involved in the sampling and data collection. After random and concealed allocation, the drugs were administered to each participant in the order of their participation in the study.

Both creams were produced by the Goldaru Pharmaceutical Company in Isfahan and were similar in shape, color, and size. In addition to the medication, the participants received seven applicators, an information booklet on how to take the medicine, dietary and health recommendations, abstaining from sexual intercourse during treatment or using a condom during intercourse, and a form to document the use of the medication after each application. They were also told how to take the medication in the form of an applicator equivalent to five grams for a week at bedtime and to come back for a follow-up 10–15 days after starting the treatment. They were also asked to pay attention to hygiene during the treatment period and not to use vaginal douches, vaginal creams, and other medications for vaginal candidiasis.

Follow up

During the follow-up examinations, the patient's complaints were asked again and recorded in the checklist. In addition, the patient was examined, the clinical signs were recorded, the pH of the secretions was measured, a sample of the vaginal secretions was taken for culture, and the results were recorded on the appropriate forms. The patient's improvement, level of satisfaction, and side effects were recorded. All untreated patients were treated with the routine treatment (Clotrimazole 1%).

Data collection tools

Socio-demographic characteristics form

This form, which was completed by participants before treatment, included the variables of age, education, work status, husband's education and occupation, last birth method, contraceptive use, date of current contraceptive use, gravida, para, medical history, medication history, and age at first marriage.

Clinical observations checklist

This checklist, completed by the researcher before and after the treatment, included items about the cervix's appearance, vulvovaginal erythema, amount, consistency, color, odor, and appearance of discharge. The vaginal discharge pH and culture were also evaluated.

Patient complaints checklist
This checklist completed by the participants before and after the treatment included items about vaginal odor, dysuria, urinary frequency, itching, itching in intercourse, lower abdominal pain, irritation in intercourse, and dyspareunia.

Content and face validity were used to determine the validity of the socio-demographic characteristics form, clinical observations checklist, and patient complaints checklist.

Data analysis

The collected data was analyzed using SPSS 21 software and the Kolmogorov–Smirnov test was used to assess the normality of the data. The Independent t, Pearson chi-square and Fisher exact tests were used to compare socio-demographic and obstetric characteristics between groups. The Pearson chi-square test was used to compare clinical observations, patient complaints, and microscopic evaluation before and after treatment. The chi-square test is a non-parametric (distribution-free) test used to analyze group differences when the dependent variable is measured at the nominal level[29]. An ANCOVA was also performed to compare vaginal pH after treatment with adjusting of baseline value. ANCOVA is a powerful statistical method that analyzes the differences between groups means while controlling for the effects of at least one continuous covariate to account for baseline differences[30]. The Mann–Whitney U test was used to compare level of satisfaction and patient improvement after treatment because the variables are single ordinal with no specific distribution[31]. The intention-to-treat (ITT) method was used for data analysis. The p-value < 0.05 was considered significant.

Results

The present study was performed on 126 patients referred to Al-Zahra Teaching Hospital from September 2023 to May 2024. A total of 166 women were examined, of whom 40 were excluded due to not meeting the inclusion criteria or their unwillingness to participate. Finally, 126 individuals participated in the study and were randomly assigned to Mycozin and Clotrimazole 1% groups. Four participants in the former group and three in the latter group were reluctant to continue the study (Fig. 1).

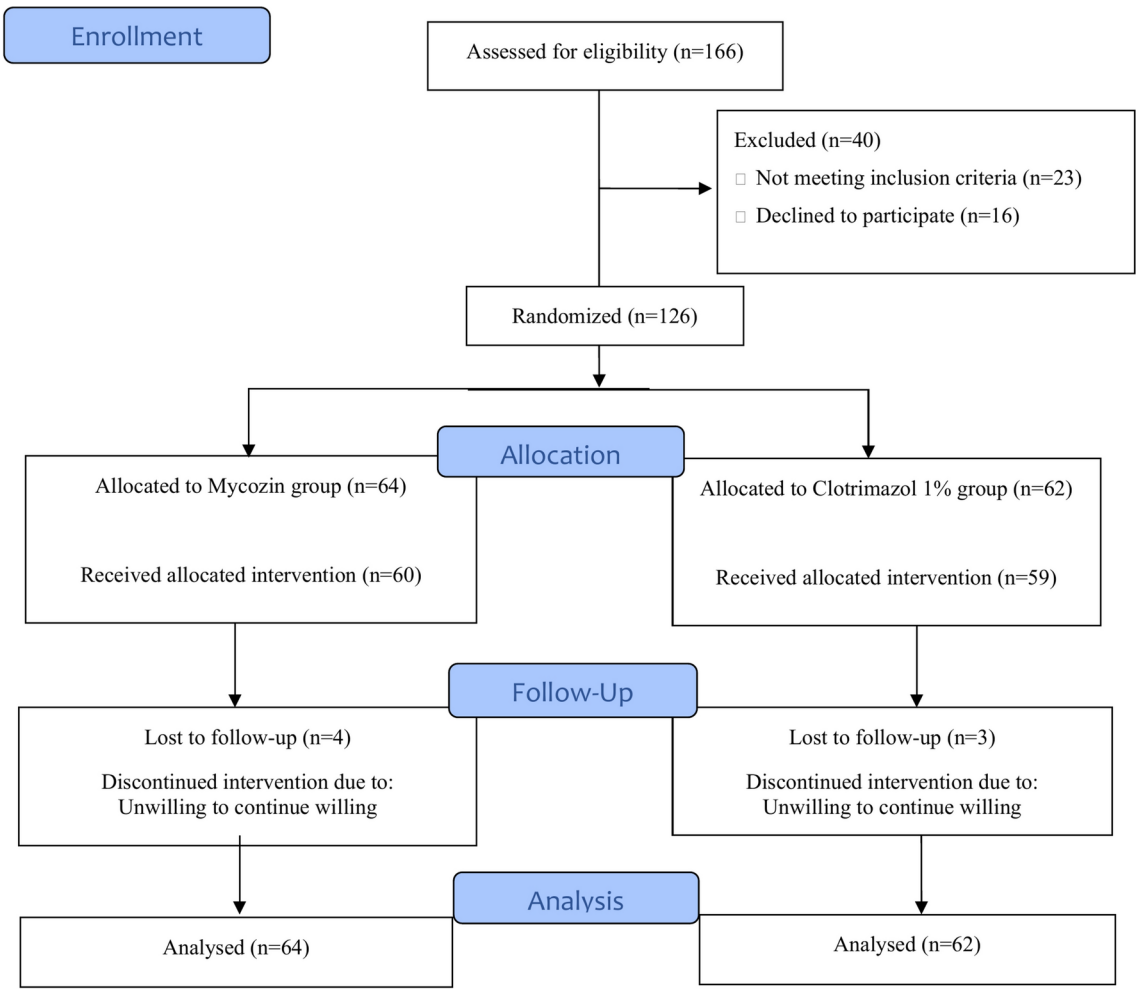

Fig. 1. Flow chart of the study.

The mean (SD) age in these two groups was 39.23 (6.59) and 39.21 (6.56) years, respectively. Most of the participants had a diploma, were housewives, and applied fertility awareness methods to prevent pregnancy. This study did not show a statistically significant difference between the two groups regarding socio-demographic characteristics (Table 1).

The mean (SD) pH before the intervention in the Mycozin and Clotrimazole 1% groups was 4.77 (0.77) and 4.81 (0.84), respectively. 10–15 days after the treatment, the mean (SD) pH in these groups was 4.92 (0.88) and 4.95 (0.83); respectively (Fig. 2). There was no statistically significant difference between the two groups regarding the mean pH after treatment based on the ANCOVA test with adjusting the baseline value (Adjusted mean difference:AMD: 0.01; 95% Confidence Interval (CI): -0.20 to 0.21, P = 0.965) (Table 2).

The frequency of negative culture, 10–15 days after the treatment, was 39 (65.0%) in the Mycozin group and 44 (74.5%) in the Clotrimazole 1% group. There was no statistically significant difference between the treatment groups regarding microscopic evaluation (Odds Ratio (OR): 0.61; 95% CI; 0.28 to 1.36, P = 0.230) (Table 2).

After the treatment the frequency of itching in the Clotrimazole group (N = 13; 22.0%) was lower than that of the Mycozin group (N = 26; 43.3%) (OR: 0.37; 95% CI: 0.17 to 0.82; P = 0.013). There was no statistically significant difference in other complaints and symptoms such as vaginal odor, dysuria, urinary frequency, itching and irritation in intercourse, dyspareunia, and lower abdominal pain between the two groups before and after the treatment (P > 0.05) (Table 3).

In the vaginal examination, there was no statistically significant difference considering cervical appearance, vulvovaginal erythema, amount, consistency, color, and appearance of discharge between the groups before the treatment (P > 0.05). Also, there was no statistically significant difference in the signs in the follow-up between the two groups (P > 0.05) (Table 3).

There was no statistically significant difference between the two groups in the level of satisfaction (P = 0.056) and patient improvement (P = 0.074) 10–15 days after the treatment (Table 4).

The side effects of treatment with Mycozin were observed in 11 patients by symptoms of intensification of itching (N = 4; 6.3%), intensification of irritation (N = 3; 4.7%), skin redness (N = 3; 4.7%), skin dryness (N = 1; 1.6%). In addition, the side effects of treatment with Clotrimazole 1% were observed in five patients with the intensification of itching (N = 1; 1.6%), intensification of irritation (N = 3; 4.8%), and skin redness (N = 1; 1.6%) (Table 5).

Discussion

The results of the study showed that Mycozin vaginal cream was as effective as Clotrimazole 1% vaginal cream in eliminating most of the symptoms, signs and laboratory results.

In the present study, there was no statistically significant difference between the two groups concerning the mean pH value of the vaginal secretions after treatment. In a review of the literature, no study examined the pH of vaginal secretions after treatment with garlic- or Clotrimazole-containing medications. In vaginal candidiasis, the vaginal pH is normal and ranges from 4–4.5[32]. In this study, the pH of vaginal secretions before treatment was in the range of 4–5, which remained constant after treatment. Given the normal pH of the vagina in candidiasis, this pH range is to be expected.

In this study, based on the culture results in SDA, patient recovery in the Mycozin group was similar to Clotrimazole 1% vaginal cream. In line with the results of the present study, Farshbaf-Khalili et al.[16] found no significant difference between the recovery of patients with vaginal candidiasis based on the results of culturing in agar in three groups receiving vaginal cream with garlic, Zataria multiflora and Clotrimazole 2%, seven and 30 days after treatment. In the study by Alizadeh et al.[15], the improvement of patients was similar in the Mycozin group as in the vaginal Miconazole group, based on the results of cultivation and smear. In contrast to the present study, the results of the study by Watson et al.[33] in asymptomatic women whose vaginal secretions were positive for Candida showed no effect of oral ingestion of three garlic tablets twice daily for two weeks before menstruation compared to the placebo group immediately after treatment on vaginal Candida colonization.

Before treatment, 68.8% of patients in the Mycozin group and 80.6% in the Clotrimazole group complained of itching. In agreement with the results of the present study, Farshbaf-Khalili et al.[16] showed that genital itching was the most common symptom experienced by patients before treatment. In our study, Clotrimazole 1% vaginal cream had a significantly better effect in eliminating itching than Mycocin, which could be because more side effects (intensification of itching) occurred in the Mycozin group than in the Clotrimazole 1% group. Contact dermatitis due to plants applied topically for medical purposes has often been described. Case reports have mentioned the possibility that garlic or thyme may cause allergic reactions (allergic contact dermatitis, irritation and itching)[34,35]. In contrast to the results of this study, Farshbaf-Khalili et al.[16] found no significant difference between the improvement of pruritus seven and 30 days after treatment in three groups receiving vaginal cream with garlic, Zataria multiflora, and Clotrimazole 2%. In the present study, both creams were similar in eliminating other symptoms and complaints of the patients except for itching. In line with the results of this study, Farshbaf-Khalili et al.[16] showed no significant difference before, seven, and 30 days after treatment between the three groups receiving vaginal cream with garlic, Zataria multiflora, and Clotrimazole 2% in terms of decrease in patients' complaints such as cheesy discharge, urine irritation, irritation and pain during intercourse. In the study by Alizadeh et al.[15] itching was the most common symptom experienced by patients before treatment, and the disappearance of all symptoms (vaginal odor, dysuria, urinary frequency, itching, itching and irritation during intercourse, and dyspareunia) in the Mycocin group was similar to that in the vaginal Miconazole group. In contrast to the present study, the study by Watson et al.[33] in women whose vaginal secretion culture was positive for Candida showed a statistically significant difference in patient-reported symptoms such as moderate and severe vaginal itching and the presence of vaginal discharge in both groups receiving three oral garlic tablets twice daily and a placebo two weeks before treatment. Using different dosage forms with longer treatment

duration (two weeks), the small sample size, the immediate post-treatment follow-up, and the comparison of the herbal medicine group with the placebo group in their study may justify this difference.

In this study, the disappearance of clinical observations in the Mycozin group was similar to Clotrimazole 1% vaginal cream. These results are consistent with those of Farshbaf-Khalili et al.[16], in which there was no significant difference in the relief of clinical symptoms of vulvovaginal erythema, abnormal cervical appearance, abnormal discharge, non-homogenous discharge, non-transparent discharge, cheesy discharge and vaginal inflammation between the groups receiving vaginal cream with garlic, Zataria multiflora and Clotrimazole 2% at seven and 30 days after treatment. Alizadeh et al.[15] showed that seven days after treatment, the effect of Mycozin and Miconazole vaginal creams was the same in eliminating the clinical symptoms of inflammation, consistency, color, odor, quantity, and appearance of vaginal discharge. Fouladi et al.[36] showed that both vaginal preparations containing thyme and Clotrimazole were effective in improving clinical symptoms such as discharge, itching, irritation, and dyspareunia.

By penetrating the membrane of Candida cells and organelles such as mitochondria, garlic can eventually lead to membrane destruction and cell death[37]. In addition to the direct effect on the fungus demonstrated in vitro, thyme extract has immunosuppressive effects and can thus destroy the fungus[38]. The mixture of garlic and thyme with its synergistic effect can be effective in Candida treatment[39].

This study showed that treatment satisfaction and patient improvement were the same in the Mycozin and Clotrimazole 1% groups. In addition, the results showed that side effects occurred in both groups. The most common side effect of the Mycozin group was intensification of itching and that of the Clotrimazole group was intensification of irritation. The least common side effect in both groups was skin dryness. Bahadoran et al.[25] showed that the most common side effect in the groups receiving vaginal cream with garlic and thyme and Clotrimazole vaginal cream was related to itching and the least common side effect in both groups was vaginal dryness. In the study by Watson et al.[30], side effects were significantly higher in the group of women with vaginal candidiasis who received oral tablets with garlic than in the placebo group. These side effects included gastrointestinal symptoms, i.e., stomach pain, garlic odor, and nausea, which may be due to oral ingestion of the drug.

The strengths of the present study were the large sample size, random allocation with allocation concealment to prevent selection bias, blinding of both participants and outcome assessor to mitigate performance and detection bias. Additionally, the use of an herbal vaginal cream containing garlic, complemented by thyme to neutralize the garlic odor and enhance its efficacy, contributed to the treatment of vaginal candidiasis. One of the weaknesses of this study was the short follow-up period to check the recurrence of vaginitis signs and symptoms. In this study, the women with chronic diseases such as diabetes, AIDS, depression, immune system disorders were excluded; so, the results cannot be generalized to women with mentioned chronic diseases. It is recommended that similar studies be conducted examining Candida species and symptom recurrence in long term follow up in women with recurrent vaginal candidiasis.

Conclusion

The results of this study show that both creams, Mycozin and Clotrimazole 1%, were effective in the treatment of vaginal candidiasis. Given the efficacy of Mycocin vaginal cream in alleviating symptoms and signs of vaginal candidiasis, its ability to yield negative results in vaginal secretion cultures, and its economical nature without serious side effects, it presents a suitable alternative or complementary therapy for treating vaginal candidiasis. This is especially relevant for patients interested in herbal remedies and those resistant to azole compounds.

Variables	Mycozin N = 64	Clotrimazole N = 62	P
	Mean (SD[a])	Mean (SD[a])	
Age (years)	39.23 (6.59)	39.21 (6.56)	0.983[b]
Age at first marriage (years)	20.95 (5.06)	19.73 (4.53)	0.154[b]
Time of current contraceptive use (months)	83.73 (59.68)	70.37 (58.10)	0.205[b]
	(N %)	(N %)	
Education level			0.421[c]
Elementary	14 (21.9)	12 (19.4)	
Intermediate	7 (10.9)	9 (14.5)	
High school	3 (4.7)	5 (8.1)	
Diploma	19 (29.7)	27 (43.5)	
University	21 (32.8)	9 (14.5)	
Work status			0.916[d]
House keeper	48 (75.0)	47 (75.8)	
Employed	16 (25.0)	15 (24.2)	
Husband's education			0.833[c]
Illiterate	5 (7.8)	2 (3.2)	
Elementary	3 (4.7)	10 (16.1)	
Intermediate	15 (23.4)	10 (16.1)	
High school	5 (7.8)	6 (9.7)	
Diploma	21 (32.8)	21 (33.9)	
University	15 (23.4)	13 (21.0)	
Husband's job			0.893[e]
Unemployed	1 (1.6)	1 (1.6)	
Worker	6 (9.4)	7 (11.3)	
Employed	16 (25.0)	12 (19.4)	
Self-employed	41 (64.1)	42 (67.7)	
Last birth method			0.353[d]
Non	11 (17.2)	8 (12.9)	
Natural vaginal delivery	20 (31.3)	27 (43.5)	
Cesarean section	33 (51.6)	27 (43.5)	
Contraception method			0.255[e]
Barrier methods	8 (12.5)	6 (9.7)	
Intra uterine device	2 (3.1)	8 (12.9)	
Fertility awareness methods	33 (51.6)	28 (45.2)	
Tubal ligation	7 (10.9)	3 (4.8)	
Vasectomy	2 (3.1)	1 (1.6)	
Injections	0 (0.0)	1 (1.6)	
Non	12 (18.8)	15 (24.2)	
Gravida			0.536[d]
0	11 (17.2)	7 (11.3)	
1–2	23 (35.9)	27 (43.5)	
≥ 3	30 (46.9)	28 (45.2)	
Continued			

Variables	Mycozin N = 64	Clotrimazole N = 62	P
	Mean (SD[a])	Mean (SD[a])	
Para			0.360[d]
0	11 (17.2)	8 (12.9)	
1–2	42 (65.6)	37 (59.7)	
≥3	11 (17.2)	17 (27.4)	
Medical history	9 (14.1)	15 (24.2)	0.148[d]
Drug history	8 (12.5)	6 (9.7)	0.614[d]

Table 1. Socio-demographic characteristics between groups (n = 126). [a]Standard deviation, [b]independent samples T, [c]Chi-square for trend, [d]Pearson Chi-square, [e]Fisher's exact test.

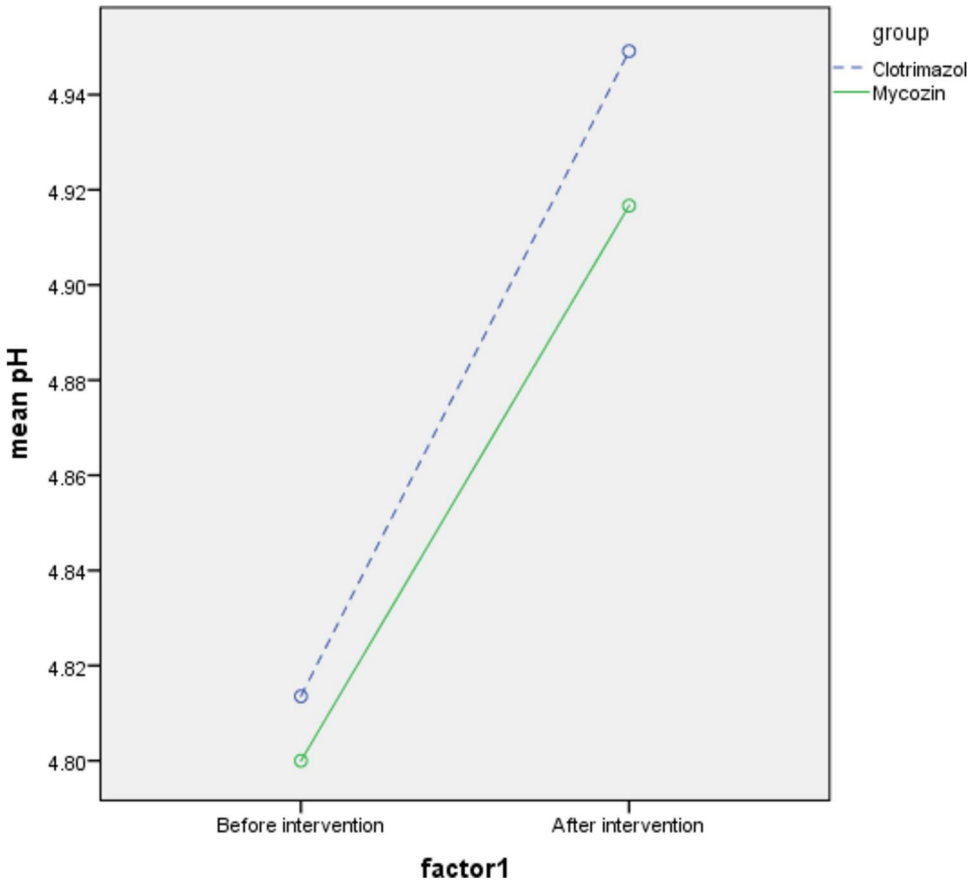

Fig. 2. Comparison of the vaginal pH between groups before and after treatment.

Variables	Mycozin (n = 64)	Clotrimazole (n = 62)	Effect size (95% CI[b])	P
Vaginal pH[a]	**Mean (SD[a])**	**Mean (SD[a])**	**Mean difference (95% CI[b])**	
Before treatment	4.77 (0.77)	4.81 (0.84)	0.04 (-0.24 to 0.33)	0.778[c]
After treatment	4.92 (0.88)	4.95 (0.83)	0.01 (-0.20 to 0.21)	0.965[d]
Positive culture	**N (%)**	**N (%)**	**Odds ratio (95% CI[b])**	
Before treatment	64 (100.0)	62 (100.0)		
After treatment	21 (35.0)	15 (25.4)	0.61 (0.28 to 1.36)	0.230[e]

Table 2. Comparison of the vaginal pH and microscopic evaluation between groups before and after treatment. [a]Standard deviation, [b]confidence interval, [c]independent samples t-test, [d]ANCOVA with adjusting the baseline value, [e]Pearson Chi-square.

Variables	Mycozin (n = 64) N (%)	Clotrimazole (n = 62) N (%)	Odds Ratio (95% Confidence Interval)	P[a]
Complaints				
Vaginal odor				
Before treatment	36 (56.3)	39 (62.9)	1.32 (0.65 to 2.70)	0.447
After treatment	21 (35.0)	26 (44.1)	1.46 (0.70 to 3.06)	0.312
Dysuria				
Before treatment	41 (64.1)	32 (51.6)	0.60 (0.30 to 1.22)	0.157
After treatment	18 (30.0)	14 (23.7)	0.73 (0.32 to 1.64)	0.440
Urinary frequency				
Before treatment	39 (60.9)	33 (53.2)	0.73 (0.36 to 1.48)	0.382
After treatment	22 (36.7)	22 (37.3)	1.03 (0.49 to 2.16)	0.944
Itching				
Before treatment	44 (68.8)	50 (80.6)	1.90 (0.83 to 4.31)	0.125
After treatment	26 (43.3)	13 (22.0)	0.37 (0.17 to 0.82)	0.013
Itching in intercourse				
Before treatment	25 (39.1)	27 (43.5)	1.20 (0.60 to 2.45)	0.609
After treatment	14 (23.3)	8 (13.6)	0.51 (0.20 to 1.34)	0.170
Lower abdominal pain				
Before treatment	43 (67.2)	39 (62.9)	0.83 (0.40 to 1.72)	0.614
After treatment	34 (56.7)	28 (47.5)	0.69 (0.33 to 1.42)	0.315
Irritation in intercourse				
Before treatment	34 (53.1)	37 (59.7)	1.31 (0.64 to 2.65)	0.458
After treatment	12 (20.0)	14 (23.7)	1.24 (0.52 to 2.98)	0.623
Dyspareunia				
Before treatment	34 (53.1)	39 (62.9)	1.50 (0.73 to 3.05)	0.266
After treatment	29 (48.3)	20 (33.9)	0.55 (0.26 to 1.15)	0.110
Clinical observations				
Abnormal cervical appearance				
Before treatment	6 (9.4)	12 (19.4)	1.20 (0.56 to 2.60)	0.109
After treatment	6 (10.0)	6 (10.2)	0.98 (0.30 to 3.24)	0.976
Vulvo-vaginal erythema				
Before treatment	44 (68.8)	45 (72.6)	1.20 (0.56 to 2.59)	0.637
After treatment	19 (31.7)	14 (23.7)	0.67 (0.30 to 1.51)	0.333
Abnormal discharge				
Before treatment	64 (100.0)	62 (100.0)		
After treatment	33 (55.0)	26 (44.1)	1.55 (0.75 to 3.20)	0.233
Non homogenous discharge				
Before treatment	62 (96.9)	62 (100.0)	2.00 (1.68 to 2.39)	0.496
After treatment	29 (48.3)	24 (40.7)	1.36 (0.66 to 2.81)	0.401
Color of discharge				
Before treatment				
Cottage cheese like	64 (100.0)	62 (100.0)		
Gray/colorless/ yellow	0 (0.0)	0 (0.0)		
After treatment			0.78 (0.38 to 1.62)	0.510
Cottage cheese like	28 (46.7)	24 (40.7)		
Gray/colorless/ yellow	32 (53.3)	35 (59.3)		
Discharge appearance				
Before treatment				
Nontransparent/Frothy	64 (100.0)	62 (100.0)		
Transparent	0 (0.0)	0 (0.0)		
After treatment			0.64 (0.31 to 1.32)	0.229
Nontransparent/Frothy	31 (51.7)	24 (40.7)		
Transparent	29 (48.3)	35 (59.3)		
Vaginal odor				
Before treatment	14 (21.9)	25 (40.3)	2.41 (1.11 to 5.27)	0.025
After treatment	11 (18.3)	17 (28.8)	1.80 (0.76 to 4.27)	0.862
Continued				

Variables	Mycozin (n = 64) N (%)	Clotrimazole (n = 62) N (%)	Odds Ratio (95% Confidence Interval)	P[a]
Macroscopic evaluation				
Before treatment	64 (100.0)	62 (100.0)		
After treatment	29 (48.3)	22 (37.3)	0.64 (0.31 to 1.32)	0.223

Table 3. Comparison of the patient complaints and clinical observations between groups before and after treatment. [a] Pearson Chi-square.

Variables	Mycozin N = 60 N (%)	Clotrimazole N = 59 N (%)	P[a]
Patient improvement			0.074
Very good	21 (32.8)	26 (41.9)	
Good	9 (14.1)	13 (21.0)	
Not bad	17 (26.6)	15 (24.2)	
Bad	13 (20.3)	5 (8.1)	
Patient satisfaction			0.056
Very satisfied	21 (32.8)	26 (41.9)	
Satisfied	9 (14.1)	13 (21.0)	
Equally satisfied and unsatisfied	14 (21.9)	15 (24.2)	
Unsatisfied	12 (18.8)	3 (4.8)	
Very unsatisfied	4 (6.3)	2 (3.2)	

Table 4. Comparison of the patient improvement and satisfaction between groups after treatment. [a] Mann–Whitney U.

Variables	Mycozin N = 60 N (%)	Clotrimazole N = 59 N (%)
Intensification of itching	4 (6.3)	1 (1.6)
Intensification of irritation	3 (4.7)	3 (4.8)
Skin redness	3 (4.7)	1 (1.6)
Skin dryness	1 (1.6)	0 (0.0)

Table 5. Side effects in study groups.

Data availability

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Author contributions

KhH, ZA, VR, LM, SM, BSh and MM contributed to the conception, and design of the study. ZA collected data and drafted the manuscript under the direct supervision of MM. LM and SM conducted laboratory tests. MM conducted the statistical analysis. KhH, VR, LM, SM, BSh and MM revised the manuscript. All authors read and approved the final manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

The study was approved by the ethics committee of Tabriz University of Medical Sciences, Iran with ethics code of IR.TBZMED.REC.1402.112. The study complies with the World Medical Association Helsinki Declaration regarding the ethical conduct of research involving human subjects. The study protocol was developed following the Consort guidelines for clinical trials and included a completed CONSORT checklist. Written informed consent was obtained from each individual participant. The principles of anonymity and confidentiality were applied and the participants were provided with the results upon their request.

Additional information

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