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ABSTRACT

Objective: To compare boric acid as an effective treatment for VVC compared to fluconazole. We also studied the efficiency of these drugs in preventing recurrence of VVC.

Design: A cross sectional, randomized, double-blind study.

Settings: Gynaecology clinic of Imam Reza hospital, Tehran - Iran

Subjects: Women with signs and symptoms related to Vulvo Vaginal Candidiasis.

Results: Seventy five patients out of total 150 patients with signs and symptoms related to Vulvo Vaginal Candidiasis were treated with boric acid powder every night for a week and the remaining 75 patients received Fluconazole. The cure rate in first group was 46.7% but the cure rate in second group was 37.3%. The difference was not statistically significant ($P>0.3$). Difference between the efficacy of the two drugs was not significant either ($P=0.47$). The recurrence rate among patients in first group was 35% while it was 32% in second group. Their difference was not statistically significant ($P=0.54$).

Conclusion: According to our findings, treatment of vaginal candidiasis with boric acid is as effective as fluconazole. The availability of boric acid and its relatively low cost suggests it as a safe and effective drug for treatment of candidiasis.

INTRODUCTION

Vulvo-Vaginal Candidiasis (VVC) is a frequent cause of mycoses of women caused by *Candida* (*C.*) species. *C. albicans* is the main causative agent (87.6%) followed by *C. glabrata* (6.2%) and *C. krusei* (2.2%) (1). *C. albicans* and *C. glabrata* are often involved in recurrent vulvovaginal candidiasis (2).

Different azole compounds are used for treating Candidiasis (1,3-6). Non-azole compounds are also used for mycotic vaginitis.

Ringdahl (11) proved that *C. albicans* also responds to azole antifungal agents like fluconazole. According to him individuals suffering from vaginitis due to *Candida* are bothered by recurrent vaginal yeast infections or experience failure of conventional therapies. He advised maintenance therapy to be started immediately after treatment of the acute episode and to be continued for six months (7,8).

Sojakova *et al* concluded that antifungal agents used to treat vaginitis may be contributing to the drug resistance problem by promoting cross-resistance to a range of clinically used antifungals (1).

The use of boric acid as a home remedy has long been in existence. Boric acid or boracic [$B(OH)_3$] is a weak acid, and acidic properties of boric acid may lead to disruption of the fungal cell wall though Ray *et al* believe that the effect of boric acid is not specific to its acidic properties (9). Clinical reports indicate success in treating vaginal candidiasis, especially non-*albicans* vaginitis with boric acid (10).

Vulvovaginal candidiasis is considered recurrent when at least four specific episodes occur in one year or at least three episodes unrelated to antibiotic therapy occur within one year (11).

Recurrent vulvovaginal candidiasis affects five percent of women of child-bearing age. The most common organism is *Candida albicans*, but an

increasing number of infections are caused by non-albicans species (7). During any treatment regimen, it is crucial that patients are carefully examined clinically and microscopically via culture-proven absence of Candida (12).

The present study has been undertaken with an aim to compare boric acid as an effective treatment for VVC compared to fluconazole. We also studied the efficiency of these drugs in preventing recurrence of VVC as well.

MATERIALS AND METHODS

This randomised double-blind study was carried out in gynecology clinic of Imam Reza hospital, Tehran - Iran. All patients with symptoms like pruritis, irritation, burning, discharge, splash dysuria and signs of inflammation including erythema, edema, excoriation, fissures were examined in the clinic. Written informed consent was obtained from every patient after they were informed about the protocol though they were blind regarding the drug they received.

Ethical committee number was obtained from our Institution Ethics Committee.

Case Selection: Microscopic examination and culturing of patients' secretions were performed to identify the etiologic agent. All patients with active acute Candida vaginitis were enrolled in the study.

Some patients were excluded from the study on the basis of our exclusion criteria like pregnancy, mixed infection and treatment with antifungal agents within last four months.

At last, study was carried out with 150 patients.

They were randomly grouped into two categories: group I with 75 patients received hand-made capsules filled with 600 mg boric acid powder every night for a week and 75 patients included in group II received 1 capsule of 150 mg Fluconazole (Pars Darou co.).

All the patients were prohibited from any other medication during the treatment and follow up. All patients and the statistician were totally blind regarding the type of medication employed.

Patients' assessment and follow up: Patients were assessed after two weeks of treatment. In every visit pelvic examination was carried out. Collected vaginal swabs were examined by direct microscopy using 10% KOH and cultured in Saboraud's dextrose agar to identify Candida species, if present.

Patients who had negative laboratory tests were followed up and were again assessed after six weeks of treatment. Patients who had positive laboratory tests especially positive culture test were considered as drug resistant and were excluded from the study. They were treated with alternate medications.

Patients were followed up to six weeks for recurrence of the disease and in order to evaluate the efficacy of these drugs in prevention of recurrence. Data were analyzed using SPSS- software.

RESULTS

One hundred and fifty patients with active acute Candida vaginitis were included in the study. Their age ranged from 18 to 45 years. Their mean age was 30 ± 5.88 years. The frequency of the signs and symptoms before and after treatment (Table 1).

Table 1

The frequency of the symptoms in two groups before & after treatment

| Grouping | Symptoms & signs before treatment | | | Symptoms & signs 2 weeks after treatment | | | Symptoms & signs 6 weeks after treatment | | |
|----------------|-----------------------------------|--------------|-----------|--|--------------|-----------|--|--------------|-----------|
| | Group I (%) | Group II (%) | Total (%) | Group I (%) | Group II (%) | Total (%) | Group I (%) | Group II (%) | Total (%) |
| Pruritis | 67 (90) | 58 (77.4) | 125 (83) | 15 (20) | 17 (22) | 34 (21) | 7 (14.6) | 7 (15.5) | 14 (15) |
| Burning | 30 (40) | 33 (44) | 63 (42) | 7 (9.3) | 8 (10.6) | 15 (11) | 3 (6.6) | 4 (8.3) | 7 (7.5) |
| Splash Dysuria | 15 (20) | 13 (17.3) | 28 (18.6) | 3 (4) | 4 (5.3) | 7 (4.5) | 1 (2.2) | 7 (4) | 3 (3.1) |
| Secretions | 45 (60) | 50 (66) | 95 (63) | 15 (20) | 12 (16) | 27 (18) | 5 (10.4) | 7 (15.5) | 12 (13) |
| Inflammation | 68 (90) | 75 (100) | 143 (95) | 154 (20) | 17 (22) | 37 (16) | 7 (14.6) | 7 (15.5) | 14 (15.5) |

As is clear from Table-1, inflammation is the commonest sign in patients suffering from vulvo vaginal candidiasis followed by pruritis, secretion, burning sensation and splash dysuria (before treatment).

Two weeks after treatment inflammation and pruritis are still the predominant signs and symptoms in both groups while discharge is also as common as the other two signs amongst patients of first group followed by burning sensation and splash dysuria in both the groups.

To find out the relationship between the kind of group variables and type of illness we used Chi-square test. We found no significant difference between group

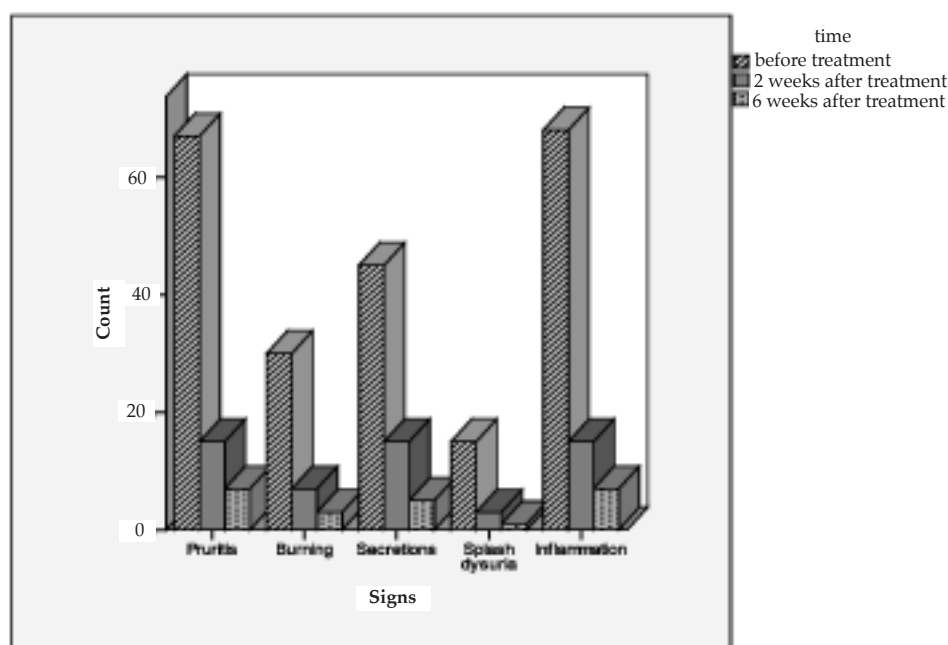
I and II in all types of signs and symptoms (pruritis, burning sensation, secretions, splash dysuria and inflammation) ($P>0.05$).

We studied the behaviour of two variables (time versus kind of signs) in two groups independently. Applying Pearson's Chi-Square test, we found no significant difference between time of illness regarding all types of signs and symptoms in group I ($P>0.05$), indicating the time of illness is independent of signs and symptoms of illness.

Figure 1 shows the number of signs and symptoms present in group I based on time of study (that is, before and after treatment) versus signs of illness.

Figure 1

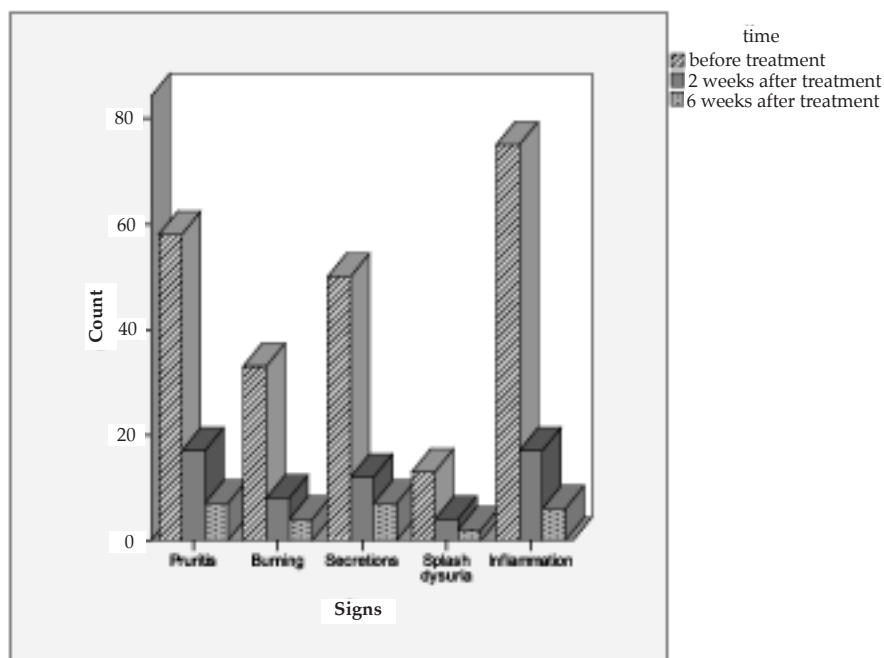
Number of signs present in group I based on time of study (that is, before and after treatment) versus kind of signs of illness



Considering the signs and symptoms based on time of illness in group II, no significant difference was found out ($P>0.05$). In this group also, the time of illness is independent of signs and symptoms of illness.

Figure 2

Number of signs present in group II based on time of study (i.e. before and after treatment) versus kind of signs of illness



As in the present study two categorical fields are specified and they have only two values, McNemar's test is applied to find out whether combinations of values between two dichotomous variables are equally likely or not. We considered six variables in two groups of study cases. In each group, we compared patients' signs and symptoms before treatment and presence of their clinical signs and symptoms after two weeks and recurrence after six weeks of treatment with boric acid and fluconazol (Table 1).

McNemar's test was run to show if there is significant difference regarding the presence of the above mentioned variables. Based on the results obtained, it can be concluded that there is significant difference between presence of the concerned variables "before treatment" and "after two weeks treatment with boric acid" ($P < 0.05$).

McNemar's test was also run to show if there is significant difference regarding the presence of concerned variables "before treatment" and "after two weeks treatment" with fluconazol. It may be concluded that there is a significant difference between "before" and "after" treatment with fluconazol regarding the presence of clinical signs and symptoms ($P < 0.05$).

Out of 75 patients treated with boric acid 46.7% patients were cured of clinical signs two weeks after treatment. Their samples cultured after two weeks were also negative. While 37.3% patient treated with Fluconazole had no clinical signs and symptoms after two weeks and the culture of their samples were negative after this period of treatment. Difference between the efficacy of two drugs was not significant ($P = 0.47$).

The cure rate is calculated on the basis of number of negative cultures of patients' samples after two weeks of treatment and lack of any clinical sign and symptom.

The cure rate in first group after two weeks of treatment was 46.7% but the cure rate in second group after two weeks of treatment was 37.3%. The difference was not statistically significant ($P > 0.3$) (Table 2).

Six weeks after treatment with boric acid 14% patients had symptoms related to vulvo vaginal candidiasis. Twenty seven percent patients were culture positive, while 15.5% patient treated with fluconazole had symptoms six weeks after treatment. Thirty seven percent patients were also culture positive (Table 2).

Table 2
Recurrence rate in both the study groups

| Grouping | Group I (%) | Group II (%) |
|--------------------------------------|----------------|-----------------|
| Outcome of Treatment | | |
| Presence of symptoms | 10.5 (14) | 11.62 (15.5) |
| Positive culture of patients samples | 20.25 (27) | 27.75 (37) |
| Recurrence rate | 26.25 (35) | 24 (32) |

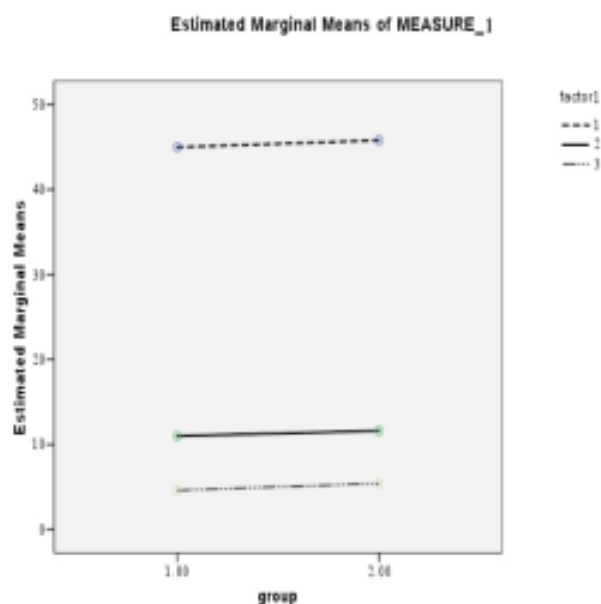
The recurrence rate based on microscopic examination of patients' samples after six weeks of treatment in boric acid group was 35% while it was 32% amongst patients treated with fluconazole. These differences were not statistically significant (P=0.54).

We are also keen to know if there is significant

difference regarding the stages of the study between the two groups. Our statistical analysis showed that there is significant difference amongst the stages of the study (P<0.05) (Figure 3). Mutual effect of the two factors, that is, stage and group, was not significant either (P>0.05) (Figure 3).

Figure 3

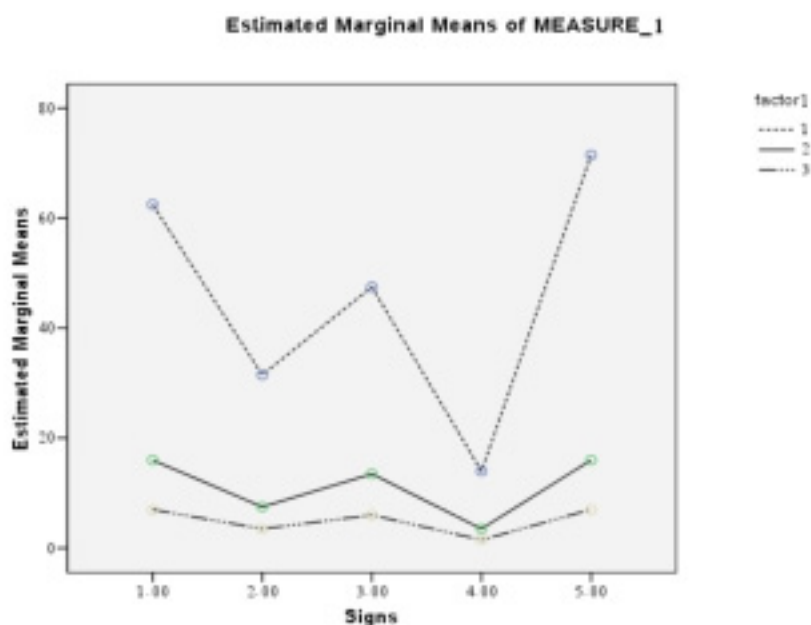
The "level of significance" of two factors, that is, stage and group in all three Stages



To find out the "level of significance" among three stages regarding the signs and symptoms of the disease (Pruritis, Burning sensation, Secretion, Splash dysuria and Inflammation) we concluded that the difference is significant (P<0.05) (Figure 4).

The "level of significance" between two groups in all three stages as a whole shows significant difference (P<0.05) (Figure 1).

Figure 4
The "level of significance" of signs between two groups in all three stages



DISCUSSION

According to Ringdahl more than 50 percent of women older than 25 years develop vulvovaginal candidiasis at some time and fewer than 5 percent of these women experience recurrences (11).

In our study all patients had signs and symptoms related to candidiasis. The clinical diagnosis was confirmed by laboratory findings.

As is conventional (9,13), we also treated a group of our patients with an azole compound i.e. fluconazole. The problem may persist despite topical or oral use of azole antifungal drugs. As conventional treatments are not always successful and may lead to drug resistance and/or recurrences (13,14), we compared the efficacy of fluconazole with a cheaper yet safer drug, that is, boric acid. We also studied the efficiency of these drugs in preventing recurrence of VVC as well.

Donders *et al* believe that for acute Candida vaginitis any oral or local anti-fungal therapy can be used but for women with recurrent vulvo-vaginal candidiasis (RVC) simple approaches are insufficient and instead, RVC should be managed as any other chronic disease and long-term, prophylactic, suppressive antifungal treatment is required (12).

In the present study we compared the efficacy of boric acid as an alternative treatment for VVC. It can be a substitute for azol drugs as it is effective against both *C. albicans* and *C. glabrata* compared with fluconazole, which is effective against *C. albicans* only (9).

In this study patients received hand made capsules of boric acid containing 600 mg boric acid powder every night for a week and 46.7% patients were cured of clinical signs two weeks after treatment whilst the mycologic cure rate varies from 40 to 100% (8). The lower cure rate in the present study compared to >90% mycological cure achieved by vaginal use of 600 mg boric acid daily for 14 days (15) may be due to our shorter duration of treatment or the species involved. We observed no boric acid side effects.

In conclusion, boric acid therapy of vaginal candidiasis has also been found to be safe and in our study we did not observe any side effect.

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