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EFFICACY OF ITRACONAZOLE VERSUS FLUCONAZOLE IN VAGINAL CANDIDIASIS

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ABSTRACT

Objective: To compare the efficacy of itraconazole 200mg twice and fluconazole 150mg single dose for one dayin the treatment of acute VVC (vulvovaginal candidiasis(VVC)). **Methods:** The study was carried out at the sub himalyan peripheral institutes Ch Bhawarna and RH Bilaspur, from September 2021 to February 2022 and comprised 50 women with mycological and clinical diagnosis of vaginal candidiasis. Based on history, clinical examination and relevant investigations the diagnosis was based. The women were divided into 2 equal groups. After the initial assessment, Group 1 was treated with capsule fluconazole 150mg stat whereas Group2 with capsule itraconazole 200mg twice for one day again. They were assessed clinically for cure and the relapse on day seven and twenty-one respectively. In the proforma all findings were recorded. Data was analysed using SPSS 12. **Results:** The overall clinical evaluation showed 50% with fluconazole and 70% cure rate with itraconazole. In Group-1, (23.00%) and in Group-2 (26.00%) showed some improvement, while (06.66%) in Group 1, and (23%) in Group 2 failed to respond to the treatment. Relapse was observed in (28.5%) and (53%) of the cured cases in Group 1 and Group 2 respectively. **Conclusion:** Compared to fluconazole; Itraconazole was found to be more effective in the treatment of vulvovaginal candidiasis (VVC) with high cure rate and low relapse rate.

INTRODUCTION

Inflammation of the vagina and the vulva is vulovovagitis. More than 90% of candida vaginitis is predominantly caused by strains of Candida albicans.[1] In a healthy vagina Candida species are commonly found in small amount. When an imbalance occurs, the change in hormonal balance, or such as change in normal acidity of a vagina or the Candida multiplies increasingly and symptoms of candidiasis like non- specific soreness, vulvovaginal pruritus, thick vulvar pain, vaginal discharge,] and dyspareunia appear.[2]

Effective management of Candida infection therefore dependson accurate diagnosis; administration of specific therapy and by good compliance of the patient.[3] There are variety of systemic and local antimycotic agents available for the treatment of VVC.[4] Topical agents can cause irritant contact dermatitis. They are sometimes messy to use. In contrast to that systemic therapy is easy to administer and therefore patient compliance is remarkably improved.[5] Oral preparation is much less painful to administer further, if the vulva is very inflamed.[6]

Fluconazole and itraconazole are both triazole antifungals. They are used for the short-term oral treatment of VVC and have proved to be safer than both ketoconazole and amphotericin B.[5] Both of them have good efficacy and safety data. The objective of the our study was to provide the single-day dosage ofitraconazole regimen to that of fluconazole in vulvovaginal candidiasis (VVC)(VVC). Today primary and secondary antifungal drug resistance has been proved by various multicenter studies.[7] In vitro sensitivity of the Candida species to antifungal drugs does not always mean successful treatment Although in vitro resistance to the drug almost always mean a high rate of failure in the treatment.[7]

In vivo response of the antifungal has hence earned importance, therefore, is the basis of this study. Asian women are mostly living in hot and humid environment and are much more prone to developing such types of infections

PATIENTS AND METHODS

This study was conducted at sub himalyan peripheral institutes from and comprised 50 women aged 16 years and above with symptomatic acute vulvovaginal candidiasis (VVC), who gave written informed consent to participate in the study. None of them had received systemic or topical antifungals within one month before enrollment. Before starting the treatment, they were all assessed For itching, burning, erythema, vaginal discharge and oedema. Pregnant women or women during puerperium were excluded from the study. In all patients in our study the diagnosis was confirmed by the direct microscopy and cultures. After establishing the diagnosis, all the subjects were randomly divided into

two groups of 25 each. Patients in Group 1 wereprescribed capsule itraconazole (200mg twice oral dose for 1 day) whereas those in Group 2 were given capsule fluconazole (150 mg single oral dose).

After treatment was gven, they were followed up on day seven and day twenty one, and each symptom and sign was assessed separately. Clinical effectiveness was recorded as improvement, cure, failure and relapse as follows.
Cure: Complete disappearance of all symptoms and signs. Improvement: Improvement but partial disappearance of signs and symptoms. Failure: Worsening or no change of symptoms and signs and relapse or reappearanceof symptoms and signs after documented cure had occurred.

Data was analysed by using SPSS version.[12] Percentages and frequency were computed to present symptoms. Findings of clinical examination before and after the treatment were computed. Time measurement was presented by mean standard deviation.

RESULTS

All the 50 patients completed the study and there was no dropout. Their ages ranged from 16 to 57 years in Group 1 (mean 35.63 ± 10.72 years) and from 22 to 54 years in Group 2 (mean 34.26 ± 8.91 years). The duration of the disease varied from seven to thirty five days inthe former (mean = 18.76 ± 10.57 days) whereas from 10 to 42 days (mean = 21.70 ± 11.42 days) in the group 2.

Patients were assessed for itching, burning, erythema and oedema and discharge. Vaginal discharge was initially present in all the patients recruited in our study. After one week, (13.3%) patients in Group 1 and (50%) in Group 2 had not responded to therapy. There was difference in treatment response between the two groups ($p \leq 0.002$).

Itching was initially present in (93%) patients in each group. In Group 1, (6.7%) patients showed treatment.

Table: Comparison of symptomatic cure rate after treatment with Itraconazole (GP 1) and Fluconazole (GP 2).

Symptoms	Itraconazole (Gp 1) (n=25)	Fluconazole (GP 2) (n=25)	p value
Vaginal Discharge	(13.3%)	(50%)	≤ 0.002
Itching	(6.7%)	(46.7%)	≤ 0.001
Burning	(10%)	(16.7%)	≤ 0.70
Erythema	(6.7%)	(26.7%)	≤ 0.03
Edema	(6.7%)	(20%)	≤ 0.25

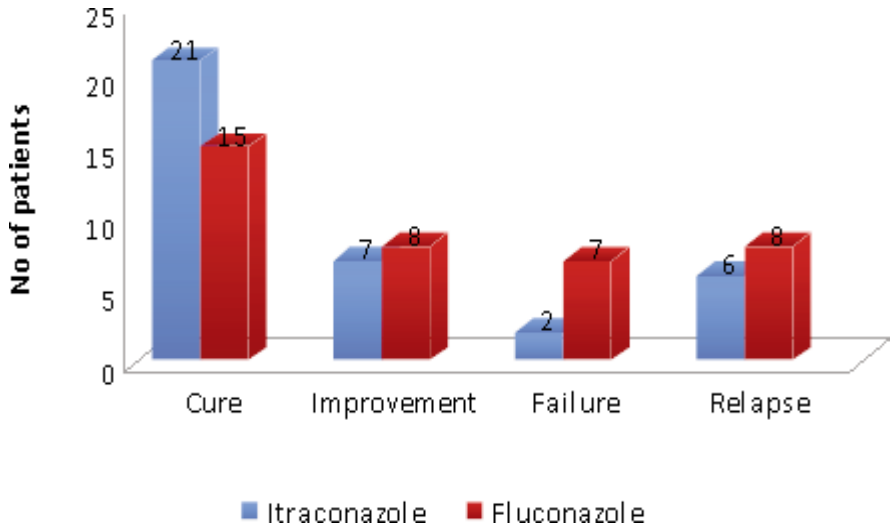

Figure: Comparison of treatment response with Itraconazole (Gp 1) and Fluconazole (GP 2).

failure on the 7th day of follow up. In Group 2, failure was observed in (46.7%) patients (p = 0.001). In Group 1 burning was initially observed in (60%) patients. (10%) patients did not respond to the drug treatment. In the Group 2, therewere initially (53%) patients with burning sensation. On the 7th dayfollow up, (16.7%) still had the remaining symptoms (p = 0.70).

Erythema was initially observed in 18 (60%) patients in each group. In Group 1, 2 (6.7%) patients actually did not respondto the therapy, while in Group 2, 8 (26.7) patients did not report improvement in symptoms (p = 0.03). Initially, 7 (23%) patients in Group 1 and 11 (36%) patients in Group 2 were observed with oedema. Two (6.7%) patients in Group 1 and 6(20%) patients in Group 2 did not respond well (p = 0.25).

At the 7th day follow up for all the symptoms, (70%) of the total in Group 1, and (50%) of Group 2 had been well cured completely; (23.33%) patients in Group 1 and

(26.6%) in Group 2 showed clinical improvement; (6.66%) in Group 1 and (23%) in Group 2 showed absolutely no response. Time taken for cure varied from 1 to 6 days (Mean 3.67 ± 1.228) in Group 1 and one to seven days (Mean 4.19 ±1.425) in Group 2. Relapse was seen in (28.5%) of the 21 cured patients in Group 1, and (53%) of the cured patients in Group 2 on day 21. Response to treatment, as such, was therefore significantly better in Group 1 compared to that of Group 2 (Figure).

DISCUSSION

Itraconazole and fluconazole are broad- spectrum safe, antifungal drugs which have gained an important place in the treatment of the vulvovaginal candidiasis(VVC). Their efficacy and safety have been evaluated in a number of comparative as well as non-comparative trials conducted indifferent areas of world.[8,9]

Eradication rate observed in our study was similar to many similar studies. Our results with fluconazole (50%) and itraconazole (70% cures) are in accordance with other earlier study.[10] Clinical cure was significantly much lower in fluconazole group than that of in the itraconazole group or clotrimazole group.

Another study also established the relationship of clinical outcomes of candidal infections and in vitro results by determination of minimum inhibitory concentration (MIC) of itraconazole and the fluconazole.[2] Clinically, itraconazole was effective in about 64.00% of the cases, whereas fluconazole was effective in 71.00%. In clinical and mycological evaluation, the responses were statistically significant for both regimens. There was a reduction in the symptoms of vaginitis and a reduction of Candida in vaginal swabs. There was no significant difference in clinical response between these two regimens.[2,3]

The results of these studies are similar to that of our study results. Clinical cure rate was significantly higher in the itraconazole group compared to that of fluconazole group. This difference between efficacy of itraconazole and fluconazole could be well explained by the fact that in our setup, due to higher availability of fluconazole women might be suffering from fluconazole-resistant strain of Candida species. Although, identification of different strains of Candida and resistance to various starins was not included in our study. Literature suggests that Candida Krusie and Candida Glabrata are often non-responsive to the fluconazole, but are very susceptible to itraconazole.

In a metaanalysis[14] on various studies conducted on the efficacy of single day dosege of fluconazole comprising 3279 patients, found a positive clinical response in whooping 94% and mycological cure in 85% of patients at the first follow up visit. Furthermore, in a similar multicentre study, total of 70% patients were cured clinically during therapy.[14]

Our findings actually do not coincide with the results of above-mentioned studies. This may be because of too much secondary drug resistance as fluconazole is a commonly prescribed drug in our area for vulvovaginal candidiasis(VVC).

In our study, those who received fluconazole reported low cure rate and clinical improvement. Failure and relapses were quite high compared to that of an earlier study done locally[16] which assessed the efficacy of the single-dose oral fluconazole forvulvovaginal candidiasis(VVC). None of the patients failed to respond and there was no relapse.[16] Our results regarding higher relapse rate with that of fluconazole compared to that of itraconazole was also consistent with international data reported.[10] Itraconazole stays in the vaginal mucosa longer than that of ketoconazole and fluconazole because of its high affinity for keratin and high lipophilicity. Therefore recurrence rate with itraconazole is much lower as suggested by a comparative study wherein recurrence rate after twenty eight days of treatment was 7% with that of itraconazole and 23% with that of fluconazole.[10]

Our study also had several limitations. The sample size was low and not adequately powered. A larger sample size, preferably actually a trial, should be undertaken. It was a single-center study. A multi-centre study is much more recommended for the future to substantiation of the findings of the current study.

CONCLUSIONS

As suggested by our study vaginal discharge was commonest presenting symptom of the vulvovaginal candidiasis(VVC). Other common presentations were burning and itching. Cutaneous involvement like oedema and erythema were the least common findings. Itraconazole was found to be much more effective in the treatment of vulvovaginal candidiasis(VVC) comparedto that of fluconazole, and therefore might represent a better choice in treating the above said condition. Relapse as well as failure were significantly high with fluconazole. Average time for relief of symptoms was lesser for the itraconazole group compared to that of fluconazole group.

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