Original Article

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Comparison of Single Dose Sertaconazole versus Three Dose Clotrimazole Regime in Treatment of Uncomplicated Vulvovaginal Candidiasis- A Prospective Study

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ABSTRACT

Introduction: Vulvovaginal candidiasis is the second most common vaginitis following bacterial vaginitis amongst the reproductive age group with variable compliance to the treatment.

Aim: To compare the efficacy of single dose sertaconazole versus multidose clotrimazole pessaries in patients with vulvovaginal candidiasis in reproductive age group.

Materials and Methods: A prospective study was conducted at a tertiary care hospital between October 2014 and September 2016 on 100 patients of reproductive age group with vulvovaginal candidiasis. Group A (n=50) were treated with single dose sertaconazole and group B (n=50) were treated with 3-dose regime clotrimazole. Pregnant females with history of antifungal treatment within past four weeks, past history of hypersensitivity to imidazole agents were excluded from the study.

Results: The mean age of patients was 28.7±5.3 years. The average duration between the appearance of symptoms and consultation was 14.8±7.6 days. The prevalence of candidiasis was most amongst the housewife's accounting for 64.3%. There was no statistically significant difference between both the groups in terms of socio-economic status and literacy rate. There was no statistically significant difference in the response to treatment between both the drugs. At the end of six weeks, 14% of the patients in group A and 18% of patients in group B had recurrence.

Conclusion: It can be a wise option to prefer sertaconazole with respect to its single dosage regime, convenience and better acceptability in uncomplicated cases of vulvovaginal candidiasis. However, no statistical significance has been observed between both the regimes.

Keywords: Antifungal agents, *Candida albicans*, Pessaries, Vaginitis

INTRODUCTION

Vulvovaginal candidiasis is defined as symptomatic vaginitis secondary to a yeast infection, affecting the mucous membrane surrounding vagina, leading to symptoms such as vulvar itching, soreness and a cheese like or watery discharge usually accompanied by dysuria or dysparenuria [1,2]. About three-quarters of women during their reproductive age have at least one episode of vulvovaginal candidiasis and approximately half have two or more episodes with *Candida albicans* being in 85-90% cases followed by *Candida glabrata* [2,3]. Clotrimazole or/and oral fluconazole has been used most commonly in the treatment of *Candida* but recent studies have shown an emerging rate of relapse with their use. Since these drugs have been used in vaginal candidiasis from long as standard treatment, fungal resistance as well as relapse rates with these drugs seems to be increasing [4-6]. Various studies have been done in the past on antifungal agents used in the treatment of vulvovaginal candidiasis [4-6], however, very few have addressed the newer agents with better characteristics like lower relapse rates. Sertaconazole is a broad-spectrum newer topical antifungal agent that belongs to the azole class of drugs, having a more extensive action in the treatment of candidiasis [6,7]. Therefore, the present study was conducted with an aim to compare the efficacy of single dose sertaconazole versus multidose clotrimazole pessaries in patients with vulvovaginal candidiasis in reproductive age group.

MATERIALS AND METHODS

A prospective study was conducted at a tertiary care hospital in Pune city, India over a period of two years between October 2014 and September 2016 on 100 consecutive symptomatic patients diagnosed with vulvovaginal candidiasis. The ethical committee approval was obtained prior to the commencement of the study. Power analysis of the study was done keeping the prevalence of vulvovaginal candidiasis as 66% [4] and an alpha error of 5%, 50 patients in each group were required in order to achieve 80% power. Written informed consent was obtained from all the patients enrolled in the study. The inclusion criteria were symptomatic patients in reproductive age group (18-45 years) with diagnosed candidiasis (on microscopic examination) who agreed to avoid sexual intercourse during the study period and exclusion criteria was pregnant females, recently biopsied or operated cervix, vaginitis due to some other cause, history of previous treatment with antifungal agents within past four weeks, un-controlled diabetes, history of chronic illness, past history of hypersensitivity to imidazole agents, patients on antibiotic/immunosuppressant therapy.

The patients were randomised using the closed envelope technique where in the patients were asked to open a closed sealed opaque envelope once the diagnosis of candidiasis was confirmed and two groups were formed. The microscopic examination was done on the specimens obtained from the posterior fornix by wet mount (bamboo shoots cluster appearance with 10% KOH) and gram stain (presence of pseudopyphaes and positive budding yeasts) techniques. These patients were informed in detail about the study protocol and subsequent follow-ups. Those who consented for the same were included in the study. Group A (n=50) patients were treated with single dose sertaconazole and group B (n=50) patients were treated with multi dosage clotrimazole pessaries. Patients in group A were taught to self insert single dose of 500 mg sertaconazole at bed time and group B were treated using 500 mg clotrimazole pessaries once a day for three days. All the patients were followed

up after two weeks of treatment to assess their condition. A local examination was repeated at one, two and four respectively to check for recurrence. All the patients underwent microscopic examination to determine the presence of *Candida* species. The final evaluation was interpreted in terms of improvement in symptoms i.e., (Pruritis and discharge) when compared to the first visit and decrease in the number of counts on microscopy. There was no lost to follow-up in the present study.

STATISTICAL ANALYSIS

All the collected data was entered in Microsoft Excel Sheet 2007. The data was then transferred and analysed using SPSS ver. 21. Qualitative data was represented in the form of frequency and percentage while quantitative data was represented using Mean±SD. Appropriate statistical tests was applied based on the type and distribution of data. A p-value of <0.05 was taken as level of significance.

RESULTS

As per the demographic parameters, the mean age of the patients was 28.7±5.3 years, body height was 156±4.3 cm and body weight was 63.7±6.8 Kg. The average duration between the appearance of symptoms and consultation was 14.8±7.6 days. Majority of the patients were married (84%) followed by unmarried (13%) and widowed/separated (3%). The prevalence of candidiasis was most amongst the housewife's accounting for 64.3%. There was no statistically significant difference between both the groups in terms of socio-economic status, literacy rate. The response to the drug administration and clinical and microbiological response is shown in [Table/Fig-1,2]. There was no statistically significant difference in the response between both the drugs. At the end of six weeks, 14% of the patients in group A and 18% of patients in group B had recurrence of symptoms which was not statistically significant (p=0.7578) and thus were treated using oral fluconazole.

Parameter	Group A n=50 (%)	Group B n=50 (%)	p-value
Clinical response			
At one week	39 (78)	35 (70)	0.4945
At two weeks	3 (6)	7 (14)	0.3178
At four weeks	2 (4)	1 (2)	1
Microscopic response			
At one week	41 (82)	39 (78)	0.6285
At two weeks	3 (6)	2 (4)	1
At four weeks	1 (2)	2 (4)	1
Recurrence at 6 weeks	7 (14)	9 (18)	0.7578

[Table/Fig-1]: Response to treatment in both the groups.

Reaction	Group A, n=50 (%)			Group B, n=50 (%)		
	Day 0	2 weeks	4 weeks	Day 0	2 weeks	4 weeks
Pruritis	41 (82)	17 (34)	2 (4)	43 (86)	13 (26)	3 (6)
Diarrhoea	17 (34)	7 (14)	0 (0)	13 (26)	2 (4)	0 (0)
Perineal pain	23 (46)	3 (6)	1 (2)	25 (50)	5 (10)	0 (0)

[Table/Fig-2]: Response to the drug administration (Day 0 represent symptoms probably due to disease and not the drug).

DISCUSSION

Vulvovaginal candidiasis results from overgrowth of various *Candida* spp. which is usually a normal commensal organism of vagina [1,5,8] and is the second most common cause of vaginitis in the reproductive age group. It has been further uncomplicated (~90%) or complicated (~10%), based on microbiological findings, host factors, and response to therapy. Uncomplicated vulvovaginal candidiasis is usually sporadic or infrequent (≤3 episodes per year) with mild to-moderate symptoms caused by *C. albicans*, which are responsive to all forms of antifungal therapy, including short-course therapy in immunocompetent women. Complicated Vulvovaginal candidiasis includes severe cases, associated with pregnancy or any concomitant conditions such as immunosuppression or diabetes [8-10].

Approximately 30% of symptomatic women remained undiagnosed after clinical evaluation [11]. The most common symptoms in patients with vulvovaginal candidiasis are severe pruritis and burning like sensation accompanied by whitish discharge. Often these symptoms can give rise to secondary problems such as dyspareunia and dysuria [2,9,10]. Odds FC et al., reported that among the many signs and symptoms of vulvovaginal candidiasis, pruritis and vaginal discharge showed a tendency to be correlated with the numbers of *Candida* in the vagina [12]. Although it has been described as "cottage cheese-like" in character, the discharge may vary from being watery to homogenously thick [2,11,12]. In present study, most common complaint in subjects of vulvovaginal candidiasis was white discharge (100% cases) followed by pruritis (91%) and dysuria (30%). In a study by Verma K et al., white discharge was seen in all patients, while pruritis and dysuria was seen in 85% and 42% patients respectively [13]. Similar observation was made by Roongpisuthipong A et al., and Wang PH et al., [14,15]. Physical examination usually reveals erythema and swelling of the labia and vulva with normal cervix. Vaginal erythema is present, together with an adherent off-white discharge typically just prior to menses [16]. In addition to clinical symptoms, an accurate diagnosis also depends on the demonstration of *Candida* in vaginal swabs using vaginal pH measurement, microscopic examination, and/or fungal culture [2,8,10,17].

Acute candidalvulvo-vaginitis can be successfully treated with azole antifungal agents belonging to the azole group due to low level of resistance. These antifungals agents are usually administered as a single dose (fluconazole 150 mg) or as a pessary in a single or three day regimens. In patients with uncomplicated either therapy has shown to be equally efficacious. Topical antimycotic treatment with antifungal drugs is usually the therapy of choice in vulvovaginal candidiasis since oral drugs can have potential adverse effects like gastrointestinal disturbances and hepatotoxicity [18,19]. Various studies have shown that oral fluconazole is as effective as seven days of intravaginal clotrimazole therapy for *Candida* vaginitis and should be reserved for non-responders [20,21].

Sertaconazole is the first compound to bring a new chemical structure: benzothiophene 3,7- di substituted, together with the already known azole matrix [22]. Its efficacy, tolerability, and safety have been widely demonstrated in previous preclinical and clinical studies [15,23]. Sertaconazole has been shown to have a powerful antifungal activity both in vitro and in vivo on a broad spectrum of fungi, especially on dermatophytes (*Trichophyton, Microsporum, Epidermophyton*) and pathogenic yeasts (mainly against *C. albicans* and *C. tropicalis*) [15]. In a study by Wang PH et al., Dellenbach P et al., and Torres J et al., single dose sertaconzaole was enough in treatment of vulvovaginal candidiasis [15,23,24]. Similar finding was noted in the present study.

LIMITATION

Small sample size remains one of the limitations of the present study.

CONCLUSION

Although sertaconazole and clotrimazole has not shown statistically significant difference, it can be a wise option to prefer sertaconazole with respect to its single dosage regime, convenience and better acceptability in uncomplicated cases of vulvovaginal candidiasis.

REFERENCES

[1] Sobel JD. Candidal vulvovaginitis. Clin Obstet Gynecol. 1993;36(1):153-65.
[2] Ilkit M, Guzel AB. The epidemiology, pathogenesis, and diagnosis of vulvovaginal candidosis: A mycological perspective. Critical Reviews in Microbiology. 2011;37(3):250-61.
[3] Mitchell H. Vaginal discharge-causes, diagnosis, and treatment. BMJ. 2004;328:1306-08.
[4] Khan F, Baqai R. In vitro antifungal sensitivity of fluconazole, clotrimazole and nystatin against vaginal candidiasis in females of child bearing age. J Ayub Med Coll Abbottabad. 2010;22(4):197-200.
[5] Badiee P, Alborzi A, Davarpanah MA, Shakiba E. Distributions and antifungal susceptibility of *candida* species from mucosal sites in HIV positive patients. Archives of Iranian Medicine. 2010;13(4):282-87.
[6] Salehei Z, Seifi Z, Mahmoudabadi AZ. Sensitivity of vaginal isolates of *candida* to eight antifungal drugs isolated from Ahvaz, Iran Jundishapur. J Microbiology. 2012;5(4):574-77.
[7] Carrillo-Munoz AJ, Tur-Tur C, Giusiano G. Sertaconazole: an antifungal agent for the topical treatment of superficial candidiasis. Expert review of Anti-Infective Therapy. 2013;11(4):347-58.
[8] Sobel JD, Faro AS, Force RW, Foxman B, Ledger WJ, Nyirjesy PR, et al. Vulvovaginal candidiasis: epidemiologic, diagnostic, and therapeutic considerations. Am J Obstet Gynecol. 1998;178(2):203-11.
[9] Pappas PG, Kaufmann CA, Andes D, Benjamin DK Jr, Calandra TF, Edwards JE Jr, et al. Infectious Diseases Society of America. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis. 2009;48:503-35.
[10] Sobel JD. Vulvaginal candidosis. Lancet. 2007;369(9577):1961-71.
[11] Anderson MR, Klink K, Cohrssen A. Evaluation of vaginal complaints. JAMA. 2004;291(11):1368-79.
[12] Odds FC, Webster CE, Mayuranathan P, Simmons PD. *Candida* concentrations in the vagina and their association with signs and symptoms of vaginal candidiasis. J Med Vet Mycol. 1988;26(5):277-83.
[13] Verma K, Bhat M, Baniya GC. A Comparative study of antifungal activity of topical per vaginal application of tablet sertaconazole and clotrimazole in cases of vulvovaginal candidiasis. IJHSR. 2015;5(2):111-15.
[14] Roongpisuthipong A, Chalermchockcharoenkit A, Sirimai K, Wanitpongpan P, Jaishuen A, Foongladda S, et al. Safety and efficacy of a new imidazole fungicide, Sertaconazole in the treatment of fungal vulvo-vaginitis: a comparative study using Fluconazole and Clotrimazole. Asian Biomedicine. 2010;4(3):443-48.
[15] Wang PH, Chao HT, Chen CL, Yuan CC. Single-dose sertaconazole vaginal tablet treatment of vulvovaginal candidiasis. Journal of the Chinese Medical Association. 2006;69(6):259-63.
[16] Eckert LO, Hawse SE, Stevens CE, Koutsky LA, Eschenbach DA, Holmes KK. Vulvovaginal candidiasis: Clinical manifestations, risk factors, management algorithm. Obstet Gynecol. 1998;92(5):757-65.
[17] Abbott J. Clinical and microscopic diagnosis of vaginal yeast infection: A prospective analysis. Ann Emerg Med. 1995;25(5):587-91.
[18] De Vos MM, Cuenca-Estrella M, Boekhout T, Theelen B, Matthijs N, Bauters T, et al. Vulvovaginal candidiasis in a Flemish patient population. Clin Microbiol Infect. 2005;11:1005-11.
[19] Martens MG, Hoffman P, El-Zaatari M. Fungal species changes in the female genital tract. J Low Genit Tract Dis. 2004;8(1):21-24.
[20] Sobel JD, Brooker D, Stein GE, Thomason JL, Wermeling DP, Bradley B, et al. Fluconazole Vaginitis Study Group. Single oral dose fluconazole compared with conventional clotrimazole topical therapy of *Candida* vaginitis. American Journal of Obstetrics and Gynecology. 1995;172(4):1263-68.
[21] Mendling W, Krauss C, Fladung B. A clinical multicenter study comparing efficacy and tolerability of topical combination therapy with clotrimazole (Canesten®, two formats) with oral single dose fluconazole (Diflucan®) in vulvovaginal mycoses. Mycoses. 2004;47(3-4):136-42.
[22] Raga MM, Moreno-Manas M, Cuberes MR, Palacin C, Castello JM, Ortiz JA. Synthesis and antimycotic activity of (benzothienyl) methyl ethers of 1-(2,4-dichlorophenyl)-2-(1Himidazol-1-yl)-ethanol and of (Z)-1-(2,4-dichlorophenyl)-2-(1H-imidazol-1-yl)ethanoneoxime. Arzneimittelforschung. 1992;42:691-94.
[23] Dellenbach P, Thomas JL, Guerin V, Oshsenbein E, ContetAudonneau N. Topical treatment of vaginal candidiasis with sertaconazole and econazole sustained-release suppositories. Int J Gynecol Obstet. 2000;71:47-52.
[24] Torres J, Marquez M, Camps F. Sertaconazole in the treatment of mycoses: From dermatology to gynecology. Int J Gynecol Obstet. 2000;71:3-20.

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