EFFICACY OF SINGLE ORAL DOSE 150mg FLUCONAZOLE IN TREATMENT OF VAGINAL CANDIDIASIS

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ABSTRACT: AIMS: This study aimed to find out the efficacy of single oral dose 150mg of fluconazole in treatment of acute vulvovaginal candidiasis, to evaluate its safety assessment and the clinical and mycological efficacy assessment. **MATERIALS AND METHODS:** This study is carried out in department of obstetrics and gynaecology Gandhi medical college sultania hospital Bhopal and with the help of microbiology department Gandhi medical college Bhopal over a period of one year. It is a hospital based clinical prospective study. **RESULTS:** Maximum age incidence was found between 21-30years. Mostly patients belonged to low socioeconomic status and were uneducated. Maximum patients were married (98%) and multiparous (92%), nulliparous formed the smallest group (8%). In factors predisposing to candidiasis, contraceptive methods were found to be important in which maximum incidence was found in patients using oral contraception about 32% and 12% of IUCD users were affected. Other factors were antibiotic treatment (5%) and diabetes (2%). Vaginal discharge and pruritis were the two commonest symptoms found. Among the signs vaginal discharge and white plaques was the commonest sign. On follow up visits 88 cases had complete clinical cure and only 6 cases showed failure and 9 recurrences. In mycological assessment maximum 135 cases showed complete cure, 6 were failure and 9 recurrence. In overall results, excellent results were found in 88cases, good in 38 cases, fair in 9 cases and recurrence in 9 cases. Recurrences were mainly due to rectal carriers. **CONCLUSION:** In conclusion fluconazole was found effective as a systemic single oral dose therapy for acute vulvovaginal candidiasis. It is proved safe in terms of tolerance and preferred by patients. So in view of its favourable patients acceptability and compliance profile, it is considered as a first line therapeutic choice for treatment of women with vaginal candidiasis.

KEYWORDS: candidiasis, fluconazole.

INTRODUCTION: Vaginitis continues to be the most prevalent infection of female genital tract. Vaginal candidiasis is one of the common cause of vaginitis in women of reproductive age[1]. Vaginal candidiasis is an infection caused by Candida albicans or related fungi. The fungi isolated in the vagina in cases of candidiasis include C. albicans in 80-90% and others such as C. Glabrata and C. Tropicalis[2].

The symptoms of vaginal candidiasis vary from irritation and discharge in a mild infection to perineal discomfort and dyspareunia in a severe infection.

Fluconazole, 2 (2,4 difluoro phenyl) analogue is a new bis-triazole antifungal agent which is well absorbed orally with a long systemic half-life, has the potential for reducing or eliminating episodes of vaginal candidiasis[3]. In this study we have carried out a trial with fluconazole a newer triazole used orally as a single dose 150mg as a minimal side effect, long half life, more effective than azole, less costly and has better compliance and patient acceptance.

MATERIAL AND METHODS: This study is carried out in department of obstetrics and gynaecology Gandhi medical college sultania hospital Bhopal and with the help of microbiology department Gandhi medical college Bhopal over a period of one year. 150 cases with symptomatic and mycologically verified candidiasis were included in study and given 150mg single oral dose fluconazole.

INCLUSION CRITERIA: Women more than 18 years of age with characteristic features of vaginal candidiasis and clinical diagnosis were confirmed by microscopy and culture.

Diagnosis of vaginal candidiasis was based on clinical parameters like Redness of vagina and vulva, 'cottage cheese', discharge or by vaginal smear and by culture results.

Only positive cases were included in the study and these confirmed cases were given 150mg. Single oral dose fluconazole and were invited for follow up visit 10 to 14 days after the initial visit and second follow up visit at 28 to 60 days. In follow up visit women were examined and vaginal swab was taken for culture and smear.

All patients under went complete general and systemic examination and laboratory investigation perform were routine and specific. Specific were vaginal smear and culture.

The patient was examined in lithotomy position internal examination was done to note condition of uterus, cervix, and fornices. The state of vagina and the amount and type of discharge noted. Two swabs taken slide was prepared by one swab and the other sent for culture.

SMEAR TECHNIQUE: Gram's smear was fixed by passing them 2 to 3 times over the flame of spirit lamp:

1. Methyl violet
2. Gram's Iodine.

Gram stain smear show budding, spore and conidia and they are gram positive.

CULTURE TECHNIQUE: Vaginal swabs were taken and put on Sabouraud's 2% glucose agar and incubated at 37'C or at room temperature for 2 to 3 days. A typical white or ivory smooth colony with yeast odour appears.

At each follow up visits clinical efficacy assessment, mycological efficacy assessment and safety assessment were done.

Clinical efficacy assessment was done by assessing signs and symptoms at follow up visits. Efficacy was noted by examiner and scored as cure, improved, failure and recurrence.

1. **CURED** – Disappearance of all signs and symptoms at both follow up visit.
2. **IMPROVE** –
   (a) Persistence of occasional signs and symptoms.
   (b) Persistence of few signs and symptoms.
3. **FAILED** – Persistence of all signs and symptoms at both visits.
4. **RECURRENCE** – Disappearance of signs and symptoms at first visit and reappearance at second visit.

Mycological efficacy assessment was done by making smear and culture from vaginal swab taken on both visit s and evaluating that smear and culture. Efficacy was noted as:

1. **CURE** – complete absences of organism in smear and culture at both visits.
2. **FAILED OR PERSISTENCE** - positive smear and culture throughout the follow up visit.
3. **RECURRENCE** - Reappearance of organism in smear and culture at long term follow up visit after short term negative smear culture.

Safety assessment was done for recording side effects of fluconazole by asking general questions at both follow up visits.

Global assessment was done by combining both clinical & mycological assessment and results are described as follows:

1 **EXCELLENT** – Mycological cure with no sign and symptoms.
2 **GOOD** - Mycological cure with occasional signs and symptoms.
3 **FAIR** – Mycological cure with few signs and symptoms.
4 **BAD –** No mycological cure and persistence of all signs and symptoms.
5 **RECURRENCE –** Mycological cure and clinical cure at short term visit and reappearance of sign and symptoms and culture positive at long term visit,

RESULTS: The study was conducted at Sultania Zanana Hospital, Bhopal during one year. A total of 150 cases who were clinically and mycologically verified candidiasis were included in the study and given 150mg single dose fluconazole. The observations are as follows:

	NUMBER	PERCENTAGE
AGE IN YEARS		
Below 20 years	12	8%
21-30 years	111	74%
31-40 years	23	15%
41 and above	4	3%
EDUCATIONAL STATUS		
uneducated	78	52%
Upto middle school	42	28%
Upto high school	22	14.6%
graduates	8	5.4%
PARITY		
nulliparous	12	8%
multiparous	138	92%
MARITAL STATUS		
Married	148	98.6%
unmarried	0	0%
Widow	2	1.4%
Total	150	100

TABLE :1 Sociodemographic features

Factors	No. of Cases	Percentage
Contraception		
Not used	62	41%
Used	88	58%
broad spectrum antibiotic treatment	8	5.3%
corticosteroid treatment	0	0%
diabetes mellitus	4	2.7%

TABLE 2: DISTRIBUTION OF CASES ACCORDING TO FACTORS PREDISPOSING TO VAGINAL CANDIDIASIS

	No. of Cases	**%**
TEMPORARY		
Oral contraception	48	32%
IUCD	18	12%
Others	6	4%
PERMANENT		
sterilized	16	10%

TABLE 3: DISTRIBUTION OF CASES ACCORDING TO METHOD OF CONTRACEPTION USED

SYMPTOMS	**No. of Cases**	**%**
Discharge	140	93%
Pruritis	122	81%
Burning sensation	92	61%
Dyspareunia	64	42%

TABLE 4: DISTRIBUTION OF CASES ACCORDING TO SYMPTOMS

CLINICAL SIGNS	**No. of cases**	**Percentage**
Discharge	140	93%
Plaque	108	72%
Redness	100	66%
Pain	76	50%

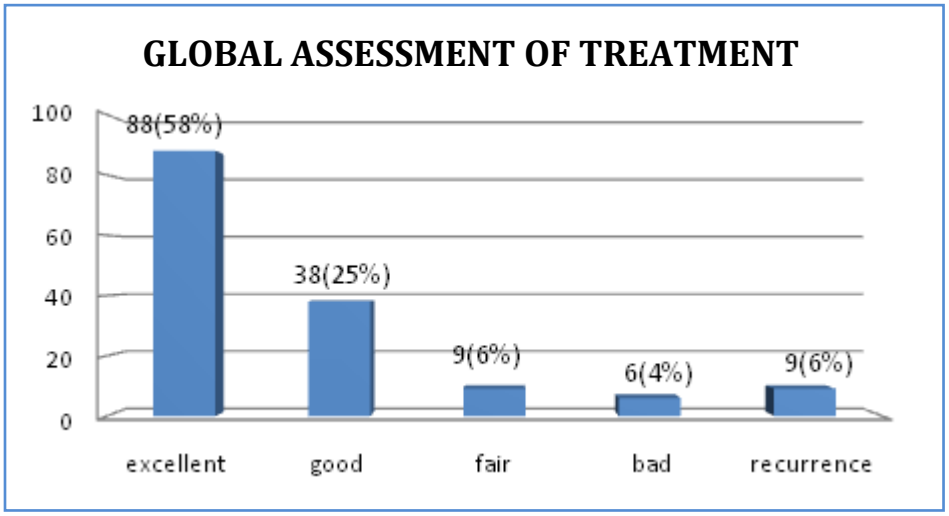
Table 5 : DISTRIBUTION OF CASES ACCORDING TO CLINICAL SIGNS

	Short term Follow up	**Long term Follow up**
cure	144(96%)	135(90%)
failed	6(4%)	6(4%)
recurrence	-	9(6%)

TABLE 6: DISTRIBUTION OF CASES ACCORDING TO MYCOLOGICAL EFFICACY ASSESSMENT

	Short term Follow up	**Long term Follow up**
cure	97(64%)	88(58%)
improve	47(31%)	47(31%)
failed	6(4%)	6(4%)
recurrence	-	9(6%)

TABLE 7: DISTRIBUTION OF CASES ACCORDING TO CLINICAL EFFICACY ASSESSMENT



DISCUSSION: A study of clinically and mycologically verified cases of vaginal candidiasis was carried out in department of obstetrics and gynaecology, Sultania Zanana Hospital, Bhopal for a period of one year. These 150 patients of vaginal candidiasis were given 150mg single dose of oral fluconazole and were invited for two follow up visits at 10-14 days and 20-60 days. Clinical, mycological and safety assessment were done at each follow up visit.

Maximum incidence of vaginal candidiasis was between the age group of 21-30 years (74%) followed by 15% between 31-40 years. All patients were married (148 out of 150) except two patients who were widow. The highest incidence of candida vaginitis in this age group is due to increased sexual activity and spread of infection from male partner and high glycogen content of vaginal epithelial cells favouring growth of candida. Erica et al found high incidence of vaginitis with maximum sexual activity[4].

Most of the patients were uneducated (52%) and only 20% were educated upto middle school. This shows that candidiasis is more common in uneducated patients.

It was found that about 138 cases (92%) were multiparous and 12 cases (8%) were nulliparous. This shows that higher incidence seen in multiparous women.

Women who take oral contraceptive pills have a higher rate of vulvovaginal candidiasis[3]. According to one theory, Candida cells have estrogen and progesterone receptors that, when stimulated, increase fungal proliferation[6]. In this study we found 32% women on oral contraceptive pills having vaginal candidiasis. Reed B et al and Sobel et al reported the same reports. Proposed mechanisms include increased adherence, receptivity, increased vaginal glycogen and increased yeast virulence.

In this study 4 patients were found to be diabetic. Hyperglycemia enhances the ability of C. albicans to bind to vaginal epithelial cells[6]. Bohanon et al found candidiasis common in diabetes.

Out of 150 patients, vaginal discharge were found in 140 cases (93%), pruritis in 122 cases (81%), burning sensation in 92 (61%), dyspareunia in 42% of the cases. This shows that vaginal discharge is the most common symptom[8]. Shaheeh et al reported discharge in all 100% of the cases and pruritis in 93% of the cases[9]. Various signs of vaginal candidiasis were recorded. The signs most commonly encountered were vaginal discharge in 140 patients (93%), white plaques in 108 cases

(72%), redness of vulva and vagina in 100 cases (66%) and pain during examination in 76 cases (50%). In study done by B. Kaplan and Rabinerson et al in Israel found the incidence of various signs as follows: vaginal discharge 89% cases, plaques in 855 cases, redness in 62% cases, pain during examination in 28% cases[7].

Clinical efficacy assessment – at short term follow up visit complete cure occur in 64% cases and at long term follow up visit 58% were cured. Improvement occurs in 47 cases (31%) in short term and long term follow up visits. Treatment failure occurs in 6 cases (4%) and recurrence occurs in 9(6%) cases.

Mycological efficacy assessment at short term follow up 96% was completely cured and long term follow up 90% cured. 6 cases (4%) were found at both follow up visits and recurrences were found in 9 cases (6%).

A meta analysis[10] on various studies conducted on the efficacy of single-day dose of fluconazole comprising 3279 patients, found a positive clinical response in 94% with a range of 88-100% and mycological cure in 85% (range 76-98%) of patients at first followup visit. Furthermore, in a similar European multicentre study, 70% patients were cured clinically during therapy and 24% improved clinically[10]. Our findings do not coincide with the results of above-mentioned studies. This may be because of secondary drug resistance as fluconazole is a commonly prescribed drug in our population for vulvovaginal candidiasis. Similarly, primary resistance of local candida species to fluconazole cannot be ruled out. The small sample size of our study necessitates further studies to validate the findings.

Global assessment was done and results were recorded as : Excellent in 80% cases (58%), good in 38 cases(25%), fair in 9 cases(6%),bad in 6 cases(6%),recurrence in 9cases(6%).

In the study done by B. Kaplan and Rabinerson et al (1997) reported excellent result in 69% 6 week follow up, from our study the recurrence rate found in 6% cases. Though we have not included recurrent cases in our study. Mostly recurrence and failure occur when associated factor like diabetes and use of antibiotic present.

Finally it can be said that fluconazole is safe and effective drug used in cases of vaginal candidiasis and achieves good control and cure in most of the patient.

This study has shown that fluconazole when given in single oral dose is effective in treatment vaginal candidiasis.

CONCLUSION: Vaginitis is most common gynaecological problem. Candidal vaginitis is most common vaginal infection affecting women of reproductive age group.

In conclusion fluconazole was found effective as a systemic single oral dose therapy for Acute Vulvovaginal Candidiasis. It is proved safe in terms of tolerance & preferred by the patients. So in view of its favourable patient's acceptability and compliance profile, it considered as a first line therapeutic choice for treatment of women with vaginal candidiasis.

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