

Clinical and Mycological Clearance of Vulvovaginal Candidiasis With Fluconazole of Kit 2, NACO, GOI**B. Archana¹, D. Subhash Reddy^{2*}, D. Sudha Vani³, D. Indira⁴, G. Jyothi Lakshmi⁵, Hetanshi Raval⁶, Niaz Mohammad⁷, Ratul Maji⁸**

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Abstract

Background: Candida albicans, along with other closely related Candida species, are the primary causative agents of vulvovaginal candidiasis (VVC)—a multifactorial infectious disease of the lower female reproductive tract resulting in pathologic inflammation. **Aims:** The present study was undertaken to know the clinical and Mycological clearance of Vulvovaginal candidiasis after treatment with Fluconazole of Kit 2 of NACO. It has been carried out in the tertiary care center over a period of 18 months. **Materials and methods:** A total of 100 patients of Clinically and Mycologically verified Candidiasis cases were included in the study and given Kit 2 of NACO and invited for follow up visit at 7 days after the initial visit and second follow up visit at 14 days. In follow up visit women were examined and vaginal swab was taken for smear. **Results:** Clinical efficacy assessment – at short term follow up visit complete cure occur in 80% short term cases and at long term follow up visit 76% were cured. Mycological efficacy assessment – at short term follow up visit complete cure occur in 93% short term cases and at long term follow up visit 86% were cured. Overall assessment - Excellent in 73 cases (73%), fair in 13 cases (13%), poor in 7 cases (7%), recurrence in 7 cases (7%). **Conclusion:** It can be said that fluconazole 150mg single dose of Kit 2 of NACO is safe and effective drug used in cases of Vulvovaginal candidiasis and achieves good control and cure in most of the patients.

Keywords: Candida albicans, vulvovaginal candidiasis, syndromic management, NACO, Fluconazole

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Introduction

VVC is defined as signs and symptoms of inflammation in the presence of Candida sp. and in the absence of other infectious etiology[1]. C. albicans is the most common species causing VVC.

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Non-albicans candida species are emerging pathogens more commonly in diabetic and immunocompromised individuals[2]. VVC presents as pruritus and vaginal discharge, typically cottage-cheese-like in character, which vary from watery to homogeneously thick, vaginal soreness, irritation, vulvar burning, dyspareunia, and dysuria. Odour is minimal and inoffensive. Examination reveals erythema and swelling of the labia and vulva, with discrete pustulopapular peripheral lesions with adherent whitish discharge. Diagnosis is based on history and physical examination[3-5]. KOH mount, wet mount and gram staining are done routinely, while positive culture is the most specific test[6]. Incidence in women below 40 years of age is 75%, of which 50% will have a second episode, and 5% will have chronic infection[7].

Syndromic management is an economical and effective treatment at the first contact between patient and health care provider recommended by the National AIDS control organization, which is Kit 2 containing Fluconazole 150mg and Secnidazole 2g for treatment of Vaginal discharge. Fluconazole is for the treatment of VVC. It acts by inhibition of C-14 α demethylase which is required for ergosterol synthesis which is a component of fungal cell wall [7-9].

Aims and Objectives: Present study was undertaken to assess the efficacy (clinical and mycological clearance) of single dose Fluconazole 150mg of kit 2 of NACO in treatment of VVC and relation with demographic data and associated risk factors.

Materials and Methods

A clinical trial without control group was conducted in a tertiary care hospital in South India to determine the clinical and mycological

clearance of vulvovaginal candidiasis after treatment with KIT 2 (containing 150mg single oral dose fluconazole and 2g single oral dose Secnidazole) of NACO, Government of India. After taking ethical approval, 100 women of more than 18 years of age, with symptomatic and microscopy verified candidiasis were included in the study. Patients with pregnancy and lactation, known allergy to Azoles, impaired renal or hepatic function and undergoing chemotherapy were excluded from the study. In the selected patients, detailed history was taken and clinical examination performed. High vaginal swabs were taken after obtaining verbal consent. Samples were then subjected to microscopy after performing Potassium Hydroxide (KOH) mount (Figure 1) and Gram's stain (Figure 2). These patients were given Kit 2 of NACO and were invited for a follow up visit at 7 days after the initial visit and second follow up visit at 14 days.



Fig 1: KOH preparation showing candida

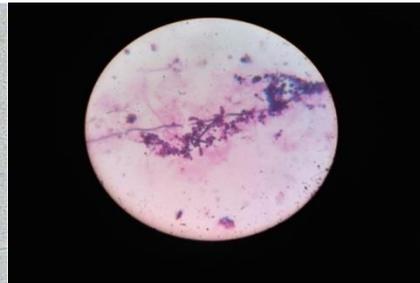


Fig 2: Gram Stain showing candida

At each follow up visit, clinical efficacy assessment, mycological efficacy assessment was done. Clinical efficacy assessment was done by assessing signs and symptoms at each visit. Efficacy was noted and scored as cure, improved, failure and recurrence.

1. Cured – Disappearance of all signs and symptoms at both follow up visits.
2. Improved – Persistence of few signs and symptoms.
3. Failed – Persistence of all signs and symptoms at both follow up visits.
4. Recurrence – Disappearance of signs and symptoms at first visit and reappearance of signs and symptoms at second visit.

Mycological efficacy assessment was done by making a smear from the vaginal swab taken on both visits and evaluating that smear. Efficacy was noted as:

1. Cured – Complete absence of organism in smear at both visits.
2. Failed – Positive smear throughout the follow up visit.
3. Recurrence – Reappearance of organism in smear at long term follow up visit after short term negative smear.

Overall 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. Fair – Mycological cure with few signs and symptoms.
3. Poor – No mycological cure and persistence of all signs and symptoms.
4. Recurrence – Mycological cure and clinical cure at short term visit and reappearance of sign and symptoms and microscopy positive at long term visit.

Data obtained was analyzed using Microsoft Excel 2017. Descriptive statistics (Mean, Median and standard deviation) and inferential statistics (t-test) were used. A p-value < 0.05 was considered statistically significant.

Results

Between December 2017 and May 2019, 100 clinically and mycologically verified candidiasis cases were included in the study and given Kit 2 of NACO.

Table 1: The characteristics of the patients

Characteristics	Frequency	Percentage
Age Group		
15-25	19	19%
26-35	45	45%
36-45	22	22%
>45	14	14%
Marital Status		
Married	92	92%
Unmarried	8	8%
Parity		
Multipara	82	82%
Nullipara	11	11%
Not Applicable	7	7%
Educational Status		
Uneducated	62	62%
Middle School	12	12%

High School	17	17%
Graduate	9	9%
Locale		
Rural	44	44%
Urban	56	56%
Contraception		
Used	67	67%
IUCD	22	22%
OCP	15	15%
Barrier	9	9%
Permanent	21	21%
Not Used	25	25%
Risk Factors		
IUCD	22	22%
OCP	15	15%
Diabetes Mellitus	6	6%
Antibiotic	5	5%
Previous h/o Candidiasis	19	19%
Other STD	4	4%
No risk factors	29	29%
Duration of Symptoms		
< 7 days	31	31%
8-14 days	24	24%
> 14 days	45	45%
Presenting Complaints		
White Discharge	100	100%
Burning Micturition	27	27%
Itching	54	54%
Presenting Signs		
Discharge	100	100%
Erythema	39	39%

The mean age was 33.51 ± 8.9313 (SD) years, with peak prevalence (45%) seen in the age group of 26-35 years. Majority (92%) of the patients were married, and 89% were primipara or multipara against nullipara (11%). The disease was more prevalent in uneducated women (62%), followed by High school (17%), Middle school (12%) and graduates (9%). Also it was more common in urban women (56%) than rural women (44%) in the present study. Contraception was used in 67 women (67%). Among them, the most common method of contraception used was IUCD (22%) followed by permanent method in 21 women (21%), OCP's in 15 women (15%) and barrier contraceptives in 9 women (9%). No method of contraception was used by 25 women (25%). Most common risk factor for VVC was IUCD in 22 women (22%), followed by previous history of Candidiasis in 19 women (19%), OCP usage in 15 women (15%), diabetes in 6 women (6%), antibiotics usage in 5 (5%)

women and other STDs in 4 women (4%). The most common associated STD is bacterial vaginosis. However, no risk factors were identified in 29 women (29%). The median duration of symptoms was 14 days (range, two days to 3 months). White discharge was the most common symptom present in all the women (100%) followed by itching which was seen in 54% of the women and Burning Micturition in 27% of the women. Resolution of these symptoms are depicted in table 4. Most common presenting sign in the present study was discharge (100%) followed by erythema in 39% cases. *Clinical efficacy assessment (Table 2):* At short term follow up visit on day 7, complete cure occurred in 80% cases, improvement occurs in 12 cases (12%) and treatment failure occurs in 8 cases (8%). At long term follow up visit on day 14, 76% were completely cured, improvement seen in 10 cases (10%), treatment failed in 7% and recurrence occurred in 7(7%) cases.

Table 2: Clinical and mycological clearance

Response to Treatment	Short Term Follow up	%age
Clinical clearance		
Cured	80	80%
Improvement	12	12%
Failed	8	8%
Recurrence		
Mycological clearance		
Cured	93	93%
Failed	7	7%
Recurrence	-	-

Mycological efficacy assessment at short term follow up visit, complete cure occurred in 93% and treatment failed in remaining 7% cases. At long term follow-up visit, 86% were cured, treatment failure occurred in 7(7%) cases and recurrence seen in 7(7%) cases.

Overall assessment was done and results were recorded as: Excellent in 73 cases (73%), fair in 13 cases (13%), poor in 7 cases (7%), recurrence in 7 cases (7%).

Table 3: Overall response to treatment

Overall Response	Number	Percentage
Excellent	73	73%
Fair	13	13%
Poor	7	7%
Recurrence	7	7%

P-value in the present study is 0.04896, which signifies that a single dose of Fluconazole of Kit 2 of NACO is effective in clinical and mycological clearance of vulvovaginal candidiasis.

Table 4: Smear positivity rate

Complaints with smear positivity	Number of cases at presenting time	Number of cases at long term visit
White Discharge with smear '+'	100	14
Burning Micturition with smear '+'	27	1
Itching with smear '+'	54	9

Discussion

Vaginal discharge is a common problem encountered in clinical practice. Majority of the cases respond well to the treatment but some can be persistent or recurrent. This can be very distressing to the patient causing social, economic and psychosexual consequences. In the present study, peak prevalence was found in age group of 26-35 years (45%). Similarly, Kavitha et al's [10] study reported majority of the patients between 26-35 years accounting for 54%. In a study by Shabana et al [11] a maximum incidence was recorded between 21-30 years (74%), while in Jacob L et al study [12], VVC was found in the age groups of 18-25 years (22.8%). Women of childbearing age groups are more vulnerable to vaginal candidiasis due to risky sexual behaviors and physiological tissue changes, caused by reproductive hormones, which increase susceptibility to Candida infection. According to Okungbowa et al study, low prevalence of VVC in older women was probably due to the increase in vaginal immunity with age as they have decreased levels of oestrogen and corticoids, and so are resistant to Candida infections [13]. In this study, VVC is more prevalent in married women (92%) than unmarried women (8%). In study conducted by Shabana et al, all patients were married (148/150) and in Leila Sekhavat et al study [14], VVC was seen in 69.5% married. Increased incidence of Candida vaginitis in married women is due to increased sexual activity, spread of infection from male partner and high glycogen content of vaginal epithelial cells favoring growth of Candida. In the present study, VVC is more prevalent in uneducated group (62%), followed by high school (17%), and followed by middle school (12%) and graduate (9%). In Shabana et al study, maximum patients were uneducated (52%) and only 20% were educated up to middle school. Similarly, in Kamy Ramesh Swaminathan study [15], most patients were illiterate (44.1%), followed by primary education (26.6%), secondary education (19.1%) and degree (10%). This shows that candidiasis is more common in uneducated patients. In this study, VVC is more prevalent in multipara (89%) than nullipara (11%). Similarly, in Shabana et al study, 92% were multiparous and 18% were nulliparous. Also, in Meena Salvi study [16], prevalence of VVC was higher in women with parity above 2 (40%) and lower in nulliparous (25.4%). This finding attributes to higher sexual activity, poor personal hygiene and higher contraceptive device use in multiparous women. In this study, VVC is more prevalent in urban women (56%) than rural women (44%). There are no available studies to compare these findings. This higher incidence could be attributed to health awareness and availability of specialists in the urban area. In this study, contraception was used in 67 women (67%). Among them, the most common was IUCD (22%) followed by permanent method in 21 women (21%), OCP's in 15 women (15%) and barrier contraceptives in 9 women (9%), while 25 women (25%) used no method of contraception. In Edith Angel-Müller et al study, no method of contraception was used by 35.59% women, surgical method by 48.68% women, hormonal methods by 31.57% women, intrauterine device by 11.84% and barrier methods by 7.89% women. In Shabana et al study [11], oral contraception was used by 32% women, IUCD by 12%, sterilization by 10% and other methods by

4%. On analyzing the data, most important risk factor predisposing to VVC, was found to be intrauterine device (22%) followed by oral contraceptive (15%). Similarly, Meena Salvi study [16] also showed higher prevalence of VVC with usage of IUCD (40%) and OCP's (28%). In Shabana et al study, higher prevalence of VVC with OCP (32%) and IUCD (12%) was noted. The association of diabetes was in 6 (6%) of the women. Increased glucose levels in the genital tissue enhance yeast adhesion and growth, and vaginal epithelial cells have a greater propensity to bind to *C. albicans* in women with diabetes [18]. The association with antibiotics, which was predominantly over the counter (OTC) was 5 (5%). History of deliberate and undulant use of antibiotics, corticosteroids usage (15%) was also a frequent risk factor in Rupal Samal et al study [19]. The most likely hypothesis is that both antibiotics and contraceptives can alter the vaginal microbiota, indirectly favoring the development of fungal infections. Previous candidiasis was the risk factor in 19 women (19%). Previous candidiasis was the most common risk factor associated with VVC prevalence (66%) in Meena Salvi study [16], which was higher than our study. All these risk factors associated in our study correlated well with Kamy Ramesh Swaminathan et al study [15], according to which, 35 (29.1%) of the women were pregnant, 16 (13.3%) of the women had previous candidiasis and 16 (13.3%) had a prolonged use of antibiotic, which were OTC, 11 (9.1%) of the women used oral contraceptive as a method of contraception and 61 (50.8%) had Copper-T inserted following a child birth. 21 (17.5%) of the women had associated other vaginal infections and like bacterial vaginitis similar to our study [15]. In the present study, white discharge was the most common symptom present in all the women (100%) followed by itching in 54% women and Burning Micturition in 27% women. Most common presenting sign in this study was discharge (100%) followed by erythema in 39% cases. In the study conducted by Shabana et al, vaginal discharge was found in 93% cases, pruritus in 81% cases, burning sensation in 61% cases, dyspareunia in 42% of the cases. The signs most commonly encountered were vaginal discharge in patients (93%), white plaques in 72%, redness of vulva and vagina in 66% and pain during examination in 50%. In Edith Angel-Müller et al study [17], the most frequent symptom was vaginal discharge (96.6%) followed by foul smell (57.6%) and pruritus (54.2%). Vaginal discharge was present in all patients on genital examination which was in concurrence with our study and erythema (47.5%) which was slightly higher than our study. Other signs in the study which were not present in our study were foul smell (70.3%) and edema (40.7%). However, in Ahmad and Khan's study of 215 women with Candida vaginitis [20], 80% complained about itching but only 20% had vaginal discharge. This observed variation in complaints and symptoms may be due to differences in microbiology (e.g., species of fungus) and culture (particularly with regard to sexual behavior as a result of differences in the studies' region of origin. In the present study, clinical efficacy assessment – at short term follow up visit, complete cure occurred in 80% cases and at long term follow up visit 76% were cured. Improvement occurred in 12 cases (12%) in short term and 10 cases (10%) in long term follow up visits. Treatment

failure occurred in 8 cases (8%) in short term and 7% in long term follow up visits and recurrence occurred in 7(7%) cases. In Edith Angel-Muller et al study[17], overall clinical cure rate with the combination of oral Secnidazole plus Fluconazole was 90.38% which was higher than our study. The study conducted by Shabana et al[11], showed 64% cured cases at short term follow up visit and 58% cured at long term follow up visit, which was lower than our study. In the present study, mycological efficacy assessment – at short term follow up visit had 93% cured cases and at long term follow up visit 86% were cured. Treatment failure occurred in 7(7%) cases and recurrence occurred in 7(7%) cases. In the Shabana et al study[11] on mycological efficacy assessment at short term follow up, 96% were completely cured and at long term follow up 90% were cured. 6 cases (4%) were found at both follow up visits and recurrences were found in 9 cases (6%) which was slightly higher than our study. In Edith Angel-Muller et al study[17] 97.1% microbiological cure rate of VVC was noted, while by Leila Sekhavat et al[14], therapy improved mycology results by 83.3%. In present study overall clearance assessment results were recorded as Excellent in 73 cases (73%), fair in 13 cases (13%), poor in 7 cases (7%), and recurrence in 7 cases (7%). In the study done by Shabana et al¹¹, Excellent was recorded in 80% cases (58%), good in 38 cases (25%), fair in 9 cases (6%), bad in 6 cases (6%), recurrence in 9 cases (6%).

Limitations of the Study

1. Sample size was small,
2. Lifestyle-related factors were missing,
3. Causative pathogen and its therapeutic susceptibility were not identified.

Conclusion

The present study has shown that single dose of Fluconazole of kit 2, NACO is able to effectively reduce the number of complaints and improve the clinical symptoms associated with Candida vaginitis. A single dose of the combination of oral Fluconazole plus Secnidazole in syndromic management of vaginal discharge allows high cure rate with efficacy of 95 - 98% and good compliance, complete treatment at the first visit thus preventing the spread of sexually transmitted disease and HIV. Immediate complete treatment prevents complications, relapse and further transmission.

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