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A COMPARATIVE STUDY ON SAFETY PROFILE OF ORAL ANTIFUNGALS TERBINAFINE AND FLUCONAZOLE IN CASES OF DERMATOPHYTOSIS.

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ABSTRACT

Objective: This study aimed to compare the safety profile of oral terbinafine and fluconazole in patients with dermatophytosis.

Method: This prospective observational study was conducted at the dermatology outpatient department of Santosh Medical College and Hospital, Ghaziabad. A total of 156 patients were included in this study. The participants were divided into two groups, A and B. Group A patients were treated with 250 mg terbinafine PO daily, and Group B was treated with fluconazole 150 mg PO daily for two-week duration. Follow-ups were done on the first, second, and fourth weeks to monitor the ADRs. The causality of ADRs was assessed using the WHO-UMC evaluation criteria, whereas the severity of ADRs was assessed using the Hartwig and Siegel scale.

Results: In Group A, 6 (7.79%) of the patients experienced ADRs, with the most common being headache 3 (27.27%) and vomiting 3 (27.27%). Group B had a 24 (30.38%) incidence of ADRs, with xerosis being the leading ADRs in 9 (23.08%) of cases. Female participants in both groups had a higher incidence of ADRs than male participants. In the 18–28 years age Group, ADRs were observed in 3 (50.00%) patients in Group A and 11 (45.83%) patients in Group B. Among individuals aged 29-38 years, ADRs occurred in 2 (33.33%) patients in Group A and 8 (33.33%) patients in Group B. In the 39-48 years age Group, A single female patient (16.67%) in Group A experienced ADRs, while 3 (12.50%) patients in Group B experienced ADRs. Among those aged 49-58 years, 2 (8.33%) patients in Group B experienced ADRs. The Causality assessment indicated that the majority of ADRs in both groups were categorized as possible, while in the severity assessment, most ADRs were classified as mild.

Conclusion: Terbinafine and fluconazole both showed ADRs however, fluconazole had a higher incidence, particularly in female patient.

INTRODUCTION

Dermatophytes are a globally distributed group of keratinophilic molds invading keratinous material in the superfacial layer of the skin and its appendages, including hair, nails, hooves, feathers, and claws in both humans and animals. These molds are responsible for a range of infections collectively termed as dermatophytosis also commonly known as ringworm or tinea.(1) The occurrence and frequency of dermatophytosis differ according to socioeconomic and geographic factors. Certain fungal skin infections manifest more frequently in regions with lower socioeconomic status attributable to factors such as overcrowded living environments, close contact with animals, and inadequate hygiene practices. Dermatophytes flourish in warm and moist environment leading to increased incidence of dermatophytosis in tropical area.(2) The prevalence of dermatophytosis in India ranges from 36.6–78.4%.(3). Various antifungal drugs are currently available for the treatment of dermatophytosis. Systemic drug used commonly includes oral terbinafine and fluconazole.(4) Terbinafine is used orally and belongs to the allylamine class of antifungal drugs. It is used as a first-line therapy for the treatment of tinea corporis and tinea cruris. It shows action by inhibiting the enzyme squalene epoxidase needed for the biosynthesis of ergosterol by fungi.(5) Fluconazole is a triazole class of drugs which inhibits the synthesis of ergosterol, an important component of fungal cell membrane. It is used in various fungal infections. It is available in oral form metabolism is primarily by kidney like other azoles from liver.(6) Dermatophytosis is currently a disease of global importance and along with developing countries it is public health problem in many parts of the world. (7)

Materials and Methods

This study included patients attending the outpatient department ofdermatology at Santosh Medical College and Hospital Ghaziabad. Ethical approval was obtained from the Institutional Ethics Committee.

Sample size: A total of 156 patients were included based on the inclusion and exclusion criteria.

Inclusion Criteria

- All newly diagnosed cases of dermatophytosis.
- Patients must be ≥ 18 years old at the start of the study.
- Patients of both genders will be enrolled

Exclusion Criteria

- Pediatric patients (<18 years)
- Pregnant women and lactating mothers
- Patents already being on anti-fungal therapy

All enrolled Patients diagnosed with dermatophytosis were randomly divided and allocated into Group A and Group B. Group A patients were treated with terbinafine at a dose of 250 mg PO once daily for two weeks Group B patients were treated with fluconazole at a dose of 150 mg PO once daily for two weeks.

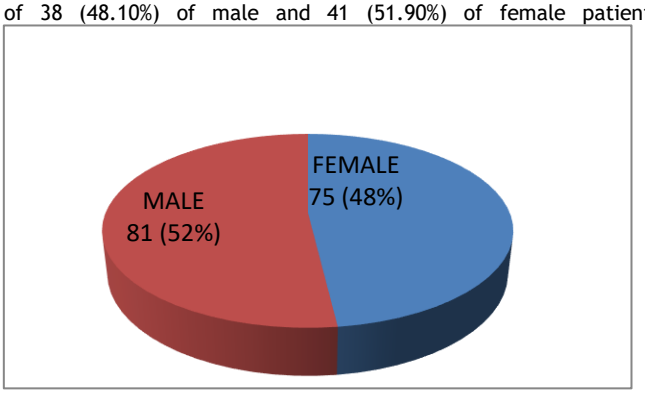
After the enrolled patients initial visit, follow-up was performed at the first, second, and fourth week telephonically and OPD visits to monitor adverse drug reactions, and if any adverse drug reactions. All adverse drug reactions were entered in ADR form version 1.4 later causality assessment and severity were assessed using WHO-UMC scale & Hertwig and Siegel scale respectively.

Statistical Analysis

The frequencies of all types of adverse drug reactions were evaluated using percentage comparisons. The causality of ADRs was assessed using the WHO-UMC evaluation criteria, whereas the severity of ADRs was assessed using the Hartwig and Siegel scale.

Results

This was a prospective, observational study. A total of 156 patients divided into two groups A (77 patients) and B (79 patients) randomly were included in the study according to inclusion and exclusion criteria. In this study, out of total 156 patients 81 (52%) males and 75 (48%) females. Group A consisted of 43 (55.85%) of male and 34 (44.15%) of female patients, while Group B consisted of 38 (48.10%) of male and 41 (51.90%) of female patients.



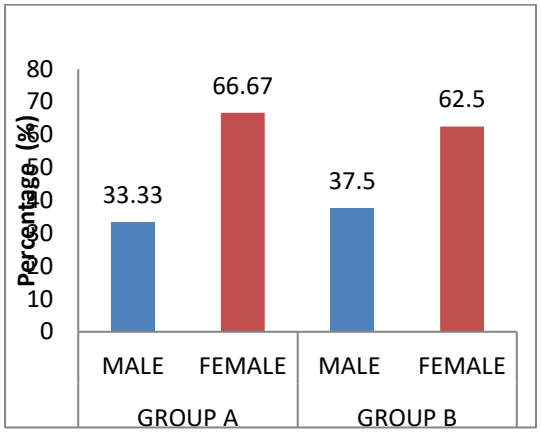
Patients enrolled in group A were treated with terbinafine at a dose of 250 mg once daily for duration of two weeks conversely, those in group B were treated with fluconazole at a dose of 150 mg once daily for the same two-week period.

In group A, 2 (33.33%) male patients and 4 (66.67%) female patients experienced adverse drug reactions. In contrast, in group B, 9 (37.50%) male patients and 15 (62.50%) female patients reported ADRs. The incidence of ADRs was notably higher in Group B than in Group A. The occurrence of ADRs was higher in females than in male in both groups.

Table 1: Age and Gender wise distribution of Patients Developed ADRs.

Age Group (In Years)	Group A			Group B		
	Male	Female	Total	Male	Female	Total
18 - 28	1	2	3	4	7	11
29 - 38	1	1	2	3	5	8
39 - 48	0	1	1	1	2	3
49 - 59	0	0	0	1	1	2
Total	2	4	6	9	15	24

In the youngest age Group A 18–28 years, Group A exhibited ADRs in a total of 3 (50.00%) patients 1 (16.67%) in male and 2 (33.33%) in female. Group B Presented ADRs in a total of 11(45.83%) patients: 4 (16.67%) male and 7 (29.17%) female.In age Group of 29-38 years in Group A total 2 (33.33%) patients experienced ADRs 1 (16.67%) in male and 1 (16.67%) in female. Conversely, in group B, 8 (33.33%) patients experienced ADRs 3 (12.50%) in male and 5 (20.83%) in female. In the age Group of 39-48 years, Group A 1 (16.67%) female patient experienced ADRs, while in group B, 3 (12.50%) patients experienced ADRs: 1 (4.17%) in male and 2 (8.33%) in female. In age Group of 49-58 years in group B 2(8.33%) patients experienced ADRs 1 (4.17%) in male and 1 (4.17%) in female.



In group A, 6 patients (7.79%) have experienced ADRs. The most common ADRs were headache 3 (27.27%), vomiting 3 (27.27%) this is followed by nausea 2 (18.18%) and pruritus with 2 cases (18.18%) abdominal discomfort were reported by 1 patient (9.09%).

Group B 24 patients (30.38%) experienced ADRs. The majority of ADRs is xerosis 09 (23.08%) followed by alopecia and xerostomia both with 06 (15.38%) cases headache, nausea and abdominal discomfort 4 (10.26%), vomiting and fatigue were reported by 03 (7.69%) patients each.

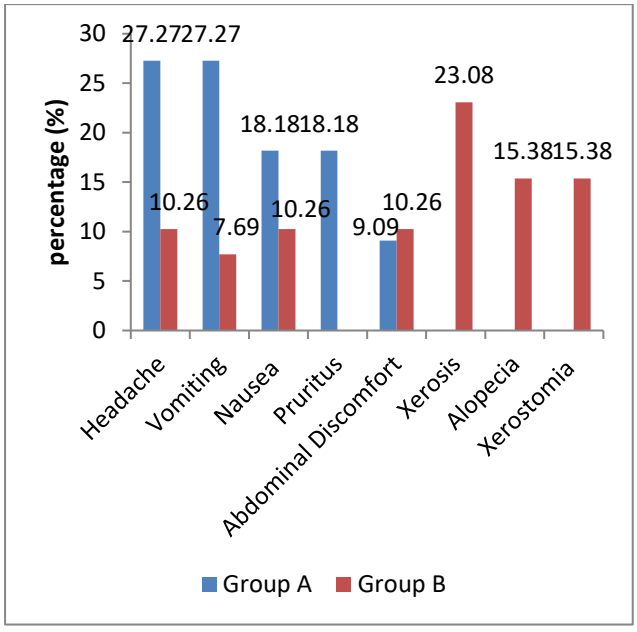


Figure 3: Adverse effects in Group A and Group B

Causality assessment of ADRs was performed using WHO-UMC scale. In group A 3 (27.27%) of cases were classified as probable and 8 (72.73%) cases were possible. In group B 15(38.46%) cases fell under the probable category and 24 (61.54%) were categorized as possible.

The severity of ADRs was assessed using the Hertwig and Seigel scale. In Group A all 11(100%) cases were categorizedmild in severity. In Group B mild severity was identified in 32 (82.05%) ADRs whereas moderate severity was noted in 7 (17.95%) cases.

DISCUSSION

This study aimed to compare the incidence and severity of adverse drug reactions in patients treated with terbinafine and fluconazole for dermatophytosis at Santosh Medical College and Hospital, Ghaziabad. In this study was observed that patients treated with fluconazole reported a greater incidence of ADRs than patients treated with terbinafine. The incidence of ADRs in female has been reported to be higher than that male in both the groups.

This gender based ADRs difference was noted by another study conducted by Matveev et al.2022,which reported that ADRs in females are higher than in males. The higher incidence of ADRs in female patients could be attributed to the unique pharmacokinetic and pharmacodynamic response to drugs in female physiology, psychological considerations and potentially higher drug usage by this category of people. (8)

In the current study patients treated with terbinafine in group A reported ADRs such as headache, nausea, vomiting, pruritus and abdominal discomfort however another study by Cohen et al. 2020 documented a lichenoid drug eruption as a result of terbinafine an ADR not observed in our study.(9)

Conversely, Group B treated with fluconazole exhibited a broader range of ADRs with xerosis being the most frequently repeated ADRs aligning with a previous study by Davis et al. 2019 on the tolerability of long-term fluconazole therapy. (10) A case report study conducted by Mahendra et al. 2006 showed fixed dose eruption caused by fluconazole which was not observed in our present study. (11)

In the present study, according to the WHO-UMC causality assessment scale in Group A patients treated with terbinafine and Group B patients treated with fluconazole most ADRs were possible category in both groups in a previous study by Padmavathi et al. 2013. This indicated that the majority of adverse cutaneous drug reactions were classified under the probable category which is similar to the present study. (12)

The severity assessment performed using the Hertwig and Siegel scale in present study majority of ADRs cases fell in mild category in contrast with a previous study by Mukherjee et al. 2020 which identified the majority of cases as being in the moderate category, presenting finding that diverge from the present study. (13)

CONCLUSION

Patients treated with oral fluconazole had higher incidence of ADRs than those treated with oral terbinafine. Females experienced a higher incidence of ADRs in both groups.

The adverse reaction profiles, including- headache, nausea, vomiting, abdominal discomfort fatigue and dizziness were similar between two groups. Pruritus, was prevalent in the terbinafine Group A absent in the fluconazole Group B. Xerosis, alopecia, fatigue and xerostomia, were prevalent in Group B fluconazole and were absent in Group A terbinafine. Overall in the present study terbinafine can be considered better than fluconazole for the treatment of dermatophytosis.

Conflicts of Interest

There are no conflicts of interest

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