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Original Research Paper

Pharmacology

A COMPARATIVE STUDY OF EFFICACY OF ITRACONAZOLE VERSUS TERBINAFINE AND THEIR COST EFFECTIVENESS IN THE TREATMENT OF RESISTANT DERMATOPHYTOSIS OF SKIN AT NALANDA MEDICAL COLLEGE, A TERTIARY CARE TEACHING HOSPITAL OF PATNA.

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ABSTRACT

Background- Dermatophytoses are common fungal infections prevalent in hot and humid climate. Itraconazole and Terbinafine are commonly used antifungal agents for the treatment of dermatophytoses. However, increased resistance is being seen with conventional doses of these drugs. Also, these infections are more common among low socio-economic population. Therefore, this study has been undertaken to compare the efficacy and cost effectiveness of Itraconazole and Terbinafine in increased dosages in resistant dermatophytoses of skin.

Objectives- To compare the efficacy of Itraconazole and Terbinafine in increased dosages in resistant dermatophytoses of skin and to select cheaper drug among them.

Materials and Methods- In this open, parallel, prospective, comparative study, 200 patients of Tinea cruris and Tinea corporis diagnosed clinically and confirmed by potassium hydroxide (KOH) test, were randomly and equally divided into two groups. Group I patients received Itraconazole 200mg twice daily while group II patients received Terbinafine 250mg twice daily for 4 weeks. Patients were evaluated at the end of 2 and 4 weeks.At the end of 4 weeks KOH test was repeated to evaluate mycological cure.

Results- At the end of 4 weeks mycological and clinical cure was seen in 92% patients in group I while 75% patients in group II. Mild adverse effects like headache, taste disturbances and gastrointestinal upset were observed in few patients of both groups but none was significant enough to discontinue therapy. Cost of therapy was more with Itraconazole than that of Terbinafine.

Conclusion- High dose Itraconazole therapy is more effective than high dose Terbinafine therapy in resistant dermatophytoses. However cost of therapy is more in case of Itraconazole. But Terbinafine has higher failure rates and the duration of treatment may require longer, thereby reducing the cost difference. Therefore, Itraconazole seems superior to Terbinafine in the treatment of resistant T.corporis and T. cruris infection in higher doses.

KEYWORDS : Itraconazole, Terbinafine, Resistant dermatophytosis

INTRODUCTION:

Dermatophytoses, the fungal infections caused by three genera of dermatophytes, namely, *Trichophyton, Epidermophyton & Microsporum,* are very common in summer and monsoon in our country due to hot and humid climate. Recent prevalence of dermatophytosis ranges from 36.6% - 78.4% in India[1]. Itraconazole and Terbinafine are the preferred drugs for the treatment of dermatophytoses[2].

Itraconazole is a synthetic triazole compound which acts by inhibiting fungal cytochrome P450 enzyme resulting into reduced ergosterol synthesis[3]. The selective toxicity of azole drugs results from their greater affinity for fungal than for human cytochrome P450 enzymes[3].Usual dose of Itraconazole in dermatophytosis of skin is 200mg/day for 1-2 weeks[2].

Terbinafine is a synthetic allylamine which also acts by interfering with ergosterol biosynthesis, but, by inhibiting fungal enzyme squalene epoxidase[3]. Standard dose of Terbinafine in dermatophytosis of skin is 250mg/day for 1-2 weeks[2].

However, now a days, widespread resistance to conventional doses of these antifungal agents are seen. An expert consensus on the management of dermatophytosis in India suggested that resistant Tinea corporis and Tinea cruris infections should be treated with higher doses of systemic drugs preferably Itraconazole and Terbinafine for a minimum duration of 4 weeks[4]. Therefore, this study was conducted to compare the efficacy of Itraconazole and Terbinafine in higher doses in resistant cases.

Also, these infections are more common among low socioeconomic population due to poor sanitary conditions, overcrowded population and lack of knowledge about hygiene. Again, recalcitrant nature of these infections need longer duration of therapy as well as adherence to the treatment. So the another objective of this study was to find out the cheaper therapy among the two.

MATERIALS AND METHODS:

This randomized, open, parallel, prospective study was conducted in the department of pharmacology at Nalanda Medical College & Hospital, Patna, between April 2019 & September 2019. 200 patients of both genders of resistant dermatophytosis of skin (Tinea corporis and Tinea cruris) attending OPD of the skin & V.D. department of Nalanda Medical College & Hospital, Patna in this period, who were willing to participate in the study and gave written and informed consent, were enrolled after fulfilling the inclusion and exclusion criteria and divided randomly into two groups of 100 each. Group I patients received 200mg Itraconazole (capsule Candiforce-200) twice daily for 4 weeks while group II patients received 250mg Terbinafine (tablet Terbinaforce 250mg) twice daily for 4 weeks.

- Inclusion criteria- patients of both genders aged between 18-55 years with clinical diagnosis of resistant Tinea corporis and Tinea cruris and confirmed by potassium hydroxide (KOH) test.

- **Exclusion criteria-**

1. Age < 18 years and > 55 years
2. Pregnant and lactating women
3. Known hypersensitivity to any of the study medications
4. Preexisting diabetic, renal, hepatic and cardiac disease patients
5. Patient on any other regular medications

A baseline liver function test was done at the beginning of the study and again at the end of 2 weeks of therapy. KOH test

was also repeated at the end of 4th week after completion of therapy.

Patients were evaluated at the end of 2nd and 4th week for any improvement in clinical symptoms and also for adverse effects. Clinical response was divided into cured, improved and not cured types. A cured case was defined as one who had complete absence of symptoms (pruritis, scaling, erythema etc.) as well as mycologically negetive KOH test after completion of therapy. Not cured was defined as neither remission of symptoms nor mycologically negetive KOH test. An improved case was in between the two who had clinically improved symptoms but mycological status was not known.

At the end of study, the results were compiled, tabulated, calculated in percentage and statistically analyzed using Chi-square tests.

RESULTS:

The demographic profile of patients and diagnosis in both the groups are shown in Table-1.

Table-1 Demographic profile and diagnosis in group I and group II

Parameters	Group I	Group II
Age (in years) (mean±SD)	35.1±14.2	34.9±13.1
Gender	Male 55 Female 45	Male 54 Female 46
Diagnosis		
Tinea corporis	10	12
Tinea cruris	14	13
Tinea corporis + Tinea cruris	76	75

The mean age of group I patients was 35.1±14.2 years and there were 55 males and 45 females. In group II, mean age was 34.9±13.1 years and there were 54 males and 46 females. Most of the patients were diagnosed with both Tinea corporis and Tinea cruris in both the groups as shown in the table-1. There was no statistically significant difference in demographic profile and diagnosis in both the groups.

Fig-1 and Fig-2 shows treatment outcomes at the end of 2 weeks and 4 weeks in group I and group II respectively. At the end of 2 weeks, in group I, there were 60% patients whose symptoms were improved but at the end of 4 weeks, 92% patients were cured. In group II, 75% patients had improved symptoms at the end of 2 weeks while the number of patients cured at the end of 4 weeks was same i.e. 75%. The result was significantly better in Itraconazole group.

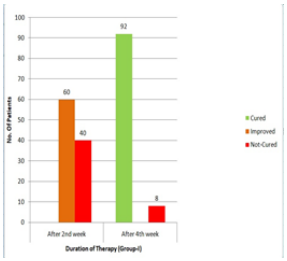

Fig-1 Treatment outcome in group I

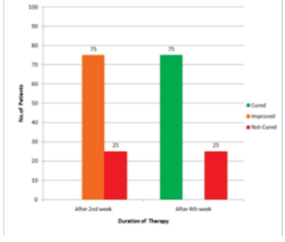

Fig-2 Treatment outcome in group II

There were 5 cases of gastric upset, 3 cases of altered taste and 1 case of headache seen among group I patients while in group II, 6 cases of gastric upset, 2 cases of altered taste, 1 case of headache and 1 case of rash were seen. These adverse effects were mild and did not require discontinuation of therapy.

Total cost of therapy of group I was Rs. 1228.00 while that of group II was Rs. 602.00.

DISCUSSION:

In our study, both Itraconazole and Terbinafine were found effective in the treatment of resistant dermatophytosis of skin but , Itraconazole came out as better drug as compared to Terbinafine in terms of efficacy as well as mycological cure rate. It is similar to other earlier studies done by A. Bhatia *et al.* and NB Shakya *et al.* in patients with T. cruris and T. corporis who also found Itraconazole superior to Terbinafine in cure rate[5][6]. However studies on toenail onychomycosis done by Sigurgeirsson B *et al.* and Bala Tripura Sundari Ankani suggests Terbinafine as more effective than Itraconazole [7][8].

Both of these drugs have similar pharmocokinetic and safety profile. Although cost of therapy is more in case of Itraconazole than terbinafine but in terms of cure rate, Itraconazole is better than Terbinafine.

CONCLUSION:

Itraconazole has higher cure rates both clinically as well as mycologically than Terbinafine. Although the cost of treatment is lower with Terbinafine for same duration of therapy, but it has higher failure rates and the duration of treatment may require longer, thereby mitigating the cost difference. Therefore, Itraconazole seems superior to Terbinafine in higher doses in the treatment of resistant T.corporis and T. cruris infection.

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