

# Comparison of Efficacy of Terbinafine and Fluconazole in Patients of Tinea Corporis

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## ABSTRACT

**Background:** Tinea corporis is a worldwide superficial fungal infection that mimics many other annular lesions. As the Tinea Corporis have a significant impact on patient's life physically and psychologically. So, physicians must have knowledge about this condition and its treatment options. **Objective:** To compare the efficacy of terbinafine versus fluconazole in patients of tinea corporis. **Study Design:** It was a randomized controlled trial. **Settings:** Department of Pharmacology, Khalifa Gulnawaz Teaching Hospital, Bannu, Khyber Pakhtunkhwa & DHQ Teaching Hospital, Bannu, Khyber Pakhtunkhwa Pakistan. **Duration:** Six months from 10 Feb to 10 Aug 2020. **Methodology:** From both the genders 102 patients aged between 20-45 years who presented with tinea corporis were included in the study. Two treatment groups were made by random allocation of patients. Patients in Group-A were treated with oral terbinafine while those in Group-B were given fluconazole. Frequency of efficacy being outcome variable was labeled upon complete resolution of the tinea corporis in 4 weeks (counted from start of treatment) and was compared between the groups. An informed written informed consent was taken from all the patients. **Results:** The patients had a mean age of 31.66±6.99 years while the mean duration of disease was 5.41±2.16 months. There were 55 (53.9%) male and 47 (46.1%) female patients with a male to female ratio of 1.2:1. The frequency of efficacy was significantly higher in patients treated with terbinafine as compared to fluconazole (90.2% vs. 64.7%; p-value=0.002). This difference was same in all subgroups as well. **Conclusion:** Oral terbinafine was found more efficacious than conventional treatment with oral fluconazole in patients with tinea corporis regardless of patient's age, gender and duration of disease which advocates preferred use of terbinafine in the treatment of such patients in future practice.

**Keywords:** Tinea Corporis, Terbinafine, Fluconazole.

## INTRODUCTION

Tinea is a fungal infection caused by dermatophytes and it is widespread geographically. Dermatophytes have three genera namely Microsporum, Epidermophyton and Trichophyton.<sup>1</sup> Most commonly encountered varieties of tinea are tinea cruris (affects inguinal region) and tinea corporis (affects trunk and limbs). Mostly, it is caused by Trichophyton species that digest keratin in the cells of the stratum corneum.<sup>2,3</sup>

According to World Health Organization, superficial mycotic infection prevalence has been estimated to be 20%-25% worldwide.<sup>4,5</sup> In clinical practice for effective treatment of dermatophytic conditions different antifungal agents both systemic and topical have been introduced. The commonly used drugs include oral griseofulvin, terbinafine, fluconazole and itraconazole. Terbinafine is the orally available allylamine antifungal. With a favorable mycological and pharmacokinetic profile, terbinafine is a first-line drug for treatment of

tinea corporis. Terbinafine acts by inhibiting the enzyme squalene epoxidase thus inhibits the synthesis of ergosterol, an important component of fungal cell membrane leading to fungal cell wall disintegration.<sup>6</sup>

An alternative is fluconazole which is given orally once a week for up to four consecutive weeks. Fluconazole, a synthetic triazole derivative, is an azole antifungal agent. Terbinafine is an allylamine. It is a synthetic antifungal agent.<sup>7</sup> Amit *et al* conducted a study and found that the efficacy of Terbinafine was slightly greater as compared to fluconazole (92.86% vs. 82.00% respectively: P > 0.05) in the treatment of tinea corporis.<sup>8</sup> Yazdanpanah *et al* reported this efficacy to be 87.5% for Terbinafine and 64.3% for Fluconazole group.<sup>9</sup> However, no single best treatment option available for treatment of Tinea Corporis. There was no local published data. So, the purpose of this study was to repeat this clinical study in local population and see the efficacy of both drugs in local population which can help us in identifying the drug with

maximum efficacy and that drug can be used for the treatment of the local population suffering from Tinea Corporis.

## METHODOLOGY

**Study Design:** Randomized controlled trial.

**Settings:** Department of Pharmacology for a period of

**Duration:** Six months from 10 Feb to 10 Aug 2020.

**Sampling Technique:** Non-probability, consecutive sampling.

**Sample Size:** Sample size of 102 patients was calculated with 95% significance level and 80% power of test with expected efficacy of terbinafine (250 mg) to be 87.5% and fluconazole (150 mg) to be 64.3%.<sup>9</sup>

**Inclusion Criteria:** Patients of both genders with age in the range of 20-45 years suffering from tinea corporis as per operational definition and who signed written informed consent to participate in the study were included in the study.

**Exclusion Criteria:** Patients with evidence of hepatic or renal disease, pregnant females, nursing mother, hypersensitivity or intolerance to treatment, patients who were taking cisapride were excluded from the study.

**Data Collection Procedure:** Two equal size study groups were made by random allocation of patients. Patients in Group I were given oral terbinafine (250 mg) daily at morning time after breakfast for 4 weeks while patients in group II were given oral fluconazole (150 mg) once weekly at morning time after breakfast for 4 weeks.

Patients were followed after the end of treatment and skin scrapings were taken from involved toes and were treated with 20% KOH. Efficacy of treatment was labeled upon negative fungal hyphae on microscopic examination of preparation (as per operational definition). All the information including patient's demographic information and efficacy of treatment was recorded. All the patients were evaluated before and after treatment by same consultant dermatologist to eliminate bias. Exclusion criteria were used to control confounding variables. Numerical variables; age and duration of disease have been presented by mean  $\pm$  SD. Categorical variables; gender and efficacy of the treatment have been presented by frequency and percentage. Chi-square test has been applied for comparison of efficacy between the two groups taking p-value  $\leq$ 0.05 as significant. To address affected modifiers, data has been stratified for age, gender, and duration of disease. Chi-square test has been applied after-stratification, taking p-value  $\leq$ 0.05 as significant.

## RESULTS

Patients had mean age of 31.66 $\pm$ 6.99 years ranging between 20 years to 45 years. There were 55 (53.9%) males and 47 (46.1%) females in the sample with a male to female ratio of 1.2:1. The duration of disease ranged from

2 months to 9 months with a mean of 5.41 $\pm$ 2.16 months as shown in Table 1.

**Table 1: Baseline Characteristics of Study Sample**

Characteristics	Participants (n=133)
Age (years)	31.66 $\pm$ 6.99
20-32 years	57 (55.9%)
33-45 years	45 (44.1%)
Gender	
Male	55 (53.9%)
Female	47 (46.1%)
Duration of Disease (months)	5.41 $\pm$ 2.16
2-5 months	51 (50.0%)
6-9 months	51 (50.0%)

In terms of mean age (p-value=0.944), mean duration of disease (p-value=0.785) and distribution of various age (p-value=0.842), gender (p-value=0.843) and duration of disease (p-value=0.552) both the groups were comparable as shown in Table 2.

**Table 2: Baseline comparison of study groups**

Characteristics	Terbinafine (n=51)	Fluconazole (n=51)	P-value
Age (years)	31.61 $\pm$ 7.11	31.71 $\pm$ 6.93	0.944
20-32 years	29 (56.9%)	28 (54.9%)	0.842
33-45 years	22 (43.1%)	23 (45.1%)	
Gender			
Male	27 (52.9%)	28 (54.9%)	0.843
Female	24 (47.1%)	23 (45.1%)	
Duration of Disease (months)	5.47 $\pm$ 2.15	5.35 $\pm$ 2.19	0.552
2-5 months	27 (52.9%)	24 (47.1%)	0.552
6-9 months	24 (47.1%)	27 (52.9%)	

Chi-square test and Independent sample t-test, statistically insignificant difference

In patients treated with terbinafine, frequency of treatment efficacy was significantly high as compared to fluconazole (90.2% vs. 64.7%; p-value=0.002) as shown in Table 3.

**Table 3: Comparison of Efficacy between the Study Groups**

Efficacy	Terbinafine (n=51)	Fluconazole (n=51)	P-value
Yes	46 (90.2%)	33 (64.7%)	0.002*
No	5 (9.8%)	18 (35.3%)	
Total	51 (100.0%)	51 (100.0%)	

Chi-square test, \* difference was observed statistically significant

This difference was same in all subgroups as well as shown in Table 4.

**Table 4: Comparison of Efficacy between the Study Groups across Various Subgroups**

Subgroups		Terbinafine (n=51)	Fluconazole (n=51)	P-value
Age (years)	20-32 years	26/29 (89.7%)	18/28 (64.3%)	0.022*
	33-45 years	20/22 (90.9%)	15/23 (65.2%)	0.038*
Gender	Male	24/27 (88.9%)	18/28 (64.3%)	0.032*
	Female	22/24 (91.7%)	15/23 (65.2%)	0.027*
Duration of Disease (months)	2-5 months	25/27 (92.6%)	16/24 (66.7%)	0.020*
	6-9 months	21/24 (87.5%)	17/27 (63.0%)	0.045*

Chi-square test, \* observed difference was statistically significant

## DISCUSSION

With about 1.5 million species, fungi are ubiquitous, however quite a few species are pathogenic to humans. Fungi invading into human host are prevented by low redox potential in tissues, temperature of 37 °C and imminent barriers.<sup>1,3</sup> But due to modern clinical practices, overcrowded population thought out the world has increased incidence of fungal infections (mycoses) throughout the world. This increase is supported by expanded use of broad-spectrum antibiotics, immunosuppressive therapies and central venous access devices.<sup>3,4</sup>

Clinical characteristics developed by dermatophytosis which is commonly known as ringworm or tinea are vesicles, inflammation, pustules and erthematous flaky skin besides particular clinical characteristics of each dermatophytosis or tinea.<sup>11,12</sup> Tinea corporis is the most common clinical form present often in the neck, in exposed glabrous skin, shoulders, torso, and extremities.<sup>2,3</sup> Fluconazole is conventionally used antifungal agent for the treatment of such patients with varying degree of success.<sup>2</sup> Recent studies claimed terbinafine, another antifungal agent to be more efficacious than fluconazole and advocated its preferred use in future dermatologic practice.<sup>8,9</sup> However, the available evidence was limited while there locally published study was found that necessitated the present study.

We observed mean age of tinea corporis patients was 31.66±6.99 years. Similar mean age of 30.4±6.6 years has been reported by Amit *et al* among Indian patients with tinea corporis.<sup>5</sup> In other Indian studies, Banerjee *et al*, Prakash *et al* and Bhatia *et al* reported similar mean age of 29.9±10.9 years, 32.1±6.6 years and 34.9±7.2 years respectively among such patients.<sup>13-15</sup>

We observed that there was a slight male predominance among patients of tinea corporis with a male to female ratio of 1.2:1. In another local study, Farooqi *et al* reported similar male predominance among patients presenting with fungal skin infections and observed it to be 1.2:1 at PNS Shifa Hospital and the Institute of Skin Diseases, Karachi.<sup>16</sup> Hussain *et al* reported similar male predominance among such patients with 1.3:1 ratio between male & female, at District Headquarter Hospital, Okara.<sup>17</sup> Bhatia *et al* (1.2:1), Pandit *et al* (1.2:1), Banerjee *et al* (1.2:1), Kalsi *et al* (1.3:1), Banerjee *et al* (1.5:1) and Prakash *et al* (1.7:1) also observed similar male predominance among such patients in India.<sup>13-15,18-20</sup>

In the present study, frequency of treatment in patients treated with terbinafine was significantly higher as compared to fluconazole (90.2% vs. 64.7%; p-value=0.002). Same differences were observed between the groups across various subgroups based on patient's age, gender and duration of disease. Our results are similar to those of Amit *et al* who also reported similar yet insignificantly higher frequency of efficacy with terbinafine as compared to fluconazole (92.86% vs. 82.00% respectively: p-value >0.05) in treating tinea corporis.<sup>8</sup> Similar higher frequency of efficacy with terbinafine in comparison with fluconazole has also been reported by Yazdanpanah *et al* (87.5% vs. 64.3%; p-value=0.239).<sup>9</sup>

In local population owing to scarcity of published data this study added research evidence on the topic. The study establishes that oral terbinafine is more efficacious than conventional treatment with fluconazole in patients with tinea corporis regardless of patient's age, gender and duration of disease which advocates preferred use of terbinafine in the treatment of such patients in future practice.

## CONCLUSION

Oral terbinafine was found more efficacious than conventional treatment with oral fluconazole in patients with tinea corporis regardless of patient's age, gender and duration of disease which advocates preferred use of terbinafine in the treatment of such patients in future practice.

## LIMITATIONS

A very strong limitation to the present study was that various side effects between the treatment groups could not be compared. Also it was limited by short follow-up of 4 weeks.

## SUGGESTIONS / RECOMMENDATIONS

Long term follow-up to compare the frequency of recurrence is also required to establish the efficacy of treatment. Such a study is highly recommended in future research.

**CONFLICT OF INTEREST / DISCLOSURE**

None.

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