

# Efficacy of Itraconazole vs Itraconazole Plus Isotretinoin in Treatment of Chronic Tinea

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## ABSTRACT

**Background:** About 20 to 25% of the global population is affected by the fungal skin infections. Different antifungal drugs used in traditional doses have developed widespread resistance, necessitating the development of an efficient antifungal treatment.

**Objective:** To assess efficacy of itraconazole vs itraconazole plus isotretinoin in treatment of chronic tinea.

**Methodology:** This was comparative study conducted at the Department of Dermatology Qazi Hussain Ahmad Complex Nowshera and alshifa clinic and skin aesthetic, Nowshera for duration of one year from November 2020 to November 2021. In both group A and B, 40 individuals were taken randomly. Treatment of group A patients was done with oral itraconazole and isotretinoin while patients of group B treatment was done with oral itraconazole alone. All patients were monitored for four weeks to assess their responsiveness to therapy and side effects.

**Results:** Complete cure response was recorded in all the patients of group A, while in group B, complete cure response was recorded in 20 (50%) patients. A statistically significant treatment response was observed between both the groups ( $p < 0.05$ ). There were 22 (55%) individuals in group A and 7 (17.5%) patients in group B who had cheilitis and dryness of the lips as major adverse effects.

**Conclusion:** Our study concludes that combination therapy with oral itraconazole and isotretinoin is efficient and safe for the treatment of chronic tinea. Our study recommends conducting study based on large sample size for better results.

## INTRODUCTION

About 20 to 25% of the global population is affected by the fungal skin infections<sup>1</sup>. Fungal infections are more in areas with hot and humid climatic conditions<sup>2</sup>. Because of its good mycological and pharmacokinetic characteristics, terbinafine is regarded a first-line medication for the treatment of fungal infections caused by tinea<sup>3</sup>. It works by preventing ergosterol formation by blocking the enzyme squalene epoxidase<sup>4</sup>. Cure rates of >90% were reported with dosages of 250 mg once day for 2 weeks in the past with this medication against dermatophytosis<sup>3,4</sup>.

Terbinafine resistance has been on the rise presently, accompanied by an increase in frequency of therapeutic failures<sup>5,6</sup>. A reduction in effective medication concentration is one of the main mechanisms of antifungal resistance<sup>7</sup>. Terbinafine was shown to be safe and effective in the treatment of dermatophytosis, with lower failure rates when given at higher dosages of 500 mg per day<sup>4</sup>.

In addition to terbinafine, itraconazole is an antifungal medication that works by blocking the cytochrome P450-dependent enzyme, thereby affecting the demethylation of lanosterol to ergosterol<sup>8,9</sup>.

It has recently been discovered that different antifungal drugs used in traditional doses have developed widespread resistance, resulting in a rise in relapse rates, necessitating the development of an efficient antifungal treatment, as well as an adequate dose and time regimen, to obtain maximal outcomes with minimal relapses. In order to boost the efficacy in the treatment, dermatologists are increasingly administering greater than usual dosages of oral antifungals and/or over longer periods of time. A patient with recurrent dermatophytosis was recently treated

satisfactorily with a combination of oral itraconazole and oral isotretinoin<sup>10</sup>. Retinoids are thought to cause enhanced desquamation of the normal epidermis, resulting in fast keratinocyte sloughing and elimination of fungal spores, lowering the fungal burden<sup>10</sup>. According to the literature data is not available about the combination therapy of oral itraconazole and oral isotretinoin. This study was therefore conducted to compare the effectiveness of oral itraconazole alone and oral itraconazole combined with oral isotretinoin for the treatment of chronic tinea.

## MATERIALS AND METHODS

This was comparative study piloted at the Department of Dermatology Qazi Hussain Ahmad Complex Nowshera and alshifa clinic and skin aesthetic, Nowshera. The study duration for this research work was one year from November 2020 to November 2021. Research and ethical committee of the hospital give approval to our study. A written consent form was signed from all the patients included in our study. The inclusion criteria for our study was all the adult patients confirmed with chronic tinea with two or more episodes in last 12 months while the exclusion criteria was patients with immunological problems, patients having known kidney, heart and liver problems, patients with diabetes mellitus, patients hypersensitive to itraconazole or isotretinoin and lactating or pregnant mothers. Totally 80 patients were included in our study. All the data of the patients was documented on predesigned Performa. 40 patients were included in both the group A and B. Group A patients were treated with oral itraconazole (100mg daily dose) combined with oral isotretinoin (20mg daily dose) while group B patients were treated with daily dose of oral itraconazole (200mg) alone. During study

period, topical therapy was not given but according to requirement oral antihistamines were permitted for itching. All patients were monitored for four weeks to assess their responsiveness to therapy and side effects.

The patients with incomplete response were followed for additional two weeks. SPSS version 23 was used for statistical analysis. For qualitative data, mean (SD) were calculated while frequency and percentages were calculated for quantitative data. Chi-square test was used for comparison of treatment response between the two groups. A p-value of less than 0.05 was taken as significant.

**RESULTS**

In our study a total of 80 patients were included. In Group A, there were 23 (57.5%) male and 17 (42.5%) female while in Group B there were 25 (62.5%) male and 15 (37.5%) were female.(Figure 1) The mean (SD) age in Group A was 32.11 (4.23) years with minimum age of 18 and maximum age of 49 years while in Group B, the mean (SD) age was 33.72 (6.11) years with minimum age of 20 and maximum age of 45 years. (Table 1) Complete cure response was recorded in all the patients of group A, while in group B, complete cure response was recorded in 20 (50%) patients.

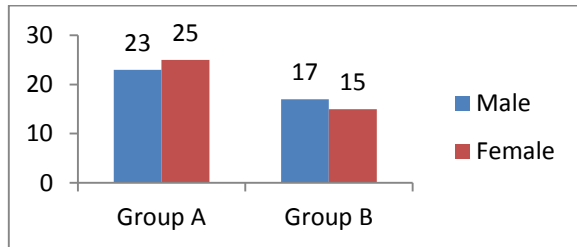


Figure 1: Gender wise distribution of patients in both the groups

Table 1: Age wise distribution of patients in both the groups

Parameter	Group A	Group B
Mean (SD) age in years	32.11 (4.23)	33.72 (6.11)
Minimum age	18	20
Maximum age	49	45

Table 2: Cure response of patients in both the groups

Response of cure	Group A n (%)	Group B n (%)	p-value
Over all complete response	40 (100%)	20 (50%)	0.029*
complete response after 4 weeks	32 (80%)	16(80%)	
complete response after 6 weeks	8 (20%)	4(20%)	
Incomplete response	00	20 (50%)	

A statistically significant treatment response was observed between both the groups (p<0.05).(Table 2) There were 22 (55%) individuals in Group A and 7 (17.5%) patients in Group B who had cheilitis and dryness of the lips as major adverse effects. No patient in either group needed treatment discontinuation.

**DISCUSSION**

A fungal skin infection increases all over the globe, and the cause has been connected to a complicated interaction between the host, environment, fungus and medication

11. A warmer and humid environment, unrestricted usage of topical corticosteroid-based combinations, increasing usage broad-spectrum antibiotics, widespread usage antifungals in agriculture, and the rise of antifungal drug resistance are all major causes <sup>12, 13</sup>. Previously, normal dosages and durations of topical or oral antifungal medications were sufficient to treat these infections, but they are now becoming more difficult to cure <sup>6</sup>. Relapses after a seemingly complete recovery are also not unusual <sup>6, 14</sup>. To boost cure rates, many tactics have been considered, including raising antifungal medication doses, expanding therapy duration,<sup>15</sup> utilizing a combination of oral antifungals <sup>16</sup>. A combined treatment with oral isotretinoin and oral itraconazole was shown to be efficacious in the management of chronic recurrent and persistent dermatophytosis. It was thought that Isotretinoin would assist eliminate the organisms by boosting the growth rate of the epidermis, which would lead to keratinocytes being shed <sup>16</sup>. This study was therefore conducted to compare the effectiveness of oral itraconazole alone and oral itraconazole combined with oral isotretinoin for the treatment of chronic tinea.

In our study, complete cure response was recorded in all the patients of group A, while in group B, complete cure response was recorded in 20 (50%) patients.. In accordance to our study, another study also compared the effectiveness of oral itraconazole alone and oral itraconazole combined with oral isotretinoin. They reported better results for combined therapy <sup>17</sup>. Dermatophytes grow at an acidic pH, and the acidic nature of the skin provides an excellent setting for the fungal growth <sup>18</sup>. Excessive skin PH is linked to high transepidermal loss of water and poor skin barrier performance <sup>19</sup>. The pH of the skin is elevated when retinoid treatment is used, which may prevent the development of dermatophytes. The keratolytic action of retinoids is well-known. They decrease corneocyte cohesion and disrupt epidermis terminal differentiation <sup>17</sup>. When used with retinoids, they boost the immune system's ability to fight off the effects of the dermatophyte, increasing antibody production and boosting T-helper cells in the peripheral circulation <sup>17</sup>.

Similar to our study, another study done by Ardeschna et al. also reported better results for combination therapy with isotretinoin and itraconazole <sup>20</sup>. A study done Holly Bartell et al. also reported comparable results <sup>21</sup>. The main limitation of our study was small sample size. Our study recommends conducting study based on large sample size for better results.

**CONCLUSION**

Our study concludes that combination therapy with oral itraconazole and isotretinoin is efficient and safe for the treatment of chronic tinea. Our study recommends conducting study based on large sample size for better results.

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