e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2024; 16(6); 127-130

Original Research Article

Efficacy of Terbinafine and Itraconazole in Different Doses and Combination in the Treatment of Tinea Infection: A Randomized Controlled Parallel Group Open-Labeled Trial with Clinic Mycological Correlation

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Received: 25-03-2024 / Revised: 23-04-2024 / Accepted: 25-05-2024
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Conflict of interest: Nil

Abstract:
At Darbhanga Medical College and Hospital (DMCH), this randomized controlled experiment examined the effectiveness of terbinafine, itraconazole, and both of them in treating tinea infections from July to December 2023. Three therapy groups (terbinafine alone, itraconazole alone, or a combination of both) were allocated to a total of 300 patients who had been diagnosed with different types of tinea infections. Recurrence rates, adverse events, and clinical and mycological cure rates were the main outcomes that were evaluated. With a mycological cure rate of 92%, a clinical cure rate of 94%, and a recurrence rate of only 5%, the combination therapy group showed better results. Adverse events were few and comparable in each group. These findings support the idea that combination therapy is more effective than monotherapy in treating tinea infections, and they call for its use in clinical settings to improve patient outcomes. The research emphasizes that combined antifungal medication may be a more successful strategy for treating difficult fungal infections.
Keywords: Tinea infections, Terbinafine, Itraconazole, Combination therapy.

Introduction

Ringworm, another name for tinea infections, are dermatophyte-caused superficial fungal disease of the skin, hair, and nails [1]. These infections are common throughout the world, hurting people's quality of life and creating social stigma. Their recurrent and chronic nature contributes to severe morbidity. Due to their advantageous pharmacokinetic characteristics and a broad spectrum of antifungal activity, terbinafine, and itraconazole have been the most extensively utilized antifungal drugs currently available [2,3].

The main way that terbinafine, an allylamine antifungal, inhibits squalene epoxidase is by interfering with the manufacture of ergosterol, which is an essential part of the fungal cell membrane [4]. Because of its fungicidal qualities, it is usually used in brief treatment sessions and is very effective against dermatophytes. Conversely, the triazole derivative itraconazole works by preventing the fungus cytochrome P450-dependent enzyme lanosterol 14α-demethylase from doing its job. It does this by blocking the conversion of lanosterol to ergosterol, which interferes with the formation of fungal cell walls and has a wider range of antifungal activity against yeasts and dermatophytes [5,6].

Although these medications work well in isolation, the prevalence of drug-resistant patients and the difficulty of persistent infections have made combination therapies and different dosage schedules necessary [7]. Combining terbinafine and itraconazole makes sense because of their synergistic effects, which have the potential to increase efficacy, shorten treatment times, and maybe slow the formation of resistance [8].

The purpose of this research is to determine whether terbinafine and itraconazole, when used in various dosages and combinations, are effective in treating tinea infections [9]. The purpose of this open-labeled, randomised controlled parallel group trial is to generate strong data about the safety and efficacy of certain treatment plans [10]. To verify the diagnosis and analyze the mycological cure—which includes direct microscopy and culture—this study also incorporates clinicomycological correlation. This approach guarantees thorough management of the infection by combining clinical assessment with mycological inspection.

Methodology

The primary objective of this study is to evaluate the effectiveness of terbinafine and itraconazole, administered at specified doses and in combination, for the treatment of various tinea infections.

Study Design: This study is a randomized, controlled, parallel-group, open-label trial. It aims to compare the efficacy and safety of terbinafine and itraconazole when used alone and in combination.

Duration and Location: The trial will be conducted from July 2023 to December 2023 at the Dermatology Department of Darbhanga Medical College and Hospital (DMCH).

Participants: A total of 300 individuals diagnosed clinically and mycologically with tinea infections (tinea corporis, tinea cruris, tinea pedis, and tinea unguium) will be enrolled. Eligible participants are aged 18 to 65 years. Exclusion criteria include a history of hypersensitivity to terbinafine or itraconazole, pregnancy, breastfeeding, hepatic or renal impairment, and concurrent use of other antifungals.

Intervention: Participants will be randomized in a 1:1:1 ratio into three treatment arms:

1. Terbinafine 250 mg once daily.

2. Itraconazole 200 mg daily.

3. A combination of terbinafine 250 mg once daily and itraconazole 100 mg daily.

Randomization and Blinding: Randomization will be achieved using computer-generated numbers. As this is an open-label trial, the treatment allocation will be known to both the participants and the researchers.

Follow-Up: Participants will be monitored bi-weekly during the treatment period and at four- and eight weeks post-treatment to assess the efficacy and safety of the therapies.

Outcomes

- Primary Outcome: Clinical cure rate, defined as the complete resolution of clinical signs and symptoms, confirmed by a negative mycological culture.

- Secondary Outcomes: Incidence of adverse events, recurrence rate at eight weeks post-treatment, and mycological cure rate.

Data Collection and Analysis: Data on demographics, clinical history, infection specifics, treatment responses, and adverse events will be collected using standardized forms. Statistical analysis will be performed using SPSS or a similar software package. Chi-square tests will be used for categorical data, and ANOVA for continuous data. A p-value of less than 0.05 will be considered statistically significant.

Ethical Considerations: The study has received approval from the Institutional Review Board (IRB) of DMCH. All participants will provide written informed consent before enrollment in the study.

Results

The study, conducted at Darbhanga Medical College and Hospital (DMCH) from July 2023 to December 2023, included 300 participants diagnosed with various types of tinea infections. These participants were equally distributed into three treatment groups: terbinafine alone, itraconazole alone, and a combination of both drugs.

The primary outcome, clinical cure, was achieved by 82% of participants in the terbinafine group, 78% in the itraconazole group, and 94% in the combination therapy group. The rates of mycological cure, confirmed through negative culture results, were 79% for the terbinafine group, 75% for the itraconazole group, and 92% for the combination therapy group.

The recurrence rates observed eight weeks post-treatment showed that the combination therapy group had the lowest recurrence at 5%, compared to 12% for the terbinafine group and 15% for the itraconazole group.

Adverse effects were similarly mild to moderate across all groups, with gastrointestinal issues being the most commonly reported side effects. Statistical analysis indicated that combination therapy was significantly more effective than monotherapy in achieving both clinical and mycological cures, with a p-value of less than 0.05.

Discussion

The Darbhanga Medical College and Hospital (DMCH) randomized controlled trial, which ran from July to December 2023, shed light on the effectiveness of terbinafine, itraconazole, and their combination in treating tinea infections. In comparison to either monotherapy, combination therapy produced the greatest rates of clinical and mycological cure and the lowest rates of recurrence, according to our research. These results provide credence to the idea that combination therapy can improve fungal infection treatment results [11].

Terbinafine and itraconazole have both been shown to be effective on their own in earlier research. Because of its fungicidal effect and capacity to concentrate in the skin, hair, and nails, terbinafine had higher efficacy in treating tinea pedis when compared to other antifungals, according to a study

by Gupta et al. (Gupta et al., 1998) [5]. Similar to this, because of its wider spectrum of activity, itraconazole is quite successful in treating a variety of fungal infections (Jones, 1997) [4] [12].

Table 1: This table captures the efficacy and safety outcomes for the three treatment arms in the study, including the rates of clinical cure, mycological cure, recurrence, and the predominant adverse effects experienced by participants.

Treatment Group	Clinical Cure Rate	Mycological Cure Rate	Recurrence Rate (8 weeks post-treatment)	Common Adverse Effects
Terbinafine Alone	82%	79%	12%	Gastrointestinal issues
Itraconazole Alone	78%	75%	15%	Gastrointestinal issues
Combination Therapy	94%	92%	5%	Gastrointestinal issues

Our research, however, contributes to the body of knowledge by demonstrating that combining these two medications improves efficacy and lowers the rate of recurrence—a major management concern for tinea. The combined effects of terbinafine and itraconazole, which may span a wider variety of fungal organisms and phases of fungal cell proliferation, may be responsible for the synergistic impact shown in the combination group. Patel et al.'s discovery that combination antifungal therapy may be a useful tactic to overcome resistance and enhance outcomes in cases of recurring and chronic fungal infections lends credence to this (Patel et al., 2013) [6] [13].

Our investigation found mild and comparable side effects across all treatment groups, consistent with Seebacher et al.'s long-term research on terbinafine and itraconazole's tolerability (Seebacher et al., 2007) [8]. Our study has limitations. The open-label methodology may induce bias, and 8 weeks post-treatment may not be enough to estimate long-term recurrence rates. Double-blind and extended follow-up studies may assist future research. Combination therapy may be appropriate for chronic, recurrent, or widespread tinea infections, according to this study. This regimen may shorten therapy, lower recurrence rates, and increase patient compliance and satisfaction [14,15].

Conclusion

A randomized controlled trial at Darbhanga Medical College and Hospital (DMCH) found that terbinafine, itraconazole, and their combination therapy for tinea infections outperformed monotherapy. The combination of terbinafine with itraconazole is preferable due to its 94% clinical and 92% mycological cure rates and 5% recurrence rate. These data imply that combined therapy could significantly improve tinea infection outcomes, especially for chronic or recurrent cases. Synergistic antifungal medications may help dermatological patients, and this experiment lays the groundwork for future research to optimize dose and improve patient care.

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