STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

Official Study Title
Comparing the Efficacy of Oral Fluconazole Versus Oral Itraconazole in Treating Resistant Tinea Corporis

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1. INTRODUCTION

Dermatophytes are among the most common causes of superficial fungal infections worldwide, affecting keratinized tissues such as skin, hair, and nails. These organisms belong primarily to the genera *Trichophyton*, *Epidermophyton*, and *Microsporum*. Dermatophytosis is clinically classified according to the site of involvement, including tinea corporis, tinea capitis, tinea cruris, tinea pedis, and related conditions.

In recent years, increasing antifungal resistance has emerged as a significant clinical challenge, particularly in chronic and recurrent dermatophytosis. Host-related factors such as skin characteristics, environmental temperature, humidity, and ultraviolet exposure influence disease persistence and treatment response. Resistant dermatophytosis often requires systemic antifungal therapy when topical agents fail.

Itraconazole and fluconazole are commonly used systemic antifungal agents; however, comparative evidence regarding their efficacy in resistant tinea corporis remains limited, particularly in local populations. Differences in resistance patterns and patient characteristics justify a controlled comparison of these agents.

2. STUDY OBJECTIVE

To compare the efficacy of oral itraconazole versus oral fluconazole in the treatment of resistant tinea corporis.

3. HYPOTHESIS

Oral itraconazole is more effective than oral fluconazole in achieving complete clinical resolution of resistant tinea corporis.

4. OPERATIONAL DEFINITIONS

Resistant Tinea Corporis
Persistence of tinea corporis for six months or longer despite appropriate topical antifungal therapy, confirmed by potassium hydroxide microscopy.

Clinical Efficacy
Complete clinical resolution defined as absence of erythema, scaling, and pruritus, with no visible lesions at four weeks, assessed using the Dermatophytosis Severity Scale and patient-reported visual analog scale.

5. STUDY DESIGN

This study is a randomized controlled trial.

6. STUDY SETTING AND DURATION

The study will be conducted in the Department of Dermatology, CDA Hospital, Islamabad. The total study duration will be six months following approval from the College of Physicians and Surgeons Pakistan.

7. SAMPLE SIZE

A total sample size of 126 participants will be enrolled, with 63 participants allocated to each treatment group. The sample size was calculated using the WHO sample size calculator, assuming an efficacy of 84% for itraconazole and 62% for fluconazole, with a significance level of 0.05 and a power of 80%.

8. SAMPLING TECHNIQUE

Non-probability consecutive sampling will be used to recruit eligible participants.

9. TREATMENT INTERVENTIONS

Participants will be randomized into one of the following groups:

Group A (Itraconazole Group)
Itraconazole 200 mg orally once daily for four weeks.

Group B (Fluconazole Group)
Fluconazole 150 mg orally on alternate days for four weeks.

10. ELIGIBILITY CRITERIA

Inclusion Criteria

Participants aged 18 to 70 years of either sex with clinically diagnosed resistant tinea corporis.

Exclusion Criteria

Participants with a history of oral antifungal use within the previous three months, antibiotic use within the previous one month, or immunosuppression due to diabetes mellitus, malignancy, or immunosuppressive medications will be excluded.

11. RANDOMIZATION AND BLINDING

Participants will be randomized into treatment groups using a mobile-based randomization application. Patients will be blinded to treatment allocation.

12. DATA COLLECTION PROCEDURE

Baseline demographic and clinical data, including age, sex, body mass index, duration of lesions, education level, and area of residence, will be recorded at enrollment. Clinical severity scores for erythema, scaling, and pruritus will be documented at baseline and reassessed at four weeks to determine treatment efficacy.

13. STATISTICAL ANALYSIS PLAN

All collected data will be entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 22. Data will be reviewed for completeness and consistency prior to analysis. Continuous variables such as age, body mass index, and duration of lesions will be assessed for distribution. Normally distributed variables will be summarized as mean with standard deviation, while non-normally distributed variables will be presented as median with interquartile range. Categorical variables including sex, residence, education level, treatment group, and clinical resolution status will be summarized as frequencies and percentages.

The primary outcome measure is clinical efficacy at four weeks. Comparison of efficacy between the itraconazole and fluconazole groups will be performed using the chi-square test. Fisher's exact test will be applied where expected cell counts are less than five. Stratification will be performed to control for potential effect modifiers including age, sex, body mass index, duration of disease,

education level, and residence. All statistical tests will be two-tailed, and a p-value of 0.05 or less will be considered statistically significant.