COMPARISON OF ORAL ITRACONAZOLE VERSUS TOPICAL CLOTRIMAZOLE IN TREATMENT OF PITYRIASIS VERSICOLOR

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ABSTRACT

Objective: To compare the efficacy of single dose of oral itraconazole 400mg with 1% topical clotrimazole in the treatment of pityriasis versicolor.
Study Design: Randomized controlled trial.
Place and Duration of Study: Dermatology department, Military Hospital Rawalpindi, from Jun 2015 to Dec 2015.
Material and Methods: A total of 60 patients of pityriasis versicolor fulfilling the inclusion criteria were selected from dermatology OPD after written informed consent and approval from the hospital ethical committee. Patients were divided into two treatment groups using random numbers table. Group A received single dose of itraconazole capsule (400mg) and group B received 1% clotrimazole cream twice daily application for 2 weeks. Patient evaluation included detailed history, clinical examination and direct microscopy of skin scrapings for fungal hyphae at the baseline, at the end of 2nd and 6th week of treatment. Efficacy of treatment was assessed on the basis of clinical and mycological cure.
Results: At the end of 2 weeks of treatment, clinical cure was seen in 23 (76.6%) and 29 (96.6%) patients (p=0.05) and mycological cure in 20 (66%) and 26 (86.6%) patients in group A and B respectively (p=0.06). At follow up (end of 6 week) 21 (70%) and 28 (93.3%) patients were cured clinically (p=0.02) while 18 (60%) and 27 (90%) patients were cured mycologically (p=0.007) in group A and B respectively.
Conclusion: Topical clotrimazole (1%) was found more effective than single dose of oral itraconazole in the treatment of pityriasis versicolor.

Keywords: Itraconazole, Pityriasis versicolor, Topical clotrimazole.

INTRODUCTION

The pityriasis versicolor (PV) is a mild, chronic and recurrent superficial fungal infection of skin caused by Malassezia yeast. It is characterized by discrete or confluent scaly, discolored or depigmented patches mainly on the upper trunk[1]. There are 14 species of Malassezia predominantly M globosa, M sympodialis and M furfur[2]. Prevalence is estimated to be as high as 30% in humid tropical zone. It may occur at any age but is more common during adolescence and young adulthood, suggesting a relationship with androgen induced sebaceous activity[2].

Species of Malassezia are a part of the normal flora of the skin in seborrheic areas but some contributing factors such as the immunosuppression, poor hygiene, and application of oily preparations, creams, hot humid climate, corticosteroid abuse or genetic predisposition provoke Pityrosporum to change from saprophytic to pathogenic form[3]. Yeast on sunlight exposure produces azelaic acid which inhibits tyrosine kinase resulting in hypopigmented spots[4].

Disease is usually diagnosed on history, clinical examination and microscopic examination of the skin scrapings. Wood`s light examination shows yellow fluorescence at the site of lesion. However, diagnosis is confirmed on microscopic examination of skin scrapings for fungal hyphae giving spaghetti and meatball appearance[5].

Treatment of PV is divided into two groups: topical and systemic. Topical agents include selenium sulfide (2.5% to 5%) shampoo, ketoconazole shampoo, clotrimazole, allylamine

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cream and lotion, propylene glycol 50% in water, nystatin, salicylic acid, cicloproxolamine, tretinoin, lactic acid lotion and 1% diclofenac gel. Systemic therapy includes fluconazole, itraconazole and terbinafin and is usually reserved for cases with extensive disease[6]. Despite many therapies, there is no standard therapy with complete cure rate and topical therapy is the first line treatment. The main goal of this study was to compare the effectiveness of single dose of oral itraconazole 400mg versus 1% topical clotrimazole in the treatment of pityriasis versicolor.

MATERIAL AND METHODS

Sixty patients diagnosed clinically as pityriasis versicolor from dermatology outpatient department at Military Hospital, Rawalpindi were inducted in the study after informed consent and approval of hospital ethical committee. Sample size was calculated by using WHO sample size calculator and sample size was 30 patients in each group. Non probability consecutive sampling was done. Diagnosis of pityriasis versicolor was confirmed with the help of skin scraping test by dissolving the scales in 10% KOH solution and observed under the microscope for fungal hyphae.

Patients ageing from 15 to 60 years and who had not received any systemic or topical antifungal therapy during last 1 month were included in the study. Pregnant or lactating females and those with history of hepatic disease, renal disease, malignancy or undergoing any sort of chemotherapy or radiotherapy were excluded. Detailed history and clinical examination was performed and all relevant clinical details were recorded on especially designed proforma. Patients were randomly allocated into two treatment groups. Group A received single oral dose of capsule itraconazole (400mg) and group B received 1% clotrimazole cream twice daily topical application for 2 weeks.

The assessment was done on the basis of clinical and mycological cure at the baseline and at the 2nd and 6th week after starting the therapy. Clinical assessment was performed on the basis of scoring the severity of erythema, scaling and pruritus from zero to 3 (3=severe, 2= moderate, 1=mild, 0=absent). Mycological cure included negative skin scraping test on microscopic examination.

Data were entered and analyzed in SPSS version 12. The quantitative variables like age and duration of illness were calculated by taking mean and standard deviation. The qualitative variables like gender and efficacy were calculated by taking frequencies and percentages. Two groups were compared for effectiveness by using Chi-square test. A *p*-value of <0.05 was considered as significant.

Table-I: Clinical assessment at the end of second weeks.

	Group A (n=30)	Group B (n=30)	*p*-value
Clinical cure	23 (76.7%)	29 (96.6%)	0.05
Mycological cure	20 (66%)	26 (86.7%)	0.06

Table-II: Clinical assessment at the end of six weeks.

	Group A (n=30)	Group B (n=30)	*p*-value
Clinical cure	21 (70%)	28 (93.3%)	0.02
Mycological cure	18 (60%)	27 (90%)	0.007

RESULTS

Mean age was 33.4 ± 9.31 and 32.17 ± 7.04 years in groups A and B respectively. There were 23 (76.67%) males and 7 (23.33%) females in group A while 22 (73.33%) males and 8 (26.67%) females were in group B.

At the end of 2 weeks of treatment, clinical assessment revealed that 23 (76.7%) patients of group A and 29 (96.6%) patients of group B achieved clinical cure (*p*=0.05). Mycological cure at the same time was demonstrated in 20 (66%) and 26 (86.7%) patients in group A and B

respectively (*p*-value=0.06). There was no statistically significant difference between the two groups.

At follow up (end of 6 weeks), 21 (70%) and 28 (93.3%) patients were cured clinically while 18 (60%) and 27 (90%) patients were cured mycologically in group A and B respectively. Cure rate was significantly higher in patients treated with clotrimazole cream as compared to itraconazole both clinically (*p*=0.02) and mycologically (*p*=0.007) as shown in tables-I & II.

DISCUSSION

Itraconazole and clotrimazole belong to azole group and both are fungistatic. Itraconazole is highly keratophilic and lipophilic triazole which impairs fungal cell wall synthesis by inhibiting cytochrome P 450 dependent 14 alpha lanosterol demethylase enzyme and interferes with fungal ergosterol synthesis[7]. It is detectable in the sweat within 24 hours of ingestion. Side effects are uncommon and consist of nausea and abdominal discomfort[8].

Clotrimazole is cost effective and efficacious but has poor compliance due to its unpleasant odour and difficult application over a large surface area for prolonged duration. Oral itraconazole is convenient to use with better compliance and low relapse rate but it is associated with systemic side effects so short duration courses are recommended to minimize its side effects. There are a few controlled clinical trials worldwide but not a single trial in our population regarding the efficacy of single dose oral itraconazole. Even among those few listed trials, treatment response is variable. So we planned this study to compare the efficacy of single dose oral itraconazole (400mg) versus 1% topical clotrimazole twice daily for two weeks in the treatment of pityriasis versicolor.

In our study, although there was no significant difference in efficacy between the two groups at the end of 2 weeks of treatment but the number of patients cured in clotrimazole group were more as compared to itraconazole group. However at 6 weeks of follow up, the cure rate was significantly higher in clotrimazole group both clinically and mycologically.

The literature review varies regarding the efficacy of a single dose oral itraconazole. In a randomized open label trial, a single 400 mg dose of itraconazole was recorded as effective as 200 mg/day given for a week[9]. However in another study, a lower rate of response to single dose itraconazole (400mg) was recorded in comparison with single dose fluconazole (20% vs. 65% respectively, *p*=<0.05). Additionally, relapse was also found significantly more in patients receiving itraconazole as compared to fluconazole (60% vs. 35% respectively, *p*-value <0.05)[10].

A double-blind randomized controlled trial was conducted by Dehghan et al to compare the efficacy of a single dose fluconazole (400mg) versus 1% clotrimazole cream twice daily application for 2 weeks. Four weeks after treatment, they recorded significant clinical response in patients treated with clotrimazole cream as compared to fluconazole (complete response 94.9% vs. 81.2% respectively, *p*=0.044). These findings support our results regarding relative higher efficacy with 1% clotrimazole[11].

Balwada et al enrolled 40 adult patients of pityriasis versicolor. Group A was treated with topical 2% ketoconazole cream and group B with 1% clotrimazole cream. On assessment of the treatment after 14 days, 18/20 (90%) patients treated with ketoconazole cream were cured in contrast to 17/20 (85%) patients in clotrimazole treated group[12].

Sharquie et al. conducted a trial in 2010 to evaluate the efficacy of topical 1% diclofenac gel for the treatment of pityriasis versicolor (PV) in comparison with 1% topical clotrimazole cream and aqua rosa cream as a placebo control. At the end of 4 weeks, 92% of patients treated with topical clotrimazole cream had complete improvement versus 56% of the patients receiving diclofenac gel (*p*<0.009)[13].

Al Hamamy et al. evaluated the effectiveness of topical 4% KOH in comparison with 1% topical

clotrimazole solution. He did single blind comparative therapeutic study and at the end of 4 weeks, 95% of the patients showed complete response with clotrimazole[14].

As far as response to 1% clotrimazole is concerned, the results of our study are comparable with those conducted by Dehghan, Balwada, Sharquie and Al Hamamy et al[11-14]. This emphasizes the fact that 1% topical clotrimazole is more effective than single dose of itraconazole in the treatment of pityriasis versicolor.

CONCLUSION

Topical clotrimazole (1%) was found more effective than single dose of oral itraconazole in the treatment of pityriasis versicolor.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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