COMPARISON OF TWO DOSAGE REGIME OF KETOCONAZOLE IN THE TREATMENT OF PITYRIASIS VERSICOLOR (PV)

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ABSTRACT

Objective: *To evaluate the efficacy and safety of single dose (400 mg) of Ketoconazole versus 10 days 200 mg daily dose of Ketoconazole in the treatment of Pityriasis Versicolor in patients attending out patient department of Hayatabad Medical Complex, Peshawar.*

Material and Methods: *Patients suffering from extensive PV who had not received any other treatment in the last 2 months and having no history of liver disease were selected for this trial. 90 patients (age ranging from 12 to 40 years in both groups) were enrolled for the study during April 2006 till end September 2006. Liver function tests were done before starting treatment, and at intervals of 3 weeks and 6 weeks after therapy. Diagnosis of PV was made on clinical appearance and confirmed by Wood's light examination and KOH examination of mycological scrapings. Patients were divided into 2 groups, A and B. Group A received 200mg of Ketoconazole for 10 days whereas, patients in group B received single 400mg dose.*

Results: *Fifty male patients and 30 female patients completed the study in both groups. 20 patients (50 %) in group A (200 mg daily Ketoconazole for 10 days) had negative mycological and Wood's lamp examination after 3 weeks and 35 patients (87.5%) had negative mycological and Wood's lamp examination after 6 weeks of stopping therapy. While 10 patients (25%) in-group B (400 mg Ketoconazole as single dose) had negative. Wood's lamp and mycological cure after 3 weeks while 25 patients (62.5%) had Wood's lamp and mycological cure after 6 weeks of stopping therapy treatment was well tolerated in both groups and none reported any untoward side effects during or after stopping treatment..*

Conclusion: *Ketoconazole 200 mg daily for 10 days was found to be more effective in the treatment of PV as compared to a single dose therapy of 400mg. However studies involving much larger patients sample are needed to establish the superiority of one form of treatment over the other.*

Key Words: *Single dose, Ketoconazole , Pityriasis versicolor.*

INTRODUCTION

Pityriasis Versicolor is a common fungal infection caused by fungi variously known as Malassezia or Pityrosporum and characterized by discrete scaly discolored or depigmented areas mainly on the upper trunk.[1] It is an anthrophilic fungus belonging to the physiological skin flora, growing in yeast form on non affected skin and in mycelial form causing clinical disease.[2] Although the disease is prevalent throughout the world it is more common in warm and humid climate. Profuse perspiration and high production of sebum by the skin makes it easier for the fungus to multiply and spread. PV usually presents during the summer season particularly affecting the young adults.[3] It is occasionally seen in children and people over the age of 50 years. Factors responsible for mycelial transition include a warm, humid environment, profuse sweating, an inherited predisposition, endogenous or exogenous Cushing's disease, immuno-suppression, or a malnourished state.[4]

.The topical antifungals work well in Pityriasis Versicolor, the main problem with the use of topical antifungals is the difficulty of applying creams and lotions to a wide body surface area. While topical therapy is ideal for this condition, which involves the stratum corneum, patients often prefer the convenience of therapy.[5] An oral drug able to eradicate the fungus with good safety profile, good tolerability and cost

GROUP WISE RESPONSE

Response	Group A (n=40)		Group B (n=40)		Chi-Square	P Value
	No	%	No	%		
Outcome after 03 weeks						
Responded	20	50	10	25	4.32	0.03
Outcome after 06 weeks						
Responded	35	87.5	25	62.5	5.40	0.02

Table 1

effective should be selected.

To evaluate the efficacy and safety of single dose (400 mg) of Ketoconazole versus 10 days 200 mg daily dose of Ketoconazole in the treatment of Pityriasis Versicolor in patients attending out patient department of Hayatabad Medical Complex, Peshawar.

MATERIAL AND METHODS

This prospective comparative clinical trial was conducted in the department of dermatology, Postgraduate Medical Institute, Hayatabad Medical Complex, Peshawar from April 2006 to September 2006. Ninety patients suffering from PV were enrolled in the study.

Inclusion Criteria

. Age > 12 years

Positive scrapping for fungus in KOH mount.

Flourescence on Wood's lamp examination.

Exclusion Criteria

Patients suffering from Chronic liver disease.

Patients who have taken systemic antifungals in previous four weeks

Pregnant and lactating mothers.

The diagnosis of PV was made on clinical appearance and was confirmed by Wood's lamp examination and demonstration of hyphae in KOH preparation. Detailed history and clinical examination was performed and all the relevant clinical details were recorded on a specially designed proforma. Patients were divided into two groups A and B. Group A received 200mg of Ketoconazole for 10 days whereas, patients in group B received single 400mg dose. At the start of treatment Wood's lamp examination, microscopic examination of KOH mount prepared from scrapping of the lesion and biochemical tests for liver and renal functions were performed. Patients were assessed clinically 3 and 6 weeks after stopping treatment. LFT, Wood's lamp examination and direct microscopy was performed on each follow up visit to asses the efficacy of treatment and look for possible Hepatotoxicity.

Efficacy of antifungal treatment was assessed by absence of fluorescence on Wood's light examination of the affected areas and disappearance of fungal hyphae from scrapping examined in a KOH mount. . Data was analysed on SPSS version 10.

RESULTS

Ninety patients were enrolled for the study. However 10 patients were lost to follow up. Forty patients received regimen A (25 males ant 15 females) and 40 patients received regimen B (27 males and 13 females). Age range was 14 to 40 for both treatment groups (mean age 20.8$\pm$ 3.4).

20 patients (50%) patients in group A and 10(25%) in group B showed mycological clearance at 3 weeks and cure rate increased to 87.5 % and 62.5% after 6 weeks of stopping therapy in group A and B respectively. (Table I)

None of the patients reported any untoward side effects during the treatment period and following 3 weeks and 6 weeks after treatment. Liver function tests remained normal during the follow up period. To test the significance of difference between the 2 groups, Chi-square test was applied. A statistically significance difference ($P < 0.05$) was observed after 3 weeks of treatment. Similarly statistically significant difference ($P < 0.05$) was also seen after 6 weeks of treatment. The level of significance was chosen as 0.05 and p value was calculated. (Table I)

DISCUSSION

Pityriasis Versicolor though harmless tends to recur especially in hot and humid climate. While treating PV, the efficacy, safety and tolerability of a drug and patient compliance should be taken into consideration.[6] Topical therapy usually suffices for localized lesions but has its drawbacks like short term efficacy with relapses due to the fact that large body areas

cannot be treated adequately leading to recurrences. The ideal treatment would be a short course of an oral antifungal drug producing high clinical and mycological cure rates and low relapse rates.[7]

Ketoconazole administered systemically is widely used in the treatment of PV Ketoconazole is widely used in our part of the world due to comparatively lower cost and free availability in the market. It is an imidazol derivative and acts by inhibiting the biosynthesis of ergosterol which is a major part of membrane lipid of pityriosporum orbiculare.[8] Ketoconazole is absorbed in the small intestine. Mean peak plasma levels of approximaly 3.5 ug/ml are reached within 1 to 2 hours following an oral administration of single 200 dose taken with a meal. Subsequent plasma elimination is biphasic with a half life of 2 hours during the first 10 hours and 8 hours thereafter. Within an hour it is carried to the skin via sweat and passive diffusion, through the blood to the skin where it remains in the stratum corneum for 10 to 12 days. Vigrous exercise 2 hours after the drug intake increases its excretion through skin and enhances its anti fungal activity against P.orbiculare.[9]

Ketoconazole has been employed to treat PV using different dosage regimens varying from 4 weeks down to single dose. A study conducted by Meisel and Wouters have established the efficacy of Ketoconazole in treating PV administered in a dose of 200mg for ten days.[10] A 10 day course of Ketoconazole was found to be effective by other investigators.[11]

Single dose regimens of 400mg Ketoconazole was effectively used to treat 22 patients. Goodless et al carried out analysis of international trials and concluded that single dose 400mg Ketoconazole is effective in selected patients.[12] A study conducted by Sadeque et al in Bangladesh concluded that frequent doses have higher cure rates as compared to single dose regimens.[13]

In the present study, mycologic cure rates of 50% in-group A and 25% in-group B were seen after 3 weeks of treatment. After 6 weeks cure rates in group A increased to 87.5% whereas 62.5% in Group B. The difference in the results of treatment in Group A and Group B after 3 and 6 weeks was statistically significant. The results of present study support the earlier studies, which showed that Ketoconazole administered in a dose of 200mg for ten days is superior to single dose of Ketoconazole.

CONCLUSION

Ketoconazole 200 mg daily for 10 days was found to be more effective in the treatment of PV as compared to single dose therapy of 400 mg. The difference in the results of 200 mg daily dosage regimen for 10 days in comparison to 400 mg single dose after 3 weeks and 6 weeks of completion of therapy was statistically significant. However studies involving larger patients sample are needed to establish the superiority of one form of treatment over the other.

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