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Comparative Evaluation of Ketoconazole 400 mg Single Dose Versus Ketoconazole 200 mg Daily for Five Days in Pityriasis Versicolor

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ABSTRACT

Introduction

Many treatments have been attempted in pityriasis versicolor with different reports of success. No direct comparative study between Ketoconazole 400 mg single dose against Ketoconazole 200 mg od for 5 days have been made earlier. The aim of this study was to study and compare the therapeutic efficacy of oral ketoconazole 400 mg single dose with oral ketoconazole 200 mg once daily for 5 days in pityriasis versicolor.

Methods

This was a comparative study conduct in Dermatology outpatient department in Chitwan Hospital, Chitwan. Patients were randomly selected to receive either ketoconazole 400 mg single dose (group A) or ketoconazole 200 mg daily for 5 days (group B). Altogether 80 patients were taken, 40 in each group. Patients were assessed after 8 weeks and both clinical and mycological evaluation was done. The treatment success (mycological cure) was defined by a negative KOH at 8 weeks post treatment. Chi-square test was used to identify the significance of the variables.

Results

The mycological cure at 8 weeks was 46% in group A and 74% in group B and the result was significant. No significant adverse event was noted in any of the groups.

Conclusions

There was significant difference in the treatment outcome in both the groups. Ketoconazole 200 mg daily for 5 days had superior efficacy than ketoconazole 400 mg single dose. There was no significant difference in the adverse events.

Keywords: ketoconazole; pityriasis versicolor.

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INTRODUCTION

Pityriasis versicolor also known as Tinea versicolor is a superficial fungal infection of the skin.[1] It is characterized by skin pigmentary changes due to colonization of the stratum corneum by a dimorphic, lipophilic fungus in the normal flora of the skin known as Malassezia furfur.[2] The disease is most prevalent in the tropics, with an incidence as high as 40%.[3]

Both topical and systemic treatments have been used to treat pityriasis versicolor. Ketoconazole has been used in various doses and duration with no definite consensus. In an international review of clinical trials,[4] it was suggested that single 400 mg of ketoconazole or short course (ketoconazole 200 mg for 5 days) may be highly effective in pityriasis versicolor and also the toxicity is minimal at theses doses. The observation that single-dose regimens (e.g., ketoconazole 400 mg or fluconazole 450 mg) may be less effective, is supported in a meta-analysis review.[5] Sadeque et al found that the relapse rate with 400 mg single dose is about 48% during the 6 months follow up period.[6] No direct comparative study has been carried out between ketoconazole 400 mg single dose and 200 mg daily for 5 days. The present study is designed to compare the efficacy of the above-mentioned regimens.

METHODS

It was a comaparative study approved by the local scientific research committee. Cases presented to dermatology OPD in Chitwan Hospital with clinical diagnosis of pityriasis versicolor, were included in to the study. A clinical and mycological evaluation was done including KOH. Patient with positive KOH exam and accepting the informed consent were taken in to the study. Patient with negative KOH exam, patient below 14 years of age, pregnant and lactating woman, patient with hepatic, renal or cardiovascular involvement and any prior treatment for pityriasis versicolor within 4 weeks were excluded from the study. They were randomized into two groups namely A and B, with help of Ralloc software. In group A, 40 patient received ketoconazole 400 mg single dose while 40 patient in group B received ketoconazole 200 mg OD for 5 days. Clinical and mycological evaluation was repeated at 8 weeks follow up. Any adverse event was also noted. Treatment success was defined as negative KOH exam at follow up. The data was compiled in Microsoft excel and entered in SPSS. Chi-square test was applied to find of the significance of the variables.

RESULTS

Of the total 80 cases, 75 patients completed the study and 5 did not turn up for follow up and thus excluded from the study. The demographic characteristics, clinical characteristics of the patients are shown below. There was no statistical difference in between the two groups.

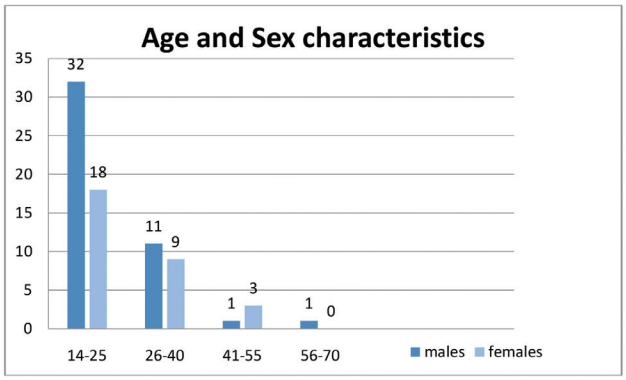

Figure 1. Demographic characteristics of the patients

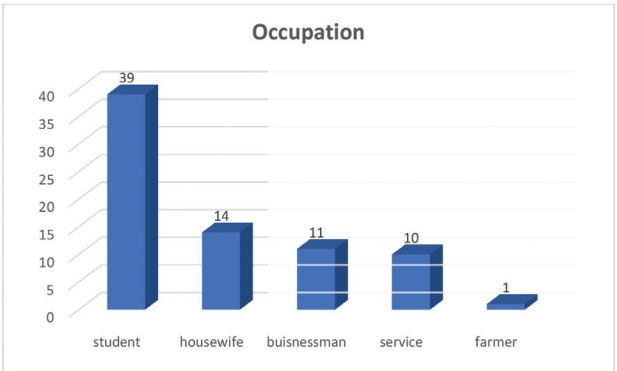

Figure 2. Demographic characteristics of the patients

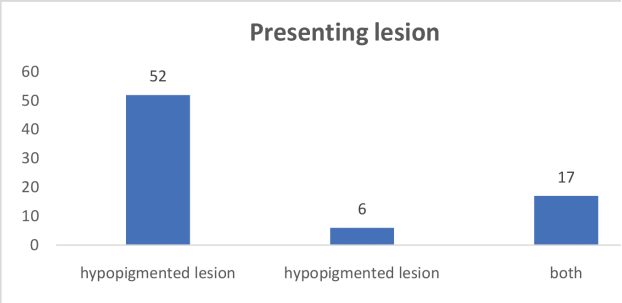

Figure 3. Clinical characteristics of the patients

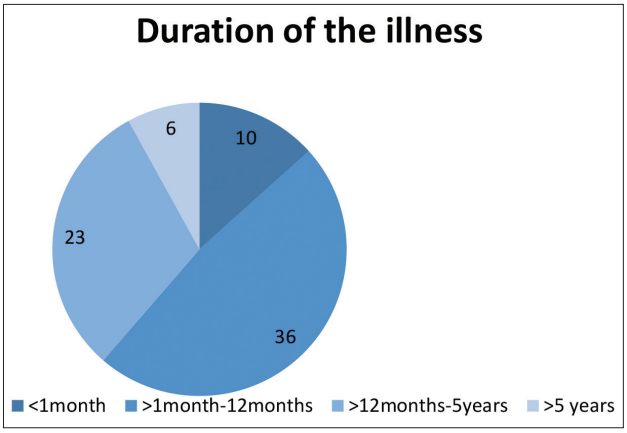

Figure 4. Clinical characteristics of the patients

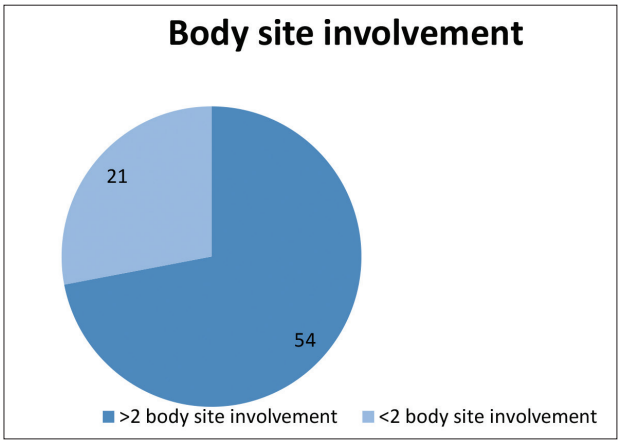

Figure 5. Clinical characteristics of the patients

Outcome of treatment

In group A, 17 (45.94%) patients out of 37 were KOH negative at week 8, while in group B, 28 (73.68%) patients out of 38 were KOH negative at week 8. It was statistically significant.

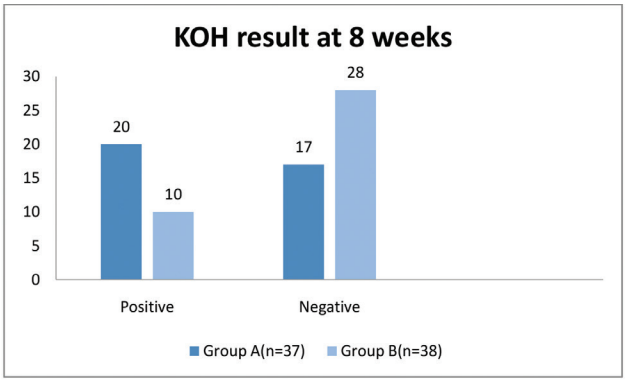

Figure 6. KOH result at 8 weeks

Scaling was decreased in most patients in both groups (only present in 9 and 6 patients in respective groups) but pigmentary changes were persistent in most of the patients at 8 weeks follow up. Only in 6 (8%) patients of group A and 9 (12%) patients of group B, it was absent. It was statistically not significant between the two groups.

Site of involvement and KOH

The mycological cure rate based on KOH examination at 8 weeks varied with number of sites involved. When the number of sites involved was less than 2; the KOH was negative in 17 patients (out of 21). Similarly, when the number of sites involved was more than 2; the KOH was negative in 28 patients (out of 54). This correlation was statistically significant.

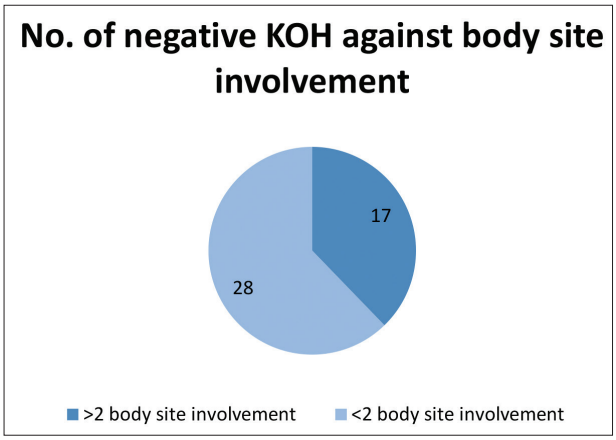

Figure 7. Site of involvement and KOH

Duration of disease and KOH examination at 8 weeks

The duration of the disease also influenced the treatment response. The mean duration of the disease was 42.45 and 45 months when the KOH was positive in group A and B respectively. Similarly, the mean duration of disease was 8.05 and 11.92 months when the KOH was negative in group A and B respectively. This difference was statistically significant.

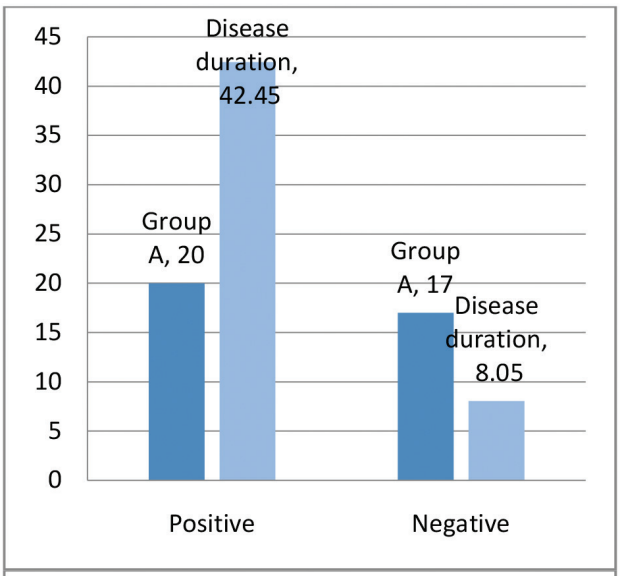

Figure 8. Duration of disease and KOH examination at 8 weeks

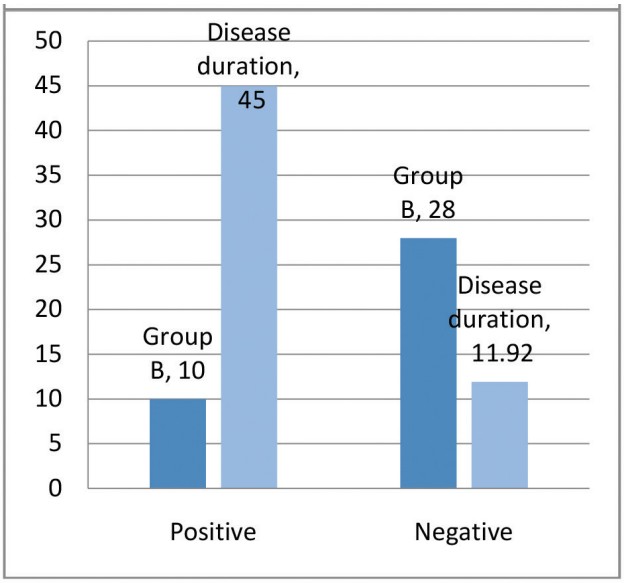

Figure 9. Duration of disease and KOH examination at 8 weeks

Adverse events

The adverse event noted in both the groups was nausea and was found in 2 (5%) out of 37 in group A and 5 (13%) out of 38 patients in group B. It was not severe enough for the treatment to be discontinued. There was no any other adverse effect related with the treatment.

DISCUSSION

Many therapeutic agents are used for the treatment of pityriasis versicolor but none is a definite treatment. Ketoconazole was the first effective, broad-spectrum oral azole developed against pityriasis versicolor and was first used in 1980[7-8] in the treatment of pityriasis versicolor with a cure rate of up to 95%. It has been tried in different doses and duration with no definite consensus. Earlier studies involved longer duration of therapy, even up to 5 weeks. Later studies have shown a good response with a single dose and for lesser duration that is even 5 days.

This was an open, randomized controlled trial, comparing the efficacy of ketoconazole 400 mg single dose with ketoconazole 200 mg once daily for 5 days. Both the study groups were well matched and similar for the various variables.

In the treatment group A, about 46% cure rate was observed after 8 weeks, while in group B, it was about 74%. The difference in the cure rate between the two groups were statistically significant (p-value <0.05). The difference in the response based on the KOH examination was also statistically significant when compared separately between the two groups. No direct comparison has been made between ketoconazole 400 mg single dose and 200 mg daily for 5 days in literature. But several of the studies as mentioned below have used these

doses in different combination. Fernandez-Nava et al found 42% cure rate with ketoconazole 400 mg single dose against 58% with ketoconazole 200 mg per day for 10 days after 1 month of follow up.[9] The cure rate of 46% with single dose of ketoconazole 400 mg stat in our study was comparable to the findings of this study. The cure rate of 76% with continuous therapy of 200 mg of ketoconazole for 5 days is higher than Fernandez-Nava's study (58%), and can be explained by the fact that the follow up examination in our study is longer.

In our study, 74% cure rate with continuous therapy of ketoconazole 200 mg daily for 5 days is comparable to study of Jain and Aggarwal with 85% cure rate though they compared it with itraconazole in similar dose with 95% cure rate at 2 weeks.[10] Bhogal et al found cure rate of 54% and 74% respectively with ketoconazole 400 mg single dose and ketoconazole 200 mg daily for 10 days which is also comparable to our study.[11]

Zaias compared ketoconazole 200 mg daily for 5 days with ketoconazole 200 mg daily for 10 days and found a mycological cure rate of 84% and 90% respectively at 1 month and concluded that 5 days course was as effective as 10 days. The finding with ketoconazole 200 mg daily for 5 days is comparable to our findings. [12]

No significant adverse event was noted in both the groups except mild nausea which was reported by 2 patients in group A and 5 patients in group B. Since the patients were instructed to take the drug in the morning in empty stomach, there was a possibility of nausea which is a known side effect of oral ketoconazole. In fact, nausea and vomiting is the most common side effects of ketoconazole.[13] The higher number in group B could be because of longer duration of therapy. But the difference was statistically not significant. It was observed that the number of site of involvement affected the cure rate. When the site of involvement was less than 2, only 4 patients were KOH positive and 17 were negative out of 21 patients. When more than 2 sites were involved, 26 patients were KOH positive out of 54 patients. This correlation was statistically significant. Similar correlation was not found with wood's lamp examination. Disease duration also had an effect on the cure rate. The mean disease duration in the patients who had KOH negative examination at 8 weeks was 8.05 and 11.92 months respectively in group A and B. While the mean disease duration in the patients who had KOH positive examination at 8 weeks was 42.45 and 45 months in group A and B respectively. Similar correlation of disease duration and positive wood's lamp examination was not seen in group A but it was significant in group B. Since we had defined KOH as the basis of mycological cure or the treatment failure, it can be concluded that patients having disease for longer duration and more sites of involvement, had a relative resistance to treatment. This finding can be a matter of further exploration in future studies.

CONCLUSIONS

There was s significant difference in cure rate between the two groups. Both the regimens were well tolerated and no significant adverse event was noted. Both disease duration and number of the site of involvement had impact on the cure rate and this should be considered in future studies to draw a conclusion.

Conflict of interest

None

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