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A Comparative Study of Efficacy, Safety and Relapse Rate of Three Drugs; Systemic Ketoconazole, Systemic Itraconazole and Topical Oxiconazole in the Treatment of Pityriasis versicolor

Amruta Mohite[1], Anil Gugle[2*], Rahul Kote[3] and Vikrant Jadhav[4]

[1]Senior Resident, Department of Skin & VD, Dr. Vasantrao Pawar Medical College & Research Centre, Nashik, India

[2]Professor & Head Department of Skin & VD, Dr. Vasantrao Pawar Medical College & Research Centre, Nashik, India; anil.gugle@yahoo.com

[3]Associate Professor, Department of Skin & VD, Dr. Vasantrao Pawar Medical College & Research Centre, Nashik, India

[4]Assistant Professor, Department of Skin & VD, Dr. Vasantrao Pawar Medical College & Research Centre, Nashik, India

Abstract

Aim: The aim of our study was to evaluate the efficacy, safety and relapse rate of systemic Ketoconazole, systemic Itraconazole and topical Oxiconazole in the treatment of pityriasis versicolor. **Study design**: 94 patients who had pityriasis versicolor were included in the study. The patients were given Ketoconazole, Itraconazole and Oxiconazole randomly and were followed up at the interval of 15 days, 1 month and 3 months for assessement of clinical and mycological cure. **Results**: In assessment of clinical parameters maximum improvement in scaling, pigmentation and pruritus was seen in Oxiconazole group compared to itraconazole and ketoconazole group. During the study it was observed that rate of clinical cure was maximum in Oxiconazole group (76.67%) as compared to Itraconazole (58.82%) and Ketoconazole group (46.66%). Mycological cure during visit 2 in Oxiconazole group was (83.33%), as compared to (88.2%) Itraconazole group and (88.7%) Ketoconazole group. During visit 3, mycological cure was present in 93.3% cases in Oxiconazole group, 94.1% in Itraconazole group and 93.3% in Ketoconazole group. During visit 4 mycological cure was assessed which showed 88.7% cure rate in Oxiconazole group compared to 88.2% in Itraconazole group and 88.7% in Ketoconazole group. These results suggested presence of relapse in 6.6% cases in both Oxiconazole and Ketoconazole group and 5.9% cases in Itraconazole group. There were no side effects with oxiconazole group while cases treated with ketoconazole and itraconazole had side effects like nausea and urticaria. **Conclusion**: According to the present study we conclude that topical Oxiconazole therapy was more effective as compared to systemic Itraconazole and Ketoconazole therapy in early improvement of scaling, pigmentation and pruritus secondary to Pityriasis versicolor with no significant side effects.

Keywords: Efficacy, Itraconazole, Ketoconazole, Pityriasis versicolor, Topical Oxiconazole

1. Introduction

Pityriasis versicolor is chronic superficial fungal infection of the stratum corneum characterized by patchy and scaly discoloration of skin. The causative organism is Malassezia furfur, a yeast like lipophilic fungus. The fungus interferes with the normal pigmentation of the skin; resulting in small, discoloured patches[1]. Most patients require treatment as spontaneous remission is uncommon. Various therapeutic regimens are used to treat Pityriasis versicolor but the relapse rate is high[2]. Oral imidazole derivatives with broad spectrum anti fungal

*Author for Correspondence

activity have offered an effective, easily administered and rapid treatment[3].

There are numerous topical agents which can be used to treat pityriasis versicolor[4]. Oxiconazole nitrate is a newer imidazole antifungal agent intended for topical treatment of superficial fungal infections. Topical Oxiconazole have proven to be well tolerated and highly effective for once daily application and duration of therapy is for 2 weeks[5].

The aim of the present study was to compare the efficacy, safety and relapse rate of systemic Ketoconazole, Itraconazole and topical Oxiconazole therapy in patients with pityriasis versicolor.

2. Material and Method

A total of 94 patients of Pityriasis versicolor were included in the study. Patients who received any kind of antifungal treatment in last 3 months were excluded.

2.1 Treatment Modalities used in this Study

1. Oral Ketoconazole 200 mg once a day for five days
2. Oral Itraconazole 200 mg once a day for five days
3. Topical Oxiconazole 1% cream once daily for two weeks

2.2 Method

The eligible patients according to the inclusion criteria were enrolled in the study and written informed consent was obtained after counselling. Liver function test of each patient was done at the time of inclusion. Clinical assessment in terms of pigmentation, erythema, scaling and pruritus was made on a scale of 0-3 (3-severe, 2-moderate, 1-mild, 0-absent) at each visit. The patients with normal liver function tests were given the drugs on sequential basis. A total of 94 patients were included in the study divided into three groups as A, B and C. There were 30 patients in groups A and C; and 34 patients in group B. Groups were as follows:

2.2.1 Group A

Patients in this group were given oral Ketoconazole 200 mg once a day for 5 days

2.2.2 Group B

Patients in this group were given oral Itraconazole 200 mg once a day for 5 days

2.2.3 Group C

Patients in this group were advised to use topical Oxiconazole 1% cream once daily for 2 weeks.

All clinically diagnosed patients of Pityriasis Versicolor were confirmed by Wood's lamp examination and KOH mount of skin scraping.

2.3 On Visit 2,3,4 (After 2 Weeks, 1 Month, 3 Months)

During these subsequent visits Patients clinical assessment in terms of resolution of scaling, pruritus, mentary changes and erythema was noted and mycological assessment with KOH mount and Wood's lamp examination was done.

Clinical evaluation was done by the naked eye appearance of the lesions for presence of scaling and disappearance of the lesions. Clinical response was assessed globally with the use of broad scale of healed, mild residual disease, moderately residual disease and not changed. The following criteria was adopted for this.

Clinical cure was achieved if lesions had healed completely or if only mild residual disease was present[6].

2.4 Mycological Cure

It was defined as negative KOH smear and negative Wood's lamp examination[7].

2.5 Relapse

It was defined as positive KOH smear and or positive Wood's lamp examination at three months follow-up once it had become negative during an initial post therapy assessment[7].

During each visit various changes were noted and clinical and mycological assessments were done in all patients in each group and were compared statistically with other two groups. A close watch on any adverse effects of the drugs were monitored during every visit and documented.

2.6 Statistical Analysis

Percentages, the standard deviation, Chi-square test, Fisher Exact test were employed using SPSS for Windows software. P value <0.05 was considered statistically significant.

3. Results

The three groups were similar with respect to sex and age. Clinical assessment of symptoms showed maximum improvement in scaling, pigmentation and pruritus was seen in Oxiconazole group compared to itraconazole and ketoconazole group.

After 2 weeks of start of treatment statistically significant clinical cure was seen with Oxiconazole group

Table 1. Comparison of clinical cure at different visits in three drug groups

Visit	Grading of clinical cure	Number of cases			P value
		OXI-(%)	ITR-(%)	KET-(%)	
Visit 2	Healed	10 (33.33)	2 (5.88)	4 (13.33)	0.015 Sig
	Mild RD	13 (43.34)	18 (52.94)	10 (33.33)	
	Moderate RD	7 (23.33)	14 (41.18)	16 (53.34)	
	No change	0 (0)	0 (0)	0 (0)	
	Total	**30 (100)**	**34 (100)**	**30 (100)**	
Visit 3	Healed	12 (40)	2 (5.88)	4 (13.33)	0.004 Sig
	Mild RD	11 (36.67)	18 (52.94)	10 (33.33)	
	Moderate RD	7 (23.33)	14 (41.18)	16 (53.34)	
	No change	0 (0)	0 (0)	0 (0)	
	Total	**30 (100)**	**34 (100)**	**30 (100)**	
Visit 4	Healed	12 (40)	2 (5.88)	4 (13.33)	0.004 Sig
	Mild RD	11 (36.37)	18 (52.94)	10 (33.33)	
	Moderate RD	7 (23.33)	14 (41.18)	16 (53.34)	
	No change	0 (0)	0 (0)	0 (0)	
	Total	**30 (100)**	**34 (100)**	**30 (100)**	

in which healed cases were 10 (33.33%) and cases with mild residual disease were 13 (43.34%) (p=0.015) as compared to itraconazole and ketoconazole group (Table 1).

During visit 3, statistically significant clinical cure was seen with Oxiconazole group in which healed cases were 12 (40%) and cases with mild residual disease were 11(36.67%) (p=0.004).

During visit 4, there was no any change seen in causing clinical cure among the cases in all the three groups as compared to visit 3 and the results also remained similar.

During visit 2, mycological cure was present in 25 (83.33%) cases in Oxiconazole group, 30 (88.2%) from Itraconazole group and 26 (88.7%) cases from Ketoconazole group. During visit 3, mycological cure was present in 28 (93.3%) cases in Oxiconazole group, 32 (94.1%) from Itraconazole group and 28 (93.3%) cases from Ketoconazole group. During visit 4, mycological cure was present in 26 (88.7%) cases in Oxiconazole group, 30 (88.2%) from Itraconazole group and 26 (88.7%) cases from Ketoconazole group. The difference in causing mycological cure among all three groups was not statistically significant (p=1, 1, 0.931) (Table 2).

In present study during visit 2, there was no any case with side effects in Oxiconazole group. 2 (5.9%) cases in Itraconazole group and 2 (6.7%) cases in Ketoconazole group had nausea. While 2 (6.7%) cases in Ketoconazole group presented with rash. Oxiconazole was better as it didn't show any side effects but difference was not statistically significant (p=0.543, 0.199).

Table 2. Comparison of mycological cure at different visits

Visit	**Number of cases**			**Fisher exact test P**
	OXI- (%)	**ITR - (%)**	**KET (%)**	
Initial visit	30 (0)	34(0)	30 (0)	-
Visit 2	25 (83.3)	30 (88.2)	26 (86.7)	1.0
Visit 3	28 (93.3)	32 (94.1)	28 (93.3)	1.0
Visit 4	26 (86.7)	30 (88.2)	26 (86.7)	0.931

4. Discussion

In present study we compared the efficacy of topical newer azole group of drug oxiconazole which has advantage of once a day application for fifteen days with systemic Ketoconazole and Itraconazole. Both drugs were given in a dose of 200mg for five days. We included total 94 patients randomly. All were assessed at the interval of 15 days, 1 month and 3 months. Clinical assessment was done by evaluating improvement in pigmentation, scaling, pruritus and erythema. Mycological assessment was done by KOH mount and Wood's lamp examination.

Regarding clinical assessment in present study during visit 2, 3 and 4 among all three groups Oxiconazole was found to be more efficacious in causing clinical cure (healed + mild residual disease) as maximum number of cases in Oxiconazole (76.67%) as compared to Itraconazole (58.82%) and Ketoconazole group (46.66%) were cured. These results were attributed mainly to Oxiconazole because of efficacy of Oxiconazole to stay in stratum

corneum for longer duration with good antifungal activity. It also has faster skin absorption, negligible systemic absorption leading to better compliance, tolerability and least side effects. It was also observed during the study that single daily topical regimen patients were more comfortable than patients taking only systemic therapy.

Our study is similar to study done by Jegasothy BV et al5 who found application of Oxiconazole cream 1% once daily for two weeks in pityriasis versicolor cases gave clinical cure in 80% cases. They concluded that once-daily use of oxiconazole cream could be valuable in patients with a history of noncompliance with multiple-daily regimens of other topical antifungal agents.

In study conducted by Gugnani HC et al[8] clinical cure was observed with use of Oxiconazole 1% cream within 2 to 4 weeks after initiating treatment which was comparable to our study.

In a study conducted in Iraq by Maytham M. Al-Hilo et al[9] showed use of systemic Itraconazole 200mg daily for 7 days causes clinical cure in 52.6% cases compared to 50% cases with use of Ketoconazole 200mg daily for 10 days after 2 weeks. This was comparable to our study.

In a study conducted by Mohanty Juthika et al[10] showed use of systemic Itraconazole 100mg twice daily for 5 to 7 days caused clinical cure in 60% cases which was comparable to our study.

In present study during visit 2, mycological cure was present in 83.33% cases in Oxiconazole group, 88.2% in Itraconazole group and 88.7% cases in Ketoconazole group. During visit 3, mycological cure was present in 93.3% cases in Oxiconazole group, 94.1% from Itraconazole group and 93.3% cases from Ketoconazole group.

Subsequently all the cases among the three groups were followed up at 3 months (visit 4) and mycological cure was assessed which showed 88.7% cure rate in Oxiconazole group compared to 88.2% in Itraconazole group and 88.7% in Ketoconazole group. These results suggested presence of relapse in 6.6% cases in both Oxiconazole and Ketoconazole group and 5.9% cases in Itraconazole group. According to present study relapse rate was comparable in all three groups it was not statistically significant.

In study done by Jegasothy BV et al[5] application of Oxiconazole cream 1% once daily for two weeks in Pityriasis versicolor cases gave mycological cure in 80% cases. This study was comparable to our study.

In a study done by Jain VK et al[6] mycological cure with systemic Itraconazole 200mg once daily for five days was 95% compared to systemic Ketoconazole 200mg once daily for five days which was 85%. The relapse rate at the end of 4 months was 5% and 15% with Itraconazole and Ketoconazole group respectively.

Honorio Silva et al[11] conducted a study in Costa Rica and reported use of systemic Itraconazole 200mg daily for 7 days causes mycological cure in 56.5% cases compared to 69.9% cases with use of Ketoconazole 200mg daily for 10 days after 2 weeks. Cases were followed at end of 1 month they found mycological cure in 84.5% and 88.9% with use of Itraconazole and Ketoconazole respectively. These results were comparable to our study.

In a study conducted in Iraq by Maytham M. Al-Hilo et al[9] use of systemic Itraconazole 200mg daily for 7 days causes relapse in 0% cases compared to 10% cases with use of Ketoconazole 200mg daily for 10 days after 2 weeks.

In present study during visit 2, there was no any case with side effects in Oxiconazole group. 5.9% cases in Itraconazole group and 6.7% cases in Ketoconazole group had nausea. While 6.7% cases in Ketoconazole group had urticarial rash. Oxiconazole was better and well tolerated as it did not show any side effects. This advantage of Oxiconazole is because of minimal systemic absorption. None of the cases had side effects in all the three drug groups during visit 3 and visit 4.

In study done by Jegasothy BV et al[5] who found application of Oxiconazole cream 1% once daily for two weeks in pityriasis versicolor cases exerts no detectable systemic effect since only a negligible amount is absorbed from the skin. Jain VK et al[6] also reported nausea in 10% of cases who had taken Ketoconazole 200mg for 5 days which is comparable to the present study.

5. Conclusion

According to the present study we conclude that topical Oxiconazole therapy was more effective as compared to systemic Itraconazole and Ketoconazole therapy in early improvement of scaling, pigmentation and pruritus secondary to Pityriasis versicolor with no significant side effects.

In the present study topical Oxiconazole therapy showed statistically significant clinical cure as compared to systemic Itraconazole and Ketoconazole while mycological cure in all the three drug groups was comparable with no statistical difference and with negligible relapse rate.

Topical therapy with Oxiconazole was well tolerated with added advantage of single daily application as compared to systemic Itraconazole and Ketoconazole therapy.

As Pityriasis versicolor is known for high relapse rate due to colonisation in follicular structures, there is a need for larger studies with longers duration follow up. There is no sufficient data on use of topical Oxiconazole 1% cream

in treatment and long term follow up for assessment of relapse rate in Pityriasis versicolor, hence more studies are needed.

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