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Original Research Article

Therapeutic efficacy of topical luliconazole versus topical ketoconazole in the treatment of pityriasis versicolor patients: a hospital based comparative study

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ABSTRACT

Background: To evaluate the clinical efficacy of 1% topical luliconazole versus 2% topical ketoconazole in pityriasis versicolor patients.
Methods: Mycological examination of all the pityriasis versicolor patient was done by using skin scrapings were collected from the skin lesions to prepare for 10% KOH mount, which was examined under the microscope to note the findings as KOH mount positive or negative for Malassezia fungi. KOH mount positive or negative was noted at 0 days, 2 weeks and 4 weeks continued treatments with luliconazole and ketoconazole.
Results: At the first days, majorities of patients 46 (92%) of luliconazole group were positive for KOH mount. At 14 days treatment with luliconazole, patients had 11 (22%) positive for KOH mount. At the 28 days treatment with luliconazole, only 2 (4%) patients were positive and most of the patients 49 (98%) were negative for KOH mount. Similarly, in ketoconazole group patients, 47 (94%) patients were positive for KOH mount in beginning of treatment. At 14 days treatment with ketoconazole 16 (32%) patients were positive and 34 (68%) patients were negative for KOH mount. And at the 28 days with treatment of ketoconazole 13 (26%) patients were positive and most of the patients 37 (74%) were negative for ketoconazole.
Conclusions: Male population as well as age 26-35 years were more prone for pityriasis versicolor infection. On two weeks of treatment luliconazole and ketoconazole had near about similar efficacy against pityriasis versicolor. But, on continue 4 weeks of treatment regimens topical luliconazole had more clinically efficacious than ketoconazole against pityriasis versicolor.

Keywords: Clinical efficacy, Gender, Luliconazole, Ketoconazole, Pityriasis versicolor

INTRODUCTION

Pityriasis versicolor (PV) is a chronic cutaneous fungal infection caused by proliferation of lipophilic yeast (*Malassezia* species) in the stratum corneum.[1,2] The most common *Malassezia* species associated with PV is *M. globosa*, with *M. sympodialis* and *M. furfur* also frequently seen.[3] In most of the cases of PV, *Malassezia*, as a part of normal skin flora, are not pathogenic unless they assume a mycelial form.[2] This may be triggered by various factors, including humidity and high temperature, hyperhidrosis, familial susceptibility, and immuno-suppression.[1,2] Consequently, PV occurs more frequently in tropical climates (as much as 40%) as compared to temperate climates.[4]

It is characterised by scaly, hypo or hyper-pigmented, irregular macules usually located on the trunk and proximal

extremities.[6] PV is difficult to cure, as relapse following treatment can be as high as 80% within 2 years.[5]

Different modalities of treatment are available for pityriasis versicolor including topical and systemic azoles, allylamines and also selenium sulphide. However, a recent evidence-based review concluded most treatment options were similarly effective in the treatment of pityriasis versicolor, but randomized controlled trials are needed to compare their relative efficacies.[6] Ketoconazole is a water-soluble imidazole derivative. It is a synthetic antimycotic with a broad spectrum of activity against dermatophytes and yeasts.[7,8]

Luliconazole is a novel, optically active imidazole antifungal.[9] The compound has a unique chemical structure, which is augmented by introduction of a ketene dithioacetate structure in the imidazole moiety. It has high potency inhibitory action against filamentous fungi, including dermatophytes. Preliminary studies suggested that luliconazole could also be effective against *Malassezia* species.[10] Objectives of this study was to evaluate the clinical efficacy of topical luliconazole versus topical ketoconazole in patients with pityriasis versicolor.

METHODS

This present study was conducted in Department of Dermatology, Madhubani Medical College, Madhubani during a period from November 2018 to October 2019. Entire subjects signed an informed consent approved by institutional ethical committee of Madhubani Medical College, Madhubani, Bihar, India was sought.

Study design

Data was collected by random sampling methods. A total of 100 subjects with irrespective of age and sex were enrolled in this study. Pityriasis versicolor skin lesions patients who were already undergoing antifungal treatment either topically or systemically and pregnant women were excluded from this study. All the 100 patients in this study were randomly allotted to two groups (A and B) with 50 patients in each group.

Method was group A patients were treated with topical luliconazole 1% cream twice daily and group B patients were treated with topical ketoconazole 2% cream twice daily for 28 days. Clinical assessment and mycological (by doing the KOH mount) assessment was done to all the patients in both the groups at the beginning and at the two follow up visits of this study. The first follow up assessment was done on the 14th day and the second follow up assessment was done on the 28th day of this study to evaluate the comparative therapeutic efficacy of both these drugs. The clinical assessment of all the patients in both the groups was done by noting the characteristic clinical features of the Pityriasis versicolor skin lesions like the presence of hypo or hyperpigmented macules or patches covered by tiny dust like scales with irregular margins and their distribution on the body over the chest, back, face, neck, upper extremities and abdomen along with the clinical examination to determine the presence of any other dermatological diseases and systemic diseases in these patients. The mycological assessment of all the patients in both the groups was done in which skin scrapings were collected from the skin lesions to prepare for 10% KOH mount, which was examined under the microscope to note the findings as KOH mount positive or negative for Malassezia fungi. At the end of this study, i.e. on the 28th day, comparative therapeutic efficacy evaluation of topical luliconazole 1% cream against topical ketoconazole 2% cream in the treatment of Pityriasis versicolor was done by noting the number of patients in both the groups of this study who attained the mycological cure, i.e., KOH mount negative for *Malassezia* fungi.

Procedures

Confirmation of the diagnosis of pityriasis versicolor was done by collecting the skin scrapings from the skin lesions of patients with pityriasis versicolor and finding both the yeast form (large number of variable size of spores producing grape-like clusters of yeast) and mycelial form (short, thick hyphae) of the *Malassezia* fungi producing the characteristic spaghetti and meat-balls appearance in 10% KOH mount preparation, which was examined under the microscope.

Statistical analysis

Data was analyzed by using simple statistical methods with the help of MS-Office software. Data was tabulated and percentages were calculated.

RESULTS

In this study, a total of 100 patients of pityriasis versicolor were enrolled. All the cases were categorized in two groups. Each group had 50 cases of pityriasis versicolor. Most of the cases were males (65%). Male and female ratio was 13:7. Majorities of patients (51%) were belonged in age group of 26-35 years (Figure 1 and 2).

In this present study, at the first days, majorities of patients 46 (92%) of luliconazole group were positive for KOH mount. At 14 days treatment with luliconazole, patients had 11 (22%) positive for KOH mount. And at the 28 days treatment with luliconazole, only 2 (4%) patients were positive and most of the patients 49 (98%) were negative for KOH mount. Similarly, in ketoconazole group patients, 47 (94%) patients were positive for KOH mount. At 14 days treatment with ketoconazole 16 (32%) patients were positive and 34 (68%) patients were negative for KOH mount. And at the 28 days with treatment of ketoconazole 13 (26%) patients

were positive and most of the patients 37 (74%) were negative for ketoconazole (Table 1).

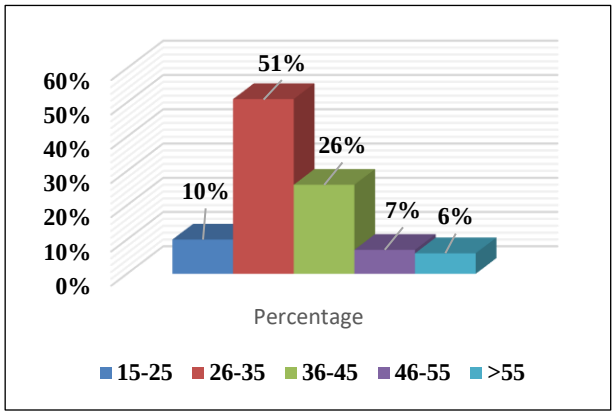

Figure 1: Age wise distribution of pityriasis versicolor patients.

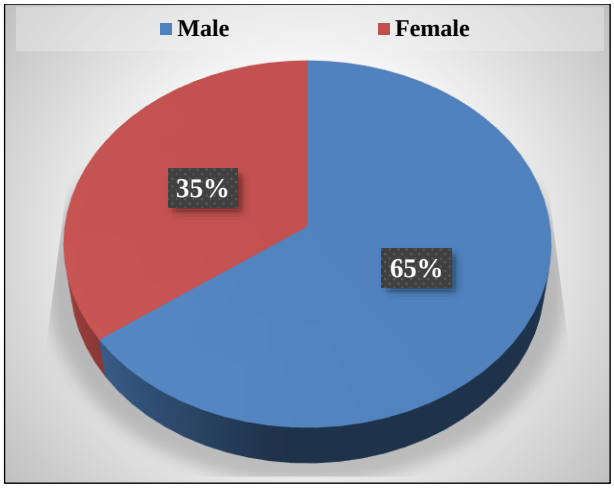

Figure 2: Gender wise distribution of pityriasis versicolor patients.

Table 1: Comparison of KOH mount sensitivity of luliconazole versus ketoconazole group patients.

	Luliconazole (%)		Ketoconazole (%)	
	KOH positive	KOH negative	KOH positive	KOH negative
At the beginning of treatment (0 days)	46 (92)	4 (8)	47 (94)	3 (6)
At 2nd follow up (2 weeks)	11 (22)	39 (78)	16 (32)	34 (68)
At the end of treatment (4 weeks)	2 (4)	49 (98)	13 (26)	37 (74)

DISCUSSION

Dermatophyte infections are one of the earliest known fungal infections of mankind and are very common throughout the world. Although dermatophytoses does not cause mortality, it does cause morbidity and poses a major health problem (Emmons and Binford et al).[11]

Imidazole preparations for topical use, such as clotrimazole, miconazole, econazole, and ketoconazole, are now well established as effective treatments in ringworm infections with a low incidence of adverse reactions.[12,13] other drugs in this group, such as tioconazole and sulconazole, are equally effective.[14,15] These older topicals have been joined by newer preparations such as sertaconazole, luliconazole, and isoconazole, although they have not been licensed in all countries.[16,17] The azole antifungals are usually available in cream, solution, or spray formulations at a 1% concentration. Most are used twice daily for 2-4 weeks, although some, such as bifonazole, are licensed for once-daily use.[18] There is little difference in the efficacy of the different azoles.[19] Luliconazole is an imidazole antifungal agent with a unique structure, as the imidazole moiety is incorporated into the ketene dithioacetate structure. Luliconazole is the R-enantiomer and has more potent antifungal activity.[20]

In this present study, 100 patients with age group 15 years to >55 years of pityriasis versicolor were enrolled. Among them 50 patients were treated with topical luliconazole 1% twice daily and 50 patients were treated with topical ketoconazole 2% twice daily for 4 weeks. Mycological assessment was performed by skin scrapings of skin lesion of pityriasis versicolor patients for 10% KOH mount. Results of this study shows that the age group 26 years to 35 years were more prone 51 (51%) to infection of pityriasis versicolor. And males (65%) were commonly infected than females (35%) with pityriasis versicolor.

In this present study, at the first days, majorities of patients 46 (92%) of luliconazole group were positive for KOH mount and 47 (94%) patients of ketoconazole group were positive for KOH mount. At second follow up on 14 days treatment with luliconazole, 11 (22%) patients were positive for KOH mount and 16 (32%) patients of ketoconazole group were positive. And at the last follow up on 28 days treatment with luliconazole, only 2 (4%) patients were positive for KOH mount and 13 (26%) patients of ketoconazole were positive for KOH mount. Thus, authors were seen that most of the patients 48 (96%) of ketoconazole group were negative for KOH mount and only 37 (74%) patients of ketoconazole were negative for KOH on 4 weeks treatment. But on 2 weeks of treatment of topical luliconazole (78% negative for KOH mount) and topical ketoconazole (68% negative for KOH mount) in pityriasis versicolor patients were near about similar effective. Hence, 1% topical luliconazole was more effective than 2% topical ketoconazole in pityriasis versicolor patients on 4 weeks of treatment.

Application of ketoconazole shampoo has varied across studies, including once daily for 3 or 14 days, and once weekly for 3 weeks.[21-24] Lange et al, conducted a multi-center, double-blind, randomized, placebo-controlled clinical trial evaluating the efficacy of a single application of ketoconazole shampoo vs. daily application for 3 days.[21] Patients used ketoconazole shampoo either daily for 3 days, ketoconazole once followed by placebo shampoo for 2 days, or placebo shampoo for 3 days. Thirty-one days from the start of treatment, there were no significant differences between the two ketoconazole regimens in mycological or complete cure rates. Both ketoconazole regimens, daily application for 3 days and one application, were significantly more effective than placebo shampoo for mycological cure (84% vs. 78% vs. 11% respectively, $p<0.001$) and complete cure (73% vs. 69% vs. 5% respectively, $p<0.001$).[21]

The anti-Malassezia activity of luliconazole has been documented and this compound has been used clinically to treat *Malassezia* infections, such as pityriasis versicolor. However, susceptibility of *M. restricta* in the new taxonomy of the species has not been determined.[25] Luliconazole showed activity comparable to or stronger than that of ketoconazole against *M. restricta*. Luliconazole is a potent antifungal drug for dermatomycotic fungi. The in vitro antifungal potency of luliconazole, because of its extremely strong anti-dermatophytic properties, is different from those of other azoles. Luliconazole demonstrates high in vitro potency against *M. restricta*. These results underscore the clinical utility of luliconazole as a potent, broadspectrum antimycotic agent.[26] This present study shows the luliconazole is more clinically efficacy than ketoconazole on 28 days of treatment regimens.

CONCLUSION

This present study concluded that the male population as well as age group 26-35 years were more prone to pityriasis versicolor infection. On two weeks of treatment regimen luliconazole and ketoconazole had near about similar efficacy against pityriasis versicolor patients. But, on continue 4 weeks of treatment with topical luliconazole had more clinically efficacious than ketoconazole against pityriasis versicolor.

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