

ORIGINAL RESEARCH



**A PROSPECTIVE STUDY ON THE COMPARISON OF EFFICACY, QUALITY OF LIFE AND MEDICATION ADHERENCE OF TRIAZOLES AND ALLYLAMINES AMONG PATIENTS WITH SUPERFICIAL MYCOTIC INFECTIONS OF SKIN AND NAILS IN A TERTIARY CARE HOSPITAL**

**Mincy. C. Das, Anu Anto, Bincy. C. M, and Babitha. M\***

Pharm.D, Department Of Pharmacy Practice, Sree Krishna College Of Pharmacy and Research Center, Trivandrum, Kerala, India

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**ABSTRACT:**

**Objective :** The main objective of the study was to compare the efficacy, quality of life and medication adherence of Triazoles and Allylamines among patients with superficial fungal infections of skin and nails.

**Methods:** Efficacy was assessed by efficacy parameters such as KOH test and changes in signs and symptom severity score, Quality of life by Dermatology Life Quality Index and Medication Adherence by Medication adherence scale 8.

**Results :** The data collected reveals that greater proportion of patients showed excellent improvement and better quality of life with Allylamines than Triazoles and medication adherence evaluated suggests that both Triazoles and Allylamines have medium adherence.

**Conclusion:** Allylamines are the best choice of antifungal therapy with excellent efficacy, better quality of life and good adherence when compared to Triazoles. Conventional azole antifungals have been associated with high rates of disease recurrence caused in part by lack of adherence to therapy, which points out that, once-daily dosing may a valuable option for physicians treating topical fungal infections. The major drawback of antifungal regimen is its long term therapy leading to poor compliance and a high relapse rate which necessitates such a study.

**KEYWORDS:** KOH, DLSO, SWO , PSO , DLQI , MAS 8 , QOL

**Corresponding author: Dr.Babitha M**  
Email id: [bincy7321@gmail.com](mailto:bincy7321@gmail.com)

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## INTRODUCTION

Infections caused by pathogenic fungi and limited to the human hair, nails, epidermis and mucosa are referred to as superficial mycotic infections. Dermatophytosis (tinea or ringworm), are the most common type of superficial mycotic infections caused by dermatophytes. They are found in soil (geophilic organisms), on animals (zoophilic), and on humans (anthropophilic). These fungi require keratin for growth and therefore, they are unable to infect mucosal surfaces. These infections involve only the outermost layers of the stratum corneum of the skin or the cuticle of the hair shaft and nails, hence constitute only cosmetic problems and rarely elicit an immune response from the host particularly in immune-suppressed or otherwise debilitated patients. According to World Health Organization (WHO), the prevalence rate of superficial mycotic infection worldwide has been found to be 20-25%. Its prevalence varies in different countries.<sup>[1]</sup> It is more prevalent in tropical and subtropical countries like India where the heat and humidity is high for most part of the year. There are several reports on intracontinental variability of the global incidence because of the change in climatic condition across the world. Tinea capitis is more common with crowded living conditions and low socioeconomic and urban settings and in Indian children. Adult blacks may have a lower incidence of dermatophytosis.

The causative species vary with geographic regions. Some species are distributed worldwide, such as *T. rubrum*, *T. mentagrophytes* var. *interdigitale*, *Microsporum canis* and *Epidermophyton floccosum*. Others have partial geographic restrictions, such as *T. schoenleinii* (Eurasia, Africa), *T. soudanense* (Africa), *T. violaceum* (Africa, Asia, and Europe) and *T. concentricum* (Pacific Islands, Far East, and India). Most cases of Tinea unguium, Tinea cruris, Tinea corporis, and Tinea pedis are caused by *T. rubrum*, which is the commonest dermatophyte in most developed countries as well as in urban areas of some developing countries.<sup>[3]</sup> Dermatophyte infections can be acquired from three sources such as most commonly from another person, from animals such as puppies or kittens and least commonly from soil. The dermatophytes are fungi that colonize skin, hair, and nails on the living host. These fungi possess greater invasive properties than those causing superficial infections, but they are limited to the keratinized tissues.<sup>[7]</sup> The progress of fungal infections depends on various parasite and host factors, such as species of organism, immunologic status of the host, type of clothing worn, and type of footwear used. Trauma plays an important role in infection where the organisms gain entry and establish themselves in the cornified

layers of traumatized or macerated skin and its integument and multiply by producing keratinase to metabolize the insoluble, tough fibrous protein. It has been speculated that factors such as cell-mediated immunity and the presence of transferrin in serum inhibit fungal propagation to the deeper tissue layers and systemic disease does not occur.<sup>[11]</sup> Classification of superficial fungal infections include Tinea Corporis, Tinea Pedis, Tinea Manuum, Tinea Cruris, Tinea Unguium, Candidiasis and Pityriasis Versicolor. The main aim of the study is to compare the efficacy, quality of life and medication adherence of triazoles and allylamines among patients with superficial fungal infections of skin and nails. Treatment options are Antibiotics ( Polyenes Eg: Amphotericin B and Heterocyclic benzofuran Eg: Griseofulvin ), Antimetabolite Eg: Flucytosine, Azoles ( Imidazoles Eg: Clotrimazole and Triazoles Eg: Fluconazole, Itraconazole ), Allylamine Eg : Terbinafine, Other topical agents Eg : Tolnaftate, Benzoic acid etc

## EFFICACY

Efficacy is the capacity for beneficial change or therapeutic effect of a given intervention, most commonly used in the practice of medicine and pharmacology.<sup>[1]</sup> In this study, efficacy is assessed by using efficacy parameters such as KOH test and changes in signs and symptoms severity score which is based on the texture/colour changes of the skin & nail, scaling, pruritis and erythema. If signs and symptoms are absent, then a score of zero will be given followed by mild, moderate and severe symptoms will be provided with 1, 2 and 3 score respectively. This score is assessed in two sections that is assessment prior to the treatment and after the treatment.

## QUALITY OF LIFE

The WHO defines Quality of Life as individuals perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.<sup>[2]</sup> The Dermatology life Quality Index (DLQI) is a ten question questionnaire used to measure the impact of skin disease on the quality of life of an affected person. It is designed for people aged 16 years and above. It was created by Dr Andrew Y Finlay and Dr Gul Karim Khan from 1990 to 1994 at the Department of Dermatology, University of Wales College of Medicine (now Cardiff University), Cardiff, UK.

## MEDICATION ADHERENCE

The WHO defines adherence to long-term therapy as "the extent to which a person's behavior in

taking medication, following a diet, and or executing life style changes and corresponds.

Treatment→Adherence→Outcomes

In Fungal infections, adherence to therapy for dermatomycosis is known to decrease with the duration of treatment and the number of applications required each day, particularly once symptoms have disappeared. Simpler dosing regimens are sought for the treatment of superficial fungal infections. Itraconazole, an Triazole antifungal, has pharmacokinetics that are considered favorable for once-daily antifungal therapy. Multiple possible causes for patient non-adherence have been postulated.<sup>[7]</sup> They include the following problems with the therapy, such as side effects, poor instructions given to the patient by the prescriber, poor physician-patient relationship, poor memory on the part of patients, and patients' inability to pay for medications. With short-term treatment, adherence can usually be enhanced with fairly simple interventions, such as patient education and follow up by telephone or e-mail, but interventions capable of increasing adherence in patients with chronic health problems tend to be complex, involving combinations of patient education, reminders, family therapy, psychological therapy, crisis intervention, and close follow up.

## MATERIALS AND METHODS

**Study sight** : Department of Dermatology of 350 bedded Cosmopolitan Multispecialty Hospital situated in Trivandrum.

**Study period** : Six months (December 2015-May 2016).

**Study design** : Prospective Observational study.

**Study people** : Patients from the department of Dermatology who were diagnosed with superficial fungal infections during the study period, were included after obtaining the permission for collection of data.

**Sample Size** : It was calculated for equivalence study of a continuous response variable from the two groups using the formula;

$$N = \frac{2(Z_{\alpha} + Z_{\beta})^2 \bar{p}(1 - \bar{p})}{\Delta^2}$$

Where

$$Z_{\alpha} = 1.96 \text{ for } \alpha = 0.05$$

$$Z_{\beta} = 0.84 \text{ for } \beta = 0.80$$

$$\bar{P} = \frac{PC + PT}{2}$$

PC = Proportion in group1

PT = Proportion in group2

$$\Delta = PT - PC$$

Minimum sample in each group is **50**

Total 130 patients were included in the study.

## Inclusion criteria

Patients on Antifungal treatment >2weeks, Patients of age between 12yrs-65yrs, Patients with or without other co-morbidities, Patients with complete Medical Records including KOH test, Patients who are willing to participate in the study, Patients with a total score ( >5) in signs and symptom severity score.

## Exclusion criteria

Pregnant and lactating women, Patients with known hypersensitivity to Allylamines or Triazoles.

## Data collection

A proforma was designed for obtaining and evaluating efficacy, medication adherence, and quality of life in patients with fungal infections. It contains relevant details such as demographics, past medical history, past medication history, diagnosis, severity score, laboratory investigations and therapeutic plan. The Institutional Ethics Committee of Cosmopolitan Hospital in its meeting held at Board room , reviewed and discussed the thesis protocol and was approved by the IEC committee.

## Data analysis

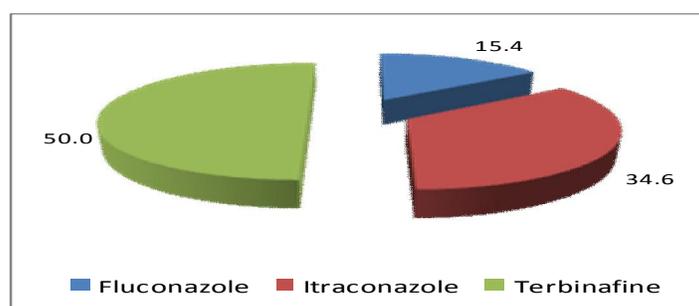
The collected data were recorded in Microsoft excel sheet and workload is entered as numeric code. KOH test results and changes in signs and symptoms score before and after the patient treatment were noted and the changes in score was analysed. Quality of life was assessed by Dermatology Life Quality Index was filled and the changes in two classes of drugs were compared. The medication adherence data were collected with the use of Medication adherence scale 8 which was self prepared and the adherence of two classes of drugs were noted and changes were compared. The whole data were analysed by using software SPSS statistics and the efficacy , quality of life and medication adherence were compared by using chi-square test with a statistical significance of  $p \leq 0.01$ .

## RESULTS

### Sample distribution

Drug	Count	Percent
Fluconazole	20	15.4
Itraconazole	45	34.6
Terbinafine	65	50.0

**Table 1 : Percentage distribution of the sample according to drug**



**Fig 1 : Percentage distribution of the sample according to drug**

Out of 130 patients enrolled in the study, 20 (15.4%) patients were prescribed with fluconazole, 45 (34.6%) patients with Itraconazole and 65 (50%)

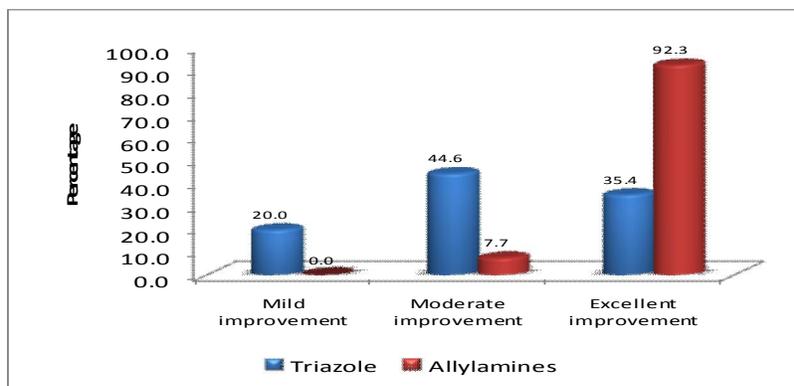
patients with Terbinafine. Thereby equal number of patients who were prescribed with Triazoles and Allylamines (each of 65) were selected randomly.

### Comparison of efficacy

Efficacy	Triazole		Allylamines	
	Count	Percent	Count	Percent
Mild improvement	13	20.0	0	0.0
Moderate improvement	29	44.6	5	7.7
Excellent improvement	23	35.4	60	92.3

\*\*:- Significant at 0.01 level

**Table 2 : Comparison of quality of life based on drug used**



**Fig 2 : Comparison of efficacy based on drug used**

The efficacy of antifungals among mycotic infection patients who were prescribed with

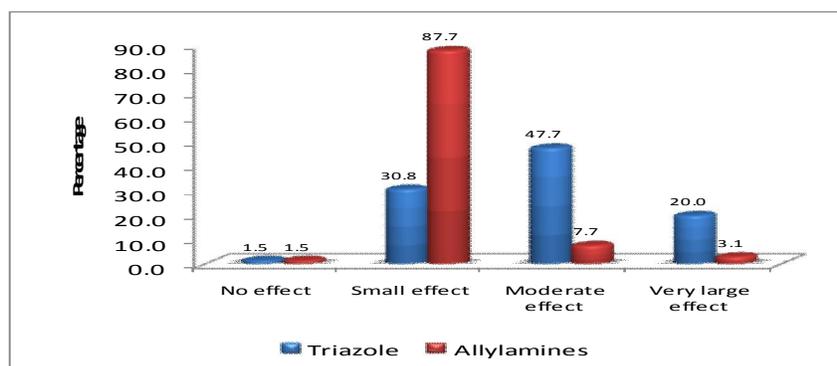
Allylamines was found to be excellent significantly ( $p \leq 0.01$ ) with a standard deviation of 46.44.

**Comparison of quality of life**

Quality of life	Triazole		Allylamines	
	Count	Percent	Count	Percent
No effect	1	1.5	1	1.5
Small effect	20	30.8	57	87.7
Moderate effect	31	47.7	5	7.7
Very large effect	13	20.0	2	3.1

\*\*:- Significant at 0.01 level

**Table 3 : Comparison of quality of life based on drug used**



**Fig 3 : Comparison of quality of life based on drug used**

The QOL among mycotic infection patients who were prescribed with Allylamines was found to be

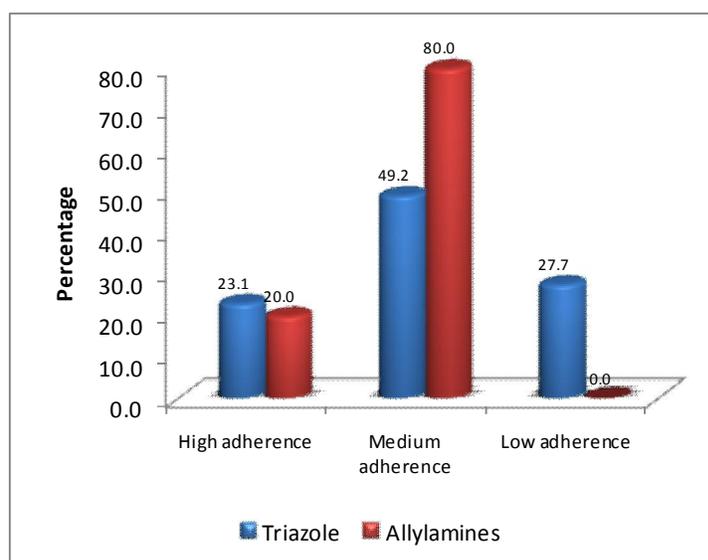
improved significantly ( $p \leq 0.01$ ) with a standard deviation of 44.62

### Comparison of medication adherence

Medication adherence	Triazole		Allylamines	
	Count	Percent	Count	Percent
High adherence	15	23.1	13	20.0
Medium adherence	32	49.2	52	80.0
Low adherence	18	27.7	0	0.0

\*\* - Significant at 0.01 level

**Table 4 : Comparison of medication adherence based on drug used**



**Fig 4 : Comparison of medication adherence based on drug used**

The adherence to medications among mycotic infection patients was found to be moderate significantly ( $p \leq 0.01$ ) with a standard deviation of 22.9 in both the cases of antifungals.

### DISCUSSION

In the comparison of efficacy [fig:2], it was found that 13 (20%), 29 (44.6%) and 23 (35.4%) patients exhibited mild, moderate and excellent improvement respectively. While Allylamines proved 5 (7.7%) and 60 (92.3%) patients with moderate and excellent improvement respectively. Hence it can be concluded that the Allylamines exhibit greater proportion of excellent improvement followed by moderate improvement than Triazoles after a follow up of 2-4 weeks. A similar study was done by Chandana T et.al; 2014

on "Comparison of safety and efficacy of Laliconazole and other antifungal agents" a prospective parallel and randomized, open-label, comparative study to evaluate the efficacy of newer antifungal drugs using the same parameters of our study with different object drugs.[1] In this, the study population was 150 patients, who met the inclusion and exclusion criteria and all the patients are aged between 18 to 80 years. Here patients received the newer antifungals randomly and the test product needed to be applied once daily for 1 week in patients with Tinea cruris/ Tinea corporis and for 2 weeks in patients with Tinea pedis. First follow up would be at 1 week and all the patients will be evaluated for clinical parameters and global clinical response. The second follow up at 4 weeks and all the patients are again needed to be assessed for the parameters.

In the Dermatology Life Quality index comparison [fig:3], 130 patients were provided with DLQI questionnaire at the time of follow up and thereby their improvement in the quality of life was assessed. It suggests that greater proportion of patients exhibited better quality of life with Allylamines than Triazoles. A similar study on the "Dermatology quality of life scales - a measure of the impact of skin diseases" by M.Morgan et.al; 1997 gives an overview of the negative impact of common chronic skin conditions, such as psoriasis, vitiligo, acne, and eczema measured by the validated quality of life instruments and states that effective treatments of the above skin conditions correlate with positive quality of life outcomes.[2] It suggests that a patient's overall satisfaction increases significantly when the physician is able to explain and empathize with the patient's skin condition. Therefore having a good relationship with the patient as well as interpersonal skills can increase patient satisfaction, which is likely to improve treatment adherence and clinical outcomes. One consistent finding in all 4 skin conditions reviewed is that effective treatment seems to correlate with positive QOL outcomes and it is logical to assume that the improvement in QOL is due to improvement of the clinical outcomes.

In the comparison of medication adherence [fig:4], it clearly shows that greater number of patients exhibit medium adherence both in the case of Triazoles and Allylamines. A study on "Increasing patient adherence in antifungal infection treatment once daily dosing of Sertaconazole" by Jeffrey M Weinberg 2009 suggest that in dermatology, adherence to therapy for dermatomycosis is known to decrease with the duration of treatment and the number of applications required each day, particularly once symptoms have disappeared.[5] It is hypothesized that its prolonged dermal retention may translate into the need for less frequent application for successful treatment in clinical practice. As former Surgeon General C. Everett Koop has pointed out, "Drugs don't work in patients who don't take them" so any modification of treatment regimens that encourages patients to be more adherent is desirable. Such modifications include simplifying regimens, customizing them to patient's particular

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lifestyles, asking patients about their medication-taking preferences, and engaging in frank discussion of the risks implicit in nonadherence, such as recurrence of disease or development of chronic conditions. Simpler dosing, such as once per day, would be particularly valuable in the treatment of cutaneous fungal infections in which symptoms may disappear soon after treatment is initiated, which can deprive patients of the reminder to continue using their medication provided by their subjective discomfort, and thereby prevent effective therapy. Conventional azole antifungals have been associated with high rates of disease recurrence caused in part by lack of adherence to therapy, which makes effective, oncedaily dosing a valuable option for physicians treating topical fungal infections.

## CONCLUSION

The present study was conducted to assess the efficacy, quality of life and medication adherence of patients with superficial mycotic infections. According to our study, we concluded that Allylamines are the best choice of antifungal therapy with excellent efficacy, better quality of life and good adherence when compared to Triazoles. It suggests that a patients' overall satisfaction increases significantly when the physician is able to explain and empathize with the patient's skin condition. Therefore having a good relationship with the patient as well as interpersonal skills can increase patient satisfaction, which is likely to improve treatment adherence and clinical outcomes. Conventional azole antifungals have been associated with high rates of disease recurrence caused in part by lack of adherence to therapy, which points out that, once-daily dosing may a valuable option for physicians treating topical fungal infections. In our country, the risk of fungal infection is high due its tropical climate. Moreover now a days, the degree of immunosuppression and the number of immunosuppressed patients are too high leading to the emergence of appropriate choice of antifungal treatments. The major drawback of antifungal regimen is its long term therapy leading to poor compliance and a high relapse rate which necessitates such a study.

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