International Journal of Research in Dermatology
Haldar S. Int J Res Dermatol. 2021 Jan;7(1):33-37
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20205591

Original Research Article

Management of dermatophytosis with a novel itraconazole formulation: a research survey

Susmit Haldar*

Calcutta Skin Institute, Kolkata, West Bengal, India

Received: 23 June 2020
Revised: 11 December 2020
Accepted: 11 December 2020

***Correspondence:**
Dr. Susmit Haldar,
E-mail: susmithaldar@gmail.com

ABSTRACT

Background: Dermatophytic infections are the most prevalent fungal infections, which affect majority of the global population. Indian climate, especially the hot and humid conditions contribute majorly to dermatophytosis. Itraconazole is an orally active triazole antifungal drug, which has demonstrated a broad spectrum of activity and a favourable pharmacokinetic profile. Itraconazole at an appropriate dosage and duration schedule has been reported to be an effective antifungal drug and has achieved optimal results.
Methods: The present survey aimed at evaluating the efficacy of the novel itraconazole formulation,
I-Tyza 100 [itraconazole 100 mg (Abbott health care pvt ltd)] with multi-particulate in solid dispersion (MPSD) technology in patients with tinea infections. The data collection was based on the proportion of patients presenting in the clinics for tinea infections, the choice and duration of therapy, real life efficacy of the drug, and for understanding the overall antifungal therapy in dermatomycosis.
Results: The responses obtained from 177 doctors were evaluated, and statistical analyses were carried out. The results suggested that clinical presentation of patients with tinea infections per week ranged between 30% and 60%. For the management of tinea infections, oral itraconazole was preferred by maximum doctors, followed by terbinafine, griseofulvin and fluconazole. Also, majority of the doctors (83%) opined that MPSD technology could improve therapeutic efficacy of the novel itraconazole formulation.
Conclusions: The survey findings indicated that the novel itraconazole formulation is a preferred oral antifungal therapy for the management of tinea infections.

Keywords: Dermatophytes, azoles, survey, itraconazole, multi-particulate in solid dispersion technology, Vegetarian capsules

INTRODUCTION

The prevalence of superficial fungal infections has increased considerably, and reports indicate that approximately 20-25% of the world's population is affected with dermatomycosis.[1] The common pathogens responsible for most of the superficial fungal infections are *Trichophyton*, *Microsporum* and *Epidermophyton*. These pathogenic fungi have the ability to form colonies in keratinized tissues like skin, hair and nails, resulting in a range of pathologic clinical presentations such as tinea pedis, tinea cruris, and other similar infections.[1,2] The ease with which they proliferate is probably one of the reasons for increased prevalence of fungal diseases. An alarmingly high prevalence of dermatophytosis, ranging from 36.6-78.4%, has been observed in India.[2]

A variety of factors such as extent of infection, site of infection and the pharmacological properties of the antifungal therapy govern the management of dermatophytosis. Topical and oral antifungals are

considered the mainstay treatment for tinea infections. However, for extensive infections, combination treatment is indicated. Combination treatment is also recommended in naïve as well as recalcitrant tinea pedis infections. Azoles are the most commonly used antifungal agents due to their anti-inflammatory, antibacterial nature and broad-spectrum antimycotic activity. Systemic antifungals are recommended in infections with vellus hair involvement; deep, inflammatory and multisite lesions; and for non-responders. Itraconazole 100-200 mg daily and terbinafine 250 mg daily are the preferred systemic agents in drug naïve cases, whereas itraconazole 200-400 mg daily is preferred in recalcitrant cases. Itraconazole is also a preferred treatment for tinea incognito and administered at a dose of 200-400 mg daily, for a minimum duration of 4-6 weeks or more.[2]

Amongst the variety of azoles, itraconazole has a distinct in vitro activity against dermatophytes. It is characterized by good oral absorption, and accumulates in the tissue due to its highly lipophilic nature.[3] It is the preferred therapy option for dermatophytic infections owing to high efficacy and favourable risk-benefit ratio; and is considered as an important therapy option in adults in case of failure of topical treatment.[3]

Quality of the drug is very important for maximizing treatment efficacy. Various factors such as size of the bead, drug polymer ratio, type of polymer, number of pellets, etc. are the important determinants for bioavailability of the drug, and ultimately affect the treatment outcome. Itraconazole formulation with homogeneity of the dispersion at molecular level will have maximum possible solubility and thus bioavailability.[4] Thus, itraconazole formulation with optimum dissolution profile is important for adequate treatment response.[5]

A novel itraconazole formulation, I-Tyza 100 (itraconazole 100 mg) with multi-particulate in solid dispersion (MPSD) technology, has demonstrated near-complete dissolution profile. This novel formulation has least pellet size variation when compared to other generic formulations.[5]

Results from another study have demonstrated improved water-solubility and bioavailability of itraconazole when formulated with hydroxypropyl methylcellulose (HPMC). Presence of HPMC, which is a water-soluble polymer, aids in dispersion, and thereby, increases the bioavailability.[6] HPMC is a commonly found cellulose in plants; and thus it is 100% vegetarian. It is a suitable material for capsules because of its flexibility and strength. It can replace gelatin which is of animal origin. Gelatin, is associated with two major drawbacks- first, the risk of developing Creutzfeldt-Jacob disease, if it is derived from animals with transmissible spongiform encephalopathy (TSE); and secondly, lesser patient preference due to religious, cultural and personal issues.[7] Considering this, especially in the Indian population which has a good number of vegetarian population, HPMC can be good alternative to gelatin. This research survey was conducted on novel itraconazole, I-Tyza 100 with MPSD technology, to assess its efficacy against dermatophytosis.

METHODS

Methodology

A survey questionnaire comprising of 17 questions (listed in annexure) was distributed to 177 health care professionals (HCP) practicing in 17 states, across different geographical regions of India between March 2019 to September 2019.

The questionnaire aimed at evaluating their clinical experience regarding the novel formulation of itraconazole, widely used for management of dermatomycosis. The survey was conducted to collect data on the proportion of patients consulting HCPs for tinea infections, the duration of therapy for which the novel itraconazole formulation would generally be prescribed, real life effectiveness ratings for the novel itraconazole formulation and understanding the overall antifungal therapy in dermatomycosis.

Survey plan

All patients who were eligible for treatment with the novel itraconazole formulation, based on the discretion of HCPs were enrolled. The data was collected from HCPs who prescribed I-tyza 100 (Abbott health care pvt ltd). The duration of the survey was approximately four months. A survey questionnaire was used to collect data and the questionnaire was filled by HCPs. The final statistical analysis of the parameters was carried out by pooling the data obtained. The following parameters were considered: proportion of patients consulting the HCPs for tinea infections, duration of therapy using the itraconazole formulation, real life effectiveness of the formulation, and understanding the overall antifungal therapy in dermatomycosis.

RESULTS

The responses obtained from 177 doctors were evaluated, and statistical analyses were carried out, using excel formulae. Average was calculated to generate the answer that got the maximum response. The major results obtained are discussed below.

Prevalence and clinical presentation of tinea infections

It was found that clinical presentation of patients with tinea infections per week was between 30% and 60% (Figure 1). The common age group of patients presenting with tinea infections was usually between 30-40 years of age. Tinea infections were found prevalent in both male and female populations. It was observed that most patients who presented with tinea infections (44.6%) were generally from the low socio-economic category (Figure 2).

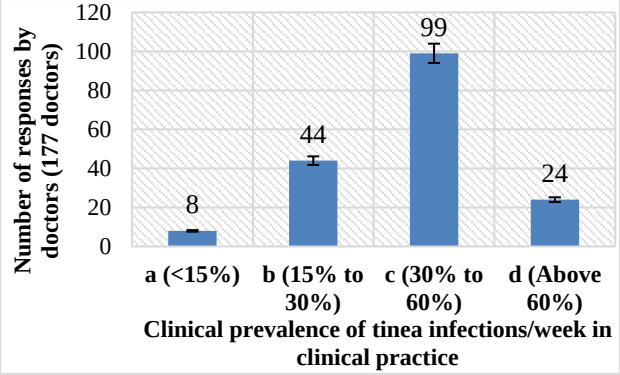

Figure 1: Percentage of patients diagnosed with tinea infections per week.

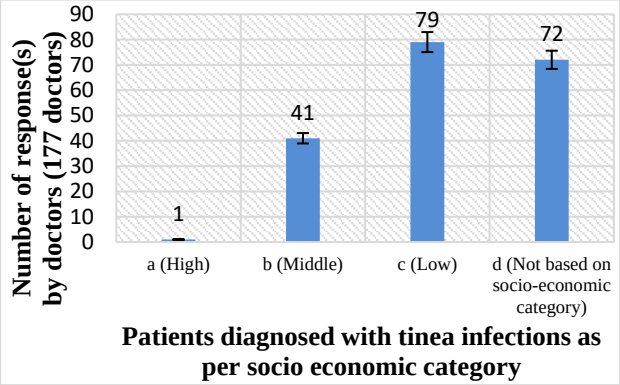

Figure 2: Percentage of patients diagnosed with tinea infections as per socio-economic category.

Management of tinea infections

Antifungal therapy

Majority of the doctors preferred the topical antifungal luliconazole for management of tinea infections over terbinafine followed by sertaconazole, amorolfine and eberconazole. Oral antifungal molecule itraconazole was preferred by maximum doctors for management of tinea infections followed by terbinafine, griseofulvin and fluconazole (Figure 3).

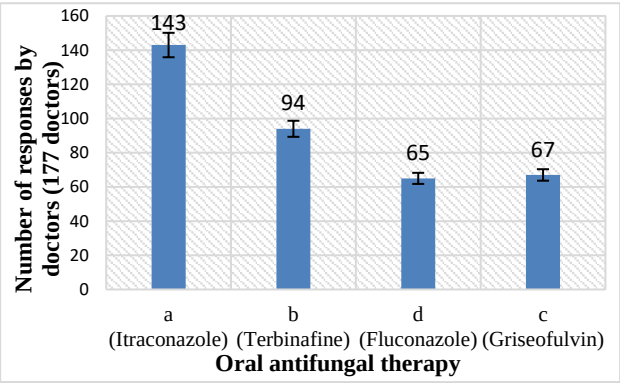

Figure 3: Clinical preference of oral antifungal molecule in management of tinea infections.

Combination therapy

Approximately 70% patients with tinea infections were prescribed with the topical and systemic therapy combination. Majority of the doctors (64.9%) preferred prescribing an antifungal soap for management of tinea infections. Selenium disulfide antifungal soap was preferred by some of the doctors (~41%) for the management of patients with tinea infections.

Itraconazole therapy

45.8% doctors were in favour of using Itraconazole (100 mg) for 21 days to 1 month. 54.8% doctors were in favour of using double dose of itraconazole (100 mg) for 21 days to 1 month. Majority of the doctors (88%) opined that itraconazole pellet manufacturing technology can play an important role in the clinical outcomes (Figure 4). Majority of the doctors (83%) were of the opinion that MPSD may improve therapeutic efficacy of novel itraconazole formulation. Approximately, 78% doctors were of the opinion that comparable biorelevant dissolution profile of novel itraconazole formulation and innovator helped in achieving equivalent results in clinical practice. 98.8% favoured the efficacy of the novel itraconazole formulation. Majority of the doctors (62.1%) supported the clinical efficacy and subsequent positive outcomes of novel itraconazole formulation. Majority of the doctors (~58%) were of the opinion that vegetarian capsules with novel itraconazole formulation can improve patient acceptance for the therapy.

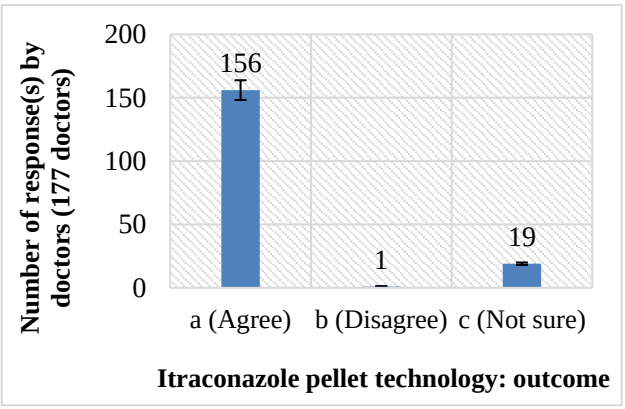

Figure 4: Response to role of novel itraconazole formulation.

DISCUSSION

Over the last few years, epidemiological studies on fungal infections, from different parts of India have shown an escalation in the prevalence of cutaneous dermatophytosis.[8] The current study concurs with the evidence of increasing prevalence of fungal infections across Indian states. Large fungal lesions often fail to clear with use of topical therapy, and require additional systemic therapy as well.[8] Clinical reports suggest that use of itraconazole 100 mg for 15 days, or 200 mg for 7 days is

more beneficial in tinea infections.[8,9] Topical therapy is found to be less effective than oral antifungals for the treatment of tinea pedis, and has to be supplemented with oral therapy for 4-8 weeks.[8] The present study is in agreement with the currently existing scientific literature that supports itraconazole as the most preferred oral antifungal therapy used for management of patients with tinea infections.

The clinical failure of antifungal drugs having low minimum inhibitory concentrations (MICs), points to quality issues with drug manufacturing, impacting the bioavailability and treatment outcomes. The process of pelletization has multiple components aiming to achieve maximum dissolution of the drug.[4] Another study highlighted the importance of processing factors involved in the pelletization process, which played an important role in dissolution and bioavailability of itraconazole.[4] The particulars involved in pelletization technology determine the gastrointestinal absorption and in-vivo bioavailability, and ultimately the skin levels and efficacy of itraconazole in dermatophytoses. In addition to these, clinical studies also demonstrated that the surface area of pellets improves the limited dissolution of poorly water-soluble drugs.[4,10] Also, in the present study, most of the doctors were of the opinion that the MPSD technology has helped in improving the efficacy of the novel itraconazole formulation.

CONCLUSION

Recalcitrant fungal infections are on the rise in Indian states. Several factors contribute to recalcitrance: such as organism type, host-immune response, skin barrier and therapeutic aspects revolving around drug delivery to the skin. Thus, the present study assessed the real-world clinical practice data and established the efficacy of novel itraconazole formulation used widely in the management of fungal infections. The survey findings indicated that the novel itraconazole formulation is a preferred oral antifungal therapy for the management of tinea infections.

ACKNOWLEDGEMENTS

We would like to thank Scientimed Solutions Pvt. Ltd. for assisting in the development of this manuscript.

Funding: The study was funded by Abbott Healthcare Pvt. Ltd
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Havlickova B, Czaika VA, Friedrich M. Epidemiological trends in skin mycoses worldwide. Mycoses. 2008;51:2-15.
2. Rajagopalan M, Inamadar A, Mittal A, Miskeen AK, Srinivas CR, Sardana K, et al. Expert consensus on the management of dermatophytosis in India (ECTODERM India). BMC Dermatol. 2018;18(1):6.
3. Korting HC, Schöllmann C. The significance of itraconazole for treatment of fungal infections of skin, nails and mucous membranes. J Dtsch Dermatol Ges. 2009;7(1):11-9.
4. Sardana K, Khurana A, Gupta A. Parameters that determine dissolution and efficacy of itraconazole and its relevance to recalcitrant dermatophytoses. Expert Rev Clin Pharmacol. 2019;12(5):443-52.
5. Verma R, Hodge S, Gargote C, Modi P, Upreti N, Yadav L, et al. Assessment of physical and dissolution characteristics of various itraconazole capsule formulations: a comparative analysis. Int J Res. 2019;5(4):765.
6. Al-Tabakha MM. HPMC capsules: current status and future prospects. J Pharm Sci. 2010;13(3):428-42.
7. Jain BV, Usman MR, Pawar SR, Patil NR, Patil PJ, Sharma SN. A vegetarian capsule: A review. Int J. 2012;2(2):10-2.
8. Sahoo AK, Mahajan R. Management of tinea corporis, tinea cruris, and tinea pedis: A comprehensive review. Indian Dermatol Online J. 2016;7(2):77-86.
9. Verma S, Madhu R. The great Indian epidemic of superficial dermatophytosis: an appraisal. Indian J Dermatol. 2017;62(3):227.
10. Zhang K, Yu H, Luo Q, Yang S, Lin X, Zhang Y, et al. Increased dissolution and oral absorption of itraconazole/Soluplus extrudate compared with itraconazole nanosuspension. Eur J Pharm Biopharm. 2013;85:1285-92.

Cite this article as: Haldar S. Management of dermatophytosis with a novel itraconazole formulation: a research survey. Int J Res Dermatol 2021;7:33-7.

ANNEXURE

No.	Questionnaire on novel itraconazole I-Tyza 100 (itraconazole 100 mg) formulation in tinea infections
Q1	In your clinical practice; per week, out of total patients what percentage of patients come with tinea?
	a (<15%) b (15% to 30%) c (30% to 60%) d (Above 60%)
Q2	What is the most common age group of patients suffering from tinea infections in your clinical practice?
	a (12-20 years) b (20-30 years) c (30-40 years) d (50 years and above)
Q3	In your clinical practice tinea is common among which gender?
	a (Male) b (Female) c (Not gender specific)
Q4	In your clinical practice, among which socio-economic category is tinea common?
	a (High) b (Middle) c (Low) d (Not based on socio-economic category)
Q5	Which topical antifungal do you prefer in management of tinea infections? Kindly rank in the order of preference?
	a (Luliconazole) b (Amorolfine) c (Terbinafine) d (Sertaconazole) e (Eberconazole) g (If any other: kindly specify molecule)
Q6	Which oral antifungal molecule do you prefer in management of tinea infections? Kindly rank in the order of preference
	a (Itraconazole) b (Terbinafine) c (Griseofulvin) d (Fluconazole) e (If any other: kindly specify molecule)
Q7	To what percentage of patients with tinea infections in your daily practice, do you prefer giving combination of systemic plus topical treatment for synergistic effect?
	a (< 40%) b (40-70%) c (70-90%) d (Almost all)
Q8	What are the co- prescriptions along with topical plus systemic antifungals?
	a (Antihistamine) b (Antibacterial) c (Dusting Powder) d (Antifungal Soap) e (Emollient/ Moisturizer) f (any other: please specify)
Q9	Do you prefer Antifungal soap in management of tinea infection?
	a (Yes) b (No) c (Not sure)
Q10	Would you like to prefer selenium disulfide as soap (with syndet base and moisturizing properties) for management of tinea infection?
	a (Yes) b (No) c (Not sure)
Q11	In your clinical practice, how long do you use itraconazole for the management of tinea infection?
	Itraconazole 100 mg a) 15 days b) 21 days to 1 month c) 2 months d) 3 months e) 6 months f) If anything else, please specify in months_____ Itraconazole (100 mg×2) a) 7 days b) 21 days to 1 month
Q12	Do you feel itraconazole pellet manufacturing technology plays an important role in the clinical outcome?
	a (Agree) b (Disagree) c (Not sure)
Q13	In your opinion, did the multi-particulate in solid dispersion (MPSD) technology help in improving the efficacy of novel itraconazole formulation?
	a (Agree) b (Disagree) c (Not sure)
Q14	Do you agree that comparable biorelevant dissolution profile of novel itraconazole formulation to innovator helped in achieving equivalent results in clinical practice?
	a (Agree) b (Disagree) c (Not sure)
Q15	Do you agree formulation with desired efficacy and affordable price will help in improving compliance to treatment in tinea infections?
	a (Agree) b (Disagree) c (Not sure)
Q16	In your clinical experience how will you rate clinical experience with novel itraconazole formulation for treating tinea?
	a (Excellent) b (Good) c (Average) d (Poor)
Q17	Would vegetarian nature of the capsules with novel itraconazole formulation play a role in patient's acceptance to therapy?
	a (Agree) b (Disagree) c (Will not make such difference)