

Indian Association of Dermatologists, Venereologists and Leprologists (IADVL) Task Force against Recalcitrant Tinea (ITART) Consensus on the Management of Glabrous Tinea (INTACT)

Abstract

Background and Aims: Dermatophytosis has always been a common superficial mycosis in India. However, the past 6-7 years have seen an unprecedented increase in the number of patients affected by recurrent, chronic, recalcitrant and steroid modified dermatophytosis involving the glabrous skin (tinea corporis, tinea cruris and tinea faciei). Importantly, there has been a notable decrease in clinical responsiveness to commonly used antifungals given in conventional doses and durations resulting in difficult-to-treat infections. Considering that scientific data on the management of the current epidemic of dermatophytosis in India are inadequate, the Indian Association of Dermatologists, Venereologists and Leprologists (IADVL) Task force Against Recalcitrant Tinea (ITART) has formulated a consensus statement on the management of dermatophytosis in India. **Methods:** Seventeen dermatologists with a focussed interest in dermatophytosis participated in a Delphi consensus method, conducted in three rounds. They responded as either “agree” or “disagree” to 132 statements prepared by the lead experts and gave their comments. Consensus was defined as an agreement of 80% or higher concurrence. Statements on which there was no consensus were modified based on the comments and were then recirculated. The results were finally analysed in a face-to-face meeting and the responses were further evaluated. A draft of the consensus was circulated among the participants and modified based on their inputs. **Results:** Consensus was achieved on 90 of the 132 statements. Direct microscopy using potassium hydroxide mount was recommended in case of diagnostic difficulty on clinical examination. Counselling of patients about strict adherence to general measures and compliance to treatment was strongly recommended as the key to successful management of dermatophytosis. A combination of systemic and topical antifungal drugs was recommended for the treatment of glabrous tinea in the current scenario. Topical corticosteroid use, whether used alone or in combination with other components, was strongly discouraged by all the experts. It was suggested that topical antifungals may be continued for 2 weeks beyond clinical resolution. Itraconazole and terbinafine were recommended to be used as the first line options in systemic therapy, whereas griseofulvin and fluconazole are alternatives. Terbinafine was agreed to be used as a first line systemic agent in treatment naïve and terbinafine naïve patients with glabrous tinea. Regular follow-up of patients to ensure compliance and monitoring of clinical response was recommended by the experts, both during treatment and for at least 4 weeks after apparent clinical cure. Longer duration of treatment was recommended for patients with chronic, recurrent and steroid modified dermatophytosis. **Conclusion:** Consensus in the management of dermatophytosis is necessary in the face of conventional regimens proving ineffective and dearth of clinical trials re-evaluating the role of available antifungals in the wake of evolving epidemiology of the infection in the country. It needs to be backed by more research to provide the required level of evidence. It is hoped that this consensus statement improves the quality of care for patients with dermatophytosis, which has emerged as a huge public health problem, imposing considerable financial burden on the country.

Keywords: Dermatophytosis, glabrous tinea, INTACT, recalcitrant, recommendations, resistance, task force

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Introduction

Dermatophytosis is the most common superficial mycosis worldwide. In India, it has been a common infection that was easily amenable to treatment with topical and systemic antifungals. However, the past few years have seen a tremendous increase in the number of patients with recalcitrant dermatophytosis across the country. There has been apparently more number of new cases as well as frequent recurrences in those earlier affected. The problem has been worsened and perhaps even been caused by the widespread use of creams containing a combination of antifungals, super potent corticosteroids and antibiotics,

either by self-medication or due to prescription by misinformed persons.^[1-5]

The current scenario of dermatophytosis in India is characterised by many atypical epidemiological, clinical and mycological manifestations compared to yesteryears [Table 1].^[1-9] Chronic, recurrent and partially responding infections are increasingly seen. A changing pattern of the dermatophyte isolates has been observed, with *Trichophyton mentagrophytes* complex emerging as the major pathogen.^[3,9] A unique clad distinct from *T. mentagrophytes/T. interdigitale* complex with multidrug resistance has recently been identified.^[10]

Table 1: Salient clinico-epidemiological features in the current scenario of dermatophytosis in India^[1-9]

Parameters	Probable reasons
Epidemiological	
Greater occurrence of dermatophytosis	Highly contagious infection, poor public awareness and inadequate access to healthcare facilities, inadequate/faulty treatments, rampant abuse of topical corticosteroid antifungal combination creams
Increasing frequency of chronic dermatophytosis	Abnormal host cell-mediated immune (CMI) response, inadequate/faulty treatments, fungal species related factors, fomites, rampant abuse of topical corticosteroid antifungal combination creams
Increasing frequency of recurrent dermatophytosis	Inadequate/faulty treatments, fungal species related factors, fomites, lifestyle related host factors
Higher incidence of infection among family members	Highly contagious infection, poor hygiene, sharing of fomites, sharing of prescriptions
Higher incidence among infants and children	Highly contagious infection, poor hygiene, high fomite transmission, inadequate and faulty treatment, topical corticosteroid abuse in the affected family members.
Changing fungal species - emergence of <i>T. mentagrophytes/T. interdigitale</i> complex as the predominant or codominant pathogen	Environment-related factors, host immunity related factors, topical high-potency corticosteroid-antibacterial-antifungal combination cream abuse, altered cutaneous flora, virulence of the fungal species
Clinical	
Extensive dermatophytosis	Topical corticosteroid usage, inadequate/faulty treatments, host immunity
Frequent involvement of uncommon sites like face and scalp	Autoinoculation from another site, fomite transmission, topical corticosteroid use on the face, misdiagnosis and faulty treatments
Inflammatory lesions, bullous/pustular lesions	Abnormal host response, fungal virulence, intermittent topical corticosteroid usage
Steroid modified tinea/tinea incognito, Tinea pseudoimbricata, Majocchi granuloma	Topical high potency corticosteroid usage-self-treatment, easy over the counter availability of topical poly-combinations, treatment by unqualified healthcare personnel, lack of awareness and inadequate knowledge of treating physicians
Atypical presentations (resembling psoriasis, eczema, impetigo, lupus, rosacea etc.)	Host immunity related factors, agent-related factors, misdiagnosis, corticosteroid application, trauma, secondary infection
Inadequate/no response to topical/systemic antifungals	Changing fungal species, poor host immunity, poor compliance, poor quality of drugs, antifungal resistance

In 2017, the Indian Association of Dermatologists, Venereologists and Leprologists (IADVL), the largest organization of dermatologists in India, constituted a task force (IADVL Task Force against Recalcitrant Tinea [ITART]) to combat this public health menace. One of ITART's activities has been the formation of a group of experts to formulate guidelines for the management of dermatophytosis in India since the standard treatment regimens are not particularly effective.^[11] It is well known that guidelines should be backed by good quality research, but there are only a few high quality epidemiological, clinical, mycological and therapeutic studies of the current epidemic of dermatophytosis in India. It was thus decided to evolve a consensus statement based on the available literature and the expertise of the panel. This statement would require periodic evaluation and updating until evidence-based guidelines can be formulated.

Methods

Design

Consensus methods are increasingly being used to solve problems in medicine. While some recommendations are likely to be outdated as new knowledge accumulates, they may help our understanding of past knowledge and identify the research gaps. Of the several methods of consensus development, the Delphi technique is one of the most popular ones in health sciences.^[12-16] It entails the development of a consensus by an expert group on a specific subject through repeated anonymous questionnaire rounds. The experts are provided with an opportunity to reflect on the results of the previous questionnaire round. The process is completed once the defined level of consensus is reached or when the experts do not agree to alter their point of view any more.

To resolve the problem of recalcitrant dermatophytoses in India, we followed the modified Delphi technique and named the consensus statement as the INdian Association of Dermatologists, Venereologists and Leprologists TAsk Force against Recalcitrant Tinea (ITART) Consensus for the management of glabrous Tinea infections (INTACT) statement.

Experts

Seventeen dermatologists comprising of members from ITART and IADVL Academy (the committee supervising the IADVL's academic activities) and others with a special interest in dermatophytosis, were selected. Most of them have research interest and publications on dermatophytosis or mycology. There was a reasonable representation from different parts of India. The chairperson and the convener of ITART were the lead experts. All members were briefed about the objectives, methods and the importance of maintaining anonymity. Their services were also utilised to draft the consensus statements.

Literature review

A detailed literature search was carried out on the epidemiology, host factors, diagnosis, etiological agents, treatment, special situations and prevention of dermatophytosis. Special emphasis was laid on published Indian literature.

Rounds

Two rounds of questions were circulated, with anonymity maintained, followed by one round of discussion. One of the lead experts circulated 132 statements and obtained the responses of experts by emails. Statements were divided into 5 parts: general statements (definitions); laboratory diagnosis; general measures in management; topical and systemic therapy and treatment in special situations such as in children, pregnancy, lactation, old age, organ dysfunctions and steroid-modified dermatophytosis [Table 2]. Eighty percent or higher agreement was considered to constitute a consensus. The experts were asked to vote by marking "agree" or "disagree" and add comments, if necessary.^[16,17]

Round 1

A document containing the list of statements was mailed to all members and their responses evaluated and recorded for consensus. Statements for which there was less than 80% agreement were modified based on the comments of the members.

Round 2

The modified statements were circulated again for voting and comments. Responses received were further evaluated. Statements for which there was less than 80% agreement were further modified based on the comments received and again circulated among the members.

Round 3

A meeting was organised to discuss and finalize the statements. It was chaired by the chairperson of ITART

Table 2: Classification of statements used for Delphi process and the detail of consensus by experts after three rounds of discussion

Category of statements	80% agreement (minimum 14 out of 17 experts agreeing with the statement)	
	Yes	No
General (n=9)	7	2
Laboratory Diagnosis (n=18)	13	5
General management (n=19)	16	3
Topical therapy (n=20)	13	7
Systemic therapy (n=47)	27	20
Special situations (n=19)	14	5
Total (n=132)	90	42

and conducted by its convener to validate the results. Those statements, wherein consensus could not be reached, were further discussed, and the relevant comments were recorded.

Using these consensus statements and appropriate review of the literature, a final draft of the consensus statement was prepared and circulated among all the members for final approval.

Results

At the end of 3 rounds, 80% or more of the experts agreed on 90 statements [Table 2] based on the evidence and their experience. The IADVL National Task Force against Recalcitrant Tinea (ITART) Consensus For Management of Glabrous Tinea Infections (INTACT) has been drafted based on these statements and the comments of members. Statements in which consensus could not be reached are also mentioned alongside. In general statements, we have defined some terms commonly related to dermatophytosis and also terms lacking any standard definition.

Definitions

1. **Glabrous tinea:** Dermatophytosis involving the skin of any site, except terminal hair-bearing areas of the scalp and face (tinea capitis/tinea barbae), palms (tinea manuum), soles (tinea pedis) and nails (tinea unguium); notwithstanding the true meaning of glabrous as “without hair”. It constitutes tinea corporis, tinea cruris and tinea faciei, and may also include involvement of hair bearing regions without invasion of hair by fungi.
2. **Chronic dermatophytosis:** Presence of glabrous tinea for a duration of six months or longer, continuous or recurrent, with or without treatment. Duration was earlier considered to be more than one year^[1,18]
3. **Recurrent dermatophytosis:** Reoccurrence of the glabrous tinea after 4 weeks of stopping treatment following clinical cure^[19]
4. **Resistant dermatophytosis:** Failure to eliminate dermatophytosis despite administration of one or more antifungal agents for an adequate dose and duration, based on clinical judgement due to proven mycological resistance to the drugs^[20,21]
5. **Naïve case:** A patient with glabrous tinea who has not received any prior treatment
6. **Recalcitrant dermatophytosis:** Persistent glabrous tinea, generally in settings like chronic, recurrent, corticosteroid-modified and resistant cases, with poor or no response to standard treatment^[19,22]
7. **Corticosteroid modified tinea:** Glabrous tinea whose morphology is altered due to topical or systemic corticosteroids, but is still recognisable or diagnosable^[3]
8. **Tinea incognito:** Glabrous tinea in which the morphology is markedly altered due to the

suppression of inflammation by corticosteroids or other immunosuppressants such that it is not easily recognisable as tinea^[3,22-24]

9. **Over-the-counter (OTC) medications:** Medications purchased from a pharmacy without prescription by a qualified healthcare professional
10. **Clinical cure:** Complete resolution of symptoms and signs with or without post-inflammatory changes at the end of treatment
11. **Mycological cure:** Complete subsidence of symptoms and signs with negative mycological reports (direct microscopy and/or culture) at the end of the treatment.

Laboratory diagnosis

Diagnosis of dermatophytosis has lately become more challenging, with atypical morphological variants being more commonly seen, of which many are attributable to topical corticosteroid abuse. When clinical diagnosis is difficult, experts recommended direct microscopic examination as an office procedure with potassium hydroxide (KOH) mount, a test with high sensitivity, to confirm dermatophytosis. The specimen should be obtained by scraping the lesion's active margin when present or from its scaly region and transported in a sterile, thick dry black sheet of paper to the laboratory, if the facility is not available in the outpatient clinic. Dermatophytes are visualised as hyaline, long, branching, septate hyphae with/without arthrospores. But direct microscopy does not help to identify the species. If feasible, the organism can be isolated by culture in modified Sabouraud's dextrose agar with antibiotics and cycloheximide, to understand the epidemiological trends in a region and for possible therapeutic implications. Macroscopic appearance of culture colony and microscopic morphology help in the identification of the various species. Laboratory diagnosis may be considered when feasible. However, there was no consensus on mycological confirmation being mandatory in patients in whom, a standard treatment has failed. There was neither consensus on the necessity of histopathology with periodic acid-Schiff (PAS) stain for the confirmation of dermatophytosis nor with regard to the species identification as a requirement for the initiation of treatment.

Antifungal susceptibility testing (AFST) studies to know the local drug susceptibility patterns and molecular diagnostic techniques required for the accurate identification of the dermatophyte species may be considered in research institutes or if reference laboratories are available. However, there was no consensus on the utility of real time polymerase chain reaction (RT-PCR) and matrix assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS) in the current scenario, since these are relatively new and the clinical implications are not known. The role of laboratory methods in the diagnosis is summarised in Table 3.^[25,26]

Table 3: Role of various laboratory methods in the diagnosis of dermatophytosis

Principle	Method	Comments
Direct microscopic examination	Direct microscopy using potassium hydroxide mount and its modifications	An office procedure with relatively high sensitivity Should be done whenever feasible, especially if there is diagnostic difficulty on clinical examination
Histopathology	Histopathology with special stain with periodic acid Schiff (PAS) stain	Indicated in suspected Majocchi granuloma or deep dermatophytosis
Isolation by culture and species identification	Fungal culture on Sabouraud's dextrose agar and other selective media, biochemical tests and hair perforation test	Sensitivity is low, but specificity is high; considered as the gold standard in the diagnosis May be performed whenever feasible for confirmation of clinical diagnosis and to understand the epidemiological trends in a region
Identification of species and subspecies by molecular diagnostic methods	Sequencing of the internal transcribed spacer (ITS) region of the ribosomal DNA, Random Amplified Polymorphic DNA (RAPD), Amplified Fragment Length Polymorphism (AFLP), mitochondrial DNA (mt DNA) restriction analysis, Sequencing of protein-encoding genes, polymerase chain reaction (PCR) fingerprinting ^[36,41]	Requires specially equipped laboratory with trained manpower Currently utilised for research purposes but may find a place in conventional diagnosis in future
Identification of species and subspecies by proteomic signature	Matrix-assisted laser desorption/ionization time of flight (MALDI-TOF) mass spectrometry	Requires specially equipped laboratory with trained manpower Currently used for research purposes but may find a place in conventional diagnosis in future
Antifungal sensitivity testing (AFST)	Microbroth dilution method	Tedious procedure requiring trained manpower Lack of reference data on minimum inhibitory concentration (MIC) of antifungal drugs used against dermatophytes ^[25,26] If facilities are available, it should be considered whenever there is a strong suspicion of antifungal resistance
Identification of mutation causing antifungal resistance	Real Time Polymerase chain reaction (RT PCR), Sequencing of DNA	Requires equipped laboratory with trained manpower; currently utilised for research purpose Whenever there is strong suspicion of antifungal resistance it may be considered

Management

General measures

Maintenance of personal hygiene is very important to avoid acquiring dermatophytosis and in preventing its spread and persistence. People living in hot and humid conditions are at greater risk of developing the infection. After every bath, the entire body surface, especially the body folds and toe clefts, should be wiped well. Washing of clothes and bed linen in hot water at 60°C and drying them in sunlight inside out may help prevent persistence of infection.^[27-30] Since direct contact and fomites play a significant role in the spread of infection, patients should not share their soaps, clothes, towels and bed linen.^[31] Furthermore, it is also important that the clothes of infected patients be stored and washed separately in order to prevent spread of infection.^[32] Regular mopping and cleaning of the house would also help to reduce the persistence of dermatophytes in the environment.^[33]

Use of synthetic and tight clothing should be avoided. Wearing bands, threads, drawstrings and rings should be discouraged as they may carry fungal elements and contribute to persistence and recurrence of infection. Comorbidities may predispose to recalcitrant or recurrent

infection. Weight loss in obese patients would help prevent recurrence of infection especially in the intertriginous area. Corticosteroids in all forms should be avoided as it results in unusual presentations, diagnostic difficulty and treatment failures. Patients should be advised not to self-medicate or share their prescriptions. Simultaneous treatment of other infected household members and close contacts is necessary.

Counselling points for patients with glabrous tinea infections are summarised in Table 4.

Experts were not in consensus with regard to pets being the source of infection in the current scenario. They did not concur on the role of bathing habits and use of emollients in the management of dermatophytosis.

To conclude, experts agreed that patients should be educated about personal hygiene, clothing, skin care, corticosteroid abuse, adherence to general measures and compliance to treatment to ensure successful outcome.

Topical therapy

The type of topical formulation could be chosen according to the site involved. Lotion and spray formulations were

Table 4: Consensus on points for counselling patients with dermatophytosis

Points for discussion with patients	Expected impact
Current scenario of dermatophytosis in India	Patients will understand the gravity of the situation and follow medical advice accurately
Taking regular bath (at least once a day)	Reduces fungal load due to exfoliation of scales
Wiping the body dry (especially intertriginous area and toe clefts)	Prevents high moisture in those parts, minimizing chances of fungal colonization
Regular washing of clothes in hot water and drying in sunlight inside out	Reduces chances of re-infection from infected clothes
Storing and washing clothes of infected patients separately	Reduces chances of transmission to contacts and family members
Regular washing of bed linen (at least once a week)	Minimizes chances of re-infection from infected linen
Avoidance of sharing of fomites like clothes, towels and soaps with others	Reduces transmission to contacts and family members
Avoidance of synthetic tight garments	Prevents occlusion, maceration, friction and barrier dysfunction
Avoidance of wearing bands, threads, draw strings and rings	Reduces chances of re-infection from such infected materials
Regular mopping and cleaning of the house	Reduces chances of persistence of dermatophytes in the environment
Losing weight in obese patients	Reduces chances of intertriginous fungal infections
Avoidance of contact with pets	May reduce zoophilic infection and transmission
Avoidance of application of topical corticosteroids	Reduces chances of unusual presentations, diagnostic difficulty and treatment failure
Strict adherence to treatment	Enhances chances of complete cure and reduces recurrence
Simultaneous treatment of other infected house members and close contacts (prophylactic treatment is not required)	Reduces chances of transmission to each other and recurrence
Avoidance of self-medication, over the counter(OTC) medications and sharing of prescriptions	Reduces chances of inadequate treatment, topical corticosteroid misuse and treatment failure

not considered more effective than creams, although they may be more convenient when larger areas are involved. However, a potential for irritation and high cost are the disadvantages of these products. A combination of systemic and topical antifungal drugs is essential in the treatment of glabrous tinea, with the extent of disease being a limiting factor for topicals. There was no consensus regarding the superiority of one topical antifungal over another and whether they should be from the same or different group as the oral antifungal prescribed. As dermatophytes grow radially, the topical antifungal should be applied inward, from beyond the margin of the lesion.^[34-36] Application may be continued twice daily until 2 weeks after achieving clinical resolution of lesions.^[3,34,35] There was no consensus on the routine use of combination of two topical antifungals.

There is no role for corticosteroids alone or in combination with antifungals in the management of dermatophytosis of the glabrous skin including inflammatory tinea.^[3] Topical azole antifungals, which have anti-inflammatory property, could be used in patients with inflammatory and corticosteroid modified tinea. There was no consensus on gradual withdrawal of topical steroid in corticosteroid modified tinea. Topical keratolytics like Whitfield's ointment have a role to play if the involved skin is not inflamed. Use of antifungal soaps was strongly discouraged, while there was difference of opinion regarding the usage of antifungal powders. The suggestion on limited application of the topical antifungals to high impact sites only, in patients with extensive dermatophytosis on concomitant

systemic antifungals, did not achieve consensus. Consensus statements for the use of topical antifungals in the treatment of dermatophytosis of the glabrous skin are discussed in Table 5.

Systemic therapy

Patients on systemic antifungals should be regularly followed to ensure adherence to treatment and to monitor the therapeutic response. The first follow up visit should be at the end of 3 weeks to assess the clinical response. If there is partial response (i.e. persistent pruritus and incomplete/minimal resolution of lesions), therapy should be continued while reassessing for contributing factors. If there is no response, change of the antifungal drug should be considered. Regular follow up should be continued both during treatment and at least up to 4 weeks after apparent clinical cure.

Panellists agreed that patients with chronic/recalcitrant dermatophytosis and corticosteroid modified tinea need to be treated for a period longer than that is conventionally recommended.^[37-39] The duration of treatment may be individualised based on clinical response. The end point of treatment for glabrous tinea should be the achievement of clinical cure.^[22]

Terbinafine may be used as first line therapy in treatment-naïve and terbinafine-naïve patients with glabrous tinea. If there is an inadequate response at the end of 3 weeks of terbinafine 250 mg once a day, increasing the dose to 250 mg twice daily may be considered in adult patients, albeit with monitoring of liver function.^[40]

Table 5: Consensus points on topical therapy in patients with glabrous tinea infections

Consensus point	Justification/comments
Topical therapy can be used as a standalone or an adjuvant therapy	Topical therapy attains high antifungal concentration at the site of infection
Antifungal preparation alone without any corticosteroid or antibacterial component should be used	Corticosteroid application can result in treatment failure and local adverse effects
Topical corticosteroid containing antifungal preparation should be avoided even for an inflammatory lesion	Topical antifungals with anti-inflammatory effect can be used
Keratolytics and Whitfield's ointment can be used in the treatment of glabrous tinea	Should be avoided if there is local inflammation
Antifungal (with few exceptions) should be applied twice a day	Twice a day application is required to achieve good clinical response
Treatment may be continued for about 2 weeks after clinical resolution	Clinical cure may not correspond with mycological cure
Topical formulation could be chosen according to the site involved	There are advantages of certain preparations; Eg. lotions in hair-bearing area
There is no added advantage in the efficacy of various formulations like lotions and sprays over the creams	Most of these preparations have advantage of being user friendly but not of added efficacy
Various classes of topical antifungals currently available are nearly equipotent	Few studies on head-to-head comparison of topical antifungals are published, but still the evidence is not sufficient to consider one molecule is superior to the other
No role for use of combination of two topical antifungals	No studies to substantiate benefits of such a combination approach and it is not practiced routinely

Itraconazole may be used as a first line option or when there is no response to terbinafine. It should be consumed immediately after food, and may be with an aerated beverage to ensure good absorption. A dose of 200 mg daily given either as two capsules of 100 mg once daily or one capsule of 100 mg twice daily in adults, is generally effective. The experts agreed on not using the unapproved higher dose formulations of itraconazole.

Experts agreed that griseofulvin and fluconazole need to be taken for a longer duration than itraconazole or terbinafine.^[6]

There was no consensus for statements such as use of systemic antifungals in all cases of tinea faciei, initiation of terbinafine in 250 BD dosage, use of fluconazole and griseofulvin as first line therapy or of ketoconazole as a reserve drug. There was also no consensus on up dosing of itraconazole and standard fixed duration of therapy for glabrous tinea infection.

Recommendations for systemic therapy of glabrous tinea infection are given in Table 6^[41-43] and are summarised in Table 7. These recommendations are based not entirely on evidence but on consensus for the current scenario of recalcitrant dermatophytosis.

Special scenarios

It is known that the presence of comorbidities may predispose an individual to recalcitrant or recurrent infections. Treatment of dermatophytosis in pregnancy, lactating women, infants, children and geriatric patients has certain limitations.

Pregnancy and lactation: Topical antifungals are the mainstay of treatment for dermatophytosis in pregnancy.

Though terbinafine is a category B drug and considered safe, experts opined that scarce human data available during the time of formulation of guidelines, precludes its routine use in pregnancy.^[44] All topical antifungals are safe during lactation, as excretion in breast milk is negligible.

Infants and children: Localised infection may be treated with topical antifungals alone. However, recurrent, chronic or corticosteroid modified tinea, which is being increasingly observed in children, warrants the use of systemic antifungals. Fluconazole is considered a safe option for children under 2 years while above 2 years of age, griseofulvin, terbinafine and itraconazole can also be given.^[45,46]

Elderly persons and in those with systemic disorders: Before initiating systemic treatment in elderly patients, particularly those with comorbidities, changes in pharmacokinetics and drug interactions should be considered. Patients with hepatic or renal dysfunction on systemic antifungals should undergo appropriate laboratory monitoring. Fluconazole is recommended as a relatively safe option in patients with hepatic dysfunction, albeit with strict monitoring of liver function. Itraconazole is a comparatively safer option in patients with renal dysfunction. In patients with cardiac illness, terbinafine is preferred while itraconazole is better avoided.^[46]

Discussion

Laboratory diagnosis

While dermatophytosis can usually be diagnosed clinically, in the recent years atypical presentations, often simulating other dermatoses are becoming increasingly common, at times leading to difficulty in diagnosis.^[5,47,48] When the

Table 6: Recommendation of Systemic treatment of glabrous tinea (tinea corporis, tinea cruris and tinea faciei)

Antifungal	Dose		Minimum duration	Precautions
	Children	Adults		
Itraconazole	3-5mg/kg/day	Naïve: 100 mg 1 or 2 capsules od	3 weeks	Drug interactions, hepatotoxicity
		CH/SMT/RCL: 100mg bd/ 100 mg 2 od	4 weeks	
Terbinafine	10-20 kg - 62.5 mg	Naïve:		Skin rash, hepatotoxicity
	20-40 kg- 125 mg	250mg/day	4 weeks	
	> 40 kg - 250 mg	CH/SMT/RCL: 250 mg bd / day	4 weeks	
Griseofulvin	10-20 mg/kg/day	Naïve: 500 mg/day	8 weeks	GI intolerance, head ache
		CH/SMT/RCL: 750 -1000 mg/ day	8 weeks	
Fluconazole	3-6 mg/kg/day	Naïve: 50-100 mg/day	4 weeks	Hepatotoxicity
		150-300 once weekly	8 weeks	
		CH/SMT/RCL: 100 mg/day	6 weeks	
		150 mg /thrice weekly*	8 weeks	

Note: Some of the dose schedules in children have been extrapolated from their uses in conditions like tinea capitis. Paediatric dose should not exceed the adult dose. References hold good for some of the drug dosages and not the duration. Duration of therapy is best individualised based on the clinical response. *Dosage in current practice and not evidence based. CH- Chronic ; SMT - Steroid modified tinea ; RCL -Recalcitrant

diagnosis is doubtful or the therapeutic response needs to be assessed, a 10-20% KOH wet mount is advocated as a simple and sensitive test whenever feasible.^[49] Certain modifications of the technique and counterstaining may improve the diagnostic accuracy.^[50]

Identification of the dermatophyte species by culture may be attempted when possible. This would help understand the epidemiological trends in the region and may have therapeutic implications too. Skin scrapings collected after wiping with alcohol swabs must be transported in a sterile, thick dry black sheet of paper and inoculated in modified Sabouraud's dextrose agar media with antibiotics and cycloheximide. The macroscopic appearance of the colony in culture and morphological features of the microconidia, macroconidia and other vegetative structures can help to identify the species.^[31] AFSTs help understand the local drug susceptibility patterns but are possible only in research institutes and reference laboratories.^[25,26,51] There is a dearth of clinically correlated mycological data which impacts the clinical utility of AFST. Histological diagnosis of dermatophytosis is not done routinely but can be useful in diagnosis of unusual clinical presentations like Majocchi granuloma and deep dermatophytosis. Staining with periodic acid Schiff (PAS) stain can ease identification of hyphae in tissue.^[52]

Molecular diagnostic techniques can accurately identify the dermatophyte species. RT-PCR is a rapid method that enables detection of dermatophytes from clinical specimens.^[53,54] Research laboratories usually rely on sequencing of the internal transcribed spacer (ITS) region of the rDNA for sub-speciation and classification of dermatophytes.^[55] Accurate subspecies identification helps understand the clinical and epidemiological implications of the genetic heterogeneity of dermatophytes.^[56]

Matrix-assisted laser desorption/ionization time of flight (MALDI-TOF) mass spectrometry is a relatively new technique that is increasingly being used to rapidly identify various microorganisms.^[57,58] It has the potential for rapid and accurate identification of different strains of dermatophytes. Molecular biological techniques have also been used to identify the genes responsible for antifungal resistance.^[59,60] There is relative lack of clinically correlated mycological data, which are essential to formulate evidence-based treatment guidelines.

General measures

Global warming has affected the climate in India in the form of increased maximum temperatures, heat waves and less rainfall. Indian Meteorological department data have shown an increase of 0.6°C in the average temperatures between 1901-10 and 2009-18. The number of days with maximum temperature exceeding 35°C in various cities in India has

Table 7: Consensus recommendation for the various facets of treatment of glabrous tinea

	Comments	Recommendation
Indications		
Glabrous tinea	Most cases in the current scenario require systemic therapy	Involvement of multiple sites Extensive disease based on clinical judgement Chronic dermatophytosis Recurrent dermatophytosis Steroid modified dermatophytosis/ Tinea incognito Failure of topical therapy Associated nail and hair involvement Immunocompromised states like hematological malignancies and therapy with immunosuppressive drugs
Choice of systemic drug		
First line	Best option considering overall efficacy and safety	Itraconazole, Terbinafine,
Alternate drugs	Prolonged duration of treatment required	Griseofulvin, Fluconazole
Complementary topical therapy		
Choice and rationale	Topical antifungal without corticosteroid and antibacterial components. There are limited laboratory/clinical studies on the efficacy and utility of combination antifungals (systemic with topical OR two systemic) for dermatophytosis of the glabrous skin	Systemic antifungal therapy should preferably be combined with topical antifungal therapy which may be of same or different class
Response		
Failure	No improvement or worsening of symptoms and signs at 3 weeks	Assessment of factors responsible for it and if detected to be corrected; if not, antifungal therapy to be changed
Total response	Complete subsidence of symptoms and signs with or without post-inflammatory changes anytime during the treatment	Completion of therapy for the stipulated period or as per the individual response
Partial Response	Partial subsidence of symptoms and signs at the end of 3 weeks	Extended duration of treatment to be considered with appropriate laboratory monitoring; double dosing of terbinafine may be considered
Cure		
Clinical cure	Complete subsidence of symptoms and signs with or without post-inflammatory changes at the end of treatment	Follow up must be at 4 weeks after apparent clinical cure to look for recurrence
Mycological cure	Complete subsidence of symptoms and signs with negative mycology reports (direct microscopy with/ without culture) at the end of the treatment	Follow up must be at 4 weeks after apparent clinical cure to look for recurrence
Laboratory monitoring		
Hepatotoxicity	All systemic antifungals are hepatotoxic	Monitoring hepatic function if the treatment is extended or if the dose is doubled
Renal toxicity	Systemic drugs used in the management of dermatophytosis do not commonly cause renal toxicity	Renal monitoring may be considered if indicated on clinical grounds
Follow up		
First follow up visit	To assess clinical response	At 3 weeks, if inadequate response
Final follow up visit	To assess recurrence	At 4 weeks after apparent clinical cure
Special situations		
Pregnancy	Teratogenicity of the drugs should be addressed	Topical antifungals with established safety [Table 8] Oral terbinafine (routine use should be avoided)
Lactating mother	Safety of the infant should be addressed	Topical antifungals Oral fluconazole

Contd...

Table 7: Contd...

	Comments	Recommendation
Children under 2 years	Safety with respect to hepatotoxicity, GI intolerance and other adverse effects should be addressed	Topical antifungals with established safety Oral fluconazole
Children above 2 years	Safety with respect to hepatotoxicity, GI intolerance and other adverse effects should be assessed	Topical antifungals with established safety Oral terbinafine, itraconazole, fluconazole and griseofulvin
Hepatic dysfunction	Monitoring of the hepatic function is mandatory	Topical antifungals Oral fluconazole
Renal dysfunction	Renal function monitoring if terbinafine is used (dose reduction if creatinine clearance is <50 ml/ min)	Topical antifungals Oral itraconazole
Cardiac dysfunction	Cardiotoxicity of drugs should be addressed	Topical antifungals Oral terbinafine

also increased.^[61,62] A hot and humid climate favours the growth of dermatophytes, while humidity can enhance penetration of fungi.^[63-65] In a study from Kerala done in 2016, 52% of patients with chronic dermatophytosis were manual labourers. About 64% of patients were exposed to the sun for more than 3 hours a day and 68% had reported excessive sweating.^[66] In another study, from Tamil Nadu, chronic infection was associated with sun exposure for more than 3 hours daily.^[67]

Patients should be advised to avoid sharing of inanimate objects or fomites (e.g., soaps, towels, clothes and bedding) with others, as these can be responsible for transmission of infection.^[32,68,69] Washing the body surface with soap and water removes fungal elements, emphasizing the need for regular bathing. Use of synthetic tight dresses and occlusive footwear is linked to increased prevalence of dermatophytosis.^[70] Tight, restrictive clothing can trap heat and moisture, leading to a conducive environment for the growth of dermatophytes. Hence, patients should be advised to avoid using synthetic or tight clothing and should preferably use loose cotton clothes.^[62]

Washing clothes in water at a temperature of 60°C or above eliminates *Trichophyton rubrum*.^[27-29] Exposure of infected socks to sunlight can reduce fungal contamination as sunlight can act as a good disinfectant.^[30] Washing or storing infected and non-infected clothes together can facilitate transmission of infection.^[32] Hence the worn clothes of patients should be stored and washed separately in hot water at 60°C and dried inside out in the sun.^[62] Similarly, ironing of clothes may also be beneficial. Waistbands, wristbands and threads, which aid the persistence of dermatophytes are better avoided.^[62]

Obese patients should be advised to lose weight to prevent recurrence of infection, especially in intertriginous areas like the groin.^[71] The nails should be examined in all patients with dermatophytosis as they may act as a focus for recurrent infection.^[72] Contact with pets should be avoided as they can be potential sources of infection, although there appears to be no role of pets in the current scenario.^[73]

Abuse of oral or topical corticosteroids frequently leads to diagnostic difficulty (due to atypical presentations of dermatophytosis) and treatment failures.^[48,74] Compliance to treatment is essential to achieve cure as patients often use antifungal drugs irregularly or stop them on getting relief from itching and achieving partial resolution.^[4,75] As infection among other family members is very common in the current scenario, treatment of all infected members simultaneously is necessary to avoid recurrences or persistence of infection.^[76]

Counselling patients about the course of disease, adherence to treatment and to general measures and avoidance of corticosteroid abuse are essential for treatment to be successful.

Pharmacological therapy

Since dermatophytes usually do not penetrate the deeper layers of the skin, the host does not necessarily develop sufficient immunity to ensure spontaneous healing.^[77] Spontaneous remission rarely occurs even when the underlying cause has been eliminated.^[78] Therefore, every patient with dermatophytosis requires topical and/or systemic antifungal therapy.

Tinea of the glabrous skin has been easily amenable to short courses of standard antifungal agents, terbinafine and itraconazole since the time these drugs were introduced. However, with increasing incidence of inadequate response to treatment, high recurrence rate and chronic infections, an extended duration of therapy is often needed. To ensure compliance, antifungal therapy should be chosen keeping affordability in mind.

Topical therapy

Topical antifungal therapy is integral to the management of glabrous tinea especially in the setting of localised infection, pregnancy, children and in the presence of some comorbidities when systemic antifungals cannot be used.^[79] Topical antifungals can be useful adjuvants to systemic antifungals in the current scenario as they may have an

Table 8: Topical antifungal preparations available in India

Class	Drug name	Preparations	FDA Pregnancy Category
Imidazoles	Ketoconazole	2 % cream, powder, lotion (with or without 1% zinc pyrithione), soap	C
	Miconazole nitrate	2 % cream, gel, powder	C
	Clotrimazole	1 % cream, lotion, powder, soap	B
	Oxiconazole	1 % cream, lotion	B
	Fenticonazole	2 % cream	Not categorised
	Bifonazole	1 % cream	B
	Eberconazole	1 % cream	C
	Sertaconazole nitrate	2 % cream, lotion	C
	Luliconazole	1 % cream, lotion, spray	C
Triazoles	Fluconazole	0.5 % gel, powder	C
Allylamines	Terbinafine hydrochloride	1% cream, gel, powder, lotion	B
Benzylamines	Butenafine	1% cream	B
Morpholones	Amorolfine hydrochloride	0.25 % cream, 5 % nail lacquer	Not categorized
Hydroxy-pyridinone	Ciclopirox olamine	8% Nail lacquer, 1% cream, 1% shampoo	B
Others	Tolnaftate	Solution (10mg/ml), cream (10mg/g)	Not assigned. To be used if benefits outweigh risk.
	Whitfield's ointment	3% salicylic acid and 6% benzoic acid in ointment base	C (due to risk of absorption of salicylic acid) WHO allows application, especially if benefits outweigh risks

additive effect and achieve high local concentration.^[80] Reaction at the site of application is rare and is the only significant adverse effect.

The ideal topical antifungal agent should have a high cure rate, low relapse rate and minimal adverse effects.^[81] Extensive infection and high cost, especially of the newer topical antifungals, are limitations to topical therapy. As dermatophytes are keratinophilic, moving radially, current practice of many dermatologists is to advise patients to apply antifungal creams from the active outer border inwards.

Topical agents are available as creams, ointments, lotions, sprays, gels, powders and soaps. Of these, antifungal soaps and powders are not recommended in the management of glabrous tinea. In India, topical antifungal, antibacterial and corticosteroid combination creams containing 3-5 components (viz. a potent corticosteroid like clobetasol propionate, ornidazole, ofloxacin and an antifungal agent) are unfortunately freely available over-the-counter.^[3] They are often used for the treatment of tinea corporis, tinea cruris and tinea faciei, leading to a variety of adverse effects.^[82] Antifungal without any corticosteroid or antibacterial only should be used for the treatment of glabrous tinea. Topical corticosteroids should never be used for tinea corporis, tinea cruris or tinea faciei. Some classes of topical antifungals such as azoles and allylamines have anti-inflammatory properties due to their inhibitory effects on cytokines and may be useful for treating patients with inflammatory lesions.^[79]

Keratolytics have been used for the treatment of dermatophytosis, especially hyperkeratotic tinea pedis.^[83,84]

Topical keratolytics, such as Whitfield's ointment (3% salicylic acid with 6% benzoic acid), can be used in the treatment of glabrous tinea, but not on the flexures or face or where the lesions are inflamed.^[85,86]

Topical antifungal agents available in India are listed in Table 8. Many are relatively new and probably have some advantages over the older ones [Table 9], but are generally more expensive.^[87-94] Since there are very few head-to-head comparison studies there is insufficient evidence to recommend one molecule over the other.^[95,96] Most topical antifungals need to be applied twice daily, but luliconazole and terbinafine may be applied once daily.^[87,92] Clotrimazole, miconazole, oxiconazole and ketoconazole are relatively less expensive.

Topical corticosteroid application adversely affects the epidermal barrier function by increasing transepidermal water loss and decreasing the ceramide content of the stratum corneum.^[97] Hence, emollient application should be encouraged, particularly in patients with corticosteroid modified tinea, to enhance the barrier function and provide symptomatic relief.^[19] Antihistamines can be used to alleviate pruritus. There are a few reports supporting the use of antifungal powders in tinea pedis,^[98,99] but antifungal powders are not recommended for other forms of tinea.

Systemic therapy

Standard indications for systemic therapy in dermatophytosis are extensive disease, involvement of multiple sites, recurrence, chronicity, failure of topical therapy, nail or hair involvement and immunocompromised status.^[22,100] In India, now a days, most patients require a

Table 9: Specific characteristics of relatively newer select topical antifungals available in India^[79,82-89]

Drug	Class	Remarks
Terbinafine	Allylamine	Fungicidal antifungal as compared to fungistatic nature of most other antifungals ^[82]
Butenafine	Benzylamine	Fungicidal antifungal as compared to fungistatic nature of most other antifungals ^[83]
Bifonazole	Imidazole	Dual mode of action by inhibition of 14 α -demethylase and microsomal HMG-CoA-reductase leading to fungicidal effect. ^[84]
Sertaconazole	Imidazole	Anti-inflammatory action. Contains a benzothiophene ring which mimics tryptophan and increases the drug's ability to form pores in the fungal cell membrane. ^[85]
Eberconazole	Imidazole	Potent anti-inflammatory activity ^[86]
Luliconazole	Imidazole	Reservoir effect. Highest antifungal activity against <i>Trichophyton spp.</i> among currently available topical antifungal drugs. ^[87]
Fenticonazole	Imidazole	Additional action of blocking cytochrome oxidases and peroxidises. ^[88]
Amorolfine	Morpholine	New class of antifungal with different mechanism of action mediated through inhibition of two different enzymes. ^[89]
Ciclopirox olamine	Hydroxypyridinone	Acts through chelation of metal ions (Fe ³⁺); inhibits cytochrome oxidase, catalase and peroxidase resulting in intracellular degradation of toxic peroxides; inhibits cellular uptake of essential compounds and alters cell permeability. ^[79]

combination of systemic and topical antifungal drugs for a longer duration than that is conventionally recommended. This is particularly true for patients with corticosteroid modified, chronic, recurrent or recalcitrant infection. Persistent papules or nodules in a healing or unresponsive lesion may indicate Majocchi granuloma, which also needs prolonged treatment.^[101,102]

Terbinafine 250 mg daily or itraconazole 200 mg daily in adults for 4-6 weeks have been recommended for treatment of chronic, widespread dermatophytosis.^[37,39] Griseofulvin 500-1000 mg daily taken after fatty meal until cure (3-6 months) has been mentioned as an alternative drug.^[37] Itraconazole and terbinafine are especially useful in sebum rich areas, as the skin pharmacokinetics (pK) are determined predominantly by their lipophilicity.^[1]

There have been concerns over increasing instances of failure to terbinafine in tinea corporis, tinea cruris and tinea faciei in the country.^[103,104] Resistance to terbinafine due to mutations in the squalene epoxidase (*SQLE*) gene of *Trichophyton interdigitale* and *T. rubrum* has been documented in studies from Chandigarh and New Delhi.^[59,60] High MIC's (Minimum inhibitory concentration) were observed and a higher dose (250 mg twice daily) or increased duration was found to be more effective in a study, hence the authors concluded that increased exposure to terbinafine, resulting in higher levels of the drug in the stratum corneum, could offset the higher MIC and the effect of *SQLE* mutation to some degree.^[40]

Itraconazole is now the most commonly prescribed oral antifungal agent for dermatophytosis. It should be taken immediately after food or with aerated beverages or acidic juice to improve its bioavailability. While the standard dosage for glabrous tinea is 100 mg once daily for 15 days or 200 mg (as 2 capsules of 100mg taken together or in a BD dose) for 1 week,^[105,106] the current scenario calls for individualisation of the duration based on clinical response and continuation of treatment until achieving cure.

Different brands of itraconazole available in India vary in the pellet morphology and thereby the resultant quality and therapeutic effect. The drug-polymer ratio, polymer type, coating thickness, bead size and number determine the dissolution of a capsule of itraconazole.^[107] Morphometric analysis of pellets using dermoscopy is a simple method to quantify the quality of a brand of itraconazole.^[108] A recent study stated that a pellet count of ≥ 560 (100 mg capsule) provides a surface area comparable to the innovator brand and may be taken as a cut off for distinguishing poor quality brands.^[109] In a compliant patient whose disease is not responsive, changing to a better brand is justified. Since itraconazole follows non-linear pharmacokinetics, a dose higher than 200 mg daily may result in decreased clearance and eventually toxic levels.^[19,110]

In some parts of India, dermatologists have found good therapeutic response to griseofulvin given for 6-8 weeks although not consistently [Table 6].^[41-43] Since the levels are high in the stratum corneum, this drug could be especially useful in patients prone to increased sweating.^[110,111]

The standard dose of fluconazole in adults is 150-300 mg weekly for 4-6 weeks or 50-100 mg daily 4 weeks.^[112,113] However, it is being commonly prescribed in the dose of 150 mg thrice weekly (extrapolated from the regimen for complicated vulvovaginal candidiasis) in certain parts of India with good results. Skin pharmacokinetic (pK) studies have found that its skin levels are markedly higher with a dose of 100 mg given daily.^[19,110] Notably, fluconazole achieves high levels in stratum corneum, reaching there mainly by way of direct diffusion. Thus, its pathway of reaching the corneum is different from terbinafine and itraconazole which largely depend on sebum secretion and this makes it potentially useful in patients with dry skin and in children who have lesser sebum secretion than adults.^[19] However, a disadvantage is that the levels decrease rapidly following treatment discontinuation due to low keratin adherence.^[110]

There is paucity of literature with regard to the use of combination of oral antifungals in the treatment of dermatophytosis. Such combinations need to be first assessed in laboratories by checkerboard studies for synergistic activity before considering any clinical utility.^[114] Although few studies have proven synergistic effect of combination antifungal therapy against dermatophytes, more evidence is desirable.^[115]

Ketoconazole is an imidazole compound with a mechanism of action similar to that of triazoles. It had been used in the management of glabrous tinea in a dose of 200-400 mg daily in adults.^[116] It is no longer approved by US FDA for the management of superficial fungal infections because of hepatotoxicity, which may be asymptomatic or can present as acute liver injury.^[117,118] Though available in India, it is not recommended for routine use, but is to be used only as a reserve drug with close monitoring of liver function.

Special situations

Dermatophytosis is now the commonest dermatologic condition seen among outpatients in India.^[119-121] Comorbidities such as diabetes, anaemia and immunosuppressive diseases or immunosuppressive therapy, may alter the clinical presentation and predispose such patients to recalcitrant or recurrent infections.^[118,122,123]

Corticosteroid-modified tinea

Corticosteroid-modified tinea and tinea incognita have become common presentations of dermatophytosis in India. Some patients tend to apply the topical corticosteroid antibacterial antifungal combination creams continuously or intermittently over weeks to months and present with morphological variants such as tinea pseudoimbricata and breakthrough lesions. Studies have shown that application of more than 50 gm of 0.05% clobetasol propionate per week can result in adrenal suppression.^[124] Hence, it is quite understandable that patients may present with Cushingoid features and a low serum cortisol level. Literature states that the recovery of the hypothalamus takes about 14-30 days after cessation of corticosteroids.^[125] This explains the delay in clinical response seen in patients with steroid modified dermatophytosis, who will hence require an extended duration of treatment.^[19] Patients with steroid modified dermatophytosis with Majocchi granuloma have been shown to achieve clearance with the use of pulse therapy with itraconazole given as 200 mg BD for 7 days followed by drug free period of 14 days (up to 3 pulses).^[19,126]

Pregnancy and lactation

US FDA pregnancy category system was abolished in 2014 and is to be replaced gradually by a new system called Pregnancy and Lactation Labelling Rule (PLLR) with narrative-based labelling requirements. However, as the same is still in transition; the older category is

mentioned here. The ideal management of glabrous tinea during pregnancy is by using only safer topical antifungals [Table 8]. Though oral terbinafine is a FDA pregnancy category B drug, scarce human data precludes its routine use in pregnancy until safety data is available.^[44] Itraconazole and griseofulvin, both belong to category C, while fluconazole is a category D drug (except as a 150 mg single dose).^[44] Among the topical antifungals, clotrimazole, oxiconazole, bifonazole, terbinafine and ciclopirox olamine belong to Category B, while the newer azoles such as sertaconazole, eberconazole and luliconazole are category C drugs.^[44,127] Systemic absorption is considered to be very low with amorolfine and hence it may be safely used in pregnancy.^[44]

All topical antifungals can be used safely during lactation as their secretion in milk is negligible. Cream, gel or liquid products which are water miscible are recommended for application to the skin over the breast because ointments may expose the infant to mineral paraffin while feeding. Data regarding the use of systemic antifungals including terbinafine during lactation is scarce, and therefore they should be avoided as far as possible especially in mothers of preterm infants.^[44,128,129] However, fluconazole has an acceptable safety profile as its secretion in the breast milk is low.^[45,130] Experts recommend that the decision on treatment should be based on the given clinical scenario.

Children and elderly

Glabrous tinea infections have become common in children in the recent times. There are differences in epidemiology, host biology, predisposing factors and clinical presentation in children as compared to adults.^[131] Topical antifungals can be given safely in children since their percutaneous absorption is negligible. Use of topical corticosteroid-antifungal combination creams result in early deleterious effects on the skin of children and persistence of infections and thus are to be avoided.^[132,133]

When systemic antifungals are needed to be used in children, their dosage should be based on the body weight [Table 8]. Antifungals like griseofulvin, terbinafine and itraconazole can be used in children above 2 years of age to treat glabrous tinea infections.^[134-136] Considering the safety aspects, fluconazole may be the preferred systemic antifungal in infants and children below 2 years of age. Secretion and distribution pattern of this drug is not dependent on sebum and directly diffuses into the skin.^[110]

Physiological, psychological and socioeconomic factors, comorbidities (renal, hepatic, cardiac) and influence of polypharmacy should be considered while treating elderly patients.^[137] A healthy elderly patient may be treated in the same manner as a young adult. Changes in pharmacokinetics must be considered while deciding an appropriate antifungal drug in elderly patients with altered hepatic or renal

Table10: Clinically relevant drug interactions with antifungals^[111,141-144]

Antifungal drug	Drug level is decreased by	Decreases level of these drugs	Increases level of these drugs
Griseofulvin	Phenobarbital	Anticoagulants, oral contraceptives, Cyclosporin	Potentiates action of alcohol-Disufiram like reaction
Terbinafine	Rifampicin	-	Anti-depressants beta blockers, Antiarrhythmics class 1c, selective serotonin reuptake inhibitors. Caution when used with anticoagulants.
Itraconazole	H2 histamine blockers, proton pump inhibitors, rifampicin, rifabutin, INH, ritonavir, nevirapine, nortriptyline, carbamazepine, phenytoin, phenobarbital	Oral contraceptives	Glibenclamide, phenytoin, warfarin, cyclosporin, tacrolimus, digoxin, lovastatin, midazolam, triazolam, methylprednisolone, Saquinavir
Fluconazole	Rifampicin	Oral contraceptives	Sulfanylurea, nifedipine, theophylline, NSAID, warfarin, cyclosporine

functions. It is very important to check for various drug interactions before treating elderly patients on polypharmacy.

Systemic comorbidities

Appropriate laboratory monitoring is mandatory in patients with known hepatic and renal dysfunction while using systemic antifungals. No recommended dose adjustment is available for systemic antifungals in patients with hepatic impairment. Monitoring them regularly is the only option. Fluconazole, as compared to other triazoles, is characterized by high water solubility and the drug is primarily eliminated by the kidneys.^[11,138,139] Hepatic metabolism does not seem to play an important role in the elimination of the drug. Oral fluconazole with laboratory monitoring can hence be considered as a relatively safer drug in patients with hepatic dysfunction. Itraconazole is eliminated mainly through faeces and in lesser amount through the urine.^[138] Oral itraconazole is thus a safer drug in patients with renal dysfunction. Itraconazole has however been associated with congestive cardiac failure and must be avoided in patients predisposed to the same.^[140] Oral terbinafine is a relatively safer drug in patients with cardiac dysfunction.^[46] However, in patients with renal dysfunction, the dose needs modification if creatinine clearance is <50 ml/minute.

Drug interactions

Systemic antifungals should be used appropriately in patients on polypharmacy after checking for various drug interactions. Table 10 summarises clinically relevant drug interaction of commonly used systemic antifungals for dermatophytosis.^[111,141-144] Terbinafine has the least drug interactions and is generally the preferred choice of drug in patients on polypharmacy.

Limitations

We could not reach a consensus on some aspects of the management of dermatophytosis such as minimum duration of treatment for naïve cases, up dosing of oral antifungals, quality

of drugs as a cause of treatment failure and comparative efficacy of topical antifungals. Topic that was not covered in the statement is the management of dermatophytosis in immunosuppressed patients due to comorbidities and concomitant corticosteroids/immunosuppressive therapy.

Conclusion

Treatment of recalcitrant dermatophytosis has evolved into an enormous public health problem imposing immense financial burden.^[145] Consensus on the management of dermatophytosis is felt to be the need of the hour. It will definitely help to improve the quality of care to patients with dermatophytosis across the country and ease some concerns of dermatologists related to effective management of the infection in their patients. Inputs from this draft are expected to be of use to medical practitioners of other countries facing a similar situation. We realize that there is need for further studies on dermatophytes with regard to antifungal resistance, clinico-mycological and therapeutic correlation substantiated by genomic approach. Such studies have already been initiated in India.^[10,146,147] Until further evidence comes in, INTACT would serve as a management guideline and a reference document that addresses most issues related to the management of glabrous tinea.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Note for readers: "The list of statements with and without consensus is not included in this manuscript due to technical and space constraints.

They are readily available on request and readers may contact the corresponding author for the same.

Editor-in-Chief"

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