Letters in response to previously published articles

'End of the road for terbinafine' in dermatophytosis: Is it a valid conclusion?

Sir,

We read with keen interest the article by Singh and Shukla on the effectiveness of terbinafine in dermatophytosis, and wish to draw attention to some points.[1] There is no doubt that dermatophytosis has progressed from being an innocuous, easily treatable infection to one that is rapidly assuming gigantic proportions in India, with chronicity and multiple recurrences, although these terms have been only recently defined.[2] Drugs such as terbinafine that were uniformly effective in treating dermatophytosis earlier are now seldom proving so in the duration conventionally considered to be sufficient. However, to conclude regarding a mainstay agent as abysmally ineffective would require consideration of some pertinent issues.

In this prospective cohort study, 500 patients of dermatophytosis were included and treated with oral terbinafine (5 mg/kg/day) for a maximum duration of 4 weeks. The number of patients following up at the end of 2 and 4 weeks were 357 and 362 and the cure rates at these time points were found to be 2 and 30.6%, respectively. Out of 500 patients, 42% had applied topical corticosteroids in the recent past, either alone or in combination creams as over-the-counter topical preparations.[1] It is well known that the unregulated availability and use of such irrational corticosteroid–antifungal–antibacterial combinations causes a reduction in the local cellular immunity, thereby playing an important role in making the dermatophytosis notoriously recalcitrant.[3] In such a scenario, to confer the recalcitrance to merely lack of effectiveness of a hitherto effective drug, such as terbinafine, would seem as jumping the gun a little too soon; more so because the use of terbinafine in this study has not been compared with any other standard drug such as itraconazole in a parallel arm. In this study, of the total patients enrolled, 243 (48.6%) had already taken some form of oral and/or topical treatment and hence were not treatment-naïve cases. There is also a marked difference in the cure rates of dermatophytosis in this study at the end of 2 and 4 weeks from 2 to 30.6%. Hence, the use of terbinafine for a duration of 4 weeks is perhaps not adequate to determine its effectiveness in causing cure, and treatment longer than 4 weeks would have perhaps improved the cure rates much further. This seems particularly relevant in today's scenario where the conventional regimens of mainstream drugs such as terbinafine and azoles no longer seem effective in the durations prescribed in standard textbooks. In this regard, it is also useful to remember that it has been recommended that minimum duration of treatment should be 2–4 weeks in naïve cases and >4 weeks in recalcitrant cases.[2] The calculation of cure rates at the end of 4 weeks also seems fallacious (153 cured out of 362, giving a cure rate of 42.3% instead of 30.6% as mentioned in the article).

Two additional factors that do not seem to have been considered are the possibility of reinfection, because the family members were not screened; and information regarding demographic and socioeconomic variables and advice regarding hygiene were not provided. These, in all probability, could have played a role in determining the cure of infection with terbinafine. Recurrences may have been owing to reinfection from family members or the environment, or the duration of antifungal therapy given may be inadequate, as was the likely case in the index study. In a study on 150 patients of dermatophytosis from North India, the authors found high minimum inhibitory concentration (>2 μg/ml) for terbinafine in one *Trichophyton interdigitale*, four *Trichophyton mentagrophytes* and three *Trichophyton rubrum* isolates.[4] They concluded that increase in minimum inhibitory concentration is not the only factor responsible for recurrence and most of the strains were not drug-resistant, thereby further consolidating our point that the dismal cure rate of terbinafine may not be explained by its effectiveness alone.

Hence, we conclude that further well-designed studies comparing the effectiveness of terbinafine with other standard drugs, such as itraconazole, should be conducted before concluding that it is the end of the road for terbinafine.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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Access this article online

Quick Response Code:

Website: www.ijdvl.com

DOI: 10.4103/ijdvl.IJDVL_717_18

How to cite this article: Bhattacharjee R, Dogra S. 'End of the road for terbinafine' in dermatophytosis: Is it a valid conclusion?. Indian J Dermatol Venereol Leprol 0;0:0.

Received: August, 2018. **Accepted:** September, 2018.

Authors' reply

Sir,

We welcome the comments on our article[1] and thank you for the opportunity to make our humble submission in reply [Table 1]. In this pragmatic study,[1] the focus was on real-life situation in view of perceived recent loss of effectiveness of terbinafine in dermatophytic infections in India. Our objective was to find the evidence for or against the above perception. The study provides evidence that yes, there is a problem, and this is how grave it is.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Table 1: Issues raised and the replies

Issue number	Issue	Reply
1	In this prospective cohort study, 500 patients of dermatophytosis were included and treated with oral terbinafine (5 mg/kg/day) for a maximum duration of 4 weeks.	As only 10 of 500 patients were cured at 2 weeks, 490 of 500 patients received treatment for 4 weeks.
2	It is well known that the unregulated availability and use of such irrational corticosteroid-antifungal- antibacterial combinations causes a reduction in the local cellular immunity, thereby playing an important role in making the dermatophytosis notoriously recalcitrant.	Cited article[2] is an important case series (with review) of 24 male patients with genital tinea who were incorrectly using topical steroid combination creams. Data presented in this article[2] do not relate to the attributions made in this comment on our article
3	Use of terbinafine in this study has not been compared with any other standard drug like itraconazole in a parallel arm.	As mentioned,[1] aim of the study was to investigate the effectiveness of terbinafine in a pragmatic setting, and not to compare its effectiveness with other antifungal agents
4	Use of terbinafine for duration of 4 weeks is perhaps not adequate to determine its effectiveness in causing cure, and treatment longer than 4 weeks would perhaps have improved the cure rates much higher.	Weight-adjusted dose of terbinafine used in the study is higher and duration of treatment much longer than those recommended by standard textbooks, which recommend a fixed dose of 250 mg per day to be given for 1 to 3 weeks,[3] 1 to 2 weeks,[4] or 10 to 14 days,[5] for tinea corporis and tinea cruris. Please also see reply to issue number 5.

(contd.....)