

## THIABENDAZOLE VERSUS MICONAZOLE IN DERMATOPHYTOSIS

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### Summary

Thirty cases of tinea corporis who were KOH positive and having at least three lesions underwent therapeutic trials with 70% alcohol, 0.25% thiabendazole in 70% alcohol and miconazole nitrate 2% gelcream. They were followed up for 4 weeks. 100% cure was obtained with both thiabendazole and miconazole. Response was significantly earlier with thiabendazole. The drug was equally effective in *T. mentagrophyte*, *T. rubrum* and *E. floccosum* infections.

Thiabendazole, an imidazole derivative, is a well established broad spectrum anthelmintic drug. In vitro studies have revealed this drug to be an effective fungicidal and in smaller concentration fungistatic agent<sup>1,2,3,4</sup>. However, clinical trials with this drug for the treatment of ring-worm infections are scanty<sup>5,6,7</sup>. This drug is not yet available in any topical form in India or abroad. The present study was undertaken to judge the therapeutic efficacy of this drug in dermatophytosis and to compare this with that of a well established topical fungicidal drug namely miconazole nitrate<sup>8,9,10,11,12</sup>.

### Methods

Thirty cases suffering from tinea corporis having at least three lesions were selected at random from skin and STD department of Medical College,

Amritsar during the years 1977 and 1978. All the cases included for this study were positive for fungus on examination of scrapings in 10% KOH. In each patient before starting therapeutic trial scrapings from the lesions were also subjected to culture on Sabouraud's dextrose agar medium for identification of the species of fungus.

Three applicants were used viz. 70% alcohol, 0.25% thiabendazole in 70% alcohol and 2% miconazole nitrate gelcream (Daktarin by Ethnor Ltd.). In each patient three areas with lesions were demarcated for the respective applicants. Medicines were applied by the investigator twice daily. A weekly assessment was made in each case with regard to the clinical mycological alteration; the latter being on the basis of KOH examination only. The cases were followed up and assessed for 4 weeks. Clinical improvement was graded as follows:

GO no change or improvement in the lesion.

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- GI margins with non-active flat papules with mild to moderate itch.
- GII scaly lesion with nil to mild itch.
- GIII complete cure with or without pigmentation.

**Observations**

*General:*

Of the 30 cases studied 19 were males and 11 were females. Their ages ranged between 16 years and 70 years. Duration of illness varied between 5 months and 15 years. Multiple sites were involved in all the cases. Positive cultures were obtained in 25 cases-Trichophyton (T) mentagrophyte in 13 cases, T. rubrum in 11 cases and Epidermophyton (E) floccosum in 1 case. Average extent of lesions treated with 70% alcohol, thiabendazole and miconazole were 42.4 sq.cms. (6 to 180 sq.cms.), 100.2 sq.cms. (24 to 320 sq.cms.) and 83.2 sq.cms. (30 to 288 sq.cms.) respectively.

*Follow up:*

In lesions treated with 70% alcohol, scrapings in KOH persisted positive for fungus throughout the period of study and no clinical improvement in the lesions was observed at the end of 4 weeks of treatment.

In all lesions treated with thiabendazole, scrapings for fungi became nega-

tive after first week and remained so throughout the follow up period. In all the lesions some clinical improvement was observed at one week's follow-up—19 cases showed GIII, 7 cases GII and 4 cases GI response. By the third week of follow-up, all the lesions had disappeared leaving behind mild pigmentation. Average period required for cure was 10.5 days.

In all lesions treated with miconazole, scrapings for fungi became negative after first week of treatment and persisted so throughout the follow up period. At one week's follow-up some improvement was observed in all the lesions—4 cases showed GIII, 15 cases GII and 11 cases GI response. By the end of three week's treatment all the lesions showed GIII improvement except one who showed GIII response at the end of 4 weeks' treatment. Average period required for cure was 15.4 days (Table I).

In T. mentagrophyte cases, at the first week follow-up, whereas with thiabendazole cure rate was 69.2% (9 lesions), no lesion had been cured with miconazole. By the third week follow-up lesions in all the 13 cases were cured with both the drugs. In T. rubrum cases with thiabendazole at first week follow-up 72.7% (8 lesions) were cured and by third week all the lesions got cured. With miconazole, cure rates were 27.3% (3 lesions) and 90.9% (10

Table 1  
Showing cure rate with respect to thiabendazole and miconazole on weekly follow up

CURE RATE									
Drug	1st week*		2nd week		3rd week		4th week		Average duration
	No. of cases	Percentage cured	No. of cases	Percentage cured	No. of cases	Percentage cured	No. of cases	Percentage cured	
Thiabendazole	19	63.3	26	86.7	30	100	30	100	1.5 wks (10.5 days)
Miconazole	4	13.3	71	70	29	96.7	30	100	2.2 wks (15.4 days)

\* Statistically significant, P<0.01

Table 2  
Showing effects of drugs versus dermatophytes

Species	Total No. of cases	Drugs tried	Follow-up								Average duration
			1st week*		2nd week		3rd week		4th week		
			No. of cases	Per-cent-age	No. of cases	Per-cent-age	No. of cases	Per-cent-age	No. of cases	Per-cent-age	
T. mentagrophyte	13	Thiabendazole	9	69.2	11	81.6	13	100	13	100	10.2 days
		Miconazole	0	0	10	76.9	13	100	13	100	15.6 days
T. rubrum	11	Thiabendazole	8	72.7	10	90.9	11	100	11	100	9.5 days
		Miconazole	3	27.3	6	54.6	10	96.9	11	100	15.9 days
E. floccosum	1	Thiabendazole	1	100	1	100	1	100	1	100	7 days
		Miconazole	1	100	1	100	1	100	1	100	7 days

\* Statistically significant for T. mentagrophyte P is smaller than 0.01 and for T. rubrum P is smaller than 0.05.

lesions) at first week and third week follow-ups respectively. In T. mentagrophyte infections and T. rubrum infections cure with thiabendazole was quicker than with miconazole. In some T. rubrum cases the faster cure obtained with thiabendazole was particularly evident. (Table 2).

### Discussion

Therapeutic evaluation of any topical drug for the treatment of ring-worm infections poses a number of problems. The therapeutic response will be related to vehicle in which the drug is, manner of application and ability of the agent to penetrate. Matching control trials are necessary for proper evaluation.

Thiabendazole which in vitro studies was found to be very effective against various dermatophytes has not yet undergone wide clinical trials probably due to the fact that discouraging results were reported in early clinical trial by Fleishmajor et al<sup>5</sup>. Studies have revealed that the drug in ointment form is ineffective<sup>6</sup>. Battistini et al<sup>7</sup> conducted clinical trials with this drug in various formulations viz. 10% thiabendazole in vanishing cream, 10% thiabendazole suspension, 0.25% thiabendazole in 70%

alcohol and 0.25% thiabendazole in polyethylene glycol 400 vehicle. They concluded that thiabendazole is an effective antifungal agent and clears ring worm lesions as rapidly as systemically administered griseofulvin. Further topical effectiveness of thiabendazole was markedly enhanced by an alcoholic vehicle but there was negligible effect in polyethylene glycol 400 vehicle.

Thiabendazole acts as a fungicide by inhibiting primarily the terminal electron transport system of mitochondria. Other decreases in metabolic functions are secondary and follow from unavailability of energy.

In the present study thiabendazole 0.25% incorporated in 70% alcohol has given 100% cure in 3 weeks, the average duration of treatment for cure being 10.5 days. Battistine et al had also obtained 100% cure rate but with 4 weeks' treatment. In their series by 2nd week 62.5% of lesions had shown marked improvement (5 out of 8 lesions). In the present study all cases showed improvement and 86.7% showed cure (26 lesions) by the end of 2nd week of treatment. The discrepancy in the success rate

may be attributable to the fact that in the present series medicine was applied under supervision whereas the responsibility of application of the medicines was given to the patients themselves in the Battistine et al study. The difference may even be partly attributable to variable sensitivity of different species of dermatophytes. In the present study the drug has been found to be equally effective in lesions caused by *T. mentagrophyte* and *T. rubrum*. This observation is in agreement with results of earlier in vitro and in vivo studies.

Compared to miconazole, thiabendazole has been found to give earlier treatment response. After one week of treatment cure rates were 13.3% (4 cases) and 63.3% (19 cases) respectively with miconazole and thiabendazole. However, by the end of 4 week's treatment 100% cure was observed with the drugs with an average 15.4 days with miconazole and 10.5 days with thiabendazole. Similar differences in the efficacy of these two drugs have been detected in *T. mentagrophyte* and *T. rubrum* cases.

In the light of the observations in present study it is concluded that 0.25% thiabendazole in 70% alcohol is an effective topical preparation for the treatment of dermatophytosis (tinea corporis) caused by *T. mentagrophyte*, *T. rubrum* and *E. floccosum*. 100% cure rate is obtained in a shorter period with thiabendazole than with miconazole.

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