

CLOTRIMAZOLE IN THE TREATMENT OF SUPERFICIAL MYCOSES *

D. N. MULAY AND A. K. GARG

Summary

Results of a trial, conducted on the treatment of superficial mycoses of man with Clotrimazole, are given. Topical treatment with Clotrimazole cream gave very good results in the treatment of dermatophytoses and candidiasis of skin, but moderate only in tinea versicolor. Excellent results were also obtained in the treatment of candidiasis vaginitis with Clotrimazole vaginal tablets.

Clotrimazole is a tritylimidazole derivative recently developed¹ and being manufactured by the Research Laboratories of Bayer A. G. Germany, under the commercial name Canesten. The high sensitivity of Clotrimazole *in vitro* to a variety of human pathogenic fungi^{2,3} belonging both to the filamentous and yeast groups, has found its use in the therapy of various superficial mycoses of man⁴⁻¹³, including dermatophytoses, candidiasis of skin and vagina, and tinea versicolor. The present study gives the results of a trial conducted to evaluate the efficacy of Clotrimazole cream in topical treatment of various dermatomycoses, and Clotrimazole vaginal tablets in candidiasis vaginitis.

Material and Methods

172 patients with superficial mycoses attending the Skin Out Patient Department of Willingdon Hospital, New Delhi were subjected to clinical trials with

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Department of Dermatology and Venereology, Willingdon Hospital, New Delhi-110001.
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Clotrimazole (commercial name Canesten; synonym: Bay b 5097) cream/vaginal tablets. The drug content in the Canesten cream was 1% in an inert ointment base, and in each of the vaginal tablets it was 100 mg. The clinical and personal data, such as the age and sex of patients, type of lesion, duration of infection, prior infection and/or treatment if any, were recorded. The skin scrapings, nail scrapings and hair plucked from scalp lesion were obtained, and examined in KOH mounts for the presence of hyphae and/or spores of fungi. The clinical diagnosis in these 172 mycologically proved cases of fungus infection is given in Table 1.

TABLE 1
Clinical diagnosis of the 172 patients of superficial mycoses treated with Clotrimazole

S. No.	Clinical Diagnosis	No. of patients
1	Dermatophytoses	119
2	Candidiasis of skin	10
3	Candidiasis vaginitis	10
4	Tinea Versicolor	33
Total		172

Routine techniques for the isolation and identification of dermatophytes and *Candida* were adopted. The

patients who had fungal infections other than candidiasis vaginitis, were advised to apply Clotrimazole cream, at the site of the lesion, in a thin film, twice a day, and usually for 6 weeks. The patients with candidiasis vaginitis were advised to introduce one Clotrimazole vaginal tablet, deep into the vagina, every night before going to bed, for six days only. The results of the treatment were assessed by clinical improvement of the lesions, and mycological investigation of the material from the lesions.

Results

The results of the treatment in the four types of superficial mycoses are given below.

1. Treatment in Dermatophytoses

The results of the treatment of dermatophytoses with topical Clotrimazole cream are given in tables 2-4. Out of the 119 patients treated (Table No. 2), most of the patients had either tinea corporis (36.9%) or tinea cruris (36.9%), or both tinea corporis and tinea cruris (16.8%). Prevalence of infections on other parts of the body in the present series was, however, much less. The commonest dermatophyte isolated from the 96 culture positive cases was *Trichophyton rubrum* in 79.2%. The other dermatophytes were isolated less frequently as follows: *Epidermophyton floccosum*, 12.5%; *T. violaceum*, 6.3% and *T. mentagrophytes* and *Microsporum gypseum* 1.0% each.

Out of the 119 patients treated, a complete cure from the disease (i.e. clinical and mycological) was achieved in 111 (93.3%) patients. Seven (5.9%) patients, including one with tinea capitis, showed good improvement, and 1 patient, who had tinea barbae lesion, showed poor improvement in their skin condition after the treatment. There was no case in which untoward effects due to the drug was observed. The

duration in which a complete cure from the disease was achieved in the 111 patients (Table No. 3) ranged from 1 to 7 weeks, but in the majority of the cases (76 or 69.7%) it was 3 weeks or less. The average time taken for cure was, however, 2.9 weeks only.

Recurrences of lesions by the same pathogen, at the same site from which they were recovered earlier before the start of Clotrimazole treatment have so far been observed in 17 (15.3%) out of the 111 cured patients. These recurrences in the completely cured cases occurred 4 to 78 weeks after the discontinuation of Clotrimazole treatment (Table No. 4). All these 17 patients were, however, retreated successfully with Clotrimazole cream.

2. Treatment in Candidiasis of Skin

Ten cases of candidiasis of skin were treated. The distribution of lesions, and the results of the treatment in these 10 cases are summarised in Table No. 5. Out of the 10 cases treated with this drug, 9 patients got cured, and the 10th patient, though given treatment for 11 weeks did not show complete disappearance of the lesions. The duration in which complete cure was achieved ranged from 1 to 6 weeks, with the average time being 3.5 weeks only.

3. Treatment in Candidiasis Vaginitis

The results of the treatment in 10 patients of candidiasis vaginitis are given in Table 6. All the patients treated got cured in 2 to 4 weeks after the start of treatment, with the average duration of cure being 2.6 weeks only. Mycologically, 7 patients became negative for *Candida* after one week, and the rest of the 3 patients, after 2 weeks of the start of the treatment. Discharge from the vagina, which was present before treatment in all the 10 cases, disappeared after one week in 8 cases. However, slight discharge continued in

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TABLE 2

Results of the topical treatment of dermatophytoses with Clotrimazole cream

Type of tinea manifestation, and number (per cent) of patients	Species isolated, from number of patients	Improvements in number of patients :				Duration of cure in weeks
		Cured	Good	Poor	Nil	
Tinea corporis, 44 (36.9)	T. rubrum, 26	25	1	—	—	1—4
	T. violaceum, 4	4	—	—	—	1—4
	E. floccosum, 3	3	—	—	—	2—4
	M. gypseum, 1 nil*, 10	1 10	— —	— —	— —	2 1—4
Tinea cruris, 44 (36.9)	T. rubrum, 30	30	—	—	—	1—7
	T. violaceum, 1	1	—	—	—	3
	E. floccosum, 7 nil*, 6	7 6	— —	— —	— —	2—3 1—6
Tinea corporis + tinea cruris, 20 (16.8)	T. rubrum, 15	14	1	—	—	1—6
	T. mentagrophytes, 1	1	—	—	—	3
	E. floccosum, 1 nil*, 3	1 2	— 1	— —	— —	1 1, 4
Tinea pedis, 6 (5.0)	T. rubrum, 1	—	1	—	—	—
	E. floccosum, 1 nil*, 4	1 3	— 1	— —	— —	5 2—4
Tinea manus, 2 (1.6)	T. rubrum, 2	2	—	—	—	2, 3
Tinea corporis + tinea capitis, 1 (0.8)	T. violaceum, 1	—	1	—	—	—
Tinea cruris + tinea pedis, 1 (0.8)	T. rubrum, 1	—	1	—	—	—
Tinea pedis + tinea manus + tinea barbae, 1 (0.8)	T. rubrum, 1	—	—	1	—	—
Total: 119	T. rubrum, 76	71	4	1	—	1—7
	T. violaceum, 6	5	1	—	—	1—4
	T. mentagrophytes, 1	1	—	—	—	5
	E. floccosum, 12	12	12	—	—	1—5
	M. gypseum, 1 nil*, 23	1 21	— 2	— —	— —	2 1—6
Grand total:	119	111	7	1	—	1—7
Percent:	100	93.2	5.8	0.8	—	—
Average time for cure (weeks):		2.9				

* KOH positive for fungus but no dermatophyte isolated in culture.

2 patients even beyond 3 weeks, though mycologically these patients were negative for *Candida*. The slight discharge in these 2 cases might have been due to causes other than candidiasis. The other two clinical symptoms i.e. itching and soggness at the site of lesion, also disappeared within 3 weeks after the start of the treatment with this drug. Reappearance of infection was reported in one out of the 10 patients treated.

TABLE 3

Results showing duration in which cure was achieved in patients of dermatophytoses after treatment with Clotrimazole.

Weeks after treatment	Patients cured	
	Number	Percent
1	8	7.3
2	34	31.2
3	34	31.2
4	27	24.8
5	2	1.8
6	3	2.8
7	1	0.9
irregular	2	—
Average duration (weeks) for cure: 2.9		

4. Treatment in Tinea Versicolor

The results of the treatment in this mycoses are given in Table 7. Out of the 33 patients treated, 22 (66.6%) got cured, whereas the remaining 11 showed improvement in their skin condition. The duration of treatment in these cases was usually 6 weeks only. Mycologically, 29 (87.8%) of the 33 patients became negative for fungus in KOH

TABLE 4

Recurrence of dermatophytoses in cured patients after discontinuing treatment with Clotrimazole

Recurrence after weeks	Number of patients
4	1
8	1
9	2
12	1
13	1
26	4
32	2
34	2
48	1
52	1
78	1
Total	17

preparations within 2 weeks, and the remaining 4, by 3 weeks of the start of the treatment. Similarly, the furfureaceous scaling at the lesions disappeared in most of the cases, i.e. 22 (66.6%), by 2 weeks, and in the remaining cases, in 3 to 4 weeks. Hypopigmentation, the chief complaint of the patients, however, took a longer period to disappear. In 14 weeks of observation it disappeared in 22 patients only, and the rest of the 11 patients continued to show it even after this period, though during all these weeks the scrapings from the lesions remained negative for the hyphae/spores of *Malassezia furfur* in KOH preparations. Reappearance of hypopigmented scaly lesions was observed, in 4 out of the 22 cured patients, after discontinuation of Clotrimazole treatment. The

TABLE 5

Results of the treatment of candidiasis of skin with Clotrimazole cream

Site of lesion	Total No. of cases treated	No. of patients showing improvements :				Duration for cure in weeks	
		Cured	Good	Poor	Nil	Range	Average
Groins	6	6	—	—	—	1-6	3.0
Toe-webs	3	2	1	—	—	3, 5	4.0
Axilla	1	1	—	—	—	6	6.0
Total	10	9	1	—	—	1-6	3.5

skin scrapings from the lesions in these patients were once again found to be positive for hyphae and/or spores of *M. furfur* in KOH preparations.

TABLE 6
Results of the treatment of candidiasis vaginitis with Clotrimazole

Weeks after start of treatment	Number of patients showing disappearance of:				
	Candida in KOH and Culture	Discharge	Itching	Soggyness	
1	7	8	3	2	
2	3	—	5	4	
3	—	—	2	4	
4	—	2	—	—	

TABLE 7
Results of the treatment of tinea versicolor with Clotrimazole Cream

Weeks after treatment	Number of patients showing disappearance of:		
	Fungus in KOH	Scaling	Hypo-pigmentation
1	14	6	—
2	15	16	1
3	4	3	3
4	—	8	2
5	—	—	1
6	—	—	6
7	—	—	2
8	—	—	1
9	—	—	2
10	—	—	1
11	—	—	1
12	—	—	—
13	—	—	1
14	—	—	1
Total	33	33	22

Discussion

The results of the present study are in conformity with the results obtained earlier by various other workers⁸⁻¹⁷ showing Clotrimazole to be good in the topical treatment of various superficial

mycoses of man. However, these results are not in agreement with the results obtained by Poleman^{1,2} who has reported excellent (100% cure rate) results in the treatment of tinea versicolor with Clotrimazole. It may be added here that, whereas all the currently used anti-fungal remedies are specific in their action, i.e. Griseofulvin and Tolanafate for dermatophytoses, and Amphotericin B and Nystatin for yeast fungi, Clotrimazole possesses a true broad spectrum activity against both the filamentous and yeast like fungi. Interestingly, the results of the double blind clinical trials conducted with Tolanafate in dermatophytoses¹⁴, and with Nystatin in candidiasis^{15,16,17}, have shown that Clotrimazole treatment was even more efficacious than Tolanafate treatment in dermatophytoses, and Nystatin treatment in candidiasis.

Reappearance of lesions, in cured patients, after discontinuing treatment with Clotrimazole, as was observed during this study, has also been reported earlier by Gip¹⁰ and Polemann¹². However, it could not be ascertained during this study, if the reappearance of superficial mycotic lesions was due to recurrence of earlier infection or a fresh infection.

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TRUE

In 1930, Kuzrok and Lieb, 2 New York gynecologists described the muscle-stimulating actions of seminal fluid on the human uterus. In the mid 1930s Goldblatt in England and Von Euler in Sweden independently described some of the actions of seminal plasma on smooth muscle. Von Euler obtaining his material from seminal fluid and from lipid extracts of sheep vesicular glands, coined the term prostaglandins. Although use of the misnomer has continued, it is now known that prostaglandins are present in most biological tissues and fluids. It is evident from accumulating evidence that the prostaglandins may be of profound clinical importance in Dermatology. It is possible that inhibitors of prostaglandin synthesis or prostaglandin antagonists or specific combinations of both types of compounds may become important adjuncts in the treatment of cutaneous inflammatory diseases.