A single blind study of 20 patients with superficial fungal infections

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INTRODUCTION

A frequent dermatological condition involves dermatophytic infection of the skin. Some of the most commonly seen are those labeled as Tinea Pedis (athlete's foot), Tinea Corporis (ringworm of the body) and Tinea Cruris (jock itch), and these are the conditions of interest in this study. The primary genera of fungal organisms that are involved are Microsporum, Trichophyton and Epidermophyton.

Until quite recently, treatments have variously included Benzoic Acid ointment (Whitfield's Ointment), Castellani's Pant (Magenta paint) and Tolnaftate, as well as many varieties of dusting powders. These have given reasonable results, but with the advent of the imidazole type drugs, treatment has become effective, safe, non-irritant and non-staining or messy.

Two of these drugs of proven effictivity are miconazole and clotrimazole.

The purpose of this study is to compare a commercially available formulation containing miconazole nitrate (ins a cream base) with a formulation containing miconazole nitrate in a special lipid containing cream emulsion base (developed by MeyerZall Laboratories). The comparison will be made on the basis of effictivity of amelioration of symptoms and the time taken under treatment for the disappearance of symptoms.

MEDICATION

The pharmacological action and efficacy of miconazole is well known and documented. At certain rising concentrations it is capable of inhibiting not only the organisms mentioned above but also others such as Candida, Cryptococcus and Torulopsis as well as certain species of Histoplasma, Aspergillus and Nocardia. Additionally certain bacterial organisms such as Staphylococci and Streptococci are also susceptible to miconazole.

The active agent has been incorporated into a vehicle that contains certain essential fatty acids (EFAs), I particular linoleic acid (LA) and alpha linolenic acid (ALA).

The rationale of inclusion of these EFAs is:

- Both LA and ALA are precursors for the anti-inflammatory prostaglandins PGE1 and PGE3. The formation of these prostaglandins also limits the production of pro-inflammatory eicosanoid (PGE2 and leukotriene LTB4). The net effect is that any existing inflammation and/or itch accompanying the fungal infection will be reduced.
- LA and ALA are also involved in the maintenance of normal skin hydration that would assist in controlling the dryness and scaling of the condition.
- PGE1 and PGE3 resulting from the EFAs in the formulation (especially PDE1) are known to affect lymphocyte function. It is hypothesised that this may contribute to the improved efficacy of the product.

PROTOCOL

20 patients were selected having Tinea Pedis, Tinea Cruris or Tinea Corporis. The patients were included in the study if they had suffered with any of the above on a recurrent (chronic) basis.

Only macroscopic evaluations were made and therefore any patients with positively diagnosed psoriasis, pityriasis rosea, contact dermatitis or eczema were excluded so as not to be misdiagnosed.

Affected area and symptoms were noted at the beginning, before treatment was commenced and then assessments were done every week until the condition cleared, worsened or the patient withdrew. Treatment was continued for 4 weeks, but patients who were clear on or before this time were advised to continue for at least 7 days after disappearance of the symptoms, in an effort to prevent recurrence.

At the end of the 4-week period the trial was deemed complete and the study unblended.

Severity of symptoms (itch, scaling and inflammation) was rated as:

4 = very severe
3 = severe
2 = moderate
1 = mild
0 = cleared

The patients were supplied with a coded (unnamed) jar containing 50g of the experimental product of the commercially available product, and instructed to apply the product twice daily after washing and thoroughly drying the affected area.

For purposes of statistical evaluation, the patients using the **experimental product** were labeled as the **Experimental Group** and those using the **commercially available product** as the **Control Group.**

RESULTS

The results, as reflected in Tables1-3 and Fig.1 indicate that:

1. In the Experimental Group, 2 patients (20%) were clear after the first week. There were no patients clear at this point in the Control Group.
2. After 2 weeks only 2 patients (20%) in the Experimental Group had not completely cleared. In the Control Group 7 patients (70%) still experienced symptoms.
3. After three weeks only one patient in the Experimental Group was still affected. In the Control Group, 4 patients were still experiencing symptoms at this time.
4. At the 4th week's evaluation, only one patient in the Experiential Group still experience symptoms, the same patient in (3) above. In the Control Group one patient was still experiencing the same level of symptoms and another's symptoms worsened.

COMMENTS

1. Of the 20 patients, treatment was deemed unsuccessful in only one. This patient presented with an infection of the groin area and was from the Control Group. It was found that he was infected with T Rubrum, known to be difficult to treat, and neither treatment would have had better results. The patient was subsequently put on the additional medication (systemic).
    a. One patient from the Experimental Group was not clear at the four-week mark. This patient initially presented with T Cruris and although not clear of infection the treatment had brought better control and the symptoms had decreased. Contact was subsequently lost with this patient.
    b. Another patient in the Control Group was also not clear at the four-week mark. This patient also initially presented with T Cruris and although not clear of infection the treatment had brought better control and the symptoms had decreased.
    c. On closer inspection, three of the four patients presenting with T Cruris was not clear after 4 weeks. This may suggest that treatment in the area should be prolonged.
2. No irritation or other side effects were noted with either medication.
3. Whereas treatment in both groups could be seen as successful, it is important to note that that in the Experimental Group 20% of the patients were clear at one week and 80% were clear at two weeks. In the Control Group only 30% was clear at the two-week mark and 60% clear at the 3-week mark.
4. It is clear from these results that with he formulation known as Covarex, a reduction of symptoms and elimination of the infection is more rapid and this then tends to support the principle of synergy between the Imidazole active and the other parts of the formulation.

Table 1. Control Group (Daktarin)

Patient No.	0	1 W	2 W	3 W	4 W
1	4	4	2	0	
2	3	2	1	1	0
4	3	2	1	1	0
6	3	1	0		
9	1	1	1	0	
13	3	2	1	1	1
15	3	2	0		
16	4	2	1	1	2
18	3	2	1	0	
19	3	2	0		

Table 2 Experimental Group (Covarex)

Patient No.	0	1 W	2 W	3 W	4 W
3	4	2	0		
5	3	1	0		
7	2	2	1	0	
8	1	0			
10	2	1	0		
11	4	2	0		
12	3	2	0		
14	3	3	1	1	1
17	4	1	0		
20	2	0			

Table 3. Efficacy and Time to Clearance: Experimental Product vs. Control Product

Time Lapse	1 Week	2 Weeks	3 Weeks	4 weeks
Experimental. Product	2	8	9	9
Control Product	0	3	6	8

Fig 1. Efficacy and Time to Clearance:
Experimental Product vs. Control Product