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Symptomatic Assessment of Miconazole Cream in the Treatment of Tinea Pedis

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Introduction

Tinea pedis (athlete's foot), although a well recognized condition, presents some difficulties to investigators undertaking clinical studies. Classically, athlete's foot has been treated with antifungal compounds. However, rigorous attempts to recover dermatophyte fungi from lesions clinically defined as athlete's foot have yielded disappointing results. In five typical studies (Marples and Chapman 1959, Marples and Bailey 1957, Ajello, Keeney & Brogles 1945, MacGregor Edwards 1978, and Taylor *et al* 1978), fungal recovery rates of between 25% and 50% from clinically affected patients have been reported. Leyden and Kligman (1975) attribute these observations to bacterial colonization, of a fungal lesion, finally driving out the fungus.

Furthermore, purely physical conditions such as the choice of footwear can markedly influence the incidence of athlete's foot. The choice of more open footwear by women is accepted as the reason why this condition is very much a male phenomena. A study by Nickerson, Irving and Mehmert (1945) of soldiers under sub-tropical conditions has shown that athlete's foot improves markedly when the footwear is changed from boots to sandals.

Clinically, athlete's foot is very variable as regards both type and severity of lesions. Peeling of skin, erythema, maceration, pruritis, weeping and fissuring are all associated symptoms. The condition can vary from a slight itching and peeling of skin from the toe-webs to marked maceration accompanied by weeping or even bleeding.

It must be accepted that clinically athlete's foot is a heterogenous condition where environmental factors such as the type of footwear combine with biological factors (infection with pathogenic micro-organisms). This situation has presented difficulties to investigators seeking to define the performance of chemotherapeutic agents used in the treatment of athlete's foot.

The response of many investigators is to select only patients with a mycologically proven fungal infection (Zarowny, Rogers & Tindall 1975, Gentles, Jones & Roberts 1975, Male 1974) when testing antifungal compounds for efficacy in the treatment of athlete's foot. This restrictive approach will not necessarily define the activity of a drug in treating clinically diagnosed athlete's foot not proven to be infected with dermatophyte fungus.

For these reasons the current study was an attempt to monitor only the symptomatic response of athlete's foot to antifungal therapy. Miconazole nitrate cream (Daktarin*) was chosen as a modern imidazole antifungal agent with broad spectrum activity against

*Daktarin cream: Janssen Pharmaceutical Ltd.

pathogenic fungi (yeasts and dermatophytes) and many Gram-positive bacteria (Brugmans, Van Cutsem & Thienpont 1970). A number of studies (Gentles *et al* 1975, Brugmans *et al* 1970, and Botter 1971) have reported successful treatment of tinea pedis with miconazole.

Materials and Methods

Patients presenting at the medical centre of 15 collieries in the West Midlands coal fields entered the study. The criterion for inclusion in the study was the clinical diagnosis of athlete's foot. This diagnosis was based on the presence of one or more of the following signs and symptoms – pruritis, skin maceration, weeping or bleeding, erythema and peeling of the interdigital spaces.

On entry into the study patients were given miconazole nitrate cream 2% (w/v) supplied as commercial Daktarin cream. Patients were instructed to rub the cream well into the affected areas night and morning for 14 days. Clinical assessment was repeated after 14 and 21 days.

Results

329 patients entered the study; they contributed a total of 548 affected feet for analysis. The incidence and severity of the presenting symptoms are given in Table 1. As was to be expected pruritis and peeling were by far the most common symptoms; almost 80% of the infected feet had skin peeling and 80% of the patients complained of pruritis.

Following treatment the change in the states of the lesions is listed in Table 2. The average clearance rates after 14 days for all signs and symptoms was 63% whereas after 21 days the average was 79·1%. For all symptoms excluding weeping and bleeding there was a statistically significant ($p<0·05$) increase in the clearance rate 7 days after the completion of treatment.

A recent study (MacGregor Edwards 1978) in the same mining population has revealed a 50% incidence of proven dermatophyte infections in individuals suffering from athlete's foot. If these figures are projected to this study it is difficult to see how clinical treatment success can be as simple as the chemotherapeutic removal of dermatophytes.

Leyden and Kligman's attractive hypothesis of bacterial superinfection eventually driving out dermatophytes has recently been supported (Taylor *et al* 1978). The findings of this paper support this hypothesis as miconazole nitrate possesses activity against the yeasts and Gram-positive bacteria which could be expected to superinfect the lesions of athlete's foot.

Until quantitative studies of other microbiological flora of athlete's foot lesions are performed the role of bacteria and yeasts in pathogenesis must remain as speculation. However, it is likely that broad spectrum anti-infective preparations such as miconazole nitrate owe their success in the treatment of athlete's foot to their activity against Gram-positive bacteria as well as to their antifungal properties.

Table 1

Presenting signs and symptoms

Symptom/sign	*Absent*	*Slight*	*Moderate*	*Severe*	*Total with symptom*	*Total*
Peeling	117	263	144	24	431 (78·7%)	548
Maceration*	240	175	112	21	308 (63·3%)	548
Erythema	322	147	55	24	226 (41·2%)	548
Fissures	245	176	110	17	303 (55·3%)	548
Weeping/Bleeding	420	77	46	5	128 (23·4%)	548
Itching/Burning*	64	131	102	32	265 (80·6%)	329

*refers to numbers of patients; other data refers to numbers of affected feet.

Table 2

Change in status of symptoms and signs following treatment

Symptom	*Change*	*After 14 days* %		*S.E.*	*After 21 days* %		*S.E.*
Peeling	Worse	5·7		1·13	2·0		0·70
	Same	26·8		2·16	17·3		1·89
	Improved	18·5	67·5	1·89	8·0	80·7	1·36
	Cleared	49·0		2·43	72·7		2·23
Maceration	Worse	4·1		1·15	3·1		1·02
	Same	22·0		2·41	10·8		1·83
	Improved	16·5	73·9	2·16	7·0	86·1	1·51
	Cleared	57·4		2·87	79·1		2·40
Erythema	Worse	6·5		1·67	3·9		1·35
	Same	16·6		2·53	7·2		1·80
	Improved	11·0	76·9	2·12	5·8	88·9	1·62
	Cleared	65·9		3·22	83·1		2·60
Fissures	Worse	4·5		1·21	4·9		1·27
	Same	17·5		2·22	12·5		1·95
	Improved	13·0	78·0	1·97	4·5	82·6	1·22
	Cleared	65·0		2·79	78·1		2·44
Weeping/ Bleeding	Worse	6·2		2·12	5·7		2·10
	Same	10·9		2·74	5·7		2·10
	Improved	5·4	82·9	1·99	4·1	88·6	1·80
	Cleared	77·5		3·68	84·5		3·28
Itching/ Burning	Worse	5·0		1·40	4·7		1·39
	Same	18·2		2·48	13·8		2·26
	Improved	13·6	76·8	2·20	4·7	81·5	1·39
	Cleared	63·2		3·10	76·8		2·77

Discussion

The study has clearly demonstrated the efficacy of miconazole nitrate cream in controlling the symptoms of athlete's foot. After two weeks' treatment an average of 63% of all symptoms were cleared. No particular symptom was more resistant to treatment than the rest, an observation which is in contrast with the recently published findings of Taylor *et al* (1978) in a study of athlete's foot in steel-workers. These investigators noticed that skin peeling in the toe-web was rather more difficult to resolve than the other symptoms.

Of particular interest is the way in which all the symptoms continued to improve in the week following completion of the 14 day course of treatment. By the end of this week the average symptom cure rate had risen from 63% to 79%. This finding is surprising in view of the fact that coal miners are subject to high risk of re-infection from the communal bath sites which are thought to act as reservoirs of dermatophyte spores (MacGregor Edwards 1978, Gentles & Evans 1973).

Part of the effect seen could be due to increased attention to foot hygiene during treatment and to the qualities of the cream base. However, this would not explain how success could be maintained after completion of therapy, let alone the continued improvement.

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