A novel two-step kit for topical treatment of tinea pedis – an open study

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Abstract

Background Tinea pedis is a common skin disease affecting most of the population during their lifetime. Topical and systemic treatments give only temporary relief.

Objective To evaluate the efficacy and safety of a new topical treatment for moderate-to-severe tinea pedis.

Methods Fifty patients suffering from tinea pedis were treated in two stages: the active stage – single use of the novel topical solution for 45 min and novel cream twice weekly for 4 weeks; the preventive stage – cream application once weekly for 10 months.

Results Forty-five patients completed the active stage and achieved 76% cure rate. The medication was well tolerated; one patient dropped from the study because of very mild irritation. No other topical or systemic side effects were noted. Another five patients were lost to follow-up during the preventive stage. The total cure rate after the preventive stage was 70%.

Conclusions This novel treatment was found to be effective, well tolerated and safe in the treatment of moderate and severe tinea pedis during the active and the preventive stages.

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Keywords
tinea pedis, topical treatment

Conflict of interest

None declared.

Introduction

Tinea pedis is a common fungal infection in adults, affecting between 30% and 70% of the population.1,2 It often develops in persons with hyperhidrosis,3 particularly among men between 20 and 40 years of age.4 Elderly, diabetic and immunocompromised patients are also at risk.4 The aetiological pathogens most commonly associated with tinea pedis are Trichophyton rubrum, Trichophyton mentagrophytes and Epidermophyton floccosum.1–5

Fungal infection has a tendency to colonize the outer layer of the skin, the stratum corneum. This layer serves as a reservoir of food for fungi. Under conditions of moisture and the warm environment of the soles, the reaction between the fungus and the stratum corneum produces a foul smelling odour. Itching, especially between the toes, is a very common complaint.3

Following effective treatment, patients return after several weeks to months with the same complaint; therefore, preventive treatment is required. In this study, we evaluated the efficacy and safety of a new topical antifungal medication.

Patients and methods

Patients

Fifty patients, males and females suffering from moderate-to-severe tinea pedis (moccasin type, interdigitalis type and vesiculobulous type) confirmed by mycological direct smear and culture were enrolled in the study. Patients suffering from diabetic or stasis ulcers, peripheral vascular diseases or plantar keratoderma including psoriasis were excluded. Pregnant and lactating women were also excluded. All patients stopped any topical or systemic antifungal treatment 4 months before entering the study. Patients known to have an allergy to at least one of the components of the medication were also excluded.

Tinea pedis was confirmed by both KOH examination and mycological cultures of samples taken from the affected skin. Samples were divided into two parts; one was used for direct KOH examination and the second for fungal culture using Sabouraud’s Dextrose Agar (Novamed, Jerusalem, Israel) that contains...
chloramphenicol and penicillin to prevent bacterial contamination. Identification of the fungus is done on the basis of microscopic morphological characteristics of the different fungi.

The medication

The medication used in our study was a two-step kit: Pedicure™ Solution & Pedicure™ Cream (Pedicure Ltd., Tel-Aviv, Israel). The active ingredients in the solution were 0.5% climbazole and 14% glycolic acid 70%, and in the cream 0.5% climbazole and 2% urea.

Study design

The study was conducted according the rules of the local Helsinki Committee and all patients provided written informed consent before enrolment.

Classification of the severity of the disease was based on a 0–3 score of the parameters used by de Chauvin et al.6; 0 = none, 1 = mild, 2 = moderate, 3 = severe. The score was based on clinical signs and symptoms (erythema, desquamation, pruritus, pustules, vesiculation and incrustation) scored by the investigator using this four-point scale.

Treatment was divided into two stages: active and preventive.

Active stage. A single treatment with the solution (Pedicure solution); patients were instructed to put their feet in plastic bags filled with the solution for 45 min after which the feet were dried with a towel. The cream (Pedicure cream) was applied twice weekly for 4 weeks overnight for 6–8 h. The patients were asked to record any topical and/or systemic side effects that appeared during treatment.

After 4 weeks of treatment (the active stage), the patients were re-examined clinically and mycologically (KOH examination and fungal culture) by the same physician; the improvement grade and side effects were evaluated.

Preventive stage. After the active stage, the cream was applied once weekly for 10 months. Patients were evaluated (clinically and mycologically) at the end of this preventive stage.

Each patient was assessed using the following score: total cure – both clinical and mycological cure; marked improvement – more than 75% clinical cure; moderate improvement – 50–74% clinical cure; mild improvement – 25–49% clinical cure; and failure – in cases of 0–24% change. Worsening – if the clinical findings worsen compared with baseline.

Results

Of 50 patients, 24 men (mean age 42.5 years) and 26 women (mean age 47.1 years), suffering from moderate-to-severe tinea pedis, 45 patients completed the active stage, four patients did not return for follow-up and one patient experienced slight stinging after 20–30 min of treatment with the solution and discontinued the treatment. Of the 45 patients who completed the first stage, 38 patients (76%) had complete cure, two patients had marked improvement, three patients had moderate improvement and two patients had mild improvement of their soles’ skin condition (Table 1).

Ten months later (after the preventive stage), the patients were re-examined and the findings were as follows: 35 (70%) patients had no pathological finding – mycological analyses were negative (Fig. 1), 1 (2%) patient had slight dryness – mycological analysis was negative for both direct smear and culture. Four (8%) patients had recurrence of the both clinical and mycological findings. Five patients were lost to follow-up (Table 2).

<table>
<thead>
<tr>
<th>Table 1 Results of treatment at the end of the active stage</th>
<th>Number (%)</th>
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<tbody>
<tr>
<td>Entered the study</td>
<td>50 (100)</td>
</tr>
<tr>
<td>Completed active stage</td>
<td>45 (90)</td>
</tr>
<tr>
<td>Complete cure</td>
<td>38 (76)</td>
</tr>
<tr>
<td>Marked improvement</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Moderate improvement</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Mild improvement</td>
<td>2 (4)</td>
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</table>

| Figure 1 Clinical picture showing results of treatment. |

<table>
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<tr>
<th>Table 2 Results of treatment at the end of the preventive stage</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entered the study</td>
<td>50 (100)</td>
</tr>
<tr>
<td>Completed active stage</td>
<td>45 (90)</td>
</tr>
<tr>
<td>Completed preventive stage</td>
<td>40 (80)</td>
</tr>
<tr>
<td>Cured</td>
<td>35 (70)</td>
</tr>
<tr>
<td>Slight dryness</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Recurrence</td>
<td>4 (8)</td>
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</tbody>
</table>
Discussion
In tinea pedis, the fungal infection is localized in the stratum corneum, which serves as reservoir of food for fungi. Most of the topical agents used in the treatment of tinea pedis usually have only fungicidic or fungistatic properties. The two-step kit used in our study was composed of two types of active ingredients: antifungal – climbazole, and keratolitic agents glycolic acid and urea, which were used to remove scales of stratum corneum.

Climbazole (1-(4-chlorophenoxy)-1-(imidazole-1-yl) 3,3-dimethylbutan-2-one) is an imidazole antifungal. Azole antifungals prevent the synthesis of ergosterol, the major sterol component of fungal plasma membranes, by inhibiting the cytochrome P450 (CYP450)-dependent enzyme lanosterol 14-α-demethylase. The subsequent depletion of ergosterol interferes with the structural function of fungal membranes leading to leakage of cell contents. The net result is an inhibition of fungal growth and replication.7,8 Secondary effects, such as inhibition of the morphogenetic transformation of yeasts to the mycelial form, decreased fungal adherence and direct toxic effects on membrane phospholipids have been reported in the literature.9 As azole antifungals, at therapeutic concentrations, bind more tightly to the fungal CYP450-dependent enzyme lanosterol 14-α-demethylase than to the mammalian enzyme,7 these compounds are considered safe for a variety of human uses.

The results of this study indicate that the above outlined treatment was satisfactory in the treatment of fungal infection of the soles during both active and preventive stages. The treatment was well tolerated and no significant side effects were noted. Compliance with treatment is enhanced by the fact that the treatment regimen does not require daily application of the drug. This novel treatment was based on combined antifungal compounds and keratolitic agents, which probably acted synergistically.

Tinea pedis is extremely difficult to eradicate, as there are persistence conditions, mainly maceration, continuous use of topical antifungal medication is effective as a preventive therapy against recurrences.10 Patel et al.11 reported that topical treatment of tinea pedis with terbinafine and clotrimazole showed good efficacy of 75–80%, but the relapse rate in patients treated with terbinafine was 15% and among clotrimazole patients, it was 19%. Savin and Jorizzo12 found that sertaconazole nitrate cream gave 70% mycological cure after 4 weeks of treatment, but 2 weeks after cessation of treatment only 47% remained mycological cure. This finding stressed the need of prophylactic use of topical antifungal treatment. In our study, we showed similar cure rates at the end of the active stage of treatment, but prophylactic use of the medication reduced recurrences.

References