Report

Efficacy of triclosan soap against superficial dermatomycoses: a double-blind clinical trial in 224 primary school-children in Kilombero District, Morogoro Region, Tanzania

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Registered trade names for triclosan
Ciba® Irgacare® MP
Ciba® Irgasan® DP 300

Abstract

Background Superficial dermatomycoses are a common problem in tropical regions. Due to limited resources, specific antimycotic therapy is often not available. The present study was performed to assess the clinical efficacy of the antimicrobial agent Triclosan in bar soap in comparison with regular soap against selected superficial dermatomycoses in Tanzanian schoolchildren.

Methods 820 primary school children were examined for skin disorders and 224 of these were included in the soap trial. The clinical presentation of dermatomycoses was recorded using a symptom score. Samples were taken for microscopic examination and mycological culture. The study participants received either bar soap containing Triclosan or a placebo for 2 months. They were re-examined at the end of this period.

Results The benefit achieved by the addition of Triclosan was not statistically significant. Overall cure rates for Triclosan and placebo groups taken together were 21.8% for tinea versicolor, 58.3% for tinea capitis, 55.5% for tinea corporis and 68.8% for tinea pedis. This was confirmed microscopically. For the majority of the children the dermatomycoses improved significantly.

Conclusions The results strongly argue for regular soap use against common dermatomycoses as a low-cost and effective treatment. This promising finding should be considered in settings where dermatophyte infections represent a public health problem and where access to appropriate treatment and financial resources are limited.

Introduction

Superficial dermatomycoses are very common in tropical countries.[1] This is the consequence of favorable growth conditions as well as poor hygiene and poor education. Conditions such as crowding in households, sharing of fomites, and close contact with infected individuals also contribute to the high prevalence of superficial mycoses in tropical regions.[1–5]

As a result of limited resources, specific antimycotic treatment is often not locally available.

The antimicrobial effects of various endogenous peptides, such as β-defensins and cathelecidins, have been demonstrated to play an important role in innate skin defense against fungal and bacterial skin infections.[6–9]

The present placebo-controlled, double-blind clinical trial aimed to assess the clinical efficacy of triclosan 1% in bar soap against selected superficial dermatomycoses, and the overall effect of regular soap use. Triclosan shows broad-spectrum *in vitro* antimicrobial activity against most bacteria, certain molds, and yeasts, and has anti-inflammatory properties.[10–13] It has no *in vitro* efficacy against *Malassezia furfur*, a common fungal element in warm and humid areas. So far, triclosan has not been tested *in vitro* against any other pathogenic *Malassezia* species. Triclosan products for topical use are available in many countries and are widely used because of triclosan's persistent antimicrobial activity.[14] They have not yet been tested as a treatment for superficial dermatomycoses.

Study area, patients, and methods

Two primary schools near Ifakara town center, an area with previously important prevalence rates of skin disorders amongst school-children, were selected for the study;[15] 820 children aged 6–19 years (mean age, 11.6 years; 52.0% male, 48.0% female)

were examined by a team consisting of the local dermatologist, a clinical officer, and two medical students. Interviews and examinations were conducted in Swahili. The baseline examination was performed in April–May 2003. It consisted of the following: (i) a complete body examination; (ii) history taking and documentation of the clinical presentation of skin disorders applying case definitions; (iii) digital photographic documentation; (iv) sample taking (skin scrapings and/or hair clippings) and microscopic examination at local laboratory facilities using 20% potassium hydroxide (KOH) solution.[16]

The following parameters were assessed during screening and follow-up and were used for evaluation: degree of pruritus, number of lesions, and the size of the largest lesion. These parameters were used to calculate a clinical score to assess the overall degree of infection.[16]

All laboratory, clinical, and photographic documents were reviewed by an expert dermatologist (P. Schmid-Grendelmeier) for quality assurance. Inclusion criteria for the soap trial were clinically diagnosed tinea versicolor, capitis, corporis, or pedis and verbal informed consent obtained from the carers.

Thirty-four of the 278 children affected by dermatomycoses could not be admitted to the soap trial because of the following exclusion criteria: their skin disorder required immediate treatment, or treatment other than the soap had been administered. Twenty children were excluded during or after the trial because of the following exclusion criteria: their skin disorder required immediate treatment, they had received their soap less than four times, or they had been lost to follow-up. The study participants were randomly assigned to receive either soap containing triclosan or placebo soap for 2 months (see Table 1). Soap bars were replaced weekly by the principal investigator. Study participants were instructed in the presence of their carers by a clinical officer, a native Kiswahili speaker, to wash the whole body, including the head and hair, at least once per day using the study soap.

Follow-up was performed in July 2003 after 2 months of soap use and consisted of the repetition of steps (i)–(iv) as described above. During follow-up, subjective improvement was assessed by asking the children if they had experienced improvement of their skin disorder; 224 children remained for statistical evaluation.

Mycologic culture and determination of minimal inhibitory concentrations (MICs)

In the case of an uncertain microscopic diagnosis, samples were sent to the Mycology Laboratory at Zurich University Hospital for repeat microscopy and mycologic culture. Congo red stain was used for direct microscopy. Dixon agar, Sabouraud glucose agar, or mycosel agar was used for culture. *Malassezia* cultures were further examined microscopically. For species identification of dermatophytes, subcultures were prepared using phenol red agar and potato dextrose agar. The field study in Ifakara was followed by the *in vitro* assessment of the MICs of placebo soap and pure triclosan against *Malassezia* spp. at the same laboratory.

Table 1 Composition of placebo and active soap

Placebo (plain bar) soap	Active soap
0.2% titanium dioxide	0.2% titanium dioxide
0.023% tetrasodium EDTA	0.023% tetrasodium EDTA
3.0% stearic acid	3.0% stearic acid
0–5% glycerine/water 1 : 1	0–5% glycerine/water 1 : 1
q.s. dye/perfume	q.s. dye/perfume
ad 100.0% soap noodles*	ad 100.0% soap noodles*
	1.0% Irgasan DP 300

EDTA, ethylenediaminetetraacetate; q.s., as much as needed; ad, up to.
*Mettler Basic Soap: 80.0% sodium tallowate; 20.0% sodium cocoate.

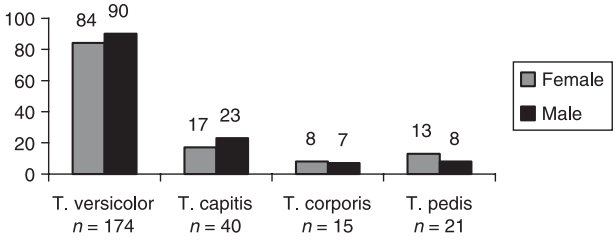

Figure 1 Number of cases according to sex amongst the 224 soap-treated children

Statistical analysis

Data were double-entered in FoxPro 2.6 (Microsoft, Seattle, WA, USA) and evaluated with STATA 8.2 (Stata Cooperation, College Station, TX, USA). Symmetry test, Wilcoxon's rank sum test, χ^2 test, Fisher's exact test, and the calculation of relative risk were used for analysis. The results of the symmetry tests were compared between the active and placebo groups using contingency tables, and testing these for difference of proportions using 95% confidence intervals.

Ethical considerations

The study protocol was approved by the ethical committees in Switzerland (Ethisches Kommittee Beider Basel) and Tanzania (Ethical Committee of the Ifakara Health Research and Development Center). Carers and study participants were provided with information about the skin disorders and the study procedures before being asked to give their verbal informed consent. Each individual who was not cured after follow-up received free treatment at the local district hospital.

Results

Of the 224 study participants (mean age, 12.4 years; 48.7% female, 51.3% male), there were 174 cases of tinea versicolor, 40 of tinea capitis, 21 of tinea pedis, and 15 of tinea corporis infection (see Fig. 1). Overall, tinea versicolor was the

Table 2 Number of samples (%) confirmed by microscopic examination during screening and follow-up (placebo vs. active soap)

	Tinea versicolor *n* (%)		Tinea capitis *n* (%)		Tinea corporis *n* (%)	
	Placebo	Active	Placebo	Active	Placebo	Active
Screening	47/58 (81.0)	55/68 (82.3)	9/21 (42.9)	14/18 (77.8)	5/7 (71.4)	5/6 (83.3)
Follow-up	35/77 (45.5)	39/76 (51.3)	8/17 (47.1)	5/14 (35.7)	1/7 (14.3)	4/7 (57.1)

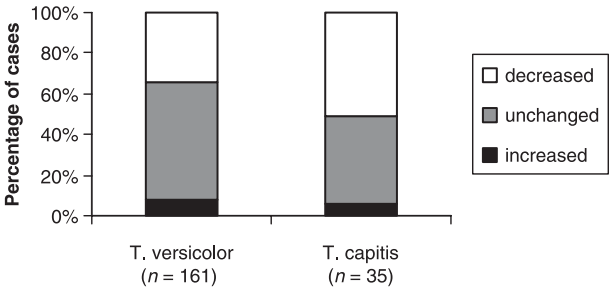

Figure 2 Degree of pruritus from screening to follow-up (after 2 months)

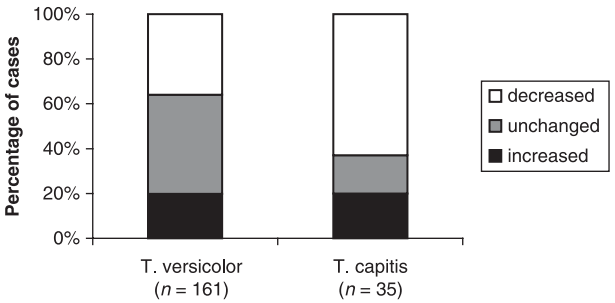

Figure 3 Number of lesions from screening to follow-up (after 2 months)

most common skin disorder, representing 70% of all fungal infections. Dermatophyte species identified by culture were *Trichophyton tonsurans*, *T. violaceum*, and *T. mentagrophytes*. Cultivation of *Malassezia* spp. was possible in one-third of the microscopically positive isolates.

If a child had two or more superficial dermatomycoses at the time of screening, each infection was regarded as a separate case.

Evaluation of the efficacy of triclosan soap

There was no significant difference between the active and placebo groups during follow-up after 2 months for any of the four forms of dermatomycoses.

In tinea versicolor, significant improvement was found in both groups for each parameter. In the other superficial dermatomycoses, triclosan soap was mildly superior for certain parameters: (i) in tinea capitis, it decreased the proportion of positive samples, whereas the placebo soap did not; however, the relative risk for a positive microscopic result did not differ significantly (see Table 2); (ii) in tinea corporis, triclosan soap decreased the average diameter of the largest lesion; however, Wilcoxon's rank sum test *P* value did not differ significantly for this parameter; (iii) in tinea versicolor, capitis, and corporis, deterioration was slightly more frequent in the placebo group; (iv) the cure rate of tinea pedis was slightly higher in the active group.

Evaluation of the efficacy of soap

As there was no significant difference between the active and placebo groups, the results of the two groups were combined to assess the overall effect of soap use on dermatomycoses. The typical signs and symptoms were reduced for all disorders from screening to follow-up. The degree of pruritus decreased significantly for tinea versicolor and tinea capitis; it also decreased in tinea corporis and tinea pedis (symmetry test *P* values: 0.000, 0.0098, 0.0916, and 0.2231, respectively; see Fig. 2).

The number of lesions decreased significantly for tinea versicolor, capitis, and corporis (symmetry test *P* values: 0.000, 0.0038, and 0.0460, respectively; see Fig. 3).

From screening to follow-up, the proportion of microscopically confirmed fungal infections was reduced from 81.0% (102/126) to 48.4% (74/153) for tinea versicolor, from 59.0% (23/39) to 41.9% (13/31) for tinea capitis, and from 76.9% (10/13) to 35.7% (5/14) for tinea corporis.

One hundred and ninety-seven of the 218 study participants (90.4%) reported a subjective improvement of their skin disorders with soap use. A comparison of the symptom score between screening and follow-up confirmed the significant overall improvement for tinea versicolor and capitis infections (*P* values of 0.000 and 0.0001, respectively; $P = 0.1718$ for tinea corporis) (see Fig. 4).

Thirty-five of the 161 children with tinea versicolor (21.8%), 58.3% (21/36) with tinea capitis, 55.5% (5/9) with tinea corporis, and 68.8% (11/16) with tinea pedis were cured after 2 months of soap use.

Determination of MICs

Neither placebo soap nor triclosan was found to show *in vitro* efficacy against *Malassezia sympodialis* originating from the laboratory in Zurich.

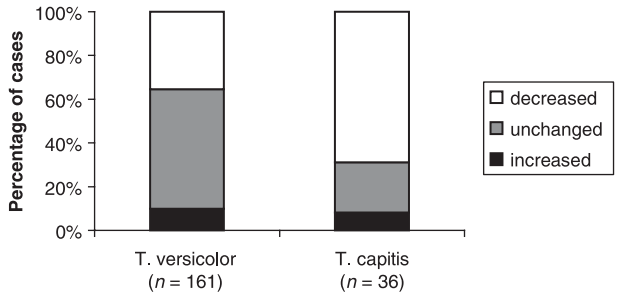

Figure 4 Overall degree of infection from screening to follow-up (after 2 months)

Discussion

Nine of every 10 study children reported a subjective improvement of their skin disorders with soap use. Soaps were well accepted and regarded as effective for reducing the most relevant complaints: cosmetic disturbance and pruritus. The degree of pruritus decreased significantly in all study participants.

The marked overall improvement in all the investigated dermatomycoses was also reflected by the objective parameters. Various clinical criteria, such as the number of lesions and the degree of pruritus, were reduced or disappeared in a large proportion of children. Improvement and cure rates were more striking for tinea capitis, tinea corporis, and tinea pedis than for tinea versicolor infections. The soap seemed to be more effective in less severe cases. The high cure rates in the present study confirm the findings of other authors: Improved hygiene may reduce the impact of dermatomycoses in Africa.[17–19]

Efficacy of triclosan soap

In spite of the anti-irritative and anti-inflammatory properties of triclosan soap, there was no significant difference between placebo and triclosan soaps with regard to pruritus, the general clinical score, the microscopic results, and the cure rates for all dermatomycoses.[12,20,21]

This may be explained by the application of triclosan as a "rinse-off" rather than a "leave-on" formulation, and the widespread use of petrolatum (vaseline) in the study population. This may have reduced the accumulation of triclosan on the skin.

The slightly superior efficacy of triclosan against tinea corporis and tinea capitis may be explained by its *in vitro* activity against dermatophytes such as *T. rubrum* and *T. mentagrophytes*. Nevertheless, the small sample sizes in the tinea corporis and tinea pedis populations mean that any conclusions drawn should be interpreted with caution. Bacterial superinfection in tinea capitis, corporis, and pedis may have been reduced by the soap's alkaline pH of 10, which has an antimicrobial effect.

In tinea versicolor, the repeated lack of an *in vitro* efficacy of triclosan against *Malassezia* correlates with the equal efficacy of both soaps.

Overall efficacy of soap

The decrease in pruritus observed for all four forms of dermatomycosis was probably the result of the decrease in the amount of irritants on the skin surface.

With regard to tinea versicolor, the growth of lipophilic *Malassezia* spp., which is usually enhanced by the amount of endogenous lipids[22,23] or the application of oily substances,[24–26] may have been reduced by soap use. In addition, the degree of occlusion of the skin by excessive amounts of lipids, affecting the carbon dioxide concentration and pH range, is likely to have decreased.[27–29] The use of keratolytic soaps has been recommended for the mechanical removal of infected scales.[30] A similar effect was possibly achieved by intense scrubbing with soap. The risk of spreading fungal elements to uninfected body sites and other individuals, and the chance of re-infection, may also have been reduced. In addition, asymptomatic dermatophyte carriers, for example of *T. tonsurans*, may possibly have been treated.[31–33] The antimicrobial (antibacterial and antifungal) properties of the investigated soap may explain the decrease in positive microscopic results in all investigated dermatomycoses.

The treatment of fungal infections with soap alone remains an alternative only if common antifungals are not available. Especially in severe cases of tinea capitis, systemic antifungal treatment should be applied.[34–36]

Several authors have reported a correlation between the incidence of dermatomycoses and climatic conditions, with higher incidence rates during the hot and rainy season;[37–39] however, for tinea capitis and corporis, a correlation with lower temperatures or reduced humidity may also be possible.[30,40] In the present study, the influence of climate cannot be ruled out as no control group was included. Species identification through culture was successful only in a small number of patients. *Trichophyton rubrum*, *Scopulariopsis brevicaulis*, *Ulocladium* spp., and *Phoma* spp., were isolated in four children with lesions resembling those of dermatophytes. These and other fungi can therefore not be ruled out as pathogens in other children.[41]

Conclusions

Two months of regular soap use were effective in achieving improvement or cure in a large number of superficial dermatomycoses in school-children. The intervention was well accepted by the study population. Triclosan soap did not appear to be more effective under current application practices. The study confirmed that normal soap is suitable for the treatment of superficial skin mycoses. This promising finding should be taken into consideration, especially in settings

in which dermatophyte infections represent a public health problem, access to appropriate treatment is limited, and the purchase of medicated soap represents a strain for local household budgets.[42]

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Conflicts of interest

The authors have declared no conflicts of interest.

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