Arch Dermatol Res (2003) 295 : 127–129
DOI 10.1007/s00403-003-0406-7

SHORT COMMUNICATION

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Increased scalp skin lipids in response to antidandruff treatment containing zinc pyrithione

Received: 4 December 2002 / Revised: 29 January 2003 / Accepted: 6 May 2003 / Published online: 17 June 2003

Keywords Dandruff · Lipids · Stratum corneum · Ceramide

Dandruff is a common complaint that is characterized by flakes on the scalp and by itch [1]. Much research has concentrated on the role of *Malassezia* in dandruff [2], and it is also known that dandruff scalp skin is hyperproliferative and parakeratotic [3]. It is now becoming evident that dandruff is a complex, multifactorial disorder and a better understanding of the biochemical changes occurring in scalp skin is required to provide more efficacious treatment. We reported recently [4] that the intrinsic barrier properties of the stratum corneum of dandruff scalp skin are weakened as observed in other scaling skin disorders such as xerosis. The scalp skin of dandruff sufferers is characterized by decreased intercellular lipids, particularly ceramides. In addition, we observed that dandruff sufferers have an increased response to the itch mediator, histamine. Based on these observations, we proposed that certain individuals are prone to dandruff due to an intrinsically weakened scalp permeability barrier that renders them more susceptible to skin damage through microbial metabolites and environmental insults.

The aim of this study was to investigate the changes in scalp skin intercellular lipid levels in response to treatment with an antidandruff shampoo containing zinc pyrithione (ZPT). A half-head study was conducted on Thai panellists with dandruff (n=7), following 5 weeks use of a placebo shampoo. During the study, half the head was expertly washed with shampoo containing 1% w/v ZPT and the other half was washed in the same (placebo) shampoo with no ZPT three times a week for 4 weeks. Stratum corneum samples for lipid analysis (eight sequential tape strips) were collected from a parting area before treatment and following treatment with placebo shampoo and ZPT-containing shampoo. There was an improvement in scalp condition with both the placebo and the ZPT-containing shampoos but the improvement was greater when the head was washed with ZPT. By expert visual assessment, the site grades were reduced from 2.0±1.2 to 1.4±0.5 in the placebo-treated scalp skin and from 2.9±0.9 to 0.4±0.5 in the ZPT-treated scalp skin (see reference 4 for details).

Total scalp stratum corneum lipids were analysed from tape strips taken from a parting area. Lipids were extracted in chloroform/methanol (2:1) and quantified using high-performance thin-layer chromatography exactly as described previously [4]. Total lipids were 966.6± 282.5 ng/μg protein before the test period. At the study onset, the levels of lipids were lower in dandruff scalps than in scalps of healthy volunteers (data not shown), consistent with previous findings from this laboratory [4]. During the 4-week study, total lipids increased significantly to 3000.4±1716.1 ng/μg protein (placebo shampoo), and increased further to 5377.6±2056 ng/μg protein (ZPT shampoo). It was interesting that the placebo shampoo alone also improved scalp condition, albeit to a lesser extent than ZPT-containing shampoo. It is likely that this phenomenon was due to the more thorough and regular salon washing regime reducing flakes and *Malassezia* colonization of the scalp.

The levels of individual species of scalp stratum corneum lipids are shown in Fig. 1. ZPT treatment significantly increased the levels of triglycerides, cholesterol and ceramides (P<0.05) compared with pretreatment levels and those in placebo shampoo-treated scalp skin. There was also a significant increase in cholesterol (P<0.05) following the placebo shampoo treatment. The dramatic increase in scalp lipid levels must reflect changes in both sebaceous and keratinocyte lipid synthesis.

Ceramide species were analysed in more detail (Fig. 2), since this class of lipid is pivotal to barrier functionality and is solely derived from the stratum corneum (not sebaceous in origin). The percentage of ceramide 3 significantly decreased and ceramide 3a significantly increased following ZPT shampoo only. The percentage of ceramide 6ii significantly decreased with both placebo and ZPT treatment.

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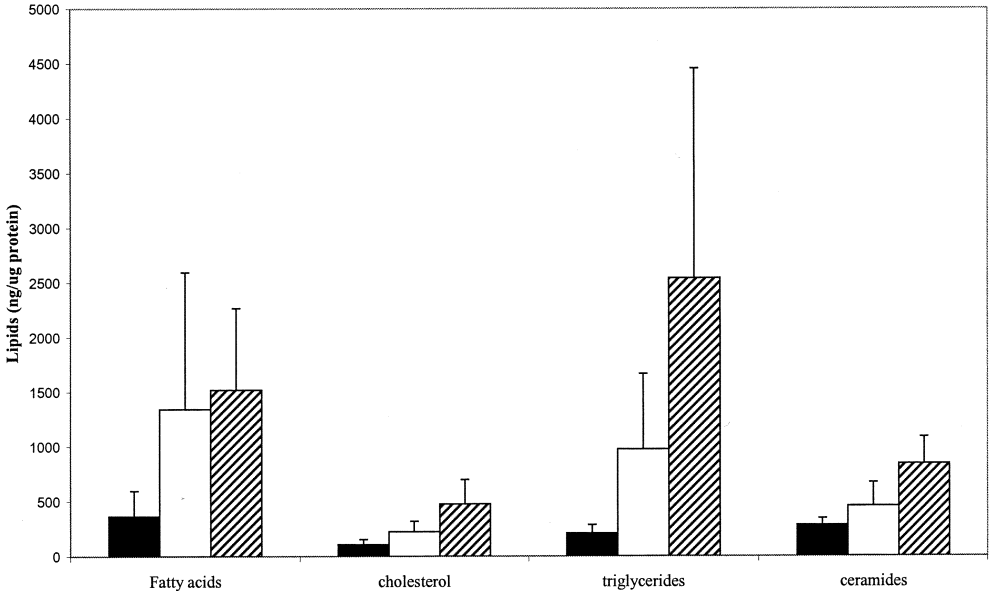

Fig. 1 Panellists of either gender were recruited. They washed their whole head with a non-antidandruff shampoo for 5 weeks and a sample was removed (*black bars*, before test phase). One side of the head was washed with shampoo containing 1% w/v ZPT (*hatched bars*), and the other half was washed with the same shampoo but containing no ZPT (*white bars*) three times a week for 4 weeks. Tape-strip samples were removed, and lipids were extracted and analysed. The results are presented as means±SD with significance set at the 5% level

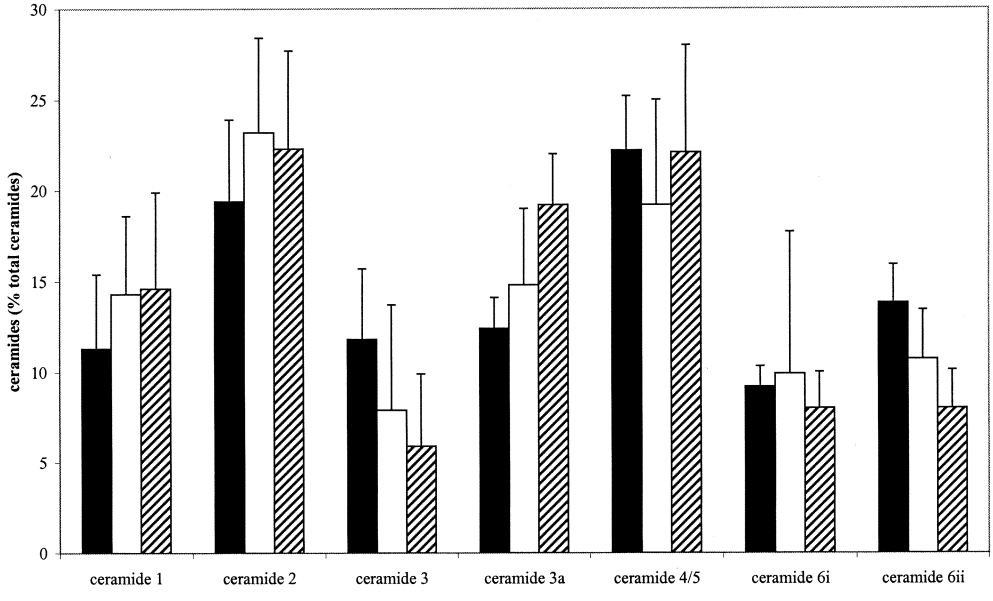

Fig. 2 Individual ceramide species expressed as a percentage of total ceramides. Samples were removed before the test period (*black bars*) and after washing three times a week for 4 weeks with either placebo shampoo (*white bars*) or shampoo containing ZPT (*hatched bars*). The results are presented as means±SD with significance set at the 5% level

The relevance of these changes is unknown, but it can be tentatively suggested that alterations in these ceramides in the scalp may influence scalp skin barrier improvement.

The changes in scalp lipid profiles were consistent with the visual improvement in scalp condition. In particular, changes in both the total amount of ceramides and the ratios of individual ceramides were evident, and this is in agreement with a role for ceramides in skin barrier function [5]. The findings of this study complement those of a recent study in which an effect of ZPT on scalp skin ultrastructure was demonstrated. ZPT normalized the parakeratotic nature of dandruff scalp skin, and improved the gross ultrastructure within the lipid-rich intercellular domains of the stratum corneum [6]. The ability of ZPT to normalize the lipid levels and restore a normal lipid ultrastructure is likely to reflect an improvement in the epidermal differentiation process of dandruff scalp skin. This may occur directly through an effect of ZPT on upregulation of barrier lipid biosynthesis, or indirectly through the antimicrobial action of ZPT.

Malassezia has been shown to have lipase and lipoxygenase activity [7, 8], which could influence scalp lipid levels. In addition, *Malassezia* can directly influence keratinocytes by modulating proinflammatory cytokine production and the cytoskeleton in vitro [9, 10]. Such effects in vivo could lead to a dysregulation of epidermal differentiation, resulting in reduced lipid biosynthesis and the inferior barrier functionality that characterizes the dandruff condition. The results of this study suggest that one mode of action by which ZPT improves the dandruff condition is through enhancing epidermal lipid biosynthesis, thereby improving scalp barrier function and leaving the individual less prone to the deleterious effects of microbial metabolites, irritants and pollutants.

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