

## Effect of Ketoconazole 2% Shampoo on Scalp Sebum Level in Patients with Seborrhoeic Dermatitis

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Twenty patients with scalp seborrhoeic dermatitis were treated twice weekly with ketoconazole 2% shampoo for 4 weeks. Clinical assessment, culture for *P. ovale* on Dixon broth and lipid measurement at two places were made before treatment and after 2 and 4 weeks. Significant improvement of the severity of seborrhoeic dermatitis ( $p < 0.001$ ) and negative mycological tests by 19 (95%) of patients were observed. The scalp lipid content remained unaltered in 11 patients with an initial lipid value over  $220 \mu\text{g}/\text{cm}^2$  but increased in those with lower initial values. This is probably due to the improvement of sebum delivery onto skin surface as a result of the elimination of the follicular occlusion.

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Seborrhoeic dermatitis of the scalp is a chronic or subacute disease characterised by erythema, desquamation and pruritus in varying degrees. Its milder form is dandruff (pityriasis simplex capitis) (1, 2). The aetiology of seborrhoeic dermatitis is not clear. Many factors, such as genetics, androgenic hormones, bacteria, psychosomatic factors, Parkinson's disease or immunological disturbances (AIDS), may play a part (1).

The role of *Pityrosporum ovale* (*P. ovale*) and sebum excretion in seborrhoeic dermatitis is controversial. In recent years many authors have suggested that the primary aetiological agent is the lipophilic yeast *P. ovale*. This has been supported by the demonstration that the oral or topical antifungal agent ketoconazole improves seborrhoeic dermatitis and dandruff (1–6). However, with quantitative cultures no significant difference has been found in the number of *P. ovale* in patients compared with controls, or between healthy and lesional skin in the patient group. IgG antibody titres against *P. ovale* have not shown any difference between the patients and controls either (7). Several studies have reported conflicting results on skin surface lipid in patients with seborrhoeic dermatitis. Some authors (8–10) have found normal sebum excretion rate and sebum levels, while Bergbrant & Faergemann (7) have observed a significantly increased amount of skin surface lipids on the forehead in patients compared to healthy individuals. No major and significant qualitative abnormalities of sebum production have been found in seborrhoeic dermatitis (8, 10–12). The disease affects skin areas with an abundance of sebaceous glands, and the increased sebum content favours the growth of *Pityrosporum* yeasts as well (13).

The aim of this study was to determine the effect of ketoconazole 2% shampoo on the scalp sebum level in patients suffering from seborrhoeic dermatitis.

### MATERIAL AND METHODS

#### Patient characteristics

Twenty outpatients with seborrhoeic dermatitis (15 males and 5 females, aged 16–40 years, mean age 27 years) were studied during the winter months. All had scalp lesions; 2 had seborrhoeic dermatitis at other sites and 3 had alopecia. Any topical treatment was stopped for at least 2 weeks before the beginning of study. Full informed consent was obtained from all patients.

#### Treatment protocol and patient assessment

Ketoconazole 2% shampoo (Nizoral<sup>®</sup>, Janssen Pharmaceutica, Belgium) was applied twice weekly for 4 weeks. The patients were examined before the treatment and 2 and 4 weeks later. At each examination lipid measurements, cultures for *P. ovale* and a clinical assessment of the severity of seborrhoeic dermatitis on a 4-point scale were made (0: no disease, 1: mild, 2: moderate and 3: severe). Moreover, each subject made his or her own assessments of the degree of scalp scaling and pruritus, using 100-mm visual analogue scales, the extremes of the scales being "none" and "severe". Because of the difficulty in assessing scalp erythema this is not reported.

#### Lipid measurements

Measurements were made with SEBUMETER<sup>®</sup> SM 810 (Courage and Khazaka, Köln, Germany). The photometrical principle of the device is based upon measurement of light transmittance through a transparent plastic film that is pressed firmly (6N) against the skin for 30 s, allowing adherence of skin lipids. The readings are expressed as  $\mu\text{g}/\text{cm}^2$ . The hair was parted to the left and to the right along the scalp median line, and measurements were made on the parting at two places: spot 1: midpoint on the hairline, and spot 2: approximately 10 cm above. All samplings were performed 36–48 h after washing the hair, according to the recommendation of Simpson & Martin (14).

#### Cultures of *P. ovale*

Cultures were taken from the scalp of all patients and inoculated onto a Dixon broth at  $37^\circ\text{C}$  for 7 days. The results were recognized as negative (below 5 colonies) or positive (above 5 colonies).

#### Statistical analysis

The Friedman's test was used to analyse the clinical grading. The linear scales and changes of sebum level were analysed using the Student's *t*-test for paired data (15). A level of  $p < 0.05$  was considered significant.

### RESULTS

#### Response of seborrhoeic dermatitis

As a result of treatment a significant improvement of the scalp scaling severity, according to the 4-point scale, was observed ( $p < 0.001$ ). The patient's own assessments, using visual analogue scales, showed a significant reduction of the scalp scaling ( $p < 0.001$ ) and pruritus ( $p < 0.001$ ). Because of the small numbers of observations, the variation of erythema at other sites and alopecia was not significant. No side-effects were observed in our patients and all of them accepted the shampoo formulation as very good.

### Cultures of *P. ovale*

All subjects were culturally positive for *P. ovale* on Dixon broth before treatment. The 2nd week the mycological examination of 11 patient (55%) was negative and at the end of the 4th week - of 19 patients (95%).

### Lipid measurements

According to the initial lipid level on the scalp before the beginning of the therapy, the subjects were divided into two groups: group 1: over 220  $\mu\text{g}/\text{cm}^2$  (11 patients with seborrhoea), and group 2: under 220  $\mu\text{g}/\text{cm}^2$  (9 patients with seborstasis). After treatment with 2% ketoconazole shampoo the amount of lipid on the scalp in group 1 remained unaltered, while in group 2 it increased considerably ( $p < 0.001$ ) (Fig. 1). There was no relationship between the scalp lipid level and the presence of *P. ovale*.

### DISCUSSION

Ketoconazole is effective against *Pityrosporum* yeasts in vitro and after topical or oral application in vivo (1-6, 16, 17). This was confirmed with 95% negative *P. ovale* tests at the end of the study.

It is reported that oral ketoconazole 200 mg daily decreases sebum excretion in patients suffering from acne and seborrhoea (18, 19). This is explained by its antiandrogen action. Other authors failed to observe such an effect (20). However, ketoconazole cream and shampoo have no percutaneous absorption of the active substance after single or multiple applications and cannot influence the glandular synthesis of androgens and thus the sebum production (21).

We ourselves were surprised to observe an increase of scalp lipid level in patient group 2. According to us, ketoconazole shampoo does not influence the sebum production but improves its delivery onto the skin surface. This is probably

due to the removal of the follicular occlusion. We suggest two possibilities:

- (1) The destroying of yeasts colonising the pilosebaceous duct contributes to the elimination of the follicular inflammation and occlusion. However, why were the two patient groups not equally affected?
- (2) Ketoconazole shampoo could reduce the follicular occlusion regardless of the incidence of *P. ovale*.

Hill et al. (22) have studied patients with *Pityrosporum* folliculitis by means of scanning electron microscopy. They have established the lack of association between the presence of yeasts and the blockage of follicles. According to them the initial event is follicular occlusion, followed by yeast and bacterial overgrowth. The beneficial effect of oral ketoconazole in patients with *Pityrosporum* folliculitis is probably associated with some direct action on the pilosebaceous follicle.

The follicular occlusion is more expressed in patients with a low lipid amount (group 2) and that explains the increase of the last after treatment. On the other hand the more efficient flow of sebum contributes to the reduction of yeasts and bacteria colonising the pilosebaceous duct.

The present study is, to our knowledge, the first attempt to assess the effect of ketoconazole shampoo on scalp sebum level in patients with seborrhoeic dermatitis. Our results support the previously reported very good clinical response of the disease. However, the mode of action of this antifungal agent on this condition remains contradictory.

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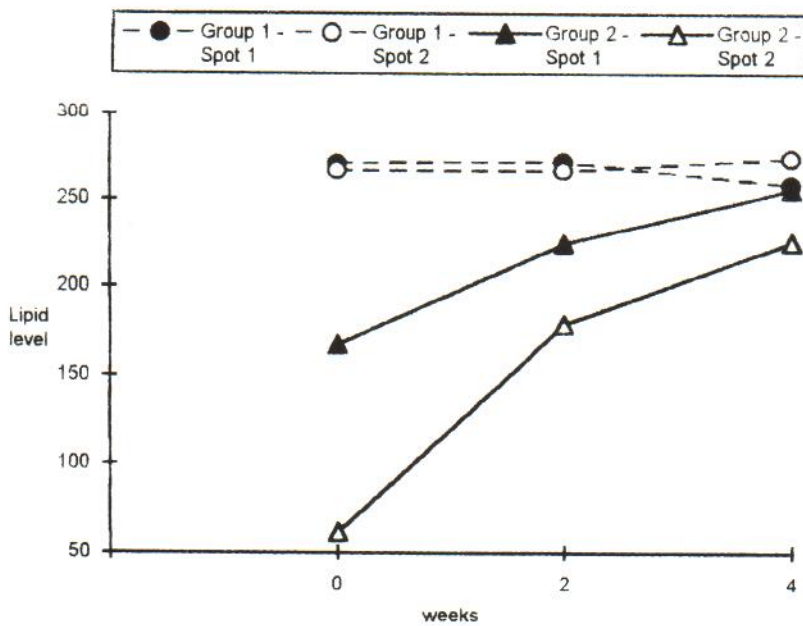


Fig. 1. Changes of scalp lipid level ( $\mu\text{g}/\text{cm}^2$ ) following application of ketoconazole 2% shampoo. ( $n_1 = 11$ ,  $n_2 = 9$ ).

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