

SEBORRHEIC DERMATITIS OF THE SCALP: results of a clinical study comparing a shampoo with ciclopiroxolamine 1.5% and zinc pyrithione 1% to a ketoconazole 2% shampoo and to a placebo

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INTRODUCTION

Thanks to several recent studies demonstrating the efficacy of antifungals in the treatment of the Seborrheic Dermatitis (SD) we know that the yeasts of genus *Malassezia* are strongly involved in the onset and the persistence of this dermatosis. With the revision of the genus *Malassezia* into 7 species in 1996, the research discovered that in SD, *M.Restricta* and *M.Globosa* were the most commonly related (1,2). A preliminary in vitro study comparing the efficacy of 1.5% Ciclopiroxolamine (CPO) and 1% Zinc Pyrithione (ZnP) combination with 2% Ketoconazole on these two species of *Malassezia* showed a synergistic inhibitory effect of the combination, higher than Ketoconazole (3).

OBJECTIVES

The aim of this phase III clinical study was to evaluate the efficacy of a 28 days treatment with 1.5% CPO/ 1% ZnP shampoo compared to a 2% Ketoconazole foaming gel and to a Placebo in a larger population of patients with moderate to severe scalp SD.

PATIENTS AND METHODS

A multicentric, controlled, single-blind clinical study was conducted on patients with a lesional score ≥ 36 of SD of the scalp. Subjects, randomised in 3 parallel groups, applied one of the above shampoos twice a week for 28 days :

- 1.5% CPO/ 1% ZnP shampoo
- 2% Ketoconazole foaming gel
- 1.5% CPO/ 1% ZnP shampoo washing base

The main efficacy criterion was the determination of a lesional score of the SD of the scalp, at baseline and at D7, D14 and D28. The score was calculated taking into account the area covered by the SD (1 to 4) and its intensity (1 to 5) evaluated on four zones on the scalp. For each zone, the surface score was then multiplied by the corresponding severity score. A lesional score ranging from 0 to 80 was calculated by the sum of the scores of each zone. The secondary criteria were clinical rating of erythema and pruritus, overall response, cosmetic acceptability, quality of life (DLQI score) and local tolerance.

RESULTS

COMPARABILITY OF THE GROUPS AT BASELINE

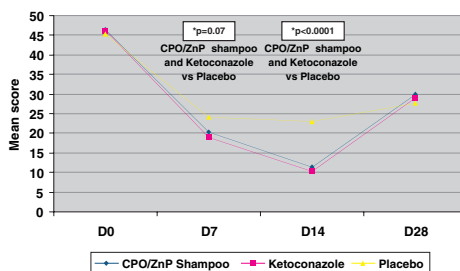
A total of 189 subjects were included.

	CPO/ZnP Shampoo N = 63	Ketoconazole foaming gel N = 66	Washing base N = 63	P value
Sex				
Male	27	34	40	P = 0.009
Female	36	32	20	
Mean age (years)	37	41	39	P = 0.255
Lesional score	46.46 \pm 1.26	46.11 \pm 1.22	45.37 \pm 1.36	P = 0.831

A variance analysis completed by Cochran-Mantel-Haenszel test was used to compare the 3 treatment groups. No statistically significant difference except on sex was found, showing comparability of the groups.

LESIONAL SCORE

LESIONAL SCORE EVOLUTION

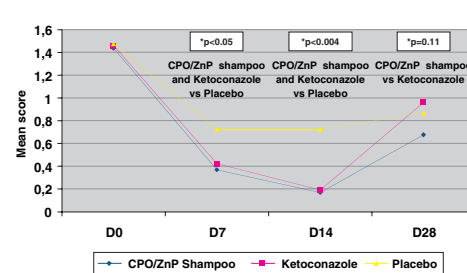


At each visit, the 2 antifungal treatments have the same significant reduction effect on the lesional score without any significant difference between the 2 groups. Compared to the washing base, the decrease of the lesional score was more important with the 2 antifungal shampoos with a slight difference at D7 (-56% and -59% versus -47%) which became highly significant at D14 (-76% and -78% versus -49%). In contrast, no significant difference was observed between the 3 groups at D28.

CLINICAL SYMPTOMS

Erythema

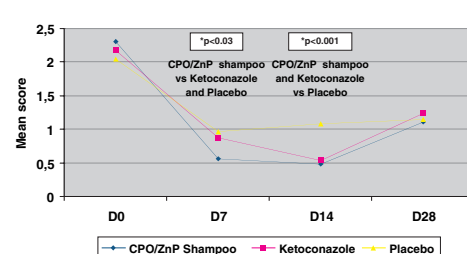
ERYTHEMA EVOLUTION



The 3 shampoos significantly reduced Erythema at each postbaseline visit. Comparison between groups revealed that the 2 antifungal shampoos induce the same improvement at D7 and D14 with a significant better result than the washing base. At D28, whereas a slight advantage for the CPO/ZnP shampoo was observed, no statistically significant difference was revealed between the 3 groups.

Pruritus

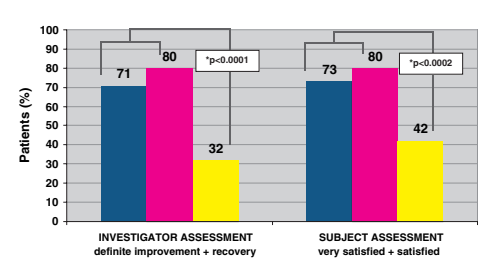
PRURITUS EVOLUTION



The pruritus was sharply improved from D7 by the 3 treatments all over the study. A significantly more important decrease of the pruritus was observed at D7 with the CPO/ZnP shampoo compared to the 2 other groups. At D14, Ketoconazole foaming gel was as effective as CPO/ZnP shampoo both being more efficient than the washing base, whereas at D28, the 3 treatments had the same effect.

OVERALL RESPONSE

OVERALL RESPONSE (D28)



Overall response judged by the investigator and the subject were similar and significantly better with both antifungal shampoos in comparison with the washing base.

COSMETIC ACCEPTABILITY

	CPO/ZnP Shampoo	ketoconazole foaming gel	Washing base
Global agreement	98%	89%	84%
Color	98%	96%	100%
Perfume	96%	95%	100%
Foaming	89%	96%	92%
Disentangling	87%	81%	76%
hairdressing	78%	76%	76%

All the shampoos scored a high level of satisfaction regarding their cosmetic qualities and hair effects with a better global agreement for the CPO/ZnP shampoo.

QUALITY OF LIFE

DLQI scores were comparable at inclusion. At D28, the 3 products demonstrated a significant improvement with a significantly higher improvement on the DLQI total mean score for the CPO/ZnP shampoo and Ketoconazole foaming gel than the placebo (4.68 points and 3.72 points respectively versus 2.07 points - $p<0.05$).

LOCAL TOLERANCE

The CPO/ZnP shampoo, Ketoconazole foaming gel and washing base were equally well tolerated, with respectively 97%, 98%, and 95% of the patients having well and very well tolerated their treatment, without any significant difference between the 3 products ($p=0.360$).

CONCLUSION

The 1.5% CPO/1% ZnP shampoo demonstrated a rapid and significant efficiency on patients with SD, equivalent to the referent product, 2% Ketoconazole foaming gel. We can suggest that the two treating shampoos have a fast action consecutive to their fungicidal properties. Once that the proliferation of yeasts was limited, the efficiency of the 3 products became comparable. The speed of action would be a factor of satisfaction and of improvement of quality of life.

¹ Nakabayasi A, Sei Y, Guillot J. Identification of *Malassezia* species isolated from patients with seborrheic dermatitis, atopic dermatitis, pityriasis versicolor and normal subjects. *Medical Mycology*. 2000;38:337-41 ² Gemmer CM, DeAngelis YM, Theelen B, Boekhout T, Dawson Jr TL Jr. Fast, noninvasive method for molecular detection and differentiation of *Malassezia* yeast species on human skin and application of the method to dandruff microbiology. *J Clin Microbiol*. 2002;40:3350-7 ³ Panizzutti C submitted to *Medical Mycology*

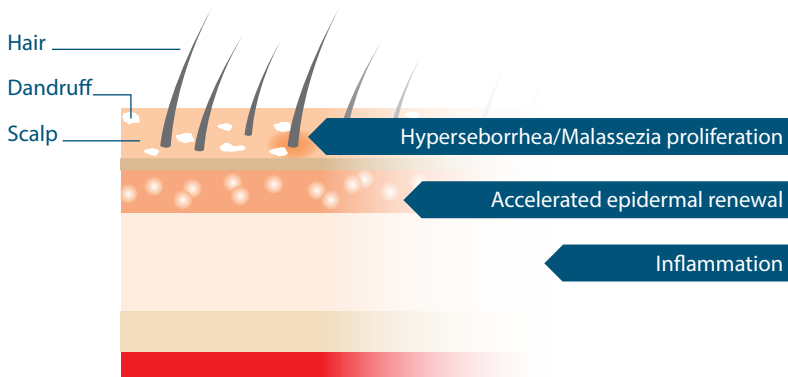
DANDRUFF

In a healthy scalp, the epidermal cell renewal (resulting in desquamation) is a normal, invisible process. When a dandruff condition is present, this cell renewal is accelerated with excessive and visible desquamation that is commonly accompanied by itching to some degree.

It is a chronic condition that might be triggered by stress, pollution, unsuitable hair products, as well as seasonal, dietary or therapeutic factors. It is not contagious or serious, but can be embarrassing and sometimes difficult to treat.

Dandruff conditions take on various clinical appearances according to the level of seborrhea and the presence of other clinical signs (redness, itching):

- Oily dandruff: Seborrheic Dermatitis
- Dry dandruff: Psoriasis



MAIN CAUSES OF DANDRUFF:

- **Hyperseborrhea proliferation:**
Excessive sebum production promotes Malassezia proliferation (since sebum creates an ideal nourishing environment).
- **Malassezia proliferation:**
Malassezia yeasts proliferate causing imbalance in the scalp and stimulating epidermal cell renewal. This excessive proliferation induces inflammation of the scalp.
- **Accelerated epidermal renewal:**
Excessive desquamation (7 to 10 days instead of 21 to 28 days).
- **Inflammation:**
Malassezia yeasts trigger an inflammatory reaction which leads to itching.

SCALP PRONE TO SEBORRHEIC DERMATITIS

- Chronic inflammatory disease marked by flare-ups
- Affects between 3 to 5% of the population
- Characterized by oily, yellowish, loose flakes on often irritated and itchy scalp
- Appears on scalp and other areas rich in oil glands, such as eyebrows, sides of a nose and backs of ears, your breastbone (sternum), groin area, and armpits
- Recurring condition, but can be effectively managed with proper treatment



RECOMMENDED TREATMENTS



Relaxation



Healthy lifestyle



Treatment products with targeted ingredients

TARGETED INGREDIENTS TO LOOK FOR:

MICRONIZED SULFUR <ul style="list-style-type: none"> • Exfoliating • Anti-fungal, anti-bacterial 	ZINC PYRITHIONE <ul style="list-style-type: none"> • Kerato reducer (improves appearance of squamous conditions of scalp) • Anti-bacterial 	PIROCTONE OLAMINE <ul style="list-style-type: none"> • Helps promote healthy scalp environment
SALICYLIC ACID <ul style="list-style-type: none"> • Exfoliating 	B-GLYCYRRHETINIC ACID <ul style="list-style-type: none"> • Anti-inflammatory 	ZINC GLYCINATE <ul style="list-style-type: none"> • Soothes sensitive scalp
ICHTHYOL <ul style="list-style-type: none"> • Calms and soothes scaly, irritated scalp • Anti-fungal, anti-bacterial, and anti-inflammatory 	KELUAMID <ul style="list-style-type: none"> • Removes flaky build-ups • Calms itching and soothes irritation 	GLYCINE <ul style="list-style-type: none"> • Calms itching
CICLOPIROX OLAMINE <ul style="list-style-type: none"> • Improves appearance of squamous conditions of scalp • Anti-fungal, anti-inflammatory 		GLYCERIN & VITAMIN B5 (PANTHENOL) <ul style="list-style-type: none"> • Nourishes and hydrates scalp and hair