Clinical efficacy of a new ciclopiroxolamine/zinc pyrithione shampoo in scalp seborrheic dermatitis treatment

Ciclopiroxolamine (CPO) and Zinc Pyrithione (ZP) antifungals are efficient at treating scalp seborrheic dermatitis. This multicentre, single-blind, clinical study was conducted to evaluate the efficacy of a shampoo containing the 1.5% CPO/1% ZP association compared to the vehicle shampoo and to 2% ketoconazole foaming gel in the treatment of seborrheic dermatitis. In 189 patients randomised to apply 1 of the 3 products twice a week for 28 days, the global lesional score, erythema, pruritus, global efficacy, quality of life (SF12 and DLQI questionnaires) and tolerance were measured at 0, 7, 14 and 28 days. The 3 products reduced lesional score, erythema and pruritus from day 7 (p < 0.0001). The 2 antifungal treatments were significantly more efficient than the vehicle in reducing lesional score, erythema and pruritus at day 14 (p < 0.0001). At day 7, the CPO/ZP shampoo was more efficient in reducing pruritus than ketoconazole gel and vehicle (p = 0.032 and p < 0.001, respectively). The global efficacy of the 2 antifungal treatments assessed at day 28 by both investigator and patient was significantly better than that of the vehicle. Only the CPO/ZP shampoo improved all DLQI questionnaire dimensions. The CPO/ZP shampoo was as rapid and efficient as ketoconazole gel in SD treatment.

Key words: ciclopirox, ketoconazole, Malassezia, seborrheic dermatitis, zinc pyrithione

Seborrheic dermatitis is a common chronic dermatological disease, which occurs in about 3-5% of the adult population [1, 2]. Malassezia yeasts, commonly found as part of the normal skin flora, could be an important factor in this disease, as they have been found in higher proportions in patients with seborrheic dermatitis or dandruff, its milder form [3-7]. M Restricta and M globosa species appeared to be the most frequently related [3, 8, 9] but the predominate M Furfur, M Sympodialis and M Obtusa has also been reported [4, 7]. Their causative role in seborrheic dermatitis is supported by several studies, which demonstrated the therapeutic efficacy of topical antifungals at improving clinical lesions and delaying symptoms recurrence [10-14], particularly by reducing the number of Malassezia yeasts [15-17].

Treatments combining keratolytic agents or topical corticosteroids and antifungals, tested for the potential complementary effect of their compounds, also proved their efficacy [13, 17, 18]. In the same way, a new association of ciclopiroxolamine (CPO) and zinc pyrithione (ZP) has been proposed on the basis of the specific properties of the two compounds. CPO is a broad-spectrum antifungal that also possesses an anti-inflammatory activity by inhibiting prostaglandin and leukotriene synthesis [19, 20]. Its efficacy in the treatment of seborrheic dermatitis and dandruff has been demonstrated in several randomised controlled trials, particularly when it is used at 1% [14, 21, 22] and 1.5% concentrations [12, 23] or in combination [13]. Concerning ZP, it is known to have both a non-specific keratolytic and antifungal activities [24, 25] and is effective in the treatment of seborrheic dermatitis and dandruff [26], mostly by normalising the altered stratum corneum ultrastructure that is observed in the scalp with dandruff [27]. The association of 1.5% CPO/1% ZP has been tested in vitro on 2 species of Malassezia (M globosa and M restricta) and showed a synergistic inhibitory and fungicidal effect, with a higher efficacy compared to 2% ketoconazole (Panizzotti C, submitted for publication). A pilot clinical study has also shown the efficacy of the CPO/ZP association at reducing the extent and severity of the lesions in 11 patients suffering from seborrheic dermatitis. The aim of this study was to confirm these preliminary results and to evaluate the clinical efficacy of a 1-month treatment with 1.5% CPO/1% ZP shampoo compared to a 2% ketoconazole foaming gel and to the non-antifungal CPO/ZP shampoo washing base, in a large population of patients with moderate to severe scalp seborrheic dermatitis.

Patients and methods

Study design
This multicentre, controlled, single blinded, randomised clinical study was designed to compare 3 parallel groups...
and was conducted from January to July 2004, by 16 dermatologists, 11 located in France and 5 in Tunisia. It was carried out according to the ethical principles stated in the Declaration of Helsinki, in conformity with local legal requirements in each country and after approval of the study protocol by the independent Ethics Committee of Tours in France.

**Patient population**

**Inclusion criteria**

Male or female patients of 18 years old and more, presenting a clinically diagnosed scalp seborrheic dermatitis including scales, erythema and pruritus and a total lesional score ≥ 36 as defined in Squire et al. [13], were recruited by French and Tunisian dermatologists. Before enrolment, each participant signed a written informed consent form.

**Exclusion criteria**

Patients presenting a seborrheic dermatitis with a lesional score < 36 or requiring an associated topical corticosteroid treatment and patients known to be allergic to one of the test components, were not included in the study. Patients who required systemic antibiotics, antifungals or corticosteroids or who had used topical corticosteroids or retinoids, or antibiotics and antifungals by topical or oral route within the week before inclusion, or those who had taken oral corticosteroids or retinoids within respectively the 14 days and the 3 months prior to study entry, were also ineligible. In the same way, patients unable to cooperate or already participating in another study, pregnant or breastfeeding women, immunodeficient patients and patients with scalp dermatosis or taking any treatment able to interfere with the evaluation of seborrheic dermatitis, were excluded.

**Treatments**

The 3 products were prepared, packed, labelled and numbered according to a computer-generated randomisation list established by the sponsor-assigned biostatistician, in order to be randomly allocated to 3 parallel groups of patients. Patients received a numbered shampoo bottle according to their order of inclusion with either the 1.5% CPO/1% ZP shampoo (Kelual DS™, Laboratoires Pierre Fabre) or a 2% ketoconazole foaming gel (Ketoderm®, Janssen Cilag Laboratory) or the non-antifungal CPO/ZP-shampoo washing base (vehicle shampoo). As the 3 treatments had a different aspect, the study was single blind: in order to keep the investigators unaware of the treatment allocation, the 3 products were packed in identical opaque 200-mL bottles. At the inclusion visit, patients received 1 bottle of shampoo with the instructions for use for a twice-a-week application during 28 days. They were instructed not to apply another substance on the scalp within the 2 hours following the treatment and the day of the visits. Patients were also required to report in their diary the changes in frequency and way of administration and at the last study visit, to return the used bottle to the investigator who had to estimate the remaining quantity (full, partially used or empty). Any treatment able to interfere with the study outcome evaluation, such as permanent waves and colorations, shampoos not provided in the study, systemic or topical treatments with antibiotics, antifungals, corticosteroids or retinoids or any topical treatment for seborrheic dermatitis was strictly forbidden during the whole study.

**Evaluation criteria**

**Main efficacy criterion**

The main efficacy criterion was assessed by the determination of a global lesional score at baseline (D0), day 7 (D7), day 14 (D14) and day 28 (D28), 2 days after the last shampoo. The lesional score ranging from 0 to 80, and was calculated taking into account the area covered by the seborrheic dermatitis lesions and its severity, as described by Squire et al. [13].

**Secondary criteria**

**Clinical symptoms**

Erythema and pruritus were graded by the investigator at D0, D7, D14 and D28, using a scale from 0 (absent) to 3 (severe).

**Global efficacy assessment by Investigators and patients**

At the final visit (D28), the global efficacy of the treatment was graded by the investigator with a global assessment of aggravation: 0, stagnation: 1, mild improvement: 2, marked improvement: 3 and recovery: 4, and by the patient using a 5-point scale from 0 (not satisfying at all) to 4 (very satisfying).

**Quality of life**

The effect of the treatment on patient’s quality of life was assessed by two questionnaires filled by the patient at the beginning (D0) and at the end of the study (D28). The first one was the French standard version of the SF-12 validated questionnaire [28], which is generally used to measure general health status. The lower the score, the more quality of life is affected. The second questionnaire specifically measures the quality of life of patients suffering from skin diseases. It was adapted with the author consent from the 10-item validated Dermatology Life Quality Index (DLQI) questionnaire [29], to be specific for the scalp simply by replacing the word “skin” by “scalp” in each question. Each item was scored using a 4-point scale from 0 (not at all) to 3 (very much). The overall score was calculated by summing the scores corresponding to each item and ranged from 0 to 30, with higher scores indicating poorer quality of life. If 1 item was unanswered, it was scored 0. If more than 1 item was missing, the DLQI was excluded from the analysis.

**Local tolerance**

Local tolerance was assessed at each post-baseline visit by the investigator. In case of an adverse event, its duration, severity and consequences were reported to the investigator and registered. Serious adverse events had to be reported to the sponsor within the 2 days following notification by the investigator.

**Statistical methods**

The statistical analysis was performed using SAS software, release 8.2. All quantitative criteria were calculated and expressed by sample size, mean, standard error (SE), median and range values, and qualitative criteria by percentage and frequency. At baseline, the comparison between the 3 treatment groups was assessed for the quantitative criteria using analysis of variance when the distribution was normal and otherwise using Kruskal-Wallis test. For the qualitative criteria, the Chi² test or the Fischer exact test was used for a sample.
size < 5 and the Kruskall-Wallis test for more than 4 classes.
Within groups time-effect analysis was performed using analysis of variance completed by the Student or Wilcoxon paired tests. For qualitative variables, the MacNemar test was used on series of differences. Between groups analysis was performed using analysis of variance for normal distributions or otherwise using Kruskall-Wallis test.
All statistical tests were two-sided and were performed at a significance level of 0.05.

Results
The flow of participants is shown in figure 1. A total of 189 patients were included in the intention-to-treat (ITT) population. According to the randomisation, 63 patients were treated by the CPO/ZP shampoo, 66 by ketoconazole foaming gel and 60 by the vehicle shampoo. Fourteen patients were excluded from per-protocol (PP) analysis due to major protocol deviations. As similar results were generally obtained for PP population, results are given for ITT population when not specified.

Demographic data and baseline clinical characteristics
Demographic data and clinical characteristics of patients at baseline are shown in table 1. The ITT population included 101 men and 88 women, aged on average of 39.33 ± 1.02 years (range 19 to 78 years). Demographic data were not statistically different between groups at inclusion except the height of the patients, which was significantly smaller in the vehicle shampoo group than in the other groups and the gender, significantly different between groups.
Concerning the clinical criteria at inclusion, no significant difference was observed between the 3 treatment groups in terms of lesional score (p = 0.831), erythema (p = 0.775) and pruritus (p = 0.072) (table 2).

Primary criterion assessment
In the 3 treatment groups, the mean lesional score highly significantly improved from baseline to each post-baseline visit (p < 0.0001) (table 3). At each visit, the 2 antifungal treatments, CPO/ZP shampoo and ketoconazole gel, had the same reducing effect on the lesional score without any significant difference between the two groups. Compared to the vehicle shampoo, the decrease of the lesional score was more important with the 2 antifungals, with a slight, non-significant difference at D7 (p = 0.071), which became highly significant at D14 (p < 0.0001). In contrast, no significant difference was observed between the 3 groups at D28, with a lesional score reduction from baseline of −16.46 ± 1.71 with CPO/ZP shampoo, −16.98 ± 1.51 with the ketoconazole gel and −17.77±1.73 with the vehicle shampoo (p = 0.857).
In the PP population analysis, the same results were globally obtained but a statistically significant difference of lesional score was achieved at D7, favouring the 2 antifungal treatments compared to the vehicle shampoo (p = 0.046).

Secondary criteria assessment
Clinical symptoms
The evaluation of erythema and pruritus evolution during treatment is shown in the figures 2 and 3, respectively.
Erythema
The 3 treatments markedly and highly significantly reduced erythema from D7 and at each pos-baseline visit \((p < 0.0001)\), producing the greatest improvement at D14, which was followed by a slight downturn at D28 although erythema score remained far below the values observed at D0.

Comparison between the 2 antifungal treatment groups revealed the same improvement at D7 and D14 without any significant difference between the CPO/ZP and ketoconazole groups \((p = 0.992\) and \(p = 0.954\) respectively), whereas a slight advantage for the CPO/ZP shampoo was observed at D28, although the difference was not statistically significant \((p = 0.115)\). By contrast, the vehicle shampoo was far less efficient than both antifungal treatments at D7 and D14 except at D28, with a significant difference between the vehicle shampoo and respectively the CPO/ZP shampoo and the ketoconazole gel \((p = 0.041\) and \(p = 0.046\) respectively) and no significant difference at D28 \((p = 0.443\) and \(p = 0.478\)).

Pruritus
The same profile was observed for pruritus, which was sharply improved from D7 by the 3 treatments all over the study \((p < 0.0001)\), with a slight downturn at D28 for the CPO/ZP and ketoconazole treatments. A better efficacy was observed at D7 for the CPO/ZP shampoo, which induced a significantly more important decrease of the pruritus than the ketoconazole gel and the vehicle shampoo \((p = 0.032\) and \(p < 0.001\) respectively), which induced the same effect \((p = 0.133)\). At D14, the ketoconazole gel was as effective as the CPO/ZP shampoo \((p = 0.365)\), both being more efficient than the vehicle shampoo \((p = 0.002\) and \(p < 0.0001\) respectively), whereas at D28, the 3 treatments had the same effect.

Global efficacy
Global efficacy of the treatments assessed at D28 by the investigator and the patient is reported in figure 4.

Investigator’s assessment
With respectively 71% and 80% of patients improved or recovered by the CPO/ZP shampoo and the ketoconazole gel, the 2 antifungal treatments had the same efficacy according to the investigator \((p = 0.557)\) and were highly significantly more efficient than the vehicle shampoo \((p < 0.0001)\) in reducing or curing seborrheic dermatitis and its symptoms.

Table 1. Demographic data of patients at baseline in the ITT population

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>Total ITT population</th>
<th>CPO/ZP shampoo group</th>
<th>Ketoconazole gel group</th>
<th>Vehicle shampoo group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>n (%) 101 (53.44)</td>
<td>27 (42.86)</td>
<td>34 (51.52)</td>
<td>40 (66.67)</td>
<td>0.009</td>
</tr>
<tr>
<td>Female</td>
<td>n (%) 88 (46.56)</td>
<td>36 (57.14)</td>
<td>32 (48.48)</td>
<td>20 (33.33)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>Mean ± SE 39.33 ± 1.02</td>
<td>37.19 ± 1.67</td>
<td>41±1.81</td>
<td>39.47 ± 1.78</td>
<td>0.255</td>
</tr>
<tr>
<td>Median (range)</td>
<td>37 (19-78)</td>
<td>34 (19-76)</td>
<td>39 (19-78)</td>
<td>37 (19-72)</td>
<td></td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>Mean ± SE 71.79 ± 0.96</td>
<td>71.83 ± 1.77</td>
<td>72.09 ± 1.63</td>
<td>71.42 ± 1.59</td>
<td>0.960</td>
</tr>
<tr>
<td>Median (range)</td>
<td>70 (40-105)</td>
<td>72 (47-105)</td>
<td>71.5 (40-105)</td>
<td>70 (48-102)</td>
<td></td>
</tr>
<tr>
<td>Height (Cm)</td>
<td>Mean ± SE 168.41 ± 0.63</td>
<td>167.22±1.10</td>
<td>167.26 ± 1.04</td>
<td>170.92 ± 1.06</td>
<td>0.023</td>
</tr>
<tr>
<td>Median (range)</td>
<td>169 (149-196)</td>
<td>167 (152-196)</td>
<td>169 (149-185)</td>
<td>171 (155-192)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Clinical characteristics of patients at baseline in the ITT population

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>CPO/ZP shampoo group</th>
<th>Ketoconazole gel group</th>
<th>Vehicle shampoo group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesional score</td>
<td>Mean ± SE 46.46 ± 1.26</td>
<td>46.11 ± 1.22</td>
<td>45.37 ± 1.36</td>
<td>0.831*</td>
</tr>
<tr>
<td>Median (range)</td>
<td>42 (36-80)</td>
<td>42 (36-72)</td>
<td>42 (36-80)</td>
<td></td>
</tr>
<tr>
<td>Erythema n (%)</td>
<td>Absent: 6 (9.52)</td>
<td>5 (7.58)</td>
<td>4 (6.67)</td>
<td>0.775§</td>
</tr>
<tr>
<td>Mild: 28 (44.44)</td>
<td>30 (45.45)</td>
<td>28 (46.67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate: 24 (38.10)</td>
<td>26 (39.39)</td>
<td>23 (38.33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe: 5 (7.94)</td>
<td>5 (7.58)</td>
<td>5 (8.33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruritus n (%)</td>
<td>Absent: 0 (0.00)</td>
<td>2 (3.03)</td>
<td>1 (1.67)</td>
<td>0.072§</td>
</tr>
<tr>
<td>Mild: 8 (12.70)</td>
<td>10 (15.15)</td>
<td>15 (25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate: 28 (44.44)</td>
<td>27 (40.91)</td>
<td>24 (40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe: 27 (42.86)</td>
<td>27 (40.91)</td>
<td>20 (33.33)</td>
<td></td>
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</tr>
</tbody>
</table>

* One factor analysis of variance. § Cochran-Mantel-Haenszel test.
**Patient’s assessment**

The same pattern is observed for the patients’ evaluation, respectively 73% and 80% of the patients treated by the CPO/ZP and ketoconazole shampoos considered they were ‘satisfied’ and ‘very satisfied’, compared to 42% of the patients treated with the vehicle shampoo (p < 0.0002).

**Tolerance**

The CPO/ZP, ketoconazole, and vehicle shampoos were equally well tolerated, with respectively 96.7%, 98.4% and 94.9% of the patients having well and very well tolerated their treatment, without any significant difference between the 3 products (p = 0.360).

Mild and moderate adverse events were experienced in 12 patients, 5 in the CPO/ZP shampoo group, 3 in the ketoconazole gel group and 4 in the vehicle shampoo group. The most common were scalp and face erythema, burning sensation, which were possibly treatment-related but did not required any treatment discontinuation and spontaneously resolved in half of cases.

**Quality of life**

Only the patients presenting available scores at inclusion and D28 were taken into consideration for the quality of life statistical analysis. Thus, 140 patients were analysed in terms of general health status (SF-12 questionnaire) and 169 for the scalp status (adapted DLQI questionnaire). Regarding the SF-12 score analysis, 47 patients treated by CPO/ZP shampoo, 49 by ketoconazole gel and 44 by the vehicle shampoo, were included. Scores were comparable at inclusion concerning the mental and physical components (p = 0.979 and p = 0.354, respectively). Comparing the evolution between D0 and D28, none of the 3 products demonstrated a significant improvement neither on the mental or physical dimension. Moreover the comparison between the 3 products in terms of mean evolution of physical and mental scores (PCS-12 and MCS-12) did not show any significant difference (p = 0.238 and p = 0.780 respectively).

**Table 3. Lesional score evolution from D0 to D28 by group of treatment in the ITT population**

<table>
<thead>
<tr>
<th>Lesional score</th>
<th>CPO/ZP shampoo group</th>
<th>Ketoconazole gel group</th>
<th>Vehicle shampoo group</th>
<th>P value&lt;sup&gt;†&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 63</td>
<td>N = 66</td>
<td>N = 60</td>
<td></td>
</tr>
<tr>
<td>D0 Mean ± SE</td>
<td>46.46 ± 1.26</td>
<td>46.11 ± 1.22</td>
<td>45.37 ± 1.36</td>
<td>0.831</td>
</tr>
<tr>
<td>Median (range)</td>
<td>42 (36-80)</td>
<td>42 (36-72)</td>
<td>42 (36-80)</td>
<td></td>
</tr>
<tr>
<td>D7 Mean ± SE</td>
<td>20.37 ± 1.79</td>
<td>19.00 ± 1.46</td>
<td>24.05 ± 1.89</td>
<td>0.071</td>
</tr>
<tr>
<td>Median (range)</td>
<td>18 (0-80)</td>
<td>16.00 (0-50)</td>
<td>23.00 (3-64)</td>
<td></td>
</tr>
<tr>
<td>Variation from baseline</td>
<td>−26.10 ± 2.10</td>
<td>−27.11 ± 1.71</td>
<td>−21.32 ± 1.78</td>
<td></td>
</tr>
<tr>
<td>P value&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>D14 Mean ± SE</td>
<td>11.32 ± 1.6&lt;sup&gt;¢&lt;/sup&gt;</td>
<td>10.20 ± 1.56&lt;sup&gt;§&lt;/sup&gt;</td>
<td>22.98 ± 2.27&lt;sup&gt;¢&lt;/sup&gt;</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Median (range)</td>
<td>6 (0-52)</td>
<td>6.00 (0-80)</td>
<td>24.50 (0-64)</td>
<td></td>
</tr>
<tr>
<td>Variation from baseline</td>
<td>−35.14 ± 1.83&lt;sup&gt;¢&lt;/sup&gt;</td>
<td>−35.91 ± 1.99&lt;sup&gt;§&lt;/sup&gt;</td>
<td>−22.38 ± 2.27&lt;sup&gt;¢&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>P value&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>D28 Mean ± SE</td>
<td>30.00 ± 1.55</td>
<td>29.12 ± 1.54</td>
<td>27.60 ± 1.81</td>
<td>0.857</td>
</tr>
<tr>
<td>Median (range)</td>
<td>32 (4-64)</td>
<td>27.50 (4-64)</td>
<td>23.00 (2-56)</td>
<td></td>
</tr>
<tr>
<td>Variation from baseline</td>
<td>−16.46 ± 1.71</td>
<td>−16.98 ± 1.51</td>
<td>−17.77 ± 1.73</td>
<td></td>
</tr>
<tr>
<td>P value&lt;sup&gt;‡&lt;/sup&gt;</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
</tbody>
</table>

* Evolution from baseline: Wilcoxon and Student paired test. † Evolution from baseline: Student paired test. ‡ Between-group comparison (a and b versus c, a versus b): variance analysis and Student-Newman-Keuls. SE: standard error. - a versus b, p=NS. - a versus c and b versus c, p<0.05.

**Figure 2. Erythema evolution from D0 to D28 in the 3 treatment groups.**

- a) CPO/ZP vs ketoconazole, p = NS
- b) CPO/ZP and ketoconazole vs vehicle shampoo: p < 0.05
- c) CPO/ZP and ketoconazole vs vehicle shampoo: p < 0.004
- d) CPO/ZP vs ketoconazole, p = 0.11.

**Figure 3. Pruritus evolution from D0 to D28 in the 3 treatment groups.**

- a) Ketoconazole vs vehicle shampoo at D0 and ketoconazole vs CPO/ZP at D14: p = NS
- b) CPO/ZP vs ketoconazole: p = 0.03 and CPO/ZP vs vehicle shampoo: p = 0.0003
- c) CPO/ZP and ketoconazole vs vehicle shampoo: p < 0.001.
Figure 4. Global efficacy of the 3 treatments assessed by the investigator and by the patients.

As concerns the DLQI scores analysis (table 4), it included 57 patients in the CPO/ZP shampoo group, 58 in the ketoconazole gel group and 54 in the vehicle shampoo group. DLQI scores were comparable at inclusion. At D28, the 3 treatments significantly improved the DLQI scores, but this improvement was higher for the CPO/ZP shampoo and the ketoconazole gel than for the vehicle shampoo, with a mean increase of the DLQI mean total score of 4.68 and 3.72 points respectively versus 2.07 points (p < 0.05 in both cases).

An analysis of the DLQI by dimension was also performed. Only the CPO/ZP shampoo induced a significant improvement from baseline for the 6 dimensions (p < 0.05 in all cases). The “work” and “treatment” dimensions as well as the “leisure” and “treatment” dimensions were not significantly improved by respectively the ketoconazole gel (p = 0.051 and p = 1.00) and the vehicle shampoo (p = 0.067 and p = 0.766) treatments.

Discussion

This randomised single blind clinical study clearly demonstrated the efficacy of the 1.5% CPO/1%ZP shampoo in the treatment of scalp seborrheic dermatitis. From 1 week of treatment and all over the treatment period, CPO/ZP shampoo highly significantly reduced the extent and severity of scaling measured by the lesional score, as well as erythema and pruritus related to the disease.

Table 4. Evolution of total DLQI score by treatment group in the ITT population

<table>
<thead>
<tr>
<th>Total DLQI score</th>
<th>CPO/ZP shampoo group n = 57</th>
<th>Ketoconazole gel group n = 58</th>
<th>Vehicle shampoo group n = 54</th>
<th>p-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>D0</td>
<td>Mean ± SE 5.98 ± 3.68</td>
<td>5 ± 3.18</td>
<td>4.74 ± 3.26</td>
<td>0.125</td>
</tr>
<tr>
<td></td>
<td>Median (Range) 5 (0–15)</td>
<td>4.50 (0–14)</td>
<td>4.50 (0–14)</td>
<td></td>
</tr>
<tr>
<td>D28</td>
<td>Mean ± SE 1.29 ± 1.83</td>
<td>1.27 ± 1.77</td>
<td>2.66 ± 2.44</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Median (Range) 1 (0–7)</td>
<td>1 (0–8)</td>
<td>2 (0–10)</td>
<td></td>
</tr>
<tr>
<td>Mean change</td>
<td>Mean ± SE -4.68 ± 3.64</td>
<td>-3.72 ± 3.59</td>
<td>-2.07 ± 3.16</td>
<td>0.0005</td>
</tr>
<tr>
<td></td>
<td>Median (Range) -4 (-13–7)</td>
<td>-3.50 (-13–4)</td>
<td>-2 (-11–8)</td>
<td></td>
</tr>
<tr>
<td>P value§</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
</tbody>
</table>

§ Time effect: paired Student test. † Intergroup comparison: Bonferroni test.
the study and were less compliant. Furthermore, though the lesional scores were rising again at D28, they were still significantly lower than baseline values. Besides, both investigators and patients assessed the global efficacy of the products at D28 and found that the 2 active shampoos were significantly more efficient than the vehicle shampoo, about 75% of patients judging that their CPO/ZP or ketoconazole treatment was “satisfying” and “very satisfying”.

Taking into account the complementary fungicidal and fungistatic properties of CPO and ZP observed in in vitro studies and the demonstrated clinical efficacy of the CPO/ZP combination in a shampoo for the treatment of moderate to severe seborrheic dermatitis, further studies on longer period of time are needed to evaluate the remanence of its effects after treatment discontinuation.

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