ABSTRACT

In spite of a variety of established therapeutic approaches to the treatment of acne vulgaris, up to 12.7% of patients cannot be cured using these methods. To overcome the limitations of established therapies, botanicals and natural mineral preparations are also used to treat acne. The aim of our study was to investigate the efficacy of topical preparations of peloid and medicinal plants from Montenegro in an acne therapy regimen.

The study design was a retrospective cohort study, with two cohorts defined by the type of topical preparation used: one cohort (n = 70) was comprised of the patients treated with Peloderm (a topical preparation containing both peloid and medicinal plants' extracts), and another cohort (n = 70) of the patients was treated with Antiacne (a topical preparation with only medicinal plants' extracts). Patients in both cohorts were treated for 18 months.

In both treatment groups, the FDA acne severity score improved gradually throughout the study visits. However, final FDA acne severity score (after 18 months of topical treatment) was significantly (T = 7.556, df = 1, p = 0.000) lower in the Peloderm group (1.0 ± 0.0) than in the Antiacne group (1.8 ± 0.9).

Both topical preparations of peloid and selected medicinal plants from Montenegro, in ratios observed in this study, are efficacious and safe options for topical treatment of acne, with the peloid preparation demonstrating somewhat greater potency.

Keywords: Peloid, acne vulgaris, topical therapy.

SAŽETAK

Uprkos velikom broju utvrđenih terapijskih metoda za lečenje akni, čak 12.7% pacijenata ne može da se trajno izleči. Da bi se prevladala ograničenja utvrđenih terapijskih metoda, sve više se u lečenju akni koriste preparati dobijeni korišćenjem lekovitih biljaka i minerala. Cilj naše studije je bilo ispitivanje efikasnosti lokalne terapije akni preparatima sačinjenim kombinovanjem peloida i lekovitih biljaka iz Crne Gore.

Studija je bila dizajnirana kao retrospektivna kohortna studija, sa dve kohorte definisane vrstom korišćenog lokalnog preparata: jednu kohortu (n = 70) su činili pacijenti lečeni Pelodermom (preparat za lokalnu primenu koji sadrži i peloid i ekstrakte lekovitih biljaka), a drugu kohortu (n = 70) pacijenti lečeni preparatom Antiakne (preparat za lokalnu primenu koji sadrži samo ekstrakte lekovitih biljaka). Pacijenti u obe kohorte su bili lečeni 18 meseci.

U obe studijske grupe, FDA skor težine akni se postepeno poboljšavao tokom lečenja. Međutim, krajnji FDA skor (posle 18 meseci lokalne terapije) je bio značajno (T = 7.556, df = 1, p = 0.000) niži u grupi sa Pelodermom (1.0 ± 0.0) nego u grupi sa Antiakne preparatom (1.8 ± 0.9).

I peloid, i izabrane lekovite biljke iz Crne Gore, pripremljeni u obliku lokalnih preparata u odnosima korišćenim u našoj studiji, su efikasni i bezbedni u lokalnoj terapiji akni, pri čemu peloid ima nešto veći terapijski efekat.

Ključne reči: Peloid, akne, lokalna terapija.
INTRODUCTION

One of the most frequent skin diseases in adolescence is acne, which affects up to 85% of the population (1). A significant percentage of the affected adolescents continue to suffer from acne in adulthood, contributing to a population prevalence of 13% (2). Usually, adult patients suffer from the most severe forms of acne.

The mainstays of acne therapy are topical preparations with proven efficacy are benzoyl peroxide, antibiotics, azelaic acid, and retinoid. In patients with mild acne, topical preparations often suffice, but in those with moderate to severe acne, systemic therapy is necessary (3). Moderate acne is treated by systemic antibiotics (especially tetracyclines) and hormonal therapy (oral contraceptives or cyproterone acetate), but severe acne requires administration of oral isotretinoin. However, many patients are not cured by these therapies (up to 12.7%), and more are unsatisfied with the therapeutic results (4). There are also considerable adverse effects of systemic acne therapy, e.g. skin reactions with minocycline, interference with growth of bones and teeth with all tetracyclines, or depression and suicide attempts with isotretinoin (5).

To overcome the limitations of established standards of care, botanicals and natural mineral preparations are also implemented in acne therapy. A recent systematic review confirmed considerable efficacy for preparations containing Mahonia, tea tree oil, and Saccharomyces (6). However, although there were numerous attempts to use peloid preparations for the treatment of a wide spectrum of diseases (7), there are no published studies about its effects on acne.

Montenegro is a coastal Mediterranean country, with some segments of coast being shallow, and contains mud rich with minerals. The aim of our study was to investigate efficacy of topical therapy of acne with preparations made by compounding peloid and medicinal plants from Montenegro.

MATERIAL AND METHODS

The preparations for use in topical acne therapy

The preparations used in our study were freshly prepared at Fontis Ltd. for each study participant. There were two study preparations for topical use: “Peloderm” and “Antiacne”.

Peloderm is a galenic ointment consisting of peloid from the Ulcinj coast of Montenegro (2%) and propylene glycol extract from the following medicinal plants: Agrimonia eupatoria, Achillea millefolium, Plantago lanceolata, Matricaria chamomilla, and Foenegreci semen, prepared according to Pharmacopoeia Yugoslavica IV rules (25%), talc (6%), and stearin-type base (55%).

The Antiacne preparation is a galenic ointment consisting of: propylene glycol extract of the following medicinal plants: Calendula officinalis, Symphytum officinale, Achillea millefolium, Salvia officinalis, prepared according to Pharmacopoeia Yugoslavica IV rules (25%), zinc oxide (15%), titanium dioxide (1%), talc (4%) and a stearin-type base (55%).

Study population

The study population comprised patients suffering from acne who were treated at Fontis Ltd outpatient facility during the period from January 2007 to January 2010. The inclusion criteria were acne with any level of severity, absence of chronic comorbidities, and a treatment-free period of 30 days prior to study initiation. The exclusion criteria were concomitant comorbidities or topical therapy of acne, advanced age (>65 years), pregnancy, and breastfeeding.

Study design and sample size

We used a retrospective cohort study design with two cohorts defined by the type of topical preparation used, as follows: one cohort comprised of patients was treated with Peloderm, and the other cohort comprised of the patients treated with Antiacne. Treatment allocation was determined by prescriber preference, lacking conflicts of interest in this study. Taking into account expected effect size of 1.56 (the effect on acne was measured by a FDA-proposed five-category ranking system) (8): probability of type I error was 0.05, the power of the study was 95%, the treatment allocation ratio between cohorts was 1, and the number needed to treat calculated was 12 patients per group. However, we chose to include 70 patients per group. The study was approved by the Ethics Committee of Fontis Health Center.

Treatment protocol

After the first visit to Fontis outpatient facility, the patients received one of the topical preparations and were instructed to apply a thin layer twice daily (in the morning and in the evening) after washing their face. The patients were then followed up through 8 visits: after 15 days (visit 1), 45 days (visit 2), 75 days (visit 3), 90 days (visit 4), 120 days (visit 5), 180 days (visit 6), 12 months (visit 7), and 18 months (visit 8). During this 18-month period, the patients were not allowed to use other systemic or topical treatments for acne. At each visit, severity of acne was rated using the FDA-proposed five-category ranking system and recorded the patient’s file.

The variables

Variables analysed were obtained retrospectively from the patients’ file. The primary outcome variable of the study was severity of acne, rated by the FDA-
proposed five-category ranking system. The following possible confounders were assessed: previous systemic or topical antibiotic treatment of acne, duration of previous antibiotic use, previous topical therapy of acne other than antibiotics, previous systemic therapy with isotretinoin, previous hormonal therapy, other previous self-medication, smoking, occasional alcohol use, body mass index, sex, age, history of acne in family members, and chronic stress.

Statistics

The results were primarily described statistically with frequencies, measures of central tendency, and measures of variability. The difference in values of numeric variables among the study groups was assessed using the Student’s T-test for independent samples, and the differences in frequencies of categorical variables’ values were tested using the Chi-square test. All tests were two-tailed, and the confidence level for rejecting the null hypothesis was set to 0.05. All calculations were performed using the SPSS statistical software, version 18.

RESULTS

Prior to allocation to topical prescription therapy (at the first visit), the patients in the study cohorts differed with respect to the FDA acne severity score, body mass index, duration of previous antibiotic use, occasional alcohol use, and chronic stress, but other characteristics were similar. Baseline characteristics of the study cohorts (70 patients treated with Peloderm and 70 patients treated with Antiacne) are shown in Table 1.

In both treatment groups, the FDA acne severity score improved gradually throughout the study visits (Peloderm group: F = 171.915, df = 8, p = 0.000; Antiacne group: F = 328.544, df = 8, p = 0.000) (Figure 1). However, final FDA acne severity score (after 18 months of topical treatment) was significantly (T = 7.556, df = 1, p = 0.000) lower in the Peloderm group (1.0 ± 0.0) than in the Antiacne group (1.8 ± 0.9). An example of the treatment effect with Peloderm is shown in Figure 2.

None of the patients in either the Peloderm and Antiacne group experienced local or systemic adverse reactions to the study medications. All enrolled patients were fully compliant with their therapeutic regimens.

DISCUSSION

Both preparations for topical treatment of acne used in our study showed considerable efficacy, with excellent safety. However, final group results in patients using Peloderm were superior. The only two ingredients which are the same in both study preparations are extracts of Achillea millefolium and zinc oxide; notwithstanding this fact, many differences in preparations exist. Differences in preparations make it difficult to ascribe the observed positive effects of both preparations, and especially the difference between the effects, to any particular ingredient.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Peloderm cohort (n=70)</th>
<th>Antiacne cohort (n=70)</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>20.7±4.4 years</td>
<td>21.0±5.3 years</td>
<td>T = -0.348 p &gt; 0.05</td>
</tr>
<tr>
<td>Body mass index*</td>
<td>19.5±2.1</td>
<td>20.5±1.9</td>
<td>T = -2.982 p = 0.003</td>
</tr>
<tr>
<td>FDA acne severity score*</td>
<td>4.5±0.6</td>
<td>5.0±0.0</td>
<td>T = -7.490 p = 0.000</td>
</tr>
<tr>
<td>Sex</td>
<td>M/F = 52/18</td>
<td>M/F = 55/15</td>
<td>χ² = 0.357 p &gt; 0.05</td>
</tr>
<tr>
<td>Previous systemic or topical antibiotic therapy of acne</td>
<td>55 (79%)</td>
<td>58 (83%)</td>
<td>χ² = 0.413 p &gt; 0.05</td>
</tr>
<tr>
<td>Duration of previous antibiotic use (0 years / 1 year / 2 years / 3 years / 4 years*)</td>
<td>0 / 10 / 38 / 8 / 14 (0% / 14% / 54% / 12% / 20%)</td>
<td>16 / 0 / 40 / 11 / 3 (23% / 0% / 57% / 16% / 4%)</td>
<td>χ² = 33.643 p = 0.000</td>
</tr>
<tr>
<td>Previous topical therapy of acne other than antibiotics</td>
<td>61 (87%)</td>
<td>52 (74%)</td>
<td>χ² = 3.717 p &gt; 0.05</td>
</tr>
<tr>
<td>Previous systemic therapy with isotretinoin</td>
<td>2 (3%)</td>
<td>1 (1.5%)</td>
<td>χ² = 0.341 p &gt; 0.05</td>
</tr>
<tr>
<td>Previous hormonal therapy</td>
<td>22 (31%)</td>
<td>17 (24%)</td>
<td>χ² = 0.889 p &gt; 0.05</td>
</tr>
<tr>
<td>Previous self-medication</td>
<td>57 (81%)</td>
<td>58 (83%)</td>
<td>χ² = 0.049 p &gt; 0.05</td>
</tr>
<tr>
<td>Smoking</td>
<td>35 (50%)</td>
<td>31 (44%)</td>
<td>χ² = 0.459 p &gt; 0.05</td>
</tr>
<tr>
<td>Occasional alcohol use*</td>
<td>28 (40%)</td>
<td>13 (19%)</td>
<td>χ² = 7.761 p = 0.005</td>
</tr>
<tr>
<td>Acne in family</td>
<td>45 (64%)</td>
<td>43 (61%)</td>
<td>χ² = 0.122 p &gt; 0.05</td>
</tr>
<tr>
<td>Chronic stress*</td>
<td>35 (50%)</td>
<td>14 (20%)</td>
<td>χ² = 13.846 p = 0.000</td>
</tr>
</tbody>
</table>

Table 1. Baseline characteristics of the study cohorts. * indicates significant difference.
Of the ingredients in the study preparations, only zinc oxide and Calendula officinalis have been evaluated for effects on acne. Zinc oxide together with chloroxylenol in the same preparation showed the same efficacy on acne and better local tolerability in a clinical trial, when compared with 5% benzoyl peroxide cream (9). It seems that the beneficial effect of zinc oxide in acne therapy could be explained by antiinflammatory properties of zinc, which suppresses cytokine-induced NO production in keratinocytes (10). Calendula officinalis was tested for treatment of acne as the only ingredient of a homeopathic topical preparation, with "good" results in a series of patients, which were not objectively evaluated (11). Salvia officinalis was tested for antimicrobial activity in vitro on 29 different aerobic and anaerobic bacteria and yeasts, but no effect was observed (12).

Since zinc oxide with established anti-acne effect was a common ingredient of both Peloderm and Antiacne preparations, at least some part of their observed efficacy in this study has to be explained by the beneficial effect of zinc. However, Peloderm was more effective than Antiacne, suggesting beneficial effects of ingredients other than zinc, especially of peloid, which was not part of Antiacne preparation.

Although previously not tested in patients with acne, peloid preparations have considerable potential beneficial effects when applied topically in this patient population. It shows antimicrobial activity on a variety of bacteria in vitro (13). Both inhibitory and stimulatory effects on some human and bacterial enzymes, like oxidoreductases (lactate dehydrogenase, malate dehydrogenase, etc.), were demonstrated in another in vitro study (14). Analytical studies (15) showed that the process of maturation of peloid is important for its potential therapeutic effects; mature mud is especially rich with organic components, such as phospholipids, phytosterols, and terpenes, which can affect human and bacterial regulatory molecules.

Figure 1. Change of average FDA acne severity score over time in groups of patients treated by Peloderm (■; n = 70) and by Antiacne (○; n = 70). Error bars = standard deviations.

Figure 2. Photographs of the affected skin area in a patient before (A) and after (B) treatment with Peloderm topical preparation.
The main limitation of our study was its observational character, precluding testing of single compound preparations, containing only one of potentially active ingredients at a time. The observed beneficial effects on acne of two complex preparations with multiple ingredients are difficult to discern; however, we still can conclude that topical preparations of both peloid and selected medicinal plants from Montenegro, in ratios specified in this study, are effective and safe options for local treatment of acne, with the peloid preparation having somewhat greater potency.

REFERENCES