

Clinical-Instrumental Assessment of A Daily Cosmetic Regimen in Ensuring Improved Skin Barrier and Tolerability in Sensitive Skin Undergoing Acne Treatment: A Prospective Open Trial

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Abstract

Introduction

Sensitive skin is common in acne patients. In these subjects, it is important to adopt, whenever possible, a multi-product holistic protocol approach to reduce acne lesions, improve skin barrier function and ensure good tolerability profile with the final goal of good treatment adherence.

Study Aim

The aim of this clinical trial was to evaluate the tolerability and efficacy of a cosmetic protocol regimen in improving facial skin conditions in subjects with sensitive and acne-prone skin. The cosmetic holistic treatment was based on the use of a specific cleanser (Biretix Cleanser) with antimicrobial activity (biopep15); a topical anti-acne product in gel formulation containing two retinoid molecules (RetinSpere® technology: hydroxy pinacolone retinoate and retinol encapsulated in glycospheres) with additional anti-inflammatory (niacinamide), antibacterial (biopep15) and keratolytic (glycolic and salicylic) activities; and a cream for adjuvant skin care (Biretix Hydramat) featuring hydrating, seborregulating and barrier renewal actives. The use of this complete cosmetic protocol (based on purify, treat, and care steps) could be particularly effective in the treatment of subjects with sensitive and acne-prone skin where treatment products can often cause excess dryness and irritation leading to lack of patient compliance and adherence.

Subjects and Methods

The study was carried out on 20 women, aged 18-45 years, with sensitive and acne prone skin. Subjects cleansed and applied the adjuvant cream twice daily, morning and evening, and used the treatment cream in the evening and the cream for the skin care both in the morning and in the evening. The primary outcome of the study was the evaluation of the tolerability and acceptability of the cosmetic treatment regimen. Secondary outcomes were the evaluation of the efficacy of the regimen on acne lesions, sebum production, skin barrier function and skin hydration. Instrumental evaluations were carried out by means of non-invasive bioengineering techniques. Skin sebum levels were measured using Sebumeter® method (Sebumeter 815, Courage+Khazak GmbH). Trans epidermal water loss (TEWL) was measured by means of the internationally recognized TEWAMETER® method (Tewameter 300® Courage+Khazaka, electronic GmbH). Skin moisturization was evaluated by means of Corneometer®. Visia® pictures were taken at baseline and after treatments to evaluate acne lesions.

Results

The Tested products were well tolerated by all the subjects. No adverse reactions or adverse events related to the cosmetic treatment were observed during the study. A significant reduction was observed in sebum production (-30%) at the end of treatment period. Skin barrier function significantly improved: TEWL was reduced by 9% at week 6. The products significantly improved skin moisturization with an increase of 20% at week 6 in comparison with baseline. Finally, this regimen significantly reduced non inflammatory acne lesions by 26% at week 6 in comparison with baseline.

Conclusion

In subjects with sensitive skin and acne lesions, the use of a specific adjuvant skin care regimen (a cleanser and a skin moisturizing cream) can ensure tolerability of treatment (gel containing a retinoid complex, antimicrobial peptide and glycolic and salicylic acid) and significantly improve skin hydration and barrier function, and reduce sebum production and acne lesions.

Keywords: Acne, Clinical Trial, Sensitive Skin, Retinoid, Antimicrobial Peptides.

Introduction

Acne is a chronic inflammatory cutaneous disease characterized by an increase in sebum secretion and abnormal keratinization it has an estimated global prevalence of 9.4%. Acne is the most common skin disorder among teenagers, affecting nearly 85% of adolescents, however, it can also occur in adult females [1-3]. Acne in adult women is not necessarily related to earlier juvenile acne and factors such as hormonal alterations, stress, environmental pollution, light exposure, and smoking can contribute to its pathogenesis. Recent epidemiological studies have shown that acne affects 12–14% of women between 25 and 50 years of age [4, 5]. In an epidemiological study conducted in France was observed a prevalence of adult acne in 41% of women, and it generally occurred on sensitive mild seborrheic skin [6].

Sensitive skin is a common condition observed in subjects with acne [25]. Patients with acne and sensitive skin can be classified in two categories: subjects with inherently sensitive skin, or patients with secondary sensitive skin caused by topical application of potentially aggressive or irritating products [7]. Sensitive skin is characterized by self-reported sensory perceptions (stinging, burning, pain, pruritus, and tingling sensations) in response to stimuli that normally should not provoke such unpleasant sensations [8]. These symptoms can be triggered by both intrinsic (e.g. age, hormonal status) and extrinsic (e.g. UV radiation, pollution, environmental temperature, chemicals) factors. The mechanisms involved in this syndrome can be different and involve neurosensory and immunological mechanisms and the alteration of epidermal barrier functions [9]. As with sensitive skin, acne can also be associated with inherent abnormalities in epidermal barrier functions. In addition, some topical and systemic medication used to treat acne vulgaris can contribute to increase trans epidermal water loss (TEWL) alternating the barrier functions [10].

In this contest, a barrier repair therapy (that combining to the topic treatment, a mild skin cleanser and an intensive moisturizing cream) represents an important tool in the management of patients with acne, particularly in presence of sensitive skin. Providing specific skin care recommendations could contribute to improving the efficacy of topical medications in reducing acne lesions [10, 11]. The aim of this clinical trial was to evaluate the tolerability and the efficacy of a cosmetic treatment regimen in improving facial skin conditions in subjects with sensitive and acne-prone skin. The cosmetic treatment regimen was based on the use of: a cleanser (Biretix Cleanser, Cantabria Labs, Madrid, Spain) with antibacterial activity (biopep15); a topical treatment product in gel formulation (Biretix Triactive, Cantabria Labs, Madrid, Spain)

containing RetinSphere® technology (hydroxypinacolone retinoate and retinol encapsulated in glycospheres), and characterized by anti-inflammatory (niacinamide), antibacterial (biopep15) and keratolytic (glycolic and salicylic) activities; an adjuvant cream for skin care (Biretix Hydramat, Cantabria Labs, Madrid, Spain) containing hydrating, seboreregulating and barrier renewal actives. The use of a complete cosmetic protocol (based on purify, treat, and care steps) and the RetinSpere® technology (that allows a slow release of the actives) could be particular effective in the treatment of subjects with sensitive and acne-prone skin.

Study Aim

To evaluate the tolerability, safety, and efficacy of a cosmetic treatment for facial care in improving skin conditions in subjects with sensitive skin with mild acne lesions.

Study Design

We conducted a 6-week, open label, prospective trial, in subjects with sensitive (self-perceived) and acne-prone skin (non-inflammatory lesions such as open and closed comedones).

Methods

The clinical-instrumental trial, conducted by COMPLIFE Italia S.r.l. CRO (Garbagnate Milanese, Italy), was performed between September 2022 and December 2022.

Subjects

The study was carried out on 20 subjects. All participants gave their written consent. Main inclusion criteria were sex (female), aged between 18 and 45 years old with sensitive (self-perceived) and acne-prone skin (non-inflammatory lesions such as open and closed comedones). Main exclusion criteria were pregnancy or breast-feeding, other clinically relevant acute or chronic diseases able to interfere with the study. Patients cleansed (Biretix Cleanser) and applied the adjuvant cream (Biretix Hydramat) twice daily, morning and evening, and used the topical treatment (Biretix Triactive) at night.

Study Outcomes

The primary outcome of the study was the evaluation of the tolerability of the cosmetic treatment in subjects with sensitive and acne-prone skin. Secondary outcomes were the evaluation of the efficacy of the treatment and the cosmetic acceptability of the products. To assess the tolerability and the efficacy of the cosmetic treatment different clinical and instrumental evaluations were carried out. The study foresaw 6 weeks of treatment; checks points were scheduled at baseline (T0) and after 3 (T3) and 6 (T6) weeks. The tolerability of the products was evaluated by the investigating

dermatologist, in collaboration with participants, based on both physical (dryness, erythema, oedema, desquamation) and functional (burning sensation, itching sensation, tight feeling, other) signs, using a score from 0 (none) to 4 (severe). Instrumental evaluations were carried out by means of non-invasive bioengineering techniques. The skin sebum content was measured using Sebumeter® method (Sebumeter 815, Courage+Khazak GmbH). Trans epidermal water loss (TEWL) was measured by means of the internationally recognized TEWAMETER method carried out in one specific point on the right cheek (Tewameter 300® Courage+Khazaka, electronic GmbH). Skin moisturization was evaluated by means of Corneometer®. The instrumental analyses were combined with the clinical evaluation of the number of non-inflammatory acne lesions (blackheads and whiteheads), visually assessed by the investigating dermatologist. In addition, digital pictures of the faces were taken with Visia®-CR (Canfield Scientific). To evaluate the cosmetic acceptability, a self-assessment questionnaire with 21

items was administered to enrolled subjects at the end of the study (T6). Data were submitted to paired Student t test; variations were considered statistically significant when the p value was < 0.05.

Results

A total of 20 female patients with a median age of 26.1 were enrolled and completed the trial.

Table 1 shows the results regarding products tolerability at baseline (T0) and at each follow-up period (T3 and T6). Treatments success was defined as the absence of both physical and functional adverse? signs. Tested products were well tolerated by all subjects. No adverse reactions or adverse events related to the cosmetic treatment were observed during the study.

Table 1: Tolerability of the products used in the cosmetic treatment. Results on skin physical (assessed by the dermatologist) and functional (self-reported by subjects) signs at each timepoint (n=20)

Physical signs					Functional signs				
		T0 n (%)	T3 n (%)	T6 n (%)			T0 n (%)	T3 n (%)	T6 n (%)
Erythema	Absent	6 (30)	7 (35)	7 (35)	Burning sensation	Absent	19 (95)	20 (100)	20 (100)
	Very mild	7 (35)	12 (60)	12 (60)		Very mild	1 (5)	0	0
	Mild	7 (35)	1 (5)	1 (5)		Mild	0	0	0
	Moderate	0	0	0		Moderate	0	0	0
	Severe	0	0	0		Severe	0	0	0
Oedema	Absent	20 (100)	20 (100)	20 (100)	Itching sensation	Absent	19 (95)	20 (100)	20 (100)
	Very mild	0	0	0		Very mild	1 (5)	0	0
	Mild	0	0	0		Mild	0	0	0
	Moderate	0	0	0		Moderate	0	0	0
	Severe	0	0	0		Severe	0	0	0
Desquamation	Absent	20 (100)	20 (100)	20 (100)	Stinging sensation	Absent	19 (95)	20 (100)	20 (100)
	Very mild	0	0	0		Very mild	1 (5)	0	0
	Mild	0	0	0		Mild	0	0	0
	Moderate	0	0	0		Moderate	0	0	0
	Severe	0	0	0		Severe	0	0	0

Skin dryness	Absent	19 (95)	20 (100)	20 (100)	Skin tightness	Absent	18 (90)	20 (100)	20 (100)
	Very mild	1 (5)	0	0		Very mild	2 (10)	0	0
	Mild	0	0	0		Mild	0	0	0
	Moderate	0	0	0		Moderate	0	0	0
	Severe	0	0	0		Severe	0	0	0

Subjects with acne are characterized by a high sebum secretion [12]. **Figure 1** shows the skin sebum levels detected over time in the subjects included in the study. The mean (standard error - SE) sebum level was 145.7 (6.1) $\mu\text{g}/\text{cm}^2$ at baseline, 116.1 (6.2) $\mu\text{g}/\text{cm}^2$ at T3, and 101.8 (8.2) $\mu\text{g}/\text{cm}^2$ at T6. The tested products thus determined a significant decrease of mean sebumeter value by -19.1% after 3 weeks (T3) and by -29.6% after 6 weeks (T6), compared to baseline value (T0). A decrease in trans epidermal water loss (TEWL) indicates an improvement in skin barrier function. The mean (SE) TEWL observed in this study was 12.3 (0.4) $\text{g}/\text{h}/\text{m}^2$ at baseline, 11.6 (0.4) $\text{g}/\text{h}/\text{m}^2$ at T3, and 11.2 (0.3) $\text{g}/\text{h}/\text{m}^2$ at T6. As shown in **Figure 2**, the tested products determined a statistically significant decrease in TEWL of -5.5% at T3 and -8.7% at T6, compared to baseline(T0). The products significantly improved skin moisturization; the mean (SE) values for skin moisturization were 48.6 (1.3) c.u.at baseline, 57.1 (1.7) c.u.at T3, and 58.4 (1.7)

c.u. at T6. The cosmetic treatment thus significantly improved skin moisturization by +18.1% at T3 and +21.5% at T6, as compared to T0 (**Figure 3**). At baseline the number of acne non-inflammatory lesions (sum of open comedones/blackheads and closed comedones/whiteheads), mean (SE), was 38.7 (2.6). After the cosmetic treatment the number of lesions was 32.6 (2.3) and 29.5 (2.2) at T3 and T6, respectively. The tested products determined a significant reduction in the number of acne non-inflammatory lesions by -6.1 lesions at T3 and by -9.2 lesions at T6, compared to T0 (**Figure 4**). Clinical images taken with Visia®-CR supported the clinical and instrumental results (**Figures 5 and 6**).The cosmetic acceptability, evaluated using a self-assessment questionnaire administrated to the subjects at the end of the study, was high. The percentage of patients that gave positive judgements (completely agree or agree, very satisfied of quite satisfied, yes) was always >80%.

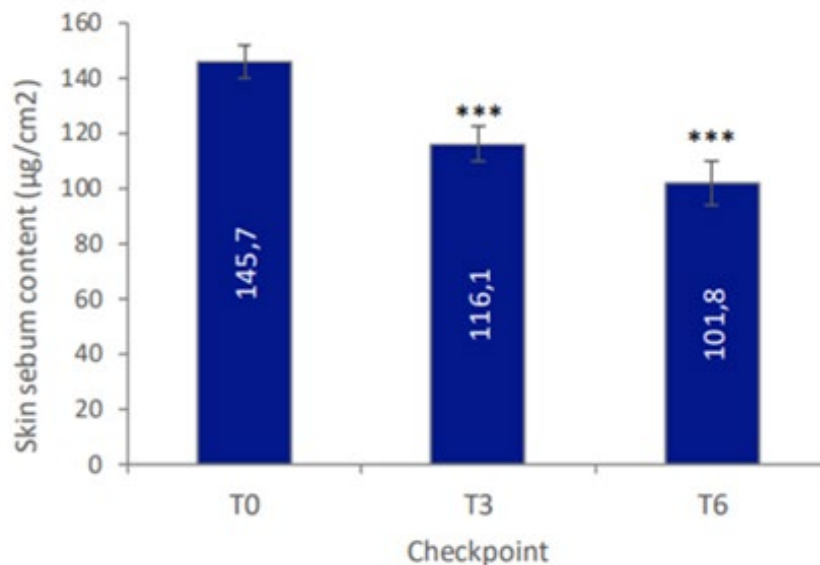


Figure 1: Mean sebumeter values obtained at each experimental time. Data are expressed as mean \pm SE. ***p<0.001

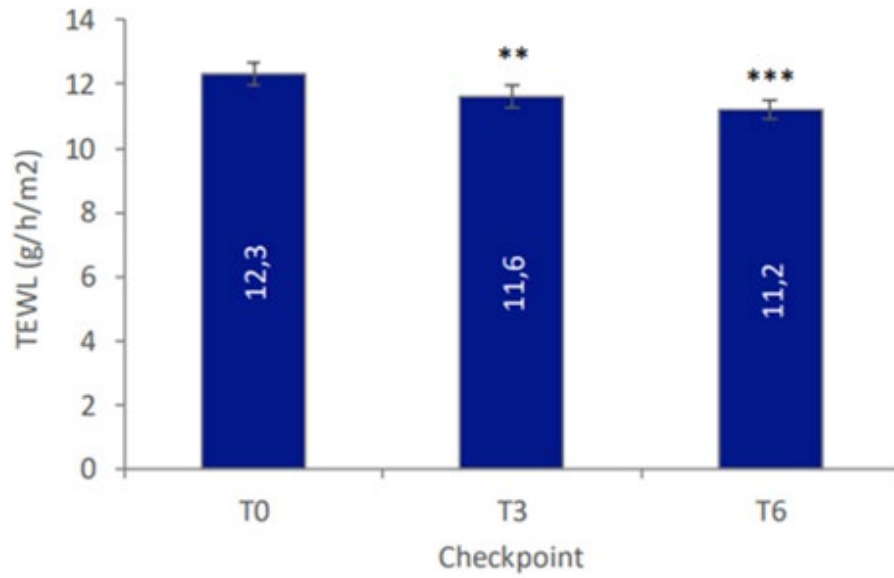


Figure 2: Mean TEWL values obtained at each experimental time. Data are expressed as mean±SE. **p<0.01, ***p<0.001

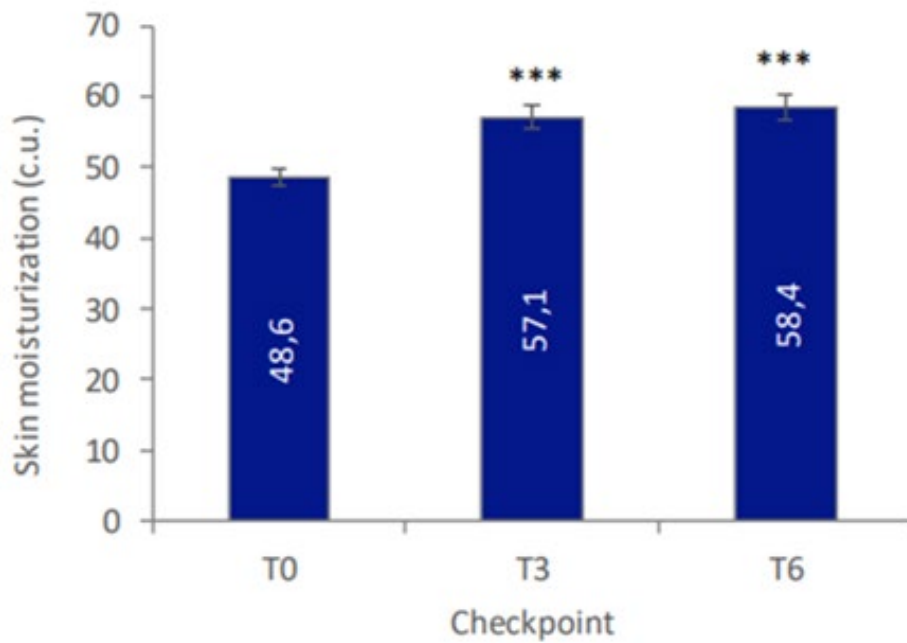


Figure 3: Mean results on skin moisturization. Data are expressed as mean±SE. ***p<0.001

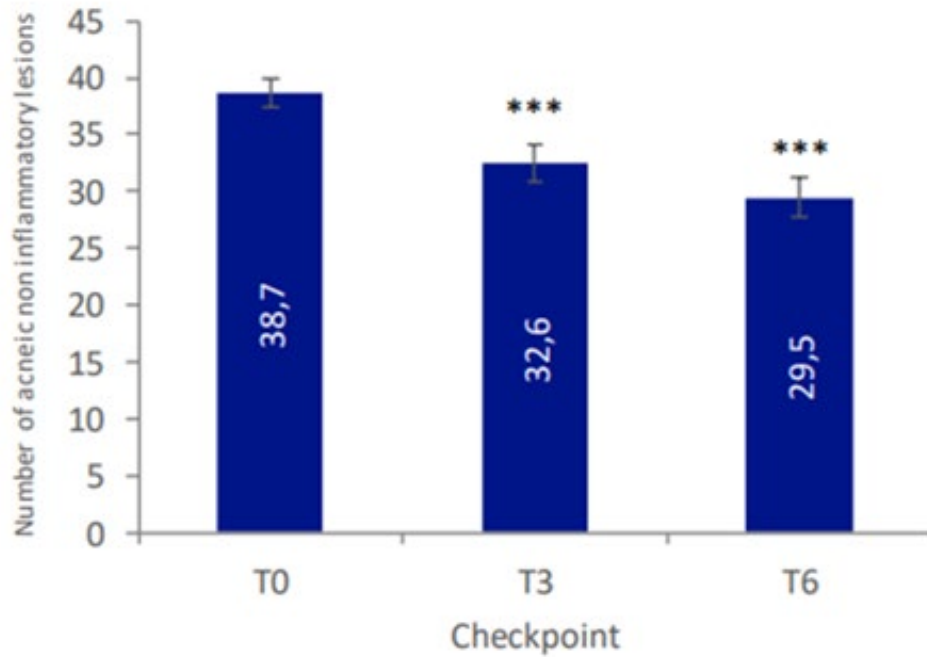


Figure 4: Mean results on acne non-inflammatory lesions. Data are expressed as mean±SE. ***p<0.001



Figure 5: Efficacy of the treatment. A) Clinical image at baseline; B) Clinical image after 6 weeks



Figure 6: Efficacy of the treatment. A) Clinical image at baseline; B) Clinical image after 6 weeks

Discussion

Acne is a very common inflammatory skin disease. Many patients affected by acne also have sensitive skin, correlated to the alteration of epidermal barrier function or secondary to the active treatments used for acne management [13]. Skin cleansing represents the first step in acne care, because it contributes to removing excess sebum and preventing follicular obstruction [14]. However, intensive washing and aggressive cleansers can be associated with an increased risk of skin barrier impairment and dry skin. For these reasons, particularly in sensitive skin, the ideal cleanser should be non-comedogenic, non-acnegenic, non-irritating, non-allergic and pH balanced [15, 16]. In addition, it is also recommended to use moisturizers during and after medical treatments to counteract the dryness associated with acne medications [17].

In this study a specific regimen combination treatment protocol composed of a cleanser, a topical treatment gel containing retinoids, antibacterial and keratolytic agents, and an adjuvant moisturizing cream was tested for the management of acne in subjects with sensitive skin. The cleanser contained Aloe Vera and Biopep15, an oligopeptide with antibacterial activity, that can interfere with lipoteichoic acid (a component of the wall of *Cutibacterium acnes*) [18]. The topical treatment gel contained: retinoids in the form of Retinsphere® technology (hydroxypinacolone retinoate and retinol in a glycosphere system, that allows a slow release of the actives, improving their chemical stability and their bioavailability); Biopep15; niacinamide 4%; and finally salicylic and glycolic acids [19, 20].

The third component of this protocol regimen was a moisturizing, sebo-regulating and barrier renewal cream with additional pigment-control agents to help prevent PIH common in these subjects [21]. In this study we demonstrated that the products used

in this cosmetic treatment regimen were well tolerated by patients with sensitive and acne-prone skin, indeed no severe adverse effects were recorded during the study. The cosmetic treatment was also effective in decreasing the non-inflammatory acne lesions and sebum production, and improving skin barrier by reducing trans epidermal water loss. In addition, this regimen protocol significantly increased skin moisturization. Previous studies evaluated the efficacy, tolerability and safety of topical products containing Retinsphere® and Biopep15 technologies in subjects with mild to moderate acne [22-24]. In this trial, in addition to the efficacy of the topical treatment containing retinoids, we confirmed that the combination of the three skin care products was well tolerated and enabled the improvement of acne lesions in subjects with acne and sensitive skin. Some limitations should be considered in evaluating our results.

This study was an uncontrolled, non-randomized trial. However, to improve the internal validity of the study, instrumental evaluations were conducted to support the clinical data. The products used during the trial determined a significant decrease in acne non-inflammatory lesions by -24% after 6 weeks. Although the clinical efficiency in terms of percentage reduction of acne lesion is slightly lower compared to other studies [23] this could be related to the limited period considered (generally the trials with the aim to assess efficacy in acne subjects are conducted for at least 12 weeks) and to the fact that in this study we enrolled only subjects with non-inflammatory predominant acne lesions. However, the duration of the trial was adequate for the evaluation of the primary outcome of the study, i.e. to confirm the tolerability and safety of this cosmetic treatment regimen in subjects with sensitive and acne prone skin.

Conclusions

The results obtained in this trial using a regimen based on the use of a cleanser, a topical treatment product containing retinoids and an antibacterial peptide, and a moisturizing, sebum-regulating and barrier renewal cream, represent an effective and well-tolerated treatment for the management of acne prone skin in subjects with sensitive skin. Further study could be useful to better evaluate the long-term efficacy of this cosmetic protocol.

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