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A MULTICENTER OPEN STUDY ON THE TOLERABILITY AND EFFICACY OF A COSMETIC TREATMENT IN MILD ACNE VULGARIS DURING THE SUMMER MONTHS

N. CASSANO, M. CARBONARA[1], M. GRANDOLFO[2], S. CALABRETTA, C. CASTELLANA, C. COVIELLO[2], S. CURIA[3], S. DATTOLA[3], C. DE CARO[3], G. FAVERO[3], G. FELICE[3], A. FERRARI[3], D. FIORENTINO[3], G. LIGUORI[3], R. LOPREIATO[3], L. OTTOMANO[3], E. PROVENZANO[3], F. SALAMINA[3], R. VERNACI[3] and G.A. VENA[2]

Istituto Dermopatico dell'Immacolata, I.D.I., I.R.C.C.S., Rome,
[1]Unit of Occupational Medicine; [2]Unit of Dermatology, University of Bari,
[3]Present address: Unit of Dermatology, University of Bari; Italy

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The improvement of acne vulgaris (AV) during summer months is a general opinion which is not universally accepted as some patients experience no change or even an aggravation of their AV during hot months. Therapeutic management of AV in summer is often difficult; in fact, most traditional anti-acne treatments are contraindicated or poorly tolerated during summer months. In this study we evaluated the tolerability and effectiveness of a cosmetic anti-acne treatment performed for 12 summer weeks in 347 patients (mean age, 19.4 yrs) with mild AV of the face. The study product (Exfoliac®) contained a mixture of alpha hydroxy acids and substances with moisturizing and/or lenitive effects. In the first 4 weeks, Exfoliac® 10 cream was applied twice a day (b.i.d.). The treatment in the following 8 weeks was decided on the basis of dermatologist's assessment of the clinical response and could consist in Exfoliac® 10 cream or Exfoliac® 15 cream, once daily (o.d.) or b.i.d. During the study period, patients used Exfoliac® cleansing gel. The cumulative results indicate a significant improvement of AV lesions and seborrhoea, irrespectively of sun exposure, and a good tolerability, even in sunbathed patients. Adverse reactions, mostly of mild severity, appeared to be independent of sunbathing or use of sunscreens and were observed in a small proportion of cases (6.8% in the first 4 weeks and 5.6% in the last 8 weeks).

Our results suggest that this type of treatment is an effective and safe approach to patients with mild AV who require treatment in the summertime.

Acne vulgaris (AV) is a common inflammatory disease of the pilosebaceous units. It is traditional opinion that AV spontaneously improves in summertime (1-3), but there is not an unanimous agreement on this and some evidence seems to indicate a great variability in seasonal fluctations of AV severity (4-6). Moreover, most conventional AV treatments are usually stopped in summer because hot climate and sun exposure can affect the tolerability profile of these treatments.

The goal of this study is to evaluate the tolerability and effectiveness of a cosmetic treatment (Exfoliac® cleansing gel, Exfoliac® 10 cream and Exfoliac® 15 cream) in mild AV during summer months.

MATERIALS AND METHODS

Subjects with mild AV (purely comedonic or with modest signs of inflammation) of the face entered the study. They did not present the following exclusion criteria: secondary acne, use of concomitant treatments

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Mailing address: Prof. G.A. Vena, M.D.
Department of Internal Medicine, Immunology and Infectious Diseases
Unit of Dermatology, University of Bari
Piazza Giulio Cesare, 11 - 70124 Bari, Italy
Phone/fax: +39 080 5478 920
e-mail: g.vena@dermatologia.uniba.it

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with potential influence on AV, hypersensitivity to any ingredients of the study products, pregnancy and lactation. Previous active treatments were interrupted for a variable period of time prior to the study start, as follows: anti-acne topical preparations for 2 weeks, chronic antinflammatory therapies (either local or systemic), systemic antibiotics for 4 weeks, and oral retinoids for 3 months. In our study population, the duration of AV ranged from 2 months to 15 years (mean, 31 months); skin phototype was defined as normal in 57% of cases, fair in 26% and dark in 17%. A heterogeneous seasonal variation of AV was observed by patients. Many patients noticed a variable degree of improvement in the previous summer independently of sun exposure, but some patients reported no change or even aggravation (26% among the patients who had not undergone sunbathing in the previous summer and 20% among those who had been exposed to sunlight) (Tab. I).

Study treatment lasted 12 weeks and was performed in the summer 2002. It was composed by two different sequential phases:

- Phase 1, from baseline visit (T0) to 4 weeks (T1), in which all patients applied Exfoliac® 10 cream b.i.d. to the face;
- Phase 2, from T1 to 12 weeks (T2), in which study treatment could be differentiated on the basis of the clinical response according to the investigator's decision, and could consist of Exfoliac® 10 cream or Exfoliac® 15 cream, applied b.i.d. or o.d.

During the 12-week study period patients used Exfoliac® cleansing gel. The composition of the study products is shown in Tab. II.

Clinical evaluations were performed at T0, T1 and T2; at each visit, tolerability and efficacy parameters were assessed. The severity of skin xerosis/scaling, erythema, burning and seborrhoea was evaluated through a four-score rating scale (0= absent; 1= mild; 2= moderate; 3= notable). For the count of AV lesions (open comedones, closed comedones and inflammatory lesions) a five-score scale was used: 0= no lesions; 1= 1-10 lesions; 2= 11-20 lesions; 3= 21-30 lesions; 4= >31 lesions).

Local adverse reactions and concomitant treatments were noted, as well as the exposure to sunlight and the use of sunscreens.

As concerns the statistical analysis, the Kolmogorov-Smirnov test showed that the evaluated parameters were not normally distributed at baseline; therefore, a non-parametric test (Wilcoxon matched-pairs signed-ranks test) was used (significance for p values <0.05). The analysis was also performed in two separate subgroups of patients, the sunbathed and the non-sunbathed, in order to assess the possible influence of the exposure to sunlight on efficacy and tolerability parameters.

Patients and physicians independently gave their judgment of the efficacy and the tolerability of the treatment. Patients were also asked about treatment acceptability.

RESULTS

Three hundred and forty-seven subjects (214 female and 133 male), aged 11 to 37 years (mean, 19.4), living in Southern Italy, were enrolled in the study. The subjects assessable at T1 and T2 were 319 and 301, respectively. The study was prematurely interrupted in 46 cases, most of whom (30) were lost to follow-up. Other reasons included clinical cure in 8 patients, poor compliance in 3, administrative reasons in 3, prohibited treatments in 1, and adverse reaction in 1. Sunbathing occurred in 112 subjects from T0 to T1 and in 163 from T1 to T2. 70 patients reported the regular use of sunscreens at T1 and 108 at T2. Compliance with the treatment was considered satisfactory in all cases but 17 at T1 and 11 at T2. The mean number of cream packs consumed was 1.8 at T1 (range: 1-3) and 1.9 at T2 (range: 1-5).

After 4 weeks of treatment with Exfoliac® 10 cream b.i.d., a significant reduction ($p<0.05$) in the number of AV lesions and in the severity of seborrhoea was noted in the whole study population, without differences related to the presence or absence of sun exposure (Tab. III). Statistical significance was seen also for the global variation of erythema, burning and xerosis/scaling, with a clinical trend towards a reduction in the first two parameters and towards a slight increase in xerosis/scaling (Tab. III). The analysis of the two subgroups confirmed the significant reduction in erythema and burning in both subgroups. Xerosis/scaling did not vary in the group of non-sunbathed patients, and increased significantly ($p<0.05$), although not in a clinically relevant way, in the sunbathed subjects. In the 2nd phase of treatment, the patients assessable at T2 received the following treatment regimens:

- Exfoliac® 10 cream b.i.d. in 173 patients (sunbathed: 97; non-sunbathed: 76),

Response	*Sun exposure*	*No sun exposure*
Not known/not applicable	16%	18%
Aggravation	7%	12%
No change	13%	14%
Slight improvement	19%	31%
Notable improvement	34%	21%
Complete remission	11%	4%

Tab. I. *Correlation between sun exposure and the response of AV during the previous summer.*

Tab. II. *Composition of the study products.*

Exfoliac® cleansing gel (pH 6)
Ammonium lactate 4.7%
Zinc lactate 0.3%
Mixture of surface-active agents 21.2%
Polyenic ester of fat acids 1%

Exfoliac® 10 cream (oil/water cream; pH 3.5)
Glycolic acid 6%
Esters of citric acid 7.3%
Vitamin A palmitate 0.3%
Zinc gluconate 0.5%
Polyoxipropylen stearyl alcohol 3%
Vitamin E acetate 0.5%
Alpha-bisabolol 0.85%
Ammonium glycyrrhetinate 0.5%

Exfoliac® 15 cream (oil/water emulsion; pH 3.5)
Glycolic acid 4.2%
Lactic acid 3.5%
Malic acid 0.5%
Salicylic acid 0.25%
Esters of citric and malic acids 11%
Vitamin A 0.3%
Zinc lactate 0.25%
Polyoxipropylen stearyl alcohol 3%
Vitamin E acetate 0.5%
Alpha-bisabolol 2%
Allantoin 1%

Tab. III. *Summary of results at T1 (after 4 weeks of treatment with Exfoliac® 10 cream b.i.d.).*

Parameter	T0 Mean score	T1 Mean score
Open comedones	2.11	1.59*
Closed comedones	2.11	1.57*
Inflammatory lesions	1.45	1.11*
Seborrhoea	1.74	1.09*
Erythema	0.97	0.67*
Burning	0.53	0.4*
Xerosis/scaling	0.31	0.39**

*$p<0.05$ *vs. T0 in both sunbathed and non sunbathed subjects*
** $p<0.05$ *vs. T0 in the sunbathed subjects, non-significant difference vs. T0 in the non-sunbathed subjects.*

	T1 Mean score	T2 Mean score	Statistical significance	Differences between sunbathed and non-sunbathed patients
Exfoliac® 10 o.d.				
Open comedones	1.50	1.11	p<0.05	n.s. in non-sunbathed patients and p<0.05 in sunbathed patients for any parameter (p=0.045 for inflammatory lesions in the sunbathed group)
Closed comedones	1.41	1.11	p<0.05	
Inflammatory lesions	1.08	0.97	p<0.05	
Exfoliac® 10 b.i.d.				
Open comedones	1.51	1.03	p<0.05	p<0.05 in the two subgroups for any parameter
Closed comedones	1.48	1.09	p<0.05	
Inflammatory lesions	1.05	0.88	p<0.05	
Exfoliac® 15 o.d.				
Open comedones	1.68	1.31	p<0.05	Inflammatory lesions in sunbathed patients and open/closed comedones in non-sunbathed: n.s.
Closed comedones	1.68	1.15	p<0.05	
Inflammatory lesions	1.43	1.12	p<0.05	
Exfoliac® 15 b.i.d.				
Open comedones	1.85	1.24	p<0.05	Inflammatory lesions in sunbathed patients: n.s.
Closed comedones	1.79	1.14	p<0.05	
Inflammatory lesions	1.17	1.00	p<0.05	

n.s.= non significant

Tab. IV. *Variation of AV lesions at T2 versus T1.*

	T1 (N.)	T2 (N.)
Irritation/scaling	8	0
Erythema/burning	7	6
Erythema/scaling	4	1
Event not specified	2	3
Erythema after sunbathing	1	3
Pustular reactions	0	2
Xerosis.	0	2
Total	**22 (6.8%)**	**17 (5.6%)**
Sunbathed patients	8	8
Non-sunbathed patients	14	9
Regular use of sunscreens	6	5
No use of sunscreens	16	12

Tab. V. *Adverse reactions reported during study treatment.*

- Exfoliac® 10 cream o.d. in 34 patients (sunbathed: 23; non-sunbathed: 11),
- Exfoliac® 15 cream b.i.d. in 62 patients (sunbathed: 30; non-sunbathed: 32),
- Exfoliac® 15 cream o.d. in 32 patients (sunbathed: 13; non-sunbathed: 19).

The combined data show a statistically significant reduction of AV lesions from T1 to T2, irrespective of the influence of sunbathing (Tab. IV). The comparison between T2 and T0 yield significant differences for seborrhoea and AV lesions for all parameters. Seborrhoea notably decreased in the entire population at T2 as compared with both T1 and T0; (.) In the analysis of the subgroups, the only non-significant result was noted in the comparison between T2 and T1 in the sunbathed patients treated with Exfoliac® 15 cream o.d.

Concerning erythema, burning and xerosis/scaling, from T1 to T2, there was a further trend towards a reduction of their severity. A statistical significance was observed in the following situations:

- entire population: xerosis/scaling, erythema and burning with Exfoliac® 10 cream b.i.d. and o.d.; erythema with Exfoliac® 15 cream o.d.;
- sunbathed patients: xerosis/scaling, erythema and burning with Exfoliac® 10 cream o.d. and b.i.d.
- non-sunbathed patients: erythema and burning with Exfoliac® 10 cream b.i.d. and Exfoliac® 15 cream o.d.

Local adverse reactions were reported by 22 patients (6.8%) at T1 and by 17 patients (5.6%) at T2. These were mild in all cases except one who complained of a moderate irritation, resulting in premature withdrawal. The frequency of adverse reactions appeared to be not notably influenced by sun exposure (Tab. V).

The opinion on efficacy, tolerability and acceptability of treatment is summarized in Table VI. In the majority of cases, both the subjects and the investigators gave positive judgments on the efficacy (95.1% and 96.3%, respectively) and tolerability (99.4%). All subjects judged positively the cosmetic acceptability of Exfoliac® cleansing gel, and the acceptability of Exfoliac® 10 cream and Exfoliac® 15 cream was considered satisfactory by most of them (98.5% and 97.5%, respectively).

DISCUSSION

The improvement of AV in summertime is a common opinion of dermatologists, especially from Western countries (1-3). This opinion is not universally accepted (4-7); some patients, with variable frequency depending on the study series, noted no change or even complained an aggravation in summer, as confirmed in our study population. It has been claimed that the hot temperature, marked humidity and sweating may be aggravating factors in AV, particularly at certain latitudes (6). Sunlight has been advocated by some authors in the treatment of AV (2), but others do not agree

	Absent	Poor	Sufficient	Fair	Good	Excellent
Patient's opinion on efficacy (%)	1.6	3.3	1.6	16.3	41.3	35.9
Investigator's opinion on efficacy (%)	0.7	3	1	11.3	58	26
Patient's opinion on tolerability (%)	0.3	0.3	2.6	7	47.2	42.6
Investigator's opinion on tolerability (%)	0.3	0.3	2.3	7	47.5	42.6
Patient's opinion on acceptability (%)						
Exfoliac® cleansing gel	0	0	0.5	5	35	59.5
Exfoliac® 10 cream	1	0.5	1.5	13	48	36
Exfoliac® 15 cream	1.5	1	1.5	19	60	17

Tab. VI. *Opinion on treatment's efficacy, tolerability and acceptability (N. of patients: 301).*

(4). Moreover, the approach to AV during the summer months is not simple. In fact, in summer, some traditional treatments are contraindicated because of the risk of adverse reactions (phototoxicity, photoallergy, hyperpigmentation). Other treatments are poorly tolerated as they augment the sensitivity and the reactivity of the skin to the sunlight. The results of our study suggest the feasibility during summer months of a cosmetic anti-acne treatment, containing a mixture of alpha hydroxy acids and other active ingredients. Alpha hydroxy acids are well known for their smoothing and exfoliating effects, mediated primarily by decreased corneocyte cohesion and increased desquamation (7-9). In this way, they can contrast the ductal hyperkeratinization, which is a key event in AV.

A placebo-controlled study demonstrated the efficacy and tolerability of Exfoliac® 15 cream (10). Our study has shown that both Exfoliac® 15 cream and Exfoliac® 10 cream cause a significant reduction in AV lesions and seborrhoea in the majority of patients, independently of sunbathing. Interestingly, the tolerability of treatment was quite good, even if associated with sun exposure, confirming previous data which demonstrated the lack of photosensitivity of the Exfoliac® line (11). In general, the tolerability parameters remained unchanged or showed a trend towards an improvement during the observational period. At T1, as expected with an exfoliating treatment, xerosis/scaling increased slightly in some cases. Local adverse reactions, mostly of mild intensity, were noticed by 6.8% and 5.6% of patients at T1 and T2, respectively, and caused premature discontinuation of the study only in 1 case. Moreover, it should be stressed that topical anti-acne treatments, especially those with comedolytic effects, usually induce mild/moderate skin irritation. The presence of moisturizing and lenitive substances in Exfoliac® products (e.g., vitamin E acetate, alpha-bisabolol, ammonium glycyrrhetinate, allantoin) and the sequential treatment regimen with increasing concentrations of alpha hydroxy acids can likely improve the tolerance of the skin to these compounds in the long term treatment.

In conclusion, the results obtained in this open multicenter study suggest that treatment with Exfoliac® products represents an effective and safe approach to patients with mild AV who needed to be treated during summer months.

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