EVALUATION OF "STEROID-SPARING" EFFECTS OF XANTHENA® CREAM IN PATIENTS WITH MILD TO MODERATE ATOPIC DERMATITIS

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Emollients play an important role in the management of atopic dermatitis (AD). The aim of this study was to evaluate the efficacy and the "steroid-sparing" activity of an emollient cream (Xanthena® cream) in patients with mild to moderate AD. Patients were asked to apply twice a day for 7 days a cream containing hydrocortisone butyrate on the lesional skin and then to apply Xanthena® cream only on the left side of affected areas. During the 2-month study period, the use of the corticosteroid cream was resumed in case of flare-up in any side.

The results obtained show significant differences of both the total severity score and the intensity of each symptom and sign of AD between the skin areas treated with Xanthena® cream and the control areas ($p<0.05$); a relevant reduction of steroid requirement was also noted in correlation with the use of this emollient cream ($p<0.05$). A significant improvement was observed even after the first month of therapy for most symptoms, except for excoriations/fissuring, oozing/crusting and burning which improved only at 2 months. Treatment was well-tolerated by the majority of patients; adverse local reactions, mostly transient and of mild intensity, were observed in 7% of cases.

Therapeutic management of atopic dermatitis (AD) is aimed at limiting triggering factors (irritants, infections, emotional stress, allergens, etc.), and at controlling xerosis, inflammation and pruritus. It is well-known that emollients play a crucial role in the baseline management of AD: they improve skin dryness and elasticity, and contribute to restore the skin barrier function and to attenuate the impact of irritants (1, 2). Emollients can be used during the active phase or flare-up of AD, in combination with other therapies, because of their specific effects on skin barrier functions, which are primarily affected in AD, and/or their mild antiinflammatory activity. Moreover, the use of emollients during the disease-free periods can help to maintain the results obtained with active treatments and to minimise the risk of relapses, thus leading to a reduction in the requirement of topical corticosteroids.

Based on these observations, we wanted to assess the effectiveness and 'steroid-sparing' activity of an emollient cream in patients with mild to moderate AD.

MATERIAL AND METHODS

Two hundreds and forty-five patients, aged 4 months to 53 years (mean age, 11.5), affected with mild to moderate AD, gave their oral informed consent to participate in the study. Exclusion criteria were concomitant skin disorders, including contact allergy and infections capable of affecting the interpretation of

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results, as well as any kind of disease which could cause the use of prohibited treatments. After suspension of any active treatment, a cream containing hydrocortisone butyrate was applied twice a day (b.i.d.) for 7 days on the lesional skin. Afterwards, patients or parents of affected children were instructed to apply b.i.d. an emollient cream (Xanthena® cream, Lofarma Laboratories, Milan, Italy) only on the left side of the areas previously treated, leaving the right side without any treatment. This therapeutic regimen was followed for 2 months, unless a flare-up of symptoms occurred; in this circumstance, the use of hydrocortisone cream could be resumed on affected areas, on any side, as needed. Study participation had to be prematurely interrupted in case of massive exposure to sun or ultraviolet radiations, treatment with systemic corticosteroids and immunomodulants or with drugs known to induce relevant influence on AD lesions. Other concomitant treatments, including antibiotics and H1-receptor antagonists, were allowed only if strictly necessary and required notification of study personnel. Non-specific preventive measures were recommended, such as reduced contact of skin with wool, synthetic textile fibres, textile dyes, aggressive cleansings, and other irritants.

The study was carried out in autumn and winter in order to limit the interference of climatic factors due to the seasonal fluctuations of AD activity and severity.

Clinical evaluations were performed at baseline (T_0) and after 4 weeks and 8 weeks of treatment (T_1 ad T_2, respectively). Disease severity was rated using a four-point scale (0= absent, 1= mild, 2= moderate, 3= notable) for the following items: erythema, xerosis, scaling, fissuring/excoriations, oozing/crusting, papulation/oedema, lichenification, atrophy, burning, and pruritus. A similar four-point scale was used to assess the impact of AD on quality of life, with particular reference to the influence on psychological aspects and mood, interference with sleep and with ordinary daily activity and social life. At each visit, the number of applications of hydrocortisone cream on either the left or the right side was recorded.

The results were analysed with Wilcoxon test (significance for $p<0.05$); for steroid requirement, descriptive parameters (mean number of applications *per* patient, proportions of patients in the study population) were also used. In order to eliminate the influence of the additional use of the corticosteroid cream on the results, a further analysis was performed, evaluating the differences of clinical scores in those patients who never used the hydrocortisone cream apart from the initial 7 days. Paired-samples sign test was used to analyse these data; values of $p<0.05$ were considered significant.

RESULTS

During the observational period, concomitant treatments were reported in only 19 cases: 2 patients required oral corticosteroids due to asthma and therefore were prematurely withdrawn; 2 patients took oral antibiotics due to respiratory infections; 15 patients used oral H1-receptor antagonists during the first phase of treatment and mostly for a few days owing to incoercible pruritus. One hundred and eighty-nine patients were included in the final 'per-protocol' analysis. The remaining cases were not assessable because of administrative reasons (lost to follow-up after baseline visit), poor compliance to protocol treatment procedures, or lack of sufficient information about efficacy parameters (clinical evaluation, use of the steroidal cream).

The evaluated patients had a mild to moderate AD, with lesions variably distributed (Tab. I). They referred the onset of AD at the mean age of 5.5 years (range: 0-38 years) whereas the mean duration of the current episode was 5.5 weeks (range: 1-52 weeks). A familiar history for atopic diseases was present in 61% of cases.

The overall response to treatment was positive; in the analysis of the assessable patients there were significant differences ($p<0.05$) in both the total disease severity and in the intensity of each sign and symptom of AD between the right side and the left side, independently of the subsequent use of steroidal cream, applied as needed (Fig. 1). A significant improvement of the quality of life items was also noted (Fig. 2). Moreover, a relevant reduction of the use of topical corticosteroid was observed in the side treated with Xanthena® cream as compared with the control side ($p<0.05$) (Tab. II). The additional analysis performed on 65 patients, who never applied the steroidal cream after the initial 7 days, showed significant differences ($p<0.05$) between the two opposite sides for each parameter at each visit, except for excoriations/fissuring, oozing/crusting and burning at visit T_1; these items, however, improved significantly on the left side at 2 months (Tab. III).

There were 11 premature withdrawals, all within the first month: 4 due to adverse reactions,

Tab. I. *Distribution of AD lesions (total patients: 189).*

Localization	N. of patients
Antecubital folds	120
Popliteal folds	108
Face	98
Neck/Extensor aspect of upper limbs	7
Wrists	4
Groin/auricular area/feet	3
Buttocks	2
Axillary folds/legs	1

Tab. II. *Use of the topical corticosteroid over the study period.*

Visit	Side	N. of days/month (mean)	N. of patients who used the corticosteroid cream
T_1	right	6	93
T_1	left	6.5	53
T_2	right	5.8	63
T_2	left	5.9	28

Left side *versus* right side at T_1 and T_2 visits: $p<0.05$

Tab. III. *Changes of clinical scores (calculated on 65 patients without additional use of steroid on both sides).*

Sign/symptom	T_0	T_1-right side	T_1-left side	T_2-right side	T_2-left side
Xerosis	1.6	1.4	0.9	1.3	0.5
Scaling	1.5	1.1	0.6	0.9	0.3
Erythema	1.5	1.1	0.8	0.9	0.5
Fissuring/excoriations	0.9	0.7*	0.6*	0.5	0.2
Papulation	0.7	0.5	0.3	0.4	0.2
Atrophy	0.6	0.4	0.2	0.3	0.1
Oozing/crusting	0.6	0.5*	0.4*	0.4	0.2
Lichenification	1.2	0.8	0.5	0.8	0.4
Burning	1	0.6*	0.5*	0.5	0.2
Pruritus	2	1.3	0.9	1.1	0.4

* *Non-significant differences between the left side and the right side.*

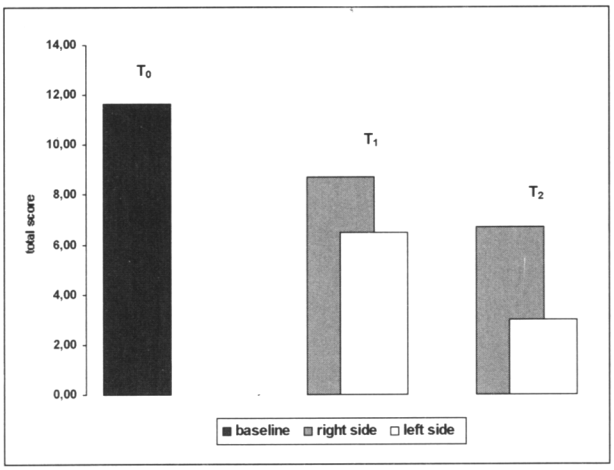

Fig. 1. *Changes of the total average clinical severity score (189 patients).*

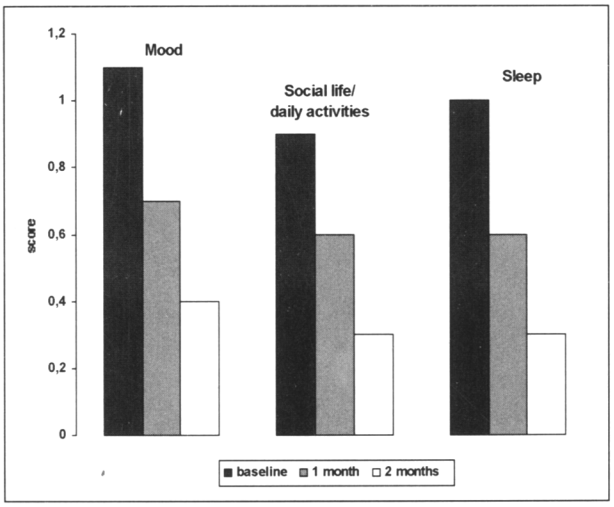

Fig. 2. *Changes of the impact on the quality of life (189 patients).*

5 due to inefficacy, and 2 owing to prohibited concomitant treatments. The tolerance to the emollient cream was good in most cases. Adverse reactions at the site of application occurred in 13 cases: transient burning in 8 patients, persistent burning associated with worsening of AD lesions in 2 patients, and irritation in 2 patients. Another local adverse event was not specified.

DISCUSSION

The results of this study demonstrate that the use of an emollient, following the initial treatment with a topical corticosteroid, can reduce the severity of lesions in most patients with mild to moderate AD. Significant differences between the side treated with the emollient cream and the control side were registered particularly in subacute and chronic forms of AD, even within the first month of treatment, with improvement of skin dryness, scaling, erythema and pruritus. The severity of fissuring/excoriations, oozing/crusting, and burning was significantly reduced as compared to the control side after 2 months of treatment.

An important finding concerns the role of emollients as 'steroid-sparing' agents (3); in our report, the number of patients who required corticosteroid treatment in the side treated with Xanthena® cream was significantly reduced as compared with the opposite side, although the mean number of monthly applications of the corticosteroid cream on the two sides was similar.

It is likely that the activity of Xanthena® cream is linked not only to the moisturizing properties but also to the synergic effects of its active ingredients. The principle components of this cream are triterpenoid glycosides, which possess lenitive and antinflammatory actions (4-10), and hyalunoric acid, which exerts moisturizing effects, acts as a scavenger of radical oxygen species, modulates phagocytosis and chemotaxis of polymorphonuclear cells and macrophages, and promotes tissue repair, though stimulation of fibroblasts and regulation of neovascularization (11-15). The relevance of these ingredients in the treatment of AD should be evaluated in future controlled studies *versus* other emollient creams.

In conclusion, this study confirms that the use of emollients is of primary importance in AD in order to reduce the risk of relapses and flare-ups and the requirement of topical corticosteroids.

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