



## CLINICAL REPORT

## A Double-Blind Study Comparing the Effect of Glycerin and Urea on Dry, Eczematous Skin in Atopic Patients

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Moisturizing creams have beneficial effects in the treatment of dry, scaly skin, but they may induce adverse skin reactions. In a randomized double-blind study, 197 patients with atopic dermatitis were treated with one of the following: a new moisturizing cream with 20% glycerin, its cream base without glycerin as placebo, or a cream with 4% urea and 4% sodium chloride. The patients were asked to apply the cream at least once daily for 30 days. Adverse skin reactions and changes in skin dryness were assessed by the patient and a dermatologist. Adverse skin reactions such as smarting (a sharp local superficial sensation) were felt significantly less among patients using the 20% glycerin cream compared with the urea-saline cream, because 10% of the patients judged the smarting as severe or moderate when using glycerin cream, whereas 24% did so using urea-saline cream ( $p < 0.0006$ ). No differences were found regarding skin reactions such as stinging, itching and dryness/irritation. The study showed equal effects on skin dryness as judged by the patients and the dermatologist. In conclusion, a glycerin containing cream appears to be a suitable alternative to urea/sodium chloride in the treatment of atopic dry skin. *Key words:* cream; dry skin; emollients; moisturizer.

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The aim of the present investigation was to compare local tolerance (primary variable) and influence on skin dryness (secondary variable) of a new moisturizing cream with 20% glycerin with its cream base as placebo, and also with an established medicinal urea cream containing 4% urea and 4% sodium chloride in patients with atopic dermatitis. The patient scored the adverse skin reactions on a category scale and the dryness on a visual analogue scale (1, 2). The dermatologist assessed the visual and tactile signs of dryness and estimated the area affected (1, 3).

### MATERIALS AND METHODS

#### Patients

A total of 197 patients with atopic dermatitis were included (4). None had known allergy to ingredients in the test creams. The patients were randomized into three groups: the glycerin group comprising 55 women and 13 men (mean age 35 years, SD 12), the urea group comprising 47 women and 16 men (mean age 32 years, SD 12), and the placebo group comprising 49 women and 17 men (mean age 34 years, SD 11). The local ethics committees approved the study and informed consent was obtained.

#### Test products

The glycerin cream contained 20% glycerin, aqua, petrolatum, canola, mineral oil, cetearylalcohol, glycerylstearate, dimethicone, PEG-100 stearate, glyceryl polymethacrylate, cholesterol, propyleneglycol, methylparaben and propylparaben. In the placebo cream, glycerin was replaced with water. The urea cream contained 4% urea and 4% sodium chloride as water-binding substances in an oil-in-water emulsion, pH about 5. Other ingredients were paraffinum liquidum, PEG-5-glycerylstearate, cetylalcohol, stearyl alcohol, stearic acid, trometamol, methylparaben, propylparaben, hydrochloric acid and water.

#### Study design

Dry, eczematous skin was treated as the patients were asked to replace their ordinary moisturizer with the test cream and to use as much cream as desired and at least once daily for 30 days. They were instructed to record their use in a patient diary and to submit the remaining amount at the end of the study for assessment of compliance. The patients were allowed to continue their use of topical corticosteroids, but to note their use in the diary. The study was carried out in February, March and April.

#### Evaluations

The patients were asked to score the degree of smarting sensation (a sharp, local, superficial effect which can be experienced during contact with for example acidic solutions), stinging, itching and dryness/irritation on a scale of 5 levels (0–4) after 2 weeks of treatment. They were also asked to note skin dryness at the beginning of the study and after one month on a visual analogue scale (14 cm). The dermatologist assessment of dry skin was done at inclusion and after 30 days according to a proposed system for dry skin and ichthyosis, where the dry skin area and severity index (DASI) is calculated as the product of the sum of severity scores and area affected in 4 body regions (3). Scaling, roughness, redness and cracks (fissures) in the worst affected area in each body region were

scored from 0 to 4, and the size of the area involved was estimated. The sum of the severity score was multiplied by the area affected in percentage. The maximum DASI score was 1600. The same dermatologist evaluated the patient at inclusion and at the end of the study. Evaluations were performed in the same room and with the same light conditions.

#### Calculations and statistics

The number of patients reporting different degrees of adverse skin reactions is shown graphically by the percent in each category stacked into a bar chart representing 100%.

Statistical significances between the glycerin cream and the other two treatments were tested using Mann-Whitney.  $P < 0.025$  was considered as significant for each of the two comparisons to obtain an overall significance level of  $p < 0.05$ .

## RESULTS

Ninety-four percent of the jars were returned to the clinic for weighing. The median consumption of glycerin cream was 306 g, of urea cream 324 g and of placebo cream 360 g. The number of applications was significantly lower for the glycerin cream compared to its placebo ( $p = 0.024$ ), but there was no difference between glycerin and urea cream ( $p = 0.33$ ). Twenty percent of the patients did not use corticosteroids during the study period, whereas the rest used corticosteroids sometimes or daily. In the glycerin group, the median number of days using corticosteroids was 8, in the urea group 7 days and in the placebo group 14 days. There was no difference between the glycerin group and the placebo ( $p = 0.18$ ) or between glycerin and urea ( $p = 0.52$ ).

Almost 40% of the patients reported some degree of smarting sensation from the use of glycerin cream or its placebo, compared with about 65% of the patients treated with the urea cream (Fig. 1). The difference in degree of smarting sensation between the glycerin cream and the urea-saline cream was statistically significant ( $p = 0.0006$ ); 10% of the patients judged the smarting as severe or moderate from the glycerin cream and more than twice as many (24%) did so from the treatment with urea cream. There was no difference in the frequency of smarting between glycerin cream and its placebo ( $p = 0.79$ ).

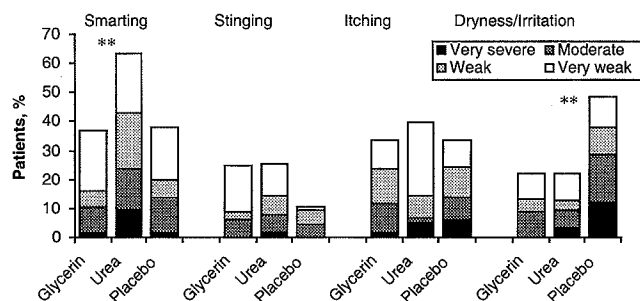


Fig. 1. The proportion of patients (%) reporting various degrees of skin reactions to the use of glycerine ( $n = 68$ ), urea ( $n = 63$ ) and placebo ( $n = 66$ ). Significant differences were observed between glycerine and urea regarding smarting ( $p = 0.0006$ ) and between glycerine and placebo regarding dryness/irritation ( $p = 0.0004$ ).

In contrast, there were no differences between treatment with the cream containing glycerin and urea regarding stinging, itching and experience of dryness/irritation ( $p = 0.83$ ,  $0.85$  and  $p = 0.97$ , respectively) (Fig. 1). Moreover, differences were not observed in stinging ( $p = 0.049$ ) or itching ( $p = 0.94$ ) between treatment with the glycerin cream and its placebo, whereas a lower degree of dryness/irritation was noted in the glycerin group than in the placebo group ( $p = 0.0004$ ) (Fig. 1).

There were no significant differences in the patients' judgement of dryness at the end of study between the three creams. During treatment with glycerin cream, 85% of the patients rated their skin improved, whereas 11% felt it became drier. In the urea group, 89% reported less dry skin and 11% more dry skin. In the placebo group, 69% reported improvement and 17% reported more dry skin. Patients in the glycerin group and those in the urea group had equal improvement of skin dryness ( $p = 0.77$ ), whereas the glycerin group had a significant improvement of dryness compared with placebo cream ( $p = 0.019$ ).

No differences were observed in disease severity measured as DASI scores between the glycerin and urea groups ( $p = 0.787$ ), nor between the glycerin and placebo groups ( $p = 0.565$ ), following one month of treatment. The DASI score decreased for the majority of the patients; 85% improved in the glycerin group, 89% in the urea group and 63% in the placebo group. Only 12% in the glycerin group and 10% in the urea group showed a deterioration of their disease, whereas 35% in the placebo group became drier during the treatment period according to the judgement of the dermatologist.

## DISCUSSION

It is well known that topical preparations can cause such unpleasant sensations as smarting, stinging and itching immediately after their application (5). Such preparations are not irritative in the ordinary sense and usually do not cause clinically noticeable skin damage. Smarting and stinging are mainly perceived in the face (5-7).

Some substances present in the tested creams are known to cause invisible skin reactions. For example, urea creams can cause smarting and stinging immediately after application, especially if applied to excoriated or fissured skin (2, 8-10). In addition, low pH and the presence of 4% sodium chloride in the urea cream are likely to contribute to the reported skin reactions (2, 9). In a previous study on atopy, a similar frequency and intensity was reported on adverse skin reactions using the same urea cream (2).

The hypothesis that glycerin cream produces a less smarting sensation than urea cream was demonstrated in the present study ( $p < 0.0006$ ) (Fig. 1). However, no difference in stinging potential was noted suggesting

different pathophysiological mechanisms. Moreover, the glycerin cream did not induce more smarting, itching and stinging than its placebo, suggesting good skin tolerability to glycerin. This is in accordance with data in the literature, where almost no reports on adverse effects from glycerin can be found, although it is used extensively (6). Other hygroscopic alcohols, such as propylene glycol and butylene glycol, can induce a variety of local effects, including irritation, sensitization and urticaria (12).

Our study showed that glycerin cream has a similar clinical effect as urea cream according to the judgement of the patients and dermatologists. The degree of improvement differed significantly between glycerin and placebo according to patient judgement, even though the patients applied the placebo cream more often than they applied the glycerin cream. Significantly more patients in the placebo group reported increased dryness/irritation than those in the glycerin group (Fig. 1).

In summary, glycerin is demonstrated to have a good skin tolerability on atopic dry skin. The cream containing 20% had a similar effect on skin dryness in patients with atopic dermatitis as the 4% urea cream with 4% sodium chloride as humectant. The study therefore suggests that the glycerin cream may have an advantage for atopic patients owing to its lower incidence and degree of smarting than the urea cream in combination with a similar effect on skin dryness.

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