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Efficacy of dexpanthenol in skin protection against irritation: a double-blind, placebo-controlled study

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Dexpanthenol is popular in treating various dermatoses and in skin care, but few controlled clinical trials have been performed. We investigated the efficacy of dexpanthenol in skin protection against irritation in a randomized, prospective, double-blind, placebo-controlled study. 25 healthy volunteers (age 18–45 years) were treated for the inner aspect of both forearms with either Bepanthol® Handbalsam containing 5% dexpanthenol or placebo ×2 daily for 26 days. From day 15–22, sodium lauryl sulfate (SLS) 2% was applied to these areas ×2 daily. Documentation comprised sebumetry, corneometry, pH value and clinical appearance (photographs). 21 volunteers completed the study, 3 were excluded because of non-compliance and 1 experienced a non-study-related, severe, adverse event. Only corneometry yielded a statistically significant difference, with decreased values following SLS challenge at the placebo sites ($P < 0.05$). Intraindividual comparisons showed superior results at the dexpanthenol-treated sites in 11 cases and in only 1 case at the placebo site. 6 volunteers experienced an irritant contact dermatitis, with more severe symptoms at the placebo site in 5 cases. In conclusion, dexpanthenol exhibits protective effects against skin irritation. The initiation of a study to evaluate the efficacy of dexpanthenol in preventing irritant occupational contact dermatitis under real workplace conditions is validated.

Key words: corneometry; dermatitis; dexpanthenol; sebumetry; skin barrier; surface pH.

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Pantothenic acid, a vitamin of the B complex and the inactive form of coenzyme A, is essential to normal epithelial function. For topical application, the stable alcoholic analogue of pantothenic acid and dexpanthenol is used, which is characterized by good skin penetration and high local concentrations when administered in water-in-oil emulsions. Amongst the dermatologic effects of dexpanthenol are increased fibroblast proliferation as well as accelerated re-epithelialization in wound healing (1). Moreover, anti-inflammatory effects have been observed in different clinical situations (1–3).

Irritant contact dermatitis is frequent in wet occupations, and barrier creams are one of the commonly recommended measures to prevent its onset. However, their actual benefit at the workplace is still regarded with scepticism (4). Most international experts consider protective creams to be no more effective compared to bland emollients in the prevention of contact dermatitis (5), thus raising the question as to the need for a separation into 'skin care' and 'skin protection' products.

Recently, *in vivo* evidence was provided for a stabilizing effect of dexpanthenol on the skin barrier function (6). The aim of the present study was therefore to evaluate the potential of dexpanthenol to serve as a 'skin protection' compound in a controlled study.

Patients and Methods

Patient selection

25 Caucasian volunteers (18–45 years old) were included in this study. Exclusion criteria comprised pregnancy and lactation, severe systemic disease, cardiovascular disease, thyroid disease, allergy to latex or compounds of the study medication, systemic anti-inflammatory medication and active skin disease at the test sites. Volunteers were included following written informed consent. This study was approved by the local ethics committee (174/03).

Study design

This was a monocentric, prospective, randomized, placebo-controlled, double-blind study comparing the effects of Bepanthol® Handbalsam containing 5% dexpanthenol (Roche Consumer Health, Deutschland GmbH, Eppstein, Germany) and its dexpanthenol-free moisturizing basis. Test sites were defined as 16 cm^2 squares on the inner aspect of both forearms directly below the elbow. Right and left test sites of each volunteer were randomly assigned to either verum or placebo treatment. Both sites were treated ×2 daily for 26 days with either verum or placebo. From day 15–22, the test sites were exposed to irritation applying sodium lauryl sulfate (SLS) 2% (Texapon ZHC, Henkel, Düsseldorf, Germany) ×2 daily in a standardized manner by means of a roller.

Measures of skin physiology

Determination of fat content in the skin surface was performed photometrically according to the sebumeter method, measuring the reduced opacity of a plastic foil compared to a control value in μg/cm^2 (sebumeter SM810, Courage & Khazaka, Köln, Germany) (7). The hydration of the stratum corneum (corneometry) was determined as an absolute value using the corneometer CM820 (Courage & Khazaka) which measures the capacitance (8). Subsequent to the corneometry, the pH value was measured electrochemically using a planar glass pH electrode (PH900, Courage & Khazaka) (9). All 3 parameters were measured ×3 at each visit. Finally, clinical symptoms were documented photographically. Each volunteer was assigned to a defined time and all measurements were then carried out at exactly the same time of the day and in the same room. All measurements were performed within 1 month, thus trying to minimize environmental changes, and they were conducted by the same investigator.

Data analyses

Measurements of fat content yielded decreasing values when measuring ×3 in a row. Thus, only the first value determined was used for subsequent data analyses. For hydration and pH, the mean of the 3 values was calculated. Cumulative data were analysed using the non-parametric Friedman test that allows comparison of 3 or more matched groups. Additionally, all individual time courses were analysed and compared intraindividually. Moreover, the difference from the value obtained at day 0 was calculated.

Results

Safety

Of the 25 volunteers included, 21 completed the study. 3 individuals were excluded for non-compliance (not on time for measurements). 1 individual experienced a severe adverse event which was classified as 'non-study-related' (this person, a technician, experienced a period of hypotension, 4 h after applying the study medication). Of the 21 volunteers completing the study, none experienced any symptoms other than dermatitis at the site of SLS challenge (see below).

Efficacy

Throughout the study period, pH measures exhibited a slight tendency to decrease. This tendency persisted throughout the study period but failed to reach statistical significance. This change was observed at the dexpanthenol as well as at the placebo sites (Fig. 1a).

Treatment of the test sites with either dexpanthenol or placebo resulted in a slight increase in fat content, which was reduced by SLS challenge and briefly raised again immediately after the SLS challenge period (days 15–22), but normalized within the next week. Due to the huge SD, these changes did not reach statistical significance. However, a tendency towards higher measures at the dexpanthenol-treated sites as well as two individuals with a profound benefit from the application of dexpanthenol can be seen from Fig. 1b.

Hydration of the stratum corneum remained fairly steady throught the study period at the dexpanthenol-treated sites. In contrast, corneometry showed a decrease at the placebo sites at the end of the SLS challenge period, which reached statistical significance at day 23 ($P < 0.05$) and showed a tendency to subsequent normalization (Fig. 1c).

In 6 volunteers, visual symptoms of irritant contact dermatitis occurred on days 19–26. These symptoms comprised erythema and papulovesicules; these individuals also reported itching at the respective sites. Both arms were affected in these individuals. There were no symptoms other than those of local inflammation. All other volunteers reported neither any symptoms nor any clinical signs of inflammation visible.

Intraindividual comparison

When the data obtained were analysed as an intraindividual comparison, thus comparing the dexpanthenol and placebo site in each individual volunteer, no differences were noted with regard to the pH values. Sebumetry yielded higher values indicating increased fat contents

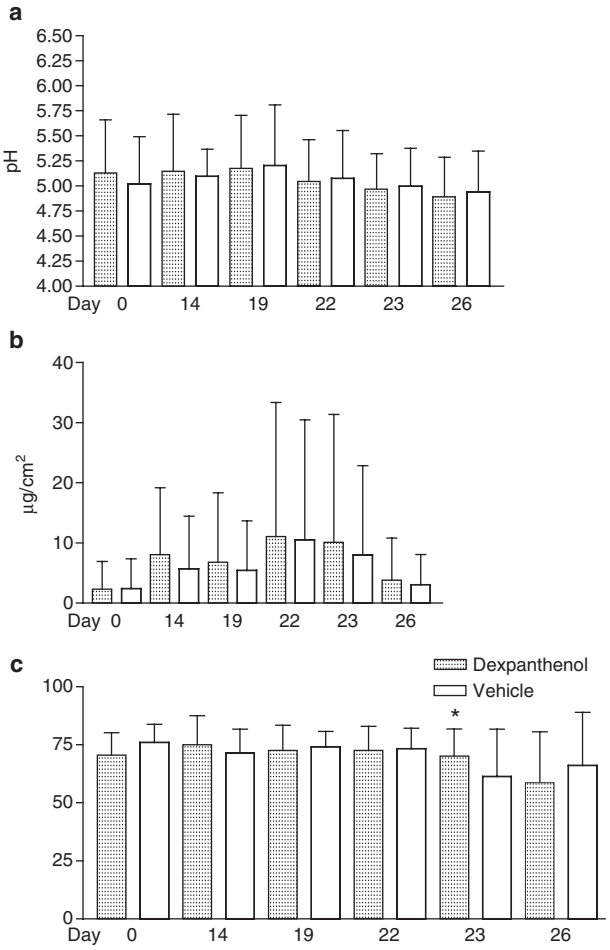

Fig. 1. Cumulative data on skin physiology. The means (sebumetry: first of 3 values obtained) and SDs are indicated. Although pH values (**a**) and sebumetry (**b**) document similar dynamics at both the dexpanthenol as well as the placebo sites, corneometry (**c**) shows a statistically significant decrease of hydration following sodium lauryl sulfate challenge on day 23 at the placebo sites (*).

for the dexpanthenol site in 2 individuals and for the placebo site in 2 others; 17 volunteers did not show any differences (Fig. 2). In contrast, higher corneometric values indicating a better hydration of the stratum corneum were observed in 11 volunteers at the dexpanthenol site and in only 1 individual at the placebo site. In 9 volunteers, no difference could be observed (Fig. 2). Finally, of the 6 volunteers with visible symptoms of irritant contact dermatitis, 5 individuals showed a clear difference between the test sites, and in all 5 cases, the placebo-treated site exhibited the more profound symptoms (Figs 2 and 3).

Discussion

Our data document the capability of dexpanthenol to protect the skin against irritant contact

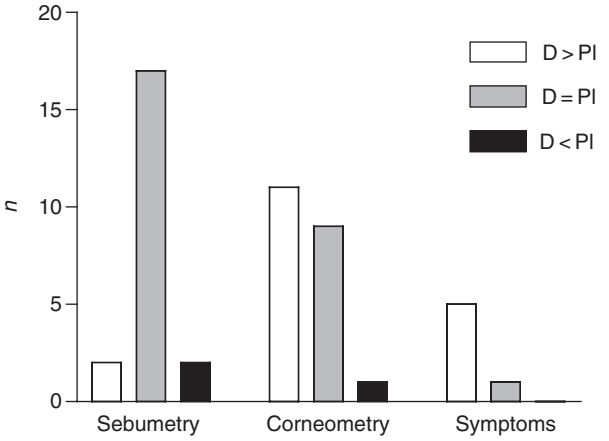

Fig. 2. Intraindividual data comparison. Volunteers with advantageous outcome at the dexpanthenol-treated sites (D) are represented by white bars, equal outcomes are indicated by grey bars and superiority of the placebo (PL) is documented by black bars. In contrast to pH values and sebumetry, which showed differences between dexpanthenol- and placebo-treated sites, both corneometry and clinical symptoms documented efficacy of dexpanthenol in prevention of skin irritation by sodium lauryl sulfate.

dermatitis. This conclusion is based mainly on corneometric data showing its ability to preserve good hydration of the stratum corneum under the influence of an irritant agent, whereas the placebo failed to do so. Sebumetry and pH values did not show significant differences between dexpanthenol and placebo. It can, however, be assumed that the 'placebo' does also exhibit beneficial effects, given the moisturizing capacity of bland emollients (10, 11). This may also explain in part why only 6 individuals developed signs of irritant contact dermatitis. Thus, the study design chosen did not favour the outcome observed.

The non-invasive methods chosen to evaluate the effects of dexpanthenol, namely corneometry, are well established for this purpose and have been used in comparable studies on the skin barrier function (12). Also, the use of SLS as a means to induce skin injury and inflammation (13, 14) represents a standard procedure. Another parameter frequently used in studies on the skin barrier function is transepidermal water loss (TEWL) (15). As sebumetry and pH measurements failed to show significant differences between the 'placebo' and dexpanthenol, but corneometry and clinical evaluation both point towards the effectiveness of the latter, a more advantageous array of methods might have been to combine clinical documentation, corneometry and TEWL.

Topical dexpanthenol has been a widely used means of skin care for decades, namely in Europe,

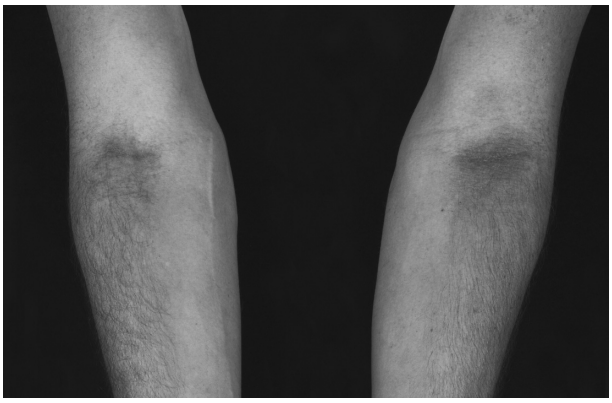

Fig. 3. Clinical efficacy of dexpanthenol in preventing sodium lauryl sulfate (SLS)-mediated irritant contact dermatitis. The test sites of volunteer number 4 on day 22 (last day of SLS challenge) show obvious differences, with the more severe skin changes visible at the placebo-treated site (left arm).

because of its moisturizing effect (1). This is also mirrored by our data. Given the role of coenzyme A in the metabolism of fatty acids and sterols, we also expected to observe effects of dexpanthenol on the fat content of the skin by sebumetry. Although dynamic changes were documented throughout the study, we were unable to identify significant differences either longitudinally or between dexpanthenol and placebo. This was attributed mainly to the pronounced SDs obtained during the measurements. Previous publications on the impact of numerous parameters including race (14) and anatomical site (16) on measurements of the skin barrier function stressed the necessity for standardization. Therefore, we not only defined a relatively homogeneous study group with regard to age and race but also tried to minimize other influences, e.g. assigning each volunteer to a defined time and having only 1 investigator performing the measurements (see *Patients and Methods*). These were strictly enforced, thus causing 3 drop-outs. Still, the SDs obtained presented a major problem in the data analyses.

Of the 21 volunteers completing the study, only 6 developed symptoms of irritant contact dermatitis. This may reflect the efficacy of dexpanthenol, but it might also document beneficial effects of the 'placebo'. The latter interpretation would be in line with a survey amongst international experts, the majority of them considering protective creams to be no more effective compared to bland emollients in the prevention of contact dermatitis (10). However, only 1 of the 6 individuals affected showed similar symptoms on both test sites, whereas the other 5 volunteers showed clear differences in favour of the dexpanthenol-treated site. Consequently, the protocol for irritation may have been too cautious. The absence of any signs or symptoms other than those of irritant contact dermatitis in the above-mentioned 6 individuals also underlines the safety of topical application of dexpanthenol.

In summary, our data document protective effects of dexpanthenol against skin irritation. Of the 3 parameters measured, skin hydration was found to be most useful in monitoring the effects of dexpanthenol. The initiation of a study to evaluate the efficacy of dexpanthenol in preventing irritant occupational contact dermatitis under real workplace conditions is feasible.

Acknowledgements

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