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SHORT COMMUNICATION

Lipid Content and Barrier Function Analysis in Uraemic Pruritus

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Dry skin, or xerosis, affects approximately 85% of haemodialysis patients (1). Itch occurrs in 50–90% of end-stage renal failure patients on dialysis. The aetiopathogenesis of uraemic pruritus is complex and largely unknown. Young et al. (2) were the first to describe the direct relationship between uraemic pruritus and the level of skin dryness, a finding subsequently later confirmed by others (1, 3, 4). Skin dryness may result from abnormal structure of the stratum corneum (SC). The aim of the current study was to determine whether uraemic xerosis might be linked to disturbances in extracellular lipid composition, which are organized in the SC in repeated bilayers created by ordering the polar regions and non-polar fragments of ceramides, cholesterol and free fatty acids. Extracellular lipids are essential for maintaining the epidermal barrier, but they may also act as signalling molecules (e.g. ceramides) evoking pruritus (5).

MATERIALS AND METHODS (See Appendix S1[1])

RESULTS

The prevalence of dry skin symptoms did not differ significantly between the control ($n=32$) and dialysis ($n=30$) groups: 50% of dialysis patients and 56.2% of control subjects showed symptoms of skin dryness ($p=0.7$). However, dry skin occurred significantly more often in patients with uraemic pruritus (80%) compared with those without itching (42%) ($p=0.002$). Skin dryness was also more severe in dialysis patients with itch (Fig. S1[1]). The mean duration of the dry skin condition did not differ significantly between patients with and without pruritus ($p=0.33$).

The intensity of itch in the patients on dialysis who had dry skin was considerably higher than in those who did not have dry skin, as measured by both the $VAS_{current}$ assessment (4.3 ± 3.2 vs. 0.7 ± 1.1 points, respectively, $p=0.01$) and the 4-item itch questionnaire (10.1 ± 4.1 vs. 6.8 ± 2.3 points, respectively, $p<0.05$). Interestingly, no correlations were observed between the intensity of pruritus and the clinical severity of the dry skin (Table SI[1]).

The mean ± SD results of the corneometric measurements showed significant differences in terms of the average epidermis moisture level in the patients on dialysis compared with the control group ($p<0.001$) (Fig. S2[1]). The mean ± SD result of forearm corneometry in patients on haemodialysis was 26.5 ± 8.7 units, and in the control group 39.1 ± 11.3 units[2].

The patients on dialysis had a higher mean value of transepidermal water loss (TEWL) within the forearm area (7.7 ± 6.0 g/h/cm^2) than the control group (6.2 ± 4.2 g/h/cm^2). Mean TEWL values on the chest and abdomen were also higher in the dialysis group, while on the lower legs mean TEWL values were slightly lower in the dialysis group compared with the control group ($p>0.05$). Comparison of the mean value of TEWL between dialysis patients with and without pruritus revealed significantly higher TEWL in patients with pruritus on the skin of the abdomen (7.8 ± 4.1 g/h/m^2 vs. 6.6 ± 6.0 g/h/m^2, respectively) and lower legs (8.3 ± 6.3 g/h/m^2 vs. 6.5 ± 5.5 g/h/m^2, respectively) ($p<0.05$).

The mean ± SD amount of isolated lipids was the same in both cohorts (0.22 ± 0.18 mg lipids/mg of epidermis). The mean relative content of ceramides 1, 2 and 3 was $13.4 \pm 3.0\%$, $13.4 \pm 4.2\%$ and $8.4 \pm 3.7\%$ in the dialysis group, compared to $10.1 \pm 3.1\%$, $9.7 \pm 3.9\%$, and $5.4 \pm 4.1\%$ in the control group ($p<0.01$ for all comparisons) (Fig. 1). Conversely, the content of cholesterol and triglycerides was significantly less in the dialysis group ($23.5 \pm 7.9\%$ and $6.8 \pm 5.8\%$) compared with the control group ($28.6 \pm 9.7\%$ and $10.5 \pm 6.4\%$), whereas the mean content of free fatty acids, cholesteryl esters and squalene did not differ between groups ($p>0.05$). The content of ceramides (1–3), cholesterol, free fatty acids, triglycerides, cholesteryl esters, and squalene did not differ significantly between the patients with pruritus and those without pruritus.

DISCUSSION

Yosipovitch et al. (9) were the first to assess abnormalities of the skin barrier in patients on dialysis in relation to pruritus. They examined the content of glycerol in the

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[2]Regarding the chest, abdomen and lower legs, dialysis patients also demonstrated significantly higher corneometry results, reflecting decreased water content in the stratum corneum compared with the control group. The hydration of the abdominal skin in patients with pruritus was considerably lower than in patients who did not experience itch; however, it was at the verge of statistical significance ($p=0.06$). The results for the remaining areas of skin did not differ significantly between patients with and without itch.

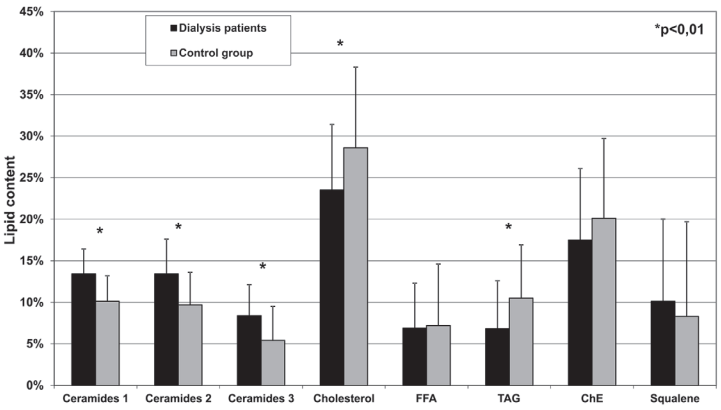

Fig. 1. Comparison of relative lipid content in stratum corneum of patients on dialysis and healthy controls.

epidermis of 38 people, including 20 who underwent dialysotherapy. They found a significant correlation between glycerol levels and skin barrier integrity in the arms. However, electron-microscopy of the epidermal barrier did not reveal any disturbances in the lamellar arrangement of extracellular lipids, or the secretion and number of lamellar granules (9). The current study shows alterations in the SC lipids in patients on dialysis. These patients had an increase in the relative content of ceramides and a decrease in cholesterol and triglycerides.

Skin barrier damage can manifest itself through clinically dry skin, which becomes rough and flaky. In the current study, dry skin was observed in 56.2% of patients on dialysis. A similar percentage was reported by Gilchrest et al. (10), who noticed skin dryness in 59.3% of subjects on dialysis. However, Ståhle-Bäckdahl (11) reported that 93.1% of 29 patients on dialysis had xerosis. Dry skin in patients on dialysis may be induced by numerous factors, such as a decrease in the moisture level in the epidermis, damage to the skin barrier, and sensitivity of the SC to external damaging factors (1, 12). Since damage to the skin barrier may result from a change in the total amount of lipids or the incorrect proportion of particular lipid classes in the extracellular matrix (a well-known phenomenon, e.g. in psoriasis), it is possible that abnormal lipid composition might also play a role in skin barrier alteration in subjects on dialysis.

TEWL reflects the integrity of the epidermal barrier. We have observed that dry skin in subjects on dialysis is connected with higher TEWL values. This finding is also supported by another report (13). Based on our results it could be concluded that skin dryness may aggravate pruritus in subjects on dialysis, as in many other pruritic conditions. It seems reasonable to recommend the use of emollients in subjects on dialysis who have itch, since such simple measures may at least partially improve pruritus in this patient group, as previously demonstrated also by our group (3, 13, 14). The reason for the reduction in hydration of the epidermis in patients on haemodialysis has not yet been sufficiently explained. It has been suggested that a fluid shift occurs in patients on dialysis, resulting in an insufficient supply of water to the skin in connection with microangiopathy of vessels (1).

In conclusion, the results of our study suggest a dysregulation of the epidermal barrier in patients on haemodialysis. These alterations might, at least in part, be explained by altered lipid composition of the SC. Impairment of the epidermal barrier leads to increased TEWL and decreased hydration of the epidermis. As a consequence, patients on dialysis may demonstrate clinical features of dry skin, which may aggravate pruritus in predisposed individuals.

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