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Original Article

Pruritus and skin hydration during dialysis

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Abstract

Background. Dry skin is frequently observed in uraemic patients and a link with the common complaint of pruritus has been suggested. Objective data on skin dryness in haemodialysed patients is sparse and equivocal. No such information exists for the many patients now receiving peritoneal dialysis. We assessed the prevalence and severity of both pruritus and skin dryness in a uraemic population receiving maintenance dialysis.

Methods. Forty-eight haemodialysis and 24 peritoneal dialysis patients were examined and skin dryness assessed by clinical grading and measurement of stratum corneum hydration using a corneometer. Forty age- and sex-matched controls were also assessed. Several biochemical parameters with possible relevance to pruritus were measured. Regular emollient therapy was prescribed to pruritic dialysis patients and efficacy assessed.

Results. Dialysis patients overall had clinically drier skin than controls, especially the peritoneal dialysis group. Stratum corneum hydration levels were significantly reduced in the peritoneal dialysis ($P<0.004$), but not the haemodialysis, population. Twenty-seven per cent of haemodialysed and 54% of peritoneal dialysis patients complained of pruritus. Pruritic patients in each dialysis group had significantly lower hydration than non-pruritic patients ($P<0.05$). Regular emollient use in pruritic patients produced a marked reduction in severity of pruritus, abolishing the symptom in nine of 21 patients treated.

Conclusion. Reduced stratum corneum hydration correlates with pruritus in patients on maintenance haemodialysis and peritoneal dialysis, and may be alleviated by simple emollient therapy.

Key words: skin dryness; uraemic pruritus; stratum corneum hydration

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Introduction

Dry skin (xerosis) has been observed in up to 85% of uraemic patients undergoing maintenance haemodialysis [1–5]. Pruritus has been reported to affect 37–86% of haemodialysed patients and severity of pruritus has been directly correlated with clinical degree of dryness [1]. Dryness of the skin has been difficult to assess objectively although reliable measurement of change in stratum corneum hydration is now possible using a corneometer, a capacitance measuring instrument [6].

One previous study of hydration in 31 haemodialysis patients showed 19 pruritic patients to have reduced stratum corneum hydration, although this was not statistically significant [1]. A recent study failed to find any association between pruritus and skin hydration in 41 haemodialysis patients [5].

We have assessed stratum corneum hydration along with several biochemical parameters that may also be relevant to the pathogenesis of pruritus in a larger population of haemodialysed patients. In addition, as peritoneal dialysis now accounts for over half the uraemic patients managed by dialysis in the United Kingdom [7], we assessed skin hydration in a population on this form of dialysis. We determined the prevalence of skin dryness and pruritus in both dialysis populations and, correcting for other possible contributing biochemical abnormalities, have considered the relevance skin dryness may have to the pathogenesis of their pruritus. Finally we assessed the benefit, if any, of regular emollient therapy in pruritic dialysis patients with dry skin.

Subjects and methods

Forty-eight patients with chronic renal failure on maintenance haemodialysis and 24 patients on peritoneal dialysis, all attending our centre and on dialysis for over 4 months, were studied (haemodialysis: 23 males, 25 females, median age 61 years, range 17–81; peritoneal dialysis: 11 males, 13 females, median age 54 years, range 19–73). Forty age- and sex-matched controls, without itch, with normal serum creatinine, on no medication, and with no significant skin disease, were also recruited.

Patients and controls were requested not to apply emollient

or any other topical agent in the 48 h prior to assessment and were requested not to bath/shower during the 12 h prior to assessment. Subjects were assessed semi-prone having been allowed to settle for at least 5 min prior to examination, in rooms with controlled temperature ($22 \pm 1°C$) and humidity ($42.5 \pm 2\%$).

Pruritus was assessed by visual analogue scale from 0 to 10 (with subsequent interpretation of $0 < X \leqslant 3$ as mild, $3 < X \leqslant 7$ as moderate, and $7 < X \leqslant 10$ as severe). Clinical assessment of skin dryness was by the graded scale: 1 = smooth, 2 = rough, 3 = rough with little scale and 4 = rough with marked scale.

The corneometer used was a CM 820 (Courage and Khazaka Electronie GmbH, Cologne, Germany). The corneometer registers the electrical capacitance of the skin surface as an indicator of stratum corneum hydration [6]. The probe, which is applied to the skin surface, consists of a plastic-foil-covered brass grid which functions as one electrode, while the skin acts as the other electrode. The capacitance is expressed digitally in arbitrary units. Measurements were taken at three sites: neck, lower back, and lower leg with three scores registered at each site and an average derived. For haemodialysis patients, scores were recorded at the start and on completion of a dialysis treatment.

Serum bilirubin, calcium, creatinine, magnesium, parathyroid hormone, phosphate, urea, thyroid function, and haemoglobin level were measured by standard technique in all dialysis patients. The plasma erythropoeitin was also measured in patients receiving this agent. Samples from haemodialysis patients were taken predialysis.

All patients with pruritus were offered 200 g of aqueous cream along with an advice sheet on usage, with the request to apply the emollient twice daily with repeat scoring of pruritus after one week.

Statistics

Comparisons between dialysis groups and between the two dialysis groups and their relevant controls were done by using the Mann–Whitney U test. Comparisons between the before and after dialysis scores were by the Wilcoxon-matched-pairs signed rank test. Box-plots incorporating these parameters have been used to display the data graphically.

Results

Skin dryness and hydration

Table 1 shows the clinical grading of skin dryness in all subjects. The widest range of skin dryness within all our patient groups was noted for the back measurements. In all areas examined, a greater proportion of dialysis patients than controls displayed dry-looking skin, with peritoneal dialysis patients clinically drier than those on haemodialysis.

A greater proportion of the pruritic dialysis patients had xerosis (on the back and leg, although not on the neck) than non-pruritic dialysis patients, again especially in the peritoneal dialysis group (Table 2).

The corneometer was shown to produce a scoring of hydration that closely matched clinical assessment of skin dryness in all three sites ($P < 0.001$) in all subjects studied (Figure 1).

The stratum corneum hydration of each of our dialysis populations, as measured by the corneometer, is compared with age/sex-matched controls (Figure 2). Peritoneal dialysis patients had overall lower hydration levels than haemodialysis patients ($P < 0.004$) and controls ($P < 0.002$) for all sites examined. The haemodialysis group showed no significant difference in the pre- to postdialysis scores and hydration scores in this group were not significantly different from controls although a trend towards these patients having a reduced hydration was suggested when back scores were compared ($P < 0.06$).

Table 1. Clinical grading of skin dryness (% of patients in each group is shown) in all subjects

		Smooth	Rough	Rough + little scale	Rough + marked scale
Neck					
Control	($n = 40$)	100	–	–	–
Haemodialysis	($n = 48$)	94	4	2	–
Peritoneal dialysis	($n = 24$)	69	31	–	–
Back					
Control	($n = 40$)	82	18	–	–
Haemodialysis	($n = 48$)	67	21	10	2
Peritoneal dialysis	($n = 24$)	25	46	25	4
Leg					
Control	($n = 40$)	18	60	22	–
Haemodialysis	($n = 48$)	25	48	23	4
Peritoneal dialysis	($n = 24$)	8	29	46	17

Pruritus, prevalence

Thirteen haemodialysis patients (27%) and thirteen peritoneal dialysis patients (54%) complained of pruritus as a current problem. Pruritus was generalized in 14 patients and predominantly affected the legs in four, back in five, face in two, and arms only in one patient. The mean duration of dialysis differed little between pruritic and non-pruritic patients in those receiving haemodialysis (pruritus, 4.0 years; non-pruritus, 4.1 years) and peritoneal dialysis (pruritus, 2.1 years; non-pruritus, 2.3 years). Severity of pruritus assessed by visual analogue scale revealed that for haemodialysis patients, pruritus was mild in four, moderate in seven, and severe in two, and for peritoneal dialysis, mild in four, moderate in five and severe in four.

Reduced stratum corneum hydration in our pruritic dialysis patients was associated with pruritus at each site examined, although only back scores continued to give a significant association when the dialysis groups were considered separately (Table 3).

Pruritus and biochemical parameters

The only significant finding in our haemodialysis group was of a greater elevation of parathyroid hormone in non-pruritic patients in comparison to those with pruritus (Table 4). In the peritoneal dialysis group, calcium/phosphate product and serum creatinine showed an association with pruritus. Thyroid function assay revealed one of our peritoneal dialysis patients to be

Table 2. Clinical grading of skin dryness in pruritic and non-pruritic dialysis patients (% of patients in each group is shown)

		Smooth	Rough	Rough + little scale	Rough + marked scale
Neck					
Pruritic haemodialysis	($n=13$)	100	–	–	–
Pruritic peritoneal dialysis	(n=13)	70	30	–	–
Non-pruritic dialysis	($n=46$)	87	11	2	–
Back					
Pruritic haemodialysis	($n=13$)	46	23	23	8
Pruritic peritoneal dialysis	($n=13$)	23	31	38	8
Non-pruritic dialysis	($n=46$)	64	30	6	–
Leg					
Pruritic haemodialysis	($n=13$)	23	31	38	8
Pruritic peritoneal dialysis	($n=13$)	8	23	46	23
Non-pruritic dialysis	($n=46$)	22	50	24	4

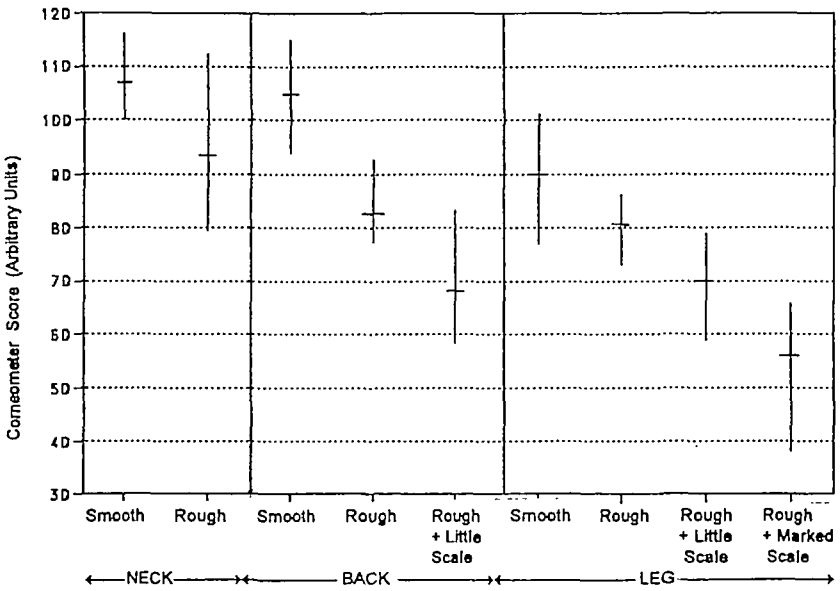

Fig. 1. Stratum corneum hydration scores and clinical grading of skin dryness in all 112 subjects studied, showing median and interquartile range.

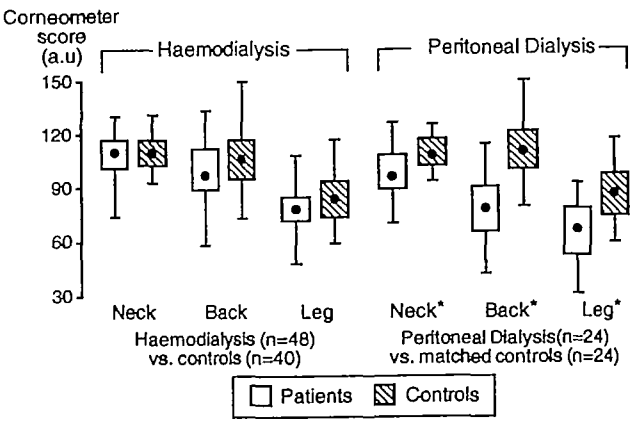

Fig. 2. Stratum corneum hydration in haemodialysis and peritoneal dialysis patients and controls when measured by corneometer (arbitrary units). Boxplot shows minimum to maximum scores, with interquartile range and median within box. (*$P<0.002$).

hypothyroid, although exclusion of the corneometer scores from this patient did not result in any alteration in the significance of observations in this study.

Seventy-three per cent of haemodialysis patients (35/48) were receiving subcutaneous erythropoeitin in comparison with 33% of peritoneal dialysis patients (8/24). The majority of pruritic patients on haemodialysis (10/13) received s.c. erythropoeitin in contrast to only 2/13 pruritic peritoneal dialysis patients. However, there was no significant difference between the plasma erythropoeitin levels or haemoglobin in either group.

Emollient application

Sixteen of 21 patients with pruritus who applied emollient twice daily for one week reported a reduction in severity of itch, with nine patients describing complete relief (Figure 3).

Table 3. Hydration scores by site in each dialysis group for pruritic and non-pruritic patients (Median scores, significance by Mann–Whitney test)

	All dialysis ($n=72$)		Haemodialysis ($n=48$)	($n=24$)	Peritoneal dialysis	
	Pruritus $n=26$	Non-pruritus $n=46$	Pruritus $n=13$	Non-pruritus $n=35$	Pruritus $n=13$	Non-pruritus $n=11$
Neck	100*	107	106	112	95	99
Back	83**	99	90**	105	68*	85
Leg	72*	77	73	79	65	66

*$P<0.05$, **$P<0.001$.

Table 4. *Pruritus and biochemical parameters in each dialysis group (median values and interquartile range)*

Parameter	Haemodialysis ($n=48$)			Peritoneal dialysis ($n=24$)		
	Pruritus	Non-pruritus	Significance	Pruritus	Non-pruritus	Significance
Calcium (mmol/l)	2.3 2.1–2.4	2.3 2.2–2.4	NS	2.4 2.3–2.5	2.1 1.5–2.5	NS
Magnesium (mmol/l)	0.9 0.7–1.1	0.9 0.5–1.2	NS	1.0 0.7–1.5	0.9 0.6–1.2	NS
Phosphate (mmol/l)	2.0 1.6–2.5	2.2 1.3–2.4	NS	2.2 1.8–2.4	2.0 1.7–2.3	NS
Calcium/ phosphate product	4.4 3.1–5.5	4.8 3.1–5.7	NS	5.1 4.4–5.7	4.3 3.5–4.7	$P=0.005$
Creatinine (mmol/l)	1022 922–1260	998 736–1290	NS	1026 868–1334	873 588–1159	$P=0.04$
Urea (mmol/l)	26.3 21.8–32.8	25.6 22.7–29.9	NS	20.7 18.4–25.0	23.1 20.4–26.5	NS
Urea (%) reduction	65 58–69	64 58–70	NS	–	–	–
Parathroid hormone (μg/l)	12.1 2.0–34.3	22.4 18.4–76.2	$P=0.03$	43.3 37.8–62.6	21.0 7.0–46.3	NS
Haemoglobin (g/dl)	10.6 9.4–11.9	8.9 8.3–10.4	NS	11.2 10.0–11.9	9.8 9.0–13.4	NS
Erythropoietin (mu/ml)	18.8 16.7–23.4	27.8 19.6–47.0	NS	14.5 14.0–27.2	14.1 13.0–19.8	NS

NS, not significant.

Discussion

Pruritus remains a common complaint of uraemic patients, particularly within the peritoneal dialysis group. Xerosis was frequently observed in both haemodialysis and peritoneal dialysis populations, with pruritus more prevalent in those patients with clinically dry skin.

Stratum corneum hydration levels were significantly reduced in the peritoneal dialysis group, but not in the haemodialysis population. We have, however, demonstrated in both dialysis populations an association between reduced stratum corneum hydration and pruritus. A significant difference was noted only with back hydration scores although all three sites examined showed a significant association when the total dialysis population was assessed. This is probably due to differences in sensitivity of the sites examined with back assessment generating the greatest range of scores.

Two studies have previously examined the possible link between stratum corneum hydration and pruritus in maintenance haemodialysis patients. Stahle-Backdahl assessed the neck, anterior chest, and leg of 31 patients, 19 with pruritus, and found a non-significant trend in all three sites [4]. This study included only 12 controls and did not consider other possible promoters of uraemic pruritus. The large variation in humidity (15–30%) in which recordings were made may also have affected the results. Yosipovitch recently assessed 41 haemodialysis patients, 73% (30/41) of whom described pruritus, and compared their hydration with that of 40 controls [5]. Skin pH was also assessed, but no other possible parameters of pruritus were measured. No correlation with pruritus was noted on assessment of forehead, upper back, volar forearm, and axilla, although decreased hydration was observed in the latter two sites. However, certain of these sites may have been particularly affected by sweating, with abnormal vascular anatomy of the volar forearm in many haemodia-

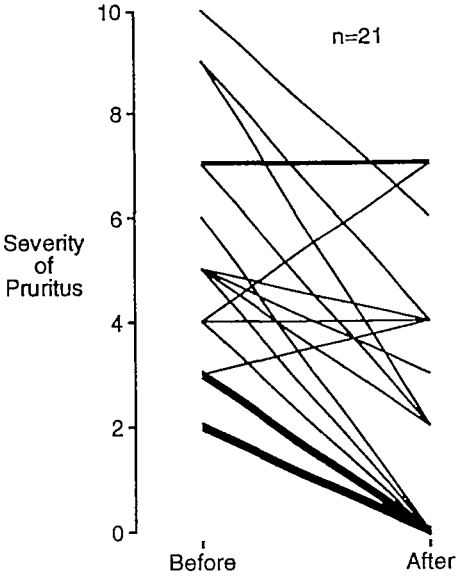

Fig. 3. Change in severity of pruritus following the regular application of emollient in dialysis patients with pruritus. (Each line corresponds to one patient.)

lysis patients possibly making this also an unreliable site for the assessment of hydration.

Our results support previous studies associating pruritus with xerosis determined purely by clinical examination [1, 2]. Although multiple factors may contribute towards the rough and scaly skin appearance of xerosis, including skin dehydration and reduced sebum excretion [8], we have demonstrated an association between reduced stratum corneum hydration and xerosis in our study population. Previous studies using the corneometer may have failed to find a statistically significant association between pruritus and skin hydration on account of smaller study size, the need to provide an optimal environment for use of the corneometer and differences in sensitivity of site examined.

This is the first report, to our knowledge, to study stratum corneum hydration in a peritoneal dialysis population. A reduction in hydration was observed in comparison both with the haemodialysis group and controls. Moreover, pruritus was twice as common in peritoneal dialysis as haemodialysis patients, with xerosis and reduced stratum corneum hydration both associated with pruritus.

The cause of this reduction in skin hydration is unclear. The fluid shift that occurs with dialysis may contribute, as might an altered cutaneous vascular supply due to the dialysis resistant, transplant responsive microangiopathy described in certain haemodialysis patients [9]. However, similar vascular change in peritoneal dialysis patients has not been described.

We also considered in this study the possible contribution of certain biochemical/haematological parameters to pruritus in our populations.

Elevated concentrations of divalent ions, namely calcium, magnesium or phosphate, have been demonstrated in the skin of patients with uraemic pruritus [10]. Microprecipitation of these ions may cause pruritus. Deranged calcium homeostasis may have contributed to pruritus in our peritoneal dialysis group with the strong correlation of calcium/phosphate product and pruritus, although there was no association of pruritus with the divalent ion concentrations assayed. Serum creatinine is an unreliable indicator of dialysis adequacy and is unlikely to be a independent marker of pruritus in those receiving peritoneal dialysis.

Parathyroid hormone (PTH) levels are reported to be higher in pruritic haemodialysis patients [11]. While this trend was evident in our peritoneal dialysis group, our pruritic haemodialysis group had significantly lower PTH levels than those without pruritus, consistent with calcium homeostasis upset in our peritoneal dialysis group, but not in those on haemodialysis.

Peritoneal dialysis patients often have residual renal function and their dialysis method does not involve the risk of blood loss which may explain the difference in erythropoeitin requirements between the dialysis groups. Whilst 35 haemodialysis patients received exogenous erythropoeitin, 10 still experienced pruritus and there was no difference in plasma erythropoeitin levels between the pruritic and non-pruritic groups. This would suggest that exogenous erythropoetin alone does not ameliorate pruritus as previously proposed by Marchi *et al.* [12].

Is our observed correlation between 'dry skin' and uraemic pruritus of pathogenic significance?

The traditional view that itch is a mild form of pain has been challenged. Separate nerve fibres for each modality have been reported [13], with sprouting of the 'itch' fibres throughout the layers of the epidermis observed in certain haemodialysis patients [14]. The stimulation of these fibres in dehydrated skin is considered to be mechanical rather than chemical [15]. The resulting low-intensity activation of the mechanoreceptors probably requires additional chemical stimuli to produce a sustained sensation of pruritus, but dry skin may promote pruritus by lowering the threshold for evoking itch [16]. Dryness of the skin is considered to contribute to pruritus in atopic eczema and senile pruritus. Reduced stratum corneum hydration has been demonstrated in both these conditions [17, 18]. Reduction in the threshold for triggering pruritus on account of skin dehydration helps explain the increased sensitivity of non-inflamed atopic skin to low concentrations of histamine [19].

We propose that in uraemic pruritus a similar mechanism operates, with dry skin lowering the threshold for pruritus, facilitating other factors to promote the sensation. This is consistent with a multifactorial aetiology to uraemic pruritus with possible contributions from secondary or tertiary hyperparathyroidism, metastatic calcification, increased levels of vitamin A, cutaneous mast cell proliferation/increased histamine release and deficient sweating [20].

Although we have not identified any additional factor(s) responsible for pruritus in our xerotic haemodialysis patients with pruritus, deranged calcium

homeostasis may have contributed to promoting itch in our xerotic peritoneal dialysis population with pruritus.

The application of emollients to the dry scaly skin of uraemic patients with pruritus has met with varying clinical benefit [3, 16]. Emollients both have rehydrating and occlusive effects [21]. Aqueous cream B.P. contains a high water content (70%) in an emulsion with emulsifying wax, liquid paraffin and white soft paraffin, combining a relatively high direct rehydrating potential with occlusion. The improvement in pruritus severity we report following emollient use, albeit in open study, supports their use in relieving the pruritus of chronic renal failure. Regular emollient therapy, by rehydrating the skin, may help to raise the threshold for pruritus.

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