

## Uremic Pruritus in Haemodialysis Patients

H. Resic<sup>1</sup>, F. Alendar<sup>2</sup>, N. Kukavica<sup>1</sup>, F. Masnic<sup>1</sup> and B. Cengic<sup>1</sup>

<sup>1</sup> Center for Haemodialysis, Clinical Center University of Sarajevo, <sup>2</sup> Clinic for Dermatovenerology, Clinical Center, University of Sarajevo, Bosnia and Herzegovina

### Abstract

**Background.** Uremic pruritus is common complaint among dialysis patients. The prevalence of renal itching in patients on dialysis is approximately 30%, but its treatment is often ineffective. The etiology of uremic pruritus remains unclear.

The aim of this study was to evaluate the prevalence and severity of pruritus, and to correlate its presence and intensity with relevant clinical and laboratory parameters.

**Methods.** Seventy-seven patients on maintenance haemodialysis were enrolled in the study. The mean age of patients was  $55,78 \pm 14,11$  and duration of dialysis was  $5,27 \pm 3,80$  years. Itch intensity was scored as mild, moderate and severe. One interviewer surveyed seventy-seven patients over three-day period. Some clinical and laboratory parameters were evaluated (age, sex, duration of dialysis, etiology of chronic renal failure (CRF), hematocrit, calcium, phosphorus, parathyroid hormone (PTH), Kt/V, calcium & phosphorus product). Ten patients with refractory pruritus were treated with UVB irradiation for two months, three times weekly, two minutes per each treatment.

**Results.** Forty-five of seventy seven patients experienced itching (58,44%). The intensity of itching was mild, moderate and severe, in 42,22%, 40,0%, 17,78% of patients, respectively. In 19 patients (42,22%) pruritus intensified during and after dialysis. There was no significant difference in the serum levels of calcium, phosphorus, PTH, hematocrit, albumin and duration of haemodialysis. However, there was a significant difference in value of Kt/V in patients with pruritus ( $p < 0,01$ ) which has been lower, as well as the product of Ca and P04 ( $p < 0,05$ ).

**Conclusions.** Our study has shown that increasing the dose of dialysis (Kt/V) leads to an improvement in uremic pruritus. Also UVB irradiation of the body, 1-2 minutes twice a week in ten patients resulted in long-lasting remission of the pruritus.

**Key words:** pruritus, hemodialysis, dialysis adequacy, UVB.

### Introduction

Uremic pruritus is one common and frequent symptom in patients with end stage renal disease (ESRD). Over the past 20 years the incidence of pruritus declined from 85% in the early 1970's to 30% in the late 1990's (1).

Many patients have complaints of pruritus, which is mostly localized in the back with symptoms worsen during dialysis (2). Many factors contribute to uremic pruritus (UP) such as: Secondary hyperparathyroidism, dry skin, hyperphosphatemia,

inadequate dialysis, increased  $\beta_2$  micro-globulin levels, high aluminum levels and immune dysfunction (3).

Histamine plays an important role in the pathophysiology of UP which is a well known prurithogen and can directly stimulate the neuron terminals on  $H_1$ , but not  $H_2$  receptors (4, 5). Dermal mast cells sit very close to afferent C neuron terminals, and interactions between these structures may play an important role in the mediation of pruritus. Skin mast cells and serum levels of histamine are increased in uremic patients (6).

In the treatment of pruritus as very important part the adequate dialysis, erythropoietin (EPO), antihistamines, ultraviolet B irradiation (UVB) and capsaicin are considered.

The aim of the present study was to evaluate the prevalence of UP in dialysis patients and their correlation with the laboratory and clinical parameters.

### Patients and methods

Seventy seven patients on maintenance haemodialysis were enrolled in the study, in the Center for haemodialysis at Clinical Center of Sarajevo. Forty one were men and thirty six were women. Their mean age was  $55,78 \pm 14,11$  in patient group with pruritus, and  $56,87 \pm 12,95$  in the group without itching. The dialysis duration was 3 times per week for 4 hours on polysulfone membranes and bicarbonate dialysis fluid. Ten patients were diabetic, and none of the patients had any previous skin disease.

The patients were questioned by a clinical psychologist, if they had pruritus during the previous two weeks, and the symptoms were classified according to the intensity (mild, moderate and severe), location and duration of HD. Patients gave their verbal consent and answered to the questions at the beginning of an interview. The severity of pruritus was assessed subjectively and scored as follows:

Severe: generalized and permanent pruritus with sleep disturbance, Moderate: generalized and permanent pruritus without sleep disturbance,

Mild: localized pruritus without sleep disturbance.

Laboratory test performed were serum calcium, phosphorus, albumin, PTH, hematocrit, Kt/V, Ca x PO4 product. Other characteristics evaluated were the etiology of renal disease, age, sex and time on dialysis.

#### Statistical analysis

Results are reported as mean  $\pm$  SD. Student's t-test and  $\chi^2$  score were used for statistical analysis. Statistical significance was defined as  $p < 0,05$ .

### Results

Correspondence to:

Halima Resic, Center for haemodialysis Clinical Center, University of Sarajevo, Bosnia and Herzegovina; Tel/fax.: ++387 33 269 071; resickcs@bih.net.ba

Forty five out of seventy seven HD patients experienced pruritus. There was no statistically significant difference

between the two groups when age, sex and duration of dialysis were compared, as shown on Table 1.

**Table 1.** Features of the HD population studied with no significant differences between the groups

	Number (%) of patients with pruritus (n = 45)	Number of patients without pruritus (n = 32)
Age	59,78±14,11	56,87±12,95
Sex m/f	26 (67,78) / 19 (42,22)	15 (46,8) / 17 (53,12)
Duration of HD treatment (years)	5,27±3,80	6,15±4,33
Diabetes as a cause of ESRD	6 (13,33%)	4 (12,5%)

Table 2 describes laboratory data of patients who reported itching and those who did not. There was significant difference ( $p < 0,05$ ) between a group with pruritus and group without pruritus in the value of Kt/V and product of calcium and phosphorus  $p < 0,001$ . Group with adequate dose of

dialysis ( $1,19 \pm 0,26$ ) and normal product of calcium and phosphorus had no pruritus. There was no significant difference between the two groups in other laboratory parameters.

**Table 2.** Laboratory parameters in HD patients

	Number of patients with pruritus No - 45	Number of patients with pruritus No - 45	P
Kt/V	1,09 ± 0,23	1,19 ± 0,25	$p < 0,01$
Ca x PO <sub>4</sub>	4,49 ± 1,5	4,05 ± 0,97	$p < 0,05$
Phosphate (mmol/L)	1,98 ± 0,63	1,82 ± 0,41	n.s.
Albumine (g/dl)	37,53 ± 3,17	38,06 ± 3,14	n.s.
Hematocrit %	32,19 ± 5,40	33,56 ± 5,35	n.s.
PTH (pg/ml)	558 (100-1400)	264 (60-878)	

**Table 3.** Characteristics and localization of pruritus

Number of patients with pruritus (n=45)			
Mild	19 (42,2%)	Back	29 (64,4%)
Moderate	18 (40,0%)	Legs	18 (40,0%)
Severe	8 (17,7%)	Face	8 (17,7%)
		Chest	7 (11,11%)
		Other	8 (18,2%)

Of the 45 patients who reported itching 42,22% had mild

severe pruritus. Pruritus was limited to the back 29 pruritus, 40,0% moderate and 17,78% of patients had a (64,64%), legs 18 (40,0%), face and chest 15 (26%) patients (Table 3).

The patients who suffered from pruritus experienced pruritus between haemodialysis sessions three times weekly (19 patients), and other patients had none (Figure 1, Table 4). Majority of the patients were treated with medicaments. Most frequently used were antihistamines (38 patients - 84,4%), which helped relieve symptoms of pruritus in most cases (Table 4).

**Table 4.** Association of the pruritus with other factors

	Number of patients with pruritus (n = 45)	
Pruritus worsened after weekend	YES 17 (37,7%)	YES 28 (62,2%)
Pruritus associated with sleeping	YES 19 (42,2%)	YES 26 (57,5%)
Taking medicaments for pruritus	YES 38 (84,4%)	YES 7 (15,5%)
Effect of the treatment on pruritus	YES 20 (44,4%)	YES 7 (15,5%)
	Partially 18 (39,9%)	

Patients that were using antihistamines and crèmes for a long period of time without effect were subjected to UVB irradiation. There were in total 10 patients on UVB irradiation that had their whole body exposed to radiation with a session lasting for 3 minutes. After UVB therapy only 2 patients had marked hyperemia, which was the reason why UVB sessions were shortened to a period of 2 minutes. UVB radiation had a systemic effect and after two weeks patients experienced improvement, which they explained by severity of pruritus.

## Discussion

Pruritus is one of the most prevalent presentations of uremia and occurs in 60-85% of HD patients. The prevalence of pruritus at our dialysis unit was consistent with other literature reports. Our study included 77 patients, pruritus was found in 45 patients (58,44%), severe in 17,78%,

moderate in 40,0% and mild in 42,2% of the patients. Zucker et al. reported pruritus in 48% of their HD patients at the time of the study (7).

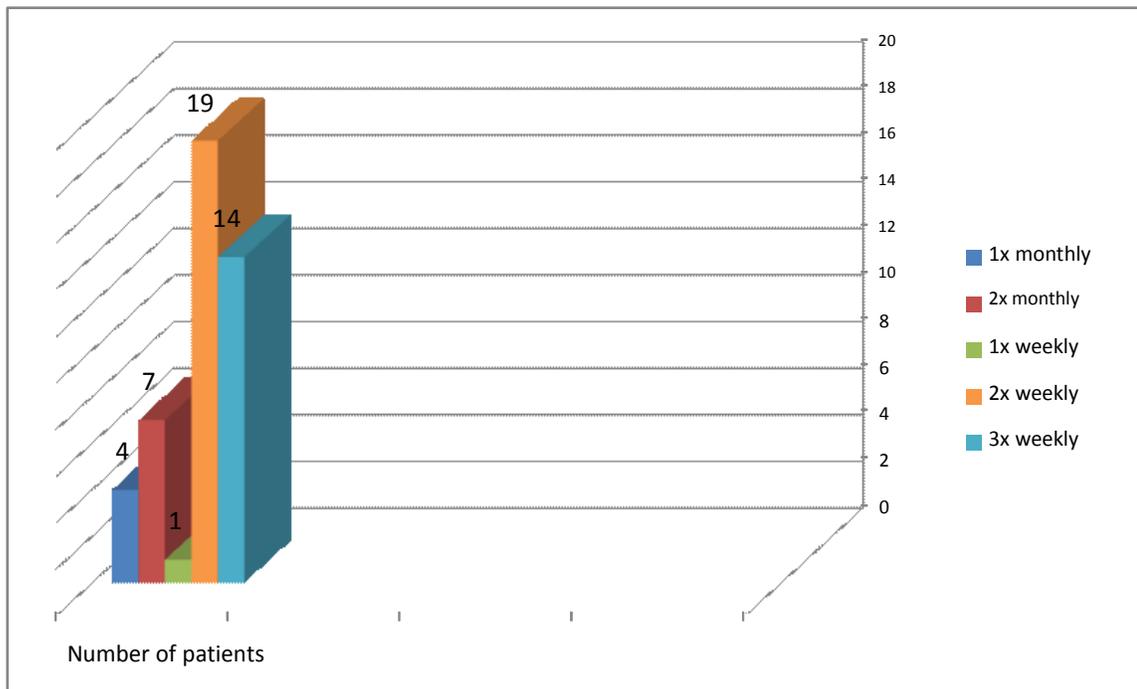
UP can be paroxysmal and localized in 56% or generalized in 44% (8). In our dialysis population UP has been localized mostly on the back (64,4%) and mainly reported between haemodialysis sessions, and in 5% of patients became worse during HD.

During the study we did not find relationship between pruritus and duration of dialysis, as seen in some studies (9). Altmeyer et al. described significant improvement of pruritus in patients who had been on HD for a longer period (10). Some authors reported that the increased serum levels of magnesium, phosphorus and calcium might have a connection with the pruritus (11).

We presented a significant correlation in CaxPO<sub>4</sub> products in patients with pruritus and without pruritus ( $p < 0,05$ ). Our statistical analysis showed no significant difference between

the two groups in the value of PTH. In majority of the reported studies there was no correlation between PTH levels and the intensity of itching (3). There was also no significant difference between pruritic and non pruritic patients when age, sex, albumin, Htc and the underlying renal disease were compared. Ten patients were diabetics. Anemia was proven by us to have no direct link with pruritus. Some studies confirmed that EPO therapy decreases pruritus in association with reduced plasma histamine levels (12). We continuously applied EPO for the last three years and we noticed an improvement in the subjective symptoms and less marked

pruritus. Furthermore, a higher Kt/V was found in patients without pruritus which is in line with the literature data (13). The most commonly reported class of medications used to treat pruritus were antihistamines, which helped relieve symptoms of pruritus and different crèmes (14). In ten patients, UP was dramatically reduced after UVB irradiation, three times weekly, 1-2 minutes. We applied this method for the first time. UVB irradiation has been consistently shown to be bioeffective in patients with the refractory uremic pruritus (15, 16).



**Figure 1.** Frequency of pruritus in HD patients

## Conclusion

Uremic pruritus in haemodialysis patients is multi-factorially conditioned. An adequate dialysis with increased Kt/V, improves symptoms of the uremic pruritus. It seems that the best therapy for refractory pruritus might be a combination of erythropoietin and UVB irradiation.

## References

- Young AW, Sweeney EW, David et al. Dermatologic evaluation of pruritus in patients on haemodialysis. *NY.st.I.Med* 1973; 73: 2670-2674.
- Pisoni RL, Wikstrom B, Elder SI. et al. Pruritus in haemodialysis patients. International results from the Dialysis Outcomes and Practice Patterns study (DOPPS). *Nephrol Dial Transplant* 2006; 21: 3495.
- Urbanos A, Schwartz RA, Szepietowski JC, Uremic pruritus –an update. *Am J Nephrol* 2001; 21: 343-350 .
- McMahon SB, Koltzenburg M. Itching for an explanation. *Trends Neurosci* 1992; 15: 497-501.
- Fantini F, Baraldi A, Sevigiani C, Spattini A, Pincelli C, Gianetti A. Cutaneous innervation in chronic renal failure patients. *Acta Derm Venereol* 1992; 72: 102-105.
- Mettang T, Fritz P, Weber I, Maelleidt C, Hubel E, Kullmann U. Uremic pruritus in patients on haemodialysis on continuous ambulatory peritoneal dialysis (CAPD). The role of plasma histamine and skin mast cells. *Clin Nephrol* 1990; 34(3): 136-141.
- Zucker J, Yosipovitch G, David M, Gafter U, Boner G, Prevalence and characterization of uremic pruritus in patients undergoing hemodialysis; Uremic pruritus is still major problem for patients with a major end stage renal disease; *J Am Acad Dermatology* 2003; 49: 842-6.
- Gilcrest BA, Stern RS, Steinman TI, Brown RS, Arndt KA, Anderson WW: Clinical features of pruritus among patients undergoing maintenance hemodialysis. *Arch Dermatology* 1982; 118: 154-156.
- Altmeyer P, Kachel HG, Yungler M, Koch KM, Holzmann H; Skin changes in long term dialysis patients. *Clinical study Hautarzt* 1982; 33: 303-309.
- Stahl-Backdahl M: Pruritus in haemodialysis patients. *Skin pharmacol* 1992; 1: 14-20.
- Colen EP, Rusell TI, Gananeis IC. Mast cells and calcium in severe uremic itching. *Am I Med Sci* 1992; 303-360.
- De Marchi S, Cecchin E, Villarta D, et al. Relief of pruritus and decreases in plasma histamine

- concentration during erythropoietin therapy in patients with uremia. *N Eng J Med* 1192; 326-969.
13. Hiroshige K, Kabashima N, Takasagi M, Kuroiwa A. Optimal dialysis improves uremic pruritus. *Am J Kidney Dis* 1995; 25: 413-419.
  14. Pauli-Magnus C, Mikus G, Alscher DM et al. Naltrexone does not relieve uremic pruritus. Results of randomized, placebo-controlled cross-over study. I. *Am.Soc Nephrol* 2000; 11: 514-519.
  15. Ada S, Seckin D, Budakoglu J, Ozdemir FN. Treatment of uremic pruritus with narrowband ultraviolet phototherapy, an open pilot study. *J Am Acad Dermatol* 2005; 53: 149.
  16. Gilcrest BA, Rowe JW, Brown RS, Steinman TI, Arndt KA, Ultraviolet phototherapy of uremic pruritus; Long term results and possible mechanisms of action; *Ann Intern Med* 1979; 91(1): 17-21.