

Original Article

Association between Pruritus and Serum Concentrations of Parathormone, Calcium and Phosphorus in Hemodialysis Patients

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ABSTRACT. Chronic renal disorders have a progressive course in most cases, and finally result in end-stage renal disease (ESRD). Hemodialysis (HD) is one of the mainstays in the treatment of these patients. Disturbance in calcium (Ca) and phosphorus (P) metabolism and alteration of serum levels of parathormone (PTH) are observed in these patients. One of the most common cutaneous manifestations in patients on HD is pruritus. The aim of this study is to evaluate the association between pruritus and serum concentrations of Ca, P and PTH in patients with chronic renal disease. This analytic, descriptive, cross-sectional study was performed on 120 patients on HD at the Fifth-Azar Hospital in Gorgan, Iran, in 2010. Information related to the patients, including age, gender, pruritus, time of pruritus and duration on dialysis, was extracted from questionnaires. Serum concentrations of intact PTH, Ca and P were measured. Data were analyzed by the chi-square test and SPSS-16 software. A *P*-value less than 0.05 was considered statistically significant. Among the 120 study patients, 50% were male and the mean age (\pm SD) was 49 ± 12.3 years. Sixty percent of the patients had pruritus, of whom 33.3% had PTH levels above the normal range. Among the 40% of the patients who did not have pruritus, 39.6% had PTH levels higher than the normal levels. The mean serum Ca and P levels were 8.44 ± 1.65 mg/dL and 5.48 ± 1.81 mg/dL, respectively. The mean (\pm SD) Ca-P product was 55.46 ± 47.16 and the mean PTH concentration was 274.34 ± 286.53 pg/mL. No significant association was found between pruritus and age, sex, serum PTH and P levels as well as Ca-P product. However, the association between serum Ca levels and pruritus was significant (*P* = 0.03). Our study showed that most patients with pruritus had serum Ca levels in the abnormal range (lower or higher), and there was no significant correlation between serum iPTH level and pruritus. Thus, good control of serum Ca levels is important to reduce pruritus in these patients.

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Introduction

Chronic renal disease has a progressive course in most cases, and finally results in end-stage renal disease (ESRD). Various treatments have been considered for these patients,

and one of the main options is hemodialysis (HD).¹ Patients with renal failure who are on treatment with HD suffer from mucosal and cutaneous lesions, which often annoy patients. These mucocutaneous manifestations may be related to uremia, previous underlying disease, drugs and/or HD treatment.² The serum levels of calcium (Ca), phosphorus (P) and parathormone (PTH) are the most important biochemical factors that get altered in these patients. One of the most common complications seen in patients on HD is pruritus, the prevalence of which in patients with chronic renal failure (CRF) is between 37% and 90%; this rate is about 80% in patients on HD.³ The etiology of pruritus has not been completely understood in these patients and its pathophysiology depends on several factors. In chronic kidney disease (CKD), there is elevated PTH concentration secondary to derangement of Ca, P and vitamin D metabolism.

Generally, hyperphosphatemia, hypocalcemia and decreased calcitriol production can all increase the PTH production and hyperplasia of parathyroid cells, finally resulting in secondary hyperparathyroidism.⁴ Hyperparathyroidism can stimulate mast cells to release histamine and increase deposition of Ca and magnesium salts on the skin. However, not all patients with severe hyperparathyroidism have pruritus. In addition, in some of the studies, no association has been found between plasma levels of PTH and cutaneous proliferation and number of mast cells.⁵ In view of the high prevalence of pruritus in patients on dialysis and its unknown etiology as well as the lack of a safe treatment for pruritus, further investigations in this field are necessary. The aim of this study is to evaluate the association between pruritus and serum levels of PTH, Ca and P in patients on HD.

Materials and Methods

This descriptive-analytic, cross-sectional study was conducted on 120 patients who were on HD at the Fifth-Azar Hospital in Gorgan in 2010. The diagnosis of ESRD was confirmed by the nephrologists. Data were collected from

questionnaires, and included age, gender, pruritus, time of developing pruritus and duration on HD. iPTH was measured by the enzyme-linked immunosorbent assay, Ca by CPC and a spectrophotometer and P by the ultraviolet technique. According to the Kidney Diseases Outcome and Quality Initiative, the acceptable level of serum Ca in patients with ESRD is 8.4–9.5 mg/dL, of P is 3.5–5.5 mg/dL and of iPTH is 150–300 pg/mL. Age, as a qualitative variable, was considered in three groups (15–35, 35–55 and 55–75 years). Data were analyzed by the chi-square test and SPSS-16 software. A *P*-value less than 0.05 was considered as being statistically significant.

Results

Among the 120 HD patients studied, half were males. The mean age \pm standard deviation was 49 ± 12.3 years, duration on dialysis was 3.84 ± 4.05 years, serum Ca concentration was 8.44 ± 1.65 m/dL, serum PTH level was 274.34 ± 286.53 pg/mL, serum P level was 5.48 ± 1.81 mg/dL and Ca–P product was 55.46 ± 47.16 .

In this study, 60% of the patients had pruritus; the PTH was higher than normal in 33.3% of them. In contrast, 39.6% of the patients without pruritus had high PTH concentrations. The association of pruritus and independent variables has been shown in Table 1. As shown, pruritus had no statistically significant difference between the two genders ($P = 1.00$). The serum PTH concentration was below normal in 55%, normal in 9.16% and above the normal limit in 35.83% of the patients. No significant association was found between age, gender, serum PTH, serum P levels and the Ca–P product and pruritus, while the association between serum Ca level and pruritus was significant ($P = 0.03$). The serum Ca was below normal in 54.2% of the patients with pruritus and 44.7% of patients without pruritus. The prevalence of pruritus, before or after dialysis, had no relationship with serum Ca and P levels ($P > 0.05$). The serum Ca and P levels showed no significant association with the serum PTH level ($P > 0.05$). The association

Table 1. Association between pruritus and independent variables in the study subjects.

Variables	Classification	With pruritus	Without pruritus	P-value
		No. (%)	No. (%)	
Gender	Male	36 (50)	24 (50)	NS
	Female	36 (50)	24 (50)	
Age groups	15–35 years	10 (13.9)	13 (27.1)	NS
	35–55 years	37 (51.4)	19 (39.6)	
	55–75 years	25 (34.7)	16 (33.3)	
Serum phosphorus level	Higher than normal	29 (40.3)	22 (45.8)	NS
	Normal	37 (51.4)	21 (43.8)	
	Lower than normal	6 (8.3)	5 (10.4)	
Serum calcium level	Higher than normal	19 (26.4)	7 (14.9)	0.03
	Normal	14 (19.4)	19 (40.4)	
	Lower than normal	39 (54.2)	21 (44.7)	
Calcium–phosphorus product	More than 55	18 (25)	13 (27.1)	NS
	Less than 55	54 (75)	35 (72.9)	
Serum parathormone level	Higher than normal	24 (33.3)	19 (39.6)	NS
	Normal	6 (8.3)	5 (10)	
	Lower than normal	42 (58.3)	24 (50)	

between Ca–P product and serum PTH in the study patients according to gender and age groups is summarized in Table 2. The only significant association seen was in the serum PTH levels in the various age groups ($P < 0.01$); the age group 15–35 years had higher serum PTH levels while most of the other age groups had lower PTH levels.

Discussion

In this study, pruritus was found in 60% of the patients. In previous studies, the reported prevalence of pruritus has been higher, while in some other studies, it has been lower than that in our study. For instance, pruritus was observed in 58.8% of the patients by Szepietowski,⁶ 41.9% by Akhiani et al,⁷ 70%

by Yazdanpanah et al⁸ and 72.8% by Omori Kentaro et al from Japan.⁹ These differences may be due to the prevailing climatic conditions. Comparison of these results shows that, generally, more than half of the patients complained of pruritus in most studies.

In the study by Narita et al, there was a significant association between serum PTH levels and pruritus.¹⁰ In the study by Yazdanpanah, the serum PTH level was normal in 60% of the patients and 84% complained of pruritus. They found a significant difference in the serum PTH levels in patients with and without pruritus.⁸ In addition, Stable-backdahlm et al also reported that the serum PTH level in HD patients with pruritus was significantly higher than in those without pruritus. However, no association was found between the severity of

Table 2. The association of calcium–phosphorus product and serum parathormone with gender and age groups in the study subjects.

Variable		Calcium–phosphorus product			Serum parathormone level			P
		Less than 55	More than 55	P	Less than normal	Normal	More than normal	
Gender	Male	47 (54)	12 (38.7)	NS	30 (45.5)	7 (63.6)	23 (53.5)	NS
	Female	40 (46)	19 (61.3)		36 (54.5)	4 (36.4)	20 (46.5)	
Age groups (years)	15–35	15 (17.2)	8 (25.8)	NS	5 (7.6)	3 (27.3)	15 (34.9)	<0.01
	35–55	39 (44.8)	15 (48.4)		32 (48.5)	7 (63.6)	17 (39.5)	
	55–75	33 (37.9)	8 (25.8)		29 (43.9)	1 (9.1)	11 (25.6)	

symptoms and the serum PTH levels.¹¹ In the present study, contrary to the three previous studies, the serum PTH concentration in patients with and without pruritus showed no significant difference ($P = 0.66$). This finding is similar to the results of Kaku et al,¹² Akhiyani et al⁷ and Szepietowski et al,⁶ in which no significant association was found between pruritus and serum PTH levels.

Narita et al and Omori Kentaro et al, in their studies, showed that male gender was an important factor for developing severe pruritus;^{9,10} in our study, there was no statistically significant association between pruritus and male and female genders ($P = 1.00$). Omori Kentaro et al reported a significant association between pruritus and age; age younger than 30 years was associated with a lower risk for pruritus,¹⁰ and no significant association was found between age and pruritus in our study.

Narita et al and Szepietowski et al found that the serum Ca concentration was significantly higher in patients with pruritus when compared with those without pruritus.^{6,10} In the present study, majority of the cases with pruritus had abnormal (increased or decreased) serum Ca levels (Table 1). A reverse association was seen between pruritus and serum Ca level in our study. Some other investigators however found no significant association between serum Ca and pruritus.^{7,11} Additionally, many studies found no association between serum P levels and pruritus.^{7,8,13} These findings were similar to our study, although Omori Kentaro et al reported a significant association between hyperphosphatemia and pruritus.¹⁰ Many studies have reported a significant association between the Ca-P product and pruritus.^{9,14}

The strong points in our study are including iPTH measurement and excluding patients with cutaneous lesions; whereas, the small sample size is a limitation in our study.

In conclusion, our study revealed a significant association between serum Ca levels and cutaneous pruritus. No significant correlation was found between serum iPTH level and pruritus. Thus, in patients with ESRD, it is important to maintain the serum Ca levels at as

close to normal as possible to reduce the prevalence of pruritus.

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