Original Article

Effects of Diabetes Mellitus, Age, and Duration of Dialysis on Parathormone in Chronic Hemodialysis Patients

Hamid Nasri¹, Soleiman Kheiri²

Departments of Internal Medicine¹ and Biostatistics and Epidemiology², Shahrekord University of Medical Sciences, Hajar Medical, Educational and Therapeutic Center, Shahrekord, Iran

ABSTRACT. Secondary hyperparathyroidism (SHPTH) can develop early in the course of chronic renal failure and becomes more prominent as kidney function declines. We studied the effect of diabetes, age, and dialysis on parathyroid function in 60 (21 women, 39 males; 44 non-diabetic, 16 diabetic) hemodialysis (HD) patients. Serum intact PTH (iPTH), calcium, phosphorus, alkaline phosphatase (ALP), and magnesium (Mg) were measured. Adequacy of HD was evaluated by calculating the urea reduction rate (URR). There were significantly lower values of serum iPTH, ALP, and dialysis adequacy among diabetic than non-diabetes HD patients. In addition, there were an inverse correlation of age and serum iPTH (r = -0.27, p = 0.034) as well as age and serum phosphorus (r = -0.28, p = 0.031). There was also a positive correlation between serum iPTH with the duration (r = 0.001, p = 0.42) and doses of dialysis treatment (r = 0.38, p = 0.002). We conclude that a significant negative correlation between age and serum phosphorus and lower parathyroid activity in diabetic HD patients, which implies more prevalence of bone disease in elderly diabetic HD patients. Further study of bone disease in this group of patients is required to evaluate its effect on outcome and different therapeutic interventions.

Keywords: Hemodialysis, Hyperparathyroidism, Parathormone, Renal, Failure, Diabetes mellitus

Introduction

Secondary hyperparathyroidism (SHPTH) is common in patients with chronic kidney disease (CKD) and is characterized by excessive serum parathyroid hormone (PTH) levels, parathyroid hyperplasia and an imbalance in calcium and phosphorus metabolism. PTH is a major uremic toxin and may be responsible for long-term con-
sequences that include renal osteodystrophy, severe vascular calcifications, alterations in cardiovascular structure and function, immune dysfunction, and anemia. These adverse effects may contribute to an increased risk of cardiovascular morbidity and mortality among end-stage renal-failure patients and some of them have been reported in our previous studies.

Secondary hyperparathyroidism develops early in the course of CKD and becomes more prominent as kidney function declines. Bone derangement and vascular calcifications are difficult to reverse when established, which mandates early management of SHPTH and consideration of factors involved in the activity of the parathyroid glands.

In spite of dramatic advances in our understanding of the pathogenesis, pathophysiology and sequelae of SHPTH, research is still required to better understand the role of parathormone in hemodialysis (HD) patients. In this regard, studies have shown that the risk of developing SHPT is not the same for all uremic patients. HD patients with diabetes mellitus (DM) may have a lower risk than non-diabetic patients of being affected by SHPTH. Studies demonstrated that diabetics on regular HD have an impaired secretion of parathyroid hormones. Moreover, duration of HD therapy and age of HD patients, with and without DM, may influence serum intact PTH (iPTH) levels.

In this study, we compare the intensity of SHPTH in diabetic and non-diabetic HD patients, and evaluate the effects of age, duration, and doses of dialysis treatment on parathyroid gland function.

**Material and methods**

This is a cross-sectional study which was conducted on patients with end-stage renal disease (ESRD) undergoing maintenance HD treatment with acetate basis dialysate and polysulfone membrane. According to the severity of the secondary hyperparathyroidism, each patient was under treatment for SHPTH with oral active vitamin D3 (Rocaltrol), calcium carbonate, and sevelamer of various doses. After an overnight fast blood samples were obtained, intact serum PTH (iPTH) was measured by the radioimmunoassay (RIA) method using DSL-8000 kits of USA (normal range of values is 10-65 pg/ml). Also peripheral venous blood samples were collected for biochemical analysis including serum pre- and post-dialysis blood urea nitrogen (BUN), calcium (Ca), phosphorus (P), alkaline phosphatase (ALP), and magnesium (Mg) were measured using standard kits.

For measurement of adequacy of HD, urea reduction rate (URR) was calculated from pre- and post-blood urea nitrogen (BUN) data. Body mass index (BMI) calculated using the standard formula (post-dialysis weight in kilograms/ square height in meters, kg/m²). Duration and frequency of HD treatment were calculated from the patients’ records. The duration of each HD session was 4 hours.

**Statistical analysis**

Data are expressed as the mean ± standard deviation (SD). Comparison between the groups was performed using Student’s t-test. Statistical correlations were assessed using partial correlation test. All statistical analyses were performed using SPSS (version 11.5.00). Statistical significance was determined at p value < 0.05.

**Results**

We studied 44 were non-diabetic (F=15, M=29) and 16 were diabetic patients (F=6,
M=10). The mean age of the patients was 46 ± 18 years. The mean duration of patients on HD was 25 ± 30 months (median: 13 months).

Table 1 shows the parameters of the study patients. The mean serum iPTH was 357 ± 395 pg/ml (median: 223 pg/ml). The mean serum ALP levels was 538 ± 746 IU/L (median: 347 IU/L).

We did not find any significant differences between age, duration of HD treatment, dialysis dose, Ca x P products, URR, serum iPTH, Ca, P, ALP or serum Mg, between males and females was found. However, we observed a significant difference of dialysis adequacy (as determined by URR) between diabetics and non-diabetic patients (p= 0.006).

Figure 1 shows that there was a significantly lower serum iPTH and ALP in diabetic than non-diabetic HD patients (p= 0.019, p= 0.022, respectively). However, there were no significant differences of serum Ca, P, Mg, and Ca x P products between diabetics and non-diabetic patients.

Figure 2 shows that there was a significant inverse correlation of serum iPTH with age (r=-0.27, p= 0.034) in the study patients.

Figure 3 shows that there was significant
inverse correlation of serum phosphorus with age ($r = -0.28$, $p = 0.031$). However, there were no significant correlations between age and serum calcium or Mg.

Other findings included a significant inverse correlation of dialysis adequacy with age as determined by URR ($r = -0.33$, $p = 0.008$), and a significant positive correlation of serum ALP with serum iPTH in the study patients ($r = 0.55$, $p < 0.001$) (adjusted for age). This association in diabetic and non-diabetic populations were ($r = 0.48$, $p = 0.091$) and ($r = 0.51$, $p = 0.001$), respectively. Significant positive correlations of serum iPTH with duration ($r = 0.001$, $p = 0.42$) and hemodialysis doses ($r = 0.38$, $p = 0.002$) were found too (data were age adjusted).

### Discussion

The principal findings of this study were the significant differences between serum iPTH, serum ALP, and URR between diabetics and non-diabetic hemodialysis patients, with lower values in the diabetic group. In addition, inverse correlations between serum phosphorus, serum ALP and the adequacy of HD with patients' age were found. Moreover, positive correlations between serum iPTH, and duration and of hemodialysis were also found.

An increase of parathyroid hormone (PTH) levels with age was reported in some studies. Endres et al, demonstrated an age-related increase in PTH, and that alterations in phosphate and calcium metabolism were consistent with it in both healthy men and women. However, several studies including ours, have suggested inverse correlation between age and serum parathyroid in hemodialysis patients. The pathophysiological basis of this age-related decline in serum iPTH levels remains unclear.

In a study conducted by Lorenzo et al revealed an inverse and significant correlation between age and protein intake, calorie intake, serum phosphorus concentration, and PTH levels in addition to a significant positive correlation between serum phosphorus and PTH levels. They suggested that a lower serum phosphorus level could be due to spontaneous reduction of protein intake, which might contribute to the relative low PTH levels observed in elderly hemodialysis patients.

Mehrotra et al, In a study on 92 maintenance hemodialysis patients concluded that age was inversely correlated with both serum phosphorus and iPTH, and that these relationships remained significant even when the data were adjusted for diabetic status, duration on dialysis, and diet. However, they suggested that reduced responsiveness of parathyroid glands may be more related to age-dependent accumulation of uremic toxins than to reduction in protein intake.

Compatible with our results, Salem found that 50% of HD patients developed serum PTH levels more than three times normal, whereas 25% developed reduced PTH levels, and that diabetic patients were less likely to have elevated PTH levels than non-diabetic patients. Moreover, Guh et al,
found that HD patients with diabetes were older, received a shorter duration of dialysis therapy, and revealed lower PTH, phosphate, albumin, BUN, and creatinine levels, as well as URRs. However, they concluded that relative hypoparathyroidism was not associated with diabetes per se, but more related to age, duration of dialysis, and levels of ionized calcium, phosphate, albumin, and magnesium. Another study by Vincenti et al. also demonstrated that diabetic patients developed significantly lower serum calcium and immunoreactive parathyroid hormone levels than non-diabetic patients. Serum iPTH was not related to total serum calcium, but was positively correlated with serum phosphorous in non-diabetic and diabetic patients, and iPTH was only correlated with alkaline phosphatase in non-diabetic patients. A third study by Inaba et al. also concluded that serum iPTH levels were significantly lower in HD patients with DM than those without DM.

We speculate from our results and the above studies that insidious malnutrition and accumulation of uremic toxins, which is often found in the elderly, might reduce the responsiveness of the parathyroid glands.

We conclude that a significant negative correlation between age and serum phosphorus and lower parathyroid activity in diabetic HD patients, which implies more prevalence of bone disease in elderly diabetic HD patients. Further study of bone disease in this group of patients is required to evaluate its effect on outcome and different therapeutic interventions.

References


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