Secondary Hyperparathyroidism and Calcium Phosphate Control in a Hemodialysis Population

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ABSTRACT

Aim: to evaluate the prevalence of secondary hyperparathyroidism and calcium phosphate control in the hemodialysis Asian population.

Methods: we evaluated 36 patients at Tan Tock Seng Hospital in Singapore, who were receiving thrice weekly maintenance hemodialysis for at least 6 months. Patients with history of previous parathyroidectomy were excluded from the study. Patient’s weight, length of dialysis per week, duration of dialysis, serum calcium, phosphate, albumin, bicarbonate, intact parathyroid hormone (iPTH), and single pool Kt/V were retrieved from patient’s medical records.

Results: the mean length of weekly dialysis session and single pool Kt/V was 13.5 hours and 1.73 respectively. The majority of patients achieved the target range of serum phosphorus (67%), corrected calcium (58%) and calcium-phosphorus product (81%). Only 25% of patients had levels of iPTH within the target range (150-300 pg/mL). Ninety four percent of the patients were on calcium-based phosphate binder and 42% on vitamin D therapy. A significant number of patients still fell out of the recommended guideline range for serum concentrations of phosphorus (11% of patients below lower target range, 22% of patients above upper target range), corrected calcium (3% below, 39% above), calcium-phosphorus product (19% above), and iPTH (58% below, 17% above). Thirty percent of the patients had levels of iPTH < 100 pg/mL.

Conclusion: compared to data reported from the USA, Europe and Japan, mean levels of phosphate, corrected calcium and Ca´P product seem better controlled in this hemodialysis Asian population. However, more than half of the patients may have oversuppression of iPTH levels and a third of patients are at increased risk of developing a dynamic bone disease.

Key words: hyperparathyroidism, calcium, phosphate, hemodialysis, adynamic bone disease.

INTRODUCTION

Phosphorus is a major constituent of bones and teeth and an essential component of metabolism and intracellular energy production. Excess dietary phosphorus is excreted by the kidneys or stored in bone tissue. Serum phosphate does not become elevated until glomerular filtration rate falls below approximately 30 ml/min/1.73m², or stage IV chronic kidney disease (CKD) according to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF–K/DOQI) classification. In endstage renal disease (ESRD), the blunted urinary excretion of phosphorus can no longer keep pace with the obligatory intestinal phosphate absorption, resulting in hyperphosphatemia.

Routine dialysis removes only up to 70% of absorbed phosphorus; therefore, hyperphosphatemia is found in the majority of patients with ESRD. Hyperphosphatemia is one of the main factors in the pathogenesis of secondary hyperparathyroidism and renal osteodystrophy. Studies have shown that elevated levels of serum phosphorus and calcium times phosphate (Ca’P) product are associated with an increased risk of death. The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (K/DOQI) Clinical Practice Guidelines for Bone Metabolism and Disease in CKD recommends maintenance of serum phosphorus between 3.5 and 5.5 mg/dL, corrected total calcium between 8.4 and 9.5 mg/dL, iPTH between 150 and 300 pg/mL and serum Ca’P product below 55 mg²/dL.

In a survey among representative samples of hemodialysis facilities and patients participating in the Dialysis Outcomes and Practice Patterns Study (DOPPS) in the United States, Europe, and Japan from 1996 to 2001, the prevalence of hyperphosphatemia among dialysis patients is very high, 52% of patients having serum phosphate levels > 5.5 mg/dL. In addition, 50% and 44% of patients had exceeded the recommended target range of corrected total calcium and Ca’P product respectively. There are only limited data available for hemodialysis Asian population outside...
Japan, which follows different diet and dialysis schedules.

METHODS

We analyzed the records of patients, who were on maintenance hemodialysis for at least 6 months, followed at Tan Tock Seng Hospital in Singapore. Patients with history of previous parathyroidectomy were excluded from the study. Thirty six patients satisfied these criteria and were included in this study. All patients were receiving thrice weekly maintenance hemodialysis with standard dialysate calcium of 2.5 meq/L. Patient’s weight, length of dialysis per week, duration of dialysis, serum calcium, phosphate, albumin, bicarbonate, intact parathyroid hormone, and single pool Kt/V were retrieved from patient’s medical records.

The average of 2 iPTH assays that were 3 months apart were analyzed together with an average of 2 concomitantly drawn calcium, phosphate, albumin, bicarbonate and single pool Kt/V. Calcium was corrected for the concomitantly drawn albumin. Serum calcium was adjusted for serum albumin according to an equation commonly used in the general population: adjusted calcium = measured calcium + [(4.0 - serum albumin in g/dL) ´ 0.8]. Patients were receiving their medicine as prescribed by their practicing nephrologists with the aim of maintaining serum phosphate, calcium, Ca ’ P product and iPTH levels according to the recommendation set by NKF-K/DOQI clinical practice guidelines for bone metabolism and disease in CKD.

Unless contraindicated, the reduction of phosphorus levels was achieved through dietary phosphate restriction and the use of phosphate binder. The main phosphate binder was calcium carbonate or acetate. In view of cost, non-calcium-, non-aluminium-based phosphate binders and calcimimetic agents were not used. Intravenous calcitriol 0.5-2 mg was given at the end of dialysis after control of hyperphosphatemia and the dose was titrated depending on the iPTH levels.

RESULTS

The baseline socio-demographic variables of the study population (n = 36) and dialysis characteristics is shown in Tables 1 and 2. There was 53% male and 47% female. The race distribution comprised 75% Chinese and 25% Malay. Diabetes was the cause of ESRD in two-third of the patients. The other remaining causes of ESRD were glomerulonephritis, hypertension, polycystic kidney disease, nephrolithiasis and trauma. The mean age was 56 ± 12 years. On average, the patients had been on chronic maintenance hemodialysis for 23 ± 17 months. Calcium-based phosphate binder was used in 94% of patients and 42% of patients received vitamin D therapy. The only non-calcium-based phosphate binder used was aluminium, which was prescribed to 11% of patients temporary.

The mineral metabolism indicators are shown in Table 3. The mean serum phosphorus concentration was 5.0 ± 1.4 mg/dL, corrected calcium 9.4 ± 0.6 mg/dL, Ca’P product 47.5 ± 13.5 mg²/dL² and the iPTH 132 ± 141 pg/mL. Table 4 shows patient characteristics by serum phosphorus, corrected total calcium, Ca’P product and iPTH levels according to the recommended guideline range set by NKF-K/DOQI.

The majority of patients achieved the target range of serum phosphorus (67%), corrected calcium (58%) and Ca’P product (81%). Only 25% of patients had levels of iPTH within the target range (150-300 pg/mL). A significant number of patients still fell out of the recommended guideline range for serum concentrations of phosphorus (11% of patients below lower target range,
22% of patients above upper target range), corrected calcium (3% below, 39% above), Ca × P product (19% above), and intact PTH (58% below, 17% above). Thirty percent of the patients had iPTH levels < 100 pg/mL and therefore at risk of developing adynamic bone disease. Eight percent of the patients developed hypercalcemia as defined by serum calcium above 10.2 mg/dL.

**DISCUSSION**

Hyperphosphatemia and secondary hyperparathyroidism is a common complication in patients with ESRD. A degree of secondary hyperparathyroidism must exist as a trade off to maintain normal bone modeling. The results of this investigation demonstrate that the majority of patients achieved the target range of serum phosphorus (67%), corrected calcium (58%) and Ca × P product (81%). These results are better than those reported in other studies. However, this difference can be explained by the difference in time on dialysis (dialysis vintage), the etiology of ESRD, the duration of weekly dialysis session and the achieved dose of dialysis. Compared to other studies, our patients had only been on chronic maintenance hemodialysis for a short period of time (mean duration on dialysis 23 ± 17 months). Neff et al found duration of dialysis to be a major factor that determines parathyroid bone disease. Recently, Chertow found dialysis vintage to be a significant predictor of hyperparathyroidism in univariate and multivariate linear regression.

Earlier studies found a low prevalence of secondary hyperparathyroidism in diabetic patients. Vincenti et al found this to be due to shorter time on dialysis and low rates of bone turnover. In our study, diabetes was the cause of ESRD in two-third of the patients, which is higher than those reported in other studies. In addition, our patients also had longer dialysis session (mean duration of weekly dialysis session 13.5 ± 1.2 hours) and higher achieved dialysis dose (mean single pool Kt/V 1.73 ± 0.27).

Calcium-based phosphate binder was used in 94% of our dialysis population. Despite the use of calcium-based phosphate binder, only 8% of our patients developed hypercalcemia as defined by serum calcium above 10.2 mg/dL. In contrast to other studies, the prevalence of hyperparathyroidism in our studies was lower. Only 17% of patients in our study developed hyperparathyroidism (defined as iPTH > 300 pg/mL). In keeping with the result of other studies, half of our patients also had oversuppression of serum iPTH. Thirty percent of our patients had iPTH levels below 100 pg/mL. It was observed that most of the cases of adynamic bone disease were found in patients with iPTH serum levels < 100 pg/mL. Treatment of secondary hyperparathyroidism with vitamin D and administration of calcium containing phosphate binder were accompanied in a large proportion of cases by the development of adynamic bone disease.

**CONCLUSION**

Compared to data reported from the USA, Europe and Japan, mean levels of phosphate, corrected calcium and Ca × P product seem better controlled in this hemodialysis Asian population. However, more than half of the patients may have oversuppression of iPTH levels and a third of patients are at increased risk of developing adynamic bone disease. This could be due to the use of mainly calcium-based phosphate binders and treatment with vitamin D. Therefore, the development of cost effective calcimimetic agents and non-calcium-, non-aluminium-based alternative treatments is of clinical value.

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**REFERENCES**