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Original Article

Analysis of the parathyroid function in maintenance hemodialysis patients from Changchun, China

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Abstract

Objective: To evaluate the parathyroid function in maintenance hemodialysis patients from 4 hemodialysis centers and to analyze the cause of the dysfunction.

Methods: This cross-sectional study included patients with chronic renal disease undergoing maintenance hemodialysis treatment at 4 hemodialysis centers in Changchun, China, between March 2014 and August 2015. A total of 337 patients were asked to complete a questionnaire including their name, gender, age, hemodialysis duration, the use of calcium carbonate and vitamin D3 supplements, health education status, hemofiltration frequency, appetite, and education level. Serum intact parathyroid hormone (iPTH), phosphorus, total calcium, blood urea nitrogen (BUN), and creatinine (Cre) levels were obtained from clinical information. Patients with iPTH data were divided into 2 groups: Normal group: the patients with an iPTH level < 100 pg/ml (28 subjects); Abnormal group: the patients with an iPTH level > 100 pg/ml (136 subjects). Intergroup differences were analyzed using the *t*-test. The enumeration data were analyzed by the χ^2 test.

Results: The iPTH levels were not monitored for 173 maintenance hemodialysis patients (51.3%) but for 164 patients (48.7%). Of the 164 patients, 28 (17.1%) had a normal serum iPTH level, while the other 136 (82.9%) had an abnormal iPTH level. The maintenance hemodialysis duration and phosphorus levels in the Abnormal group were higher than those in the Normal group ($P < 0.05$). The appetites of patients in the Abnormal group were better than those of patients in the Normal group ($P < 0.05$).

Conclusions: A lower proportion of patients on hemodialysis had a normal iPTH level. The phosphorus levels of patients on hemodialysis should be controlled via dietary interventions.

Keywords: Maintenance hemodialysis; Intact parathyroid hormone; Serum phosphorus

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Introduction

The incidence and prevalence of maintenance hemodialysis is rapidly increasing in Changchun, the capital of Jilin province in Northeast China. The number of maintenance hemodialysis patients has increased sharply in the past few years due to the high morbidity of end-stage renal disease, population aging, medical insurance coverage, and the increased number of hemodialysis centers. There are approximately 5000 maintenance hemodialysis patients in the main districts of Changchun city.

Hypocalcemia, one of the most frequent complications of maintenance hemodialysis, is directly related to patient quality of life. In fact, hypocalcemia is the typical clinical syndrome induced in cases of secondary hyperparathyroidism. The morbidity of secondary hyperparathyroidism is high in patients on maintenance hemodialysis. Many patients with chronic kidney disease develop elevated intact parathyroid hormone (iPTH) levels or secondary hyperparathyroidism, which further adds to their disease burden.[1] Secondary hyperparathyroidism results in imbalances in serum calcium and phosphorous level as well as alternations in vitamin D metabolism and can lead to renal osteodystrophy, fractures, cardiovascular disease, and even death. Accordingly, we tested the serum iPTH levels of 337 maintenance hemodialysis patients from hemodialysis centers. We then analyzed the cause of the parathyroid dysfunction and the calcium and phosphorus levels.

Materials and methods

Patient selection and characteristics

This cross-sectional study included patients with chronic renal disease who were undergoing maintenance hemodialysis treatment in Changchun, China, between March 2014 and August 2015. All patients had been on regular bicarbonate hemodialysis for >1 month, consisting of a polysulfone dialyzer membrane with a dialysis fluid of 3.0 mEq/L calcium. The patients received hemodialysis 3 times per week for 4 hours per episode. Hemofiltration was routinely received in some of the patients. A total of 337 adults from 4 hemodialysis centers in Changchun, China, were enrolled in this study. These centers were Jilin Province People's Hospital (147 subjects), Changchun Central Hospital (36 subjects), Changchun Nanguan District Hospital (118 subjects), and Jilin Xinhua Hospital (36 subjects).

Questionnaire and parameters

All patients were asked to fill in the questionnaire by providing their name, gender, age, hemodialysis duration, calcium carbonate supplementation (Yes/No), active vitamin D3 (1-α-[OH]D3) supplementation (Yes/No), health education received (Yes/No), hemofiltration frequency, appetite (good/medium/poor), and education level (>9 years/≤9 years).

The most recent levels of the following biochemical indicators were obtained from the clinical information system: serum iPTH, phosphorus, total calcium, blood urea nitrogen (BUN), and creatinine (Cre). The blood samples were obtained before hemodialysis was started. The iPTH level (normal range, 14−72 pg/ml) was then tested using the electrochemical luminescence method. Serum BUN, Cre, calcium, and phosphorus levels were determined using an auto biochemistry analysis system.

Secondary hyperparathyroidism diagnosis

The 2009 version of the Improving Global Outcomes (KDIGO) guidelines suggested an iPTH goal of 2−9 times the upper limit of normal (130−600 pg/ml).[2] According to the internal medicine textbook in China and guidelines and published data of other Asian countries,[3−5] we regarded the tangent point of iPTH level of >100 pg/ml.

Patients with iPTH data were divided into 2 groups: Normal group: patients with an iPTH level <100 pg/ml; and Abnormal group: the patients with an iPTH level >100 pg/ml.

Statistical analysis

The data are summarized as mean ± standard deviation (SD). Intergroup differences were analyzed by the *t*-test, while enumeration data were analyzed by the χ^2 test. For all comparisons, values of $P < 0.05$ were considered statistically significant.

Results

A total of 337 patients on maintenance hemodialysis were enrolled in this study. Among them, serum iPTH level was not monitored in 173 (51.3%) but monitored in 164 (48.7%) patients. Of the monitored patients, 28 (17.1%) had a normal serum iPTH level, while the other 136 (82.9%) had an abnormal level.

The patients in the Normal group (10 men, 18 women) were 60 ± 16 years of age, while those in the

Abnormal group (61 men, 75 women) were 59 ± 15 years of age. There were no gender or age-based intergroup differences at baseline ($P > 0.05$).

The mean iPTH level of the Abnormal group was higher than that of the Normal group. The highest iPTH level of the maintenance hemodialysis patients in the Abnormal group was 3080 pg/ml. The maintenance hemodialysis duration and serum phosphorus level in the Abnormal group were higher than those in the Normal group ($P < 0.05$). The mean appetite of the Abnormal group was better than that of the Normal group ($P < 0.05$) (Table 1).

There were no intergroup differences in use of calcium carbonate or active vitamin D3 (1-α-[OH]D3) supplementation; health education received; hemofiltration frequency; education level; or serum calcium, BUN, or Cre levels (Table 1).

Discussion

Secondary hyperparathyroidism, a critical complication of chronic kidney disease in maintenance hemodialysis patients, refers to an adaptive increase in serum iPTH levels due to hypocalcemia that reverts to normal if the clinical derangement is controlled. Our results indicated that the serum iPTH levels were not monitored in 51.3% of maintenance hemodialysis patients. These results are important. Health education should include monitoring iPTH, and patients should be encouraged to undergo regular iPTH testing. Only 17.1% of the maintenance hemodialysis patients had a normal iPTH level, while the others (82.9%) had an abnormal iPTH level. In Beijing, 39.1% of maintenance hemodialysis patients had iPTH levels of 150−600 pg/ml, while 29.7% had a level >600 pg/ml.[6] These findings are similar to our results.

iPTH and calcium are known to independently affect cardiovascular function. iPTH is vasodilatory and has chronotropic and inotropic effects on the heart, while hypercalcemia is associated with vascular and valvular calcification, hypertension, and left ventricular hypertrophy. Lin et al demonstrated that a low iPTH level after parathyroidectomy could improve cardiovascular outcomes in nondiabetic dialysis patients with secondary hyperparathyroidism.[7] iPTH excess could also cause abnormally high bone turnover.[3] An 8-year period study that included 106,760 maintenance hemodialysis patients indicated the hyperparathyroidism affected bone and mineral metabolism measures.[8] Thus, iPTH monitoring of maintenance hemodialysis patients should be promoted in clinical practice because it is directly related to patient mortality rates.

Table 1
Comparison of serum iPTH and other indicators between normal and abnormal groups.

Group	Number	Gender (Male/Female)	Age (years)	HD duration (years)	iPTH (pg/ml)	Calcium (mmol/L)	Phosphorus (mmol/L)	BUN (mmol/L)	Cre (μmol/L)
Normal	28	10/18	60 ± 16	4.3 ± 2.9	62.4 ± 29.9	2.11 ± 0.19	1.5 ± 0.4	17.9 ± 6.8	695.4 ± 302.5
Abnormal	136	61/75	59 ± 15	5.0 ± 3.7[a]	560.1 ± 494.2[a]	2.05 ± 0.24	2.0 ± 0.6[a]	21.1 ± 8.5	756.9 ± 273.0

Group	Calcium carbonate (Yes/No)	Vitamin D3 (Yes/No)	Hemofiltration (Yes/No)	Health education (Yes/No)	Appetite (good/medium/poor)	Schooling education (<9 years/>9 years)
Normal	24/4	21/7	26/2	26/2	9/13/6	19/9
Abnormal	112/24	83/53	112/24	112/24	80/49/7[a]	98/38

HD, hemodialysis; iPTH, intact parathyroid hormone; BUN, blood urea nitrogen; Cre, creatinine.
[a] Compared with the Normal group ($P < 0.048$).

Our results demonstrated that serum phosphorus levels of patients in the Abnormal group were higher than those in the Normal group. Moreover, the appetite of patients in the Abnormal group was better than that in the Normal group. This finding is similar to those of other observers.[9,10] Since foods high in protein are a major source of dietary phosphorus, it is plausible that increasing one's protein intake could contribute to hyperphosphatemia. Previous studies have suggested that both a higher serum iPTH level and higher dietary protein intake may contribute to higher serum phosphorus levels. Overall, our results suggest that hyperphosphatemia is associated with both a higher dietary protein intake and a higher serum iPTH level in maintenance hemodialysis patients.[9,11]

Indeed, decreased protein intake has been correlated with low serum phosphorus and relatively low iPTH levels in elderly dialysis patients.[11] The phosphorus intake of a healthy person is known to be approximately 1000–2000 mg daily; however, this level must be restricted to approximately 800 mg in adult dialysis patients. Organic phosphorus is categorized into vegetable and animal sources. Inorganic phosphorus exists as an additive in processed foods. Plant-based phosphorous-rich foods such as nuts exhibit a low gastrointestinal absorption rate, whereas animal-based phosphorus-rich foods such as yogurt have a high gastrointestinal absorption rate. In particular, the levels of inorganic phosphorus as an additive and preservative in carbonated beverages reach 80–100%.[12] As such, limiting the intake of inorganic and natural phosphorus is important. As a result, health education is a critical role in our clinical work. For example, egg white is an excellent source of protein and has a very low phosphorus-to-protein content. In addition, boiling a food lowers its phosphorus content.

The management of hyperparathyroidism in hemodialysis patients requires phosphorus level control. This is the reason why we often use phosphorus binders as the initial treatment of secondary hyperparathyroidism related to hemodialysis in the clinical setting. Most phosphorus exists in the bones and teeth, whereas only 1% exists in the blood. Thus, the phosphorus removed from the body through dialysis is extremely limited. The phosphate binders applied in the clinical setting include aluminum-containing phosphate binders, calcium-containing phosphate binders, and non-calcium-based phosphate binders. Lanthanum carbonate (LC) is a potent non-calcium-based phosphate binder. A meta-analysis demonstrated that LC has high efficacy for lowering serum phosphorus and iPTH levels without increasing serum calcium levels. Current evidence does not show a higher rate of adverse effects for LC than with other treatments, except for a higher incidence of vomiting. Moreover, LC accumulation in the blood and bone was below toxic levels.[13]

In this study, the iPTH level increased as hemodialysis duration increased. However, the calcium level did not differ between the groups, perhaps due to patients receiving supplemental calcium carbonate and active vitamin D3.

The cross-sectional design is the main limitation of our study. Thus, a future dynamic observation is required to provide more evidence for a clinical guideline. The other limitation is that only serum iPTH level was tested; evidence of the supporting morphology of the parathyroid such as ultrasonic parameters and histopathological data is lacking. Bone biopsy information is also needed but rarely collected in many parts of the world. In particular, some new parameters such as β-crosslaps[14] and fibroblast growth factor-23[15] were not included in this study, but represent future directions of research related to hemodialysis-associated secondary hyperparathyroidism.

Above all, we should recommend regular serum iPTH monitoring in maintenance hemodialysis patients. A change in monitoring frequency from quarterly to monthly can reportedly increase the percentage of patients reaching target iPTH values.[16] However, we often suggest iPTH monitoring every 3–6 months for maintenance hemodialysis patients in our own clinical practice. This protocol can be well received by patients because of its better cost-effectiveness. In addition, it is important to maintain normal phosphorus levels by controlling the diet and reducing the phosphorus intake. Such measures can prevent cardiovascular complications, abnormal mineral metabolic disease, and bone disease in maintenance hemodialysis patients. Our goal is to promote quality of life in maintenance hemodialysis patients and help them move from the hospital back to the community.

Conflicts of interest

The authors declare no conflicts of interest.

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