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Original

Secondary hyperparathyroidism in chronic hemodialysis patients in Khuzestan province, Iran

Fatemeh Hayati[1], Seyed Seifollah Beladi Mousavi[1*], Mohammad Faramarzi[1]

Abstract

Introduction: Secondary hyperparathyroidism (SHPT) describes a complex alteration in bone and mineral metabolism which caused by several changes that occurs as a direct result of decreased kidney function

Objectives: The aim of this study is to determine the prevalence of SHPT and its relationship in end-stage renal disease (ESRD) patients living in the province of Khuzestan, Iran.

Patients and Methods: This cross-sectional study was conducted on hemodialysis patients in . Blood samples were obtained to check of intact parathyroid hormone (iPTH) level and routine laboratory studies including serum calcium, phosphorus, and alkaline phosphatase.

Results: One hundred twelve hemodialysis (HD) patients (49 females [43.7%] and 63 males [56.3%]) with mean age of 52.6±15.3 years were enrolled in the study. Seventy-eight patients had intact PTH above 300 ρg/mL, 22 patients had intact PTH between 150-300 ρg/mL and 12 patients had intact PTH below 50 ρg/mL. There was no significant difference in prevalence of SHPT between diabetic and nondiabetic HD. All of our patients had hyperphosphatemia.

Conclusion: According to the results of the study, a very significant percent of our HD patients have SHPT and the serum phosphorus level of these patients are outside the ranges suggested by K/DOQI guidelines. Hence, according to the consequences of SHPTH on progress of atherosclerosis and vascular calcification and therefore high rate of myocardial ischemia and heart failure among HD patients, more attention to this aspect of HD patients is necessary.

Keywords: Hemodialysis, Parathyroid hormone, End-stage renal disease, Secondary hyperparathyroidism

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Introduction

End-stage renal disease (ESRD) is a life-threatening disease with significant complication and the incidence and prevalence of this disease have significantly increased in recent years and imposes a major social and economic burden for healthcare systems (1,2). As seen worldwide, it is well-established that diabetic nephropathy particularly from type 2 diabetes, and hypertensive nephrosclerosis are the leading causes of ESRD in developed and developing countries possibly because of increasing prevalence of obesity, diabetes and hypertension (1-3).

Secondary hyperparathyroidism (SHPT) describes a complex alteration in bone and mineral metabolism – caused by several changes – that occurs as a direct result of decreased kidney function (4,5). The major factors responsible for SHPT in ESRD are hypocalcemia, hyperphosphatemia, deficiency of activated vitamin D and a decrease in the activation of the calcium-sensing receptor in the parathyroid glands. It is suggested that skeletal resistance to the calcemic effect of PTH is also another factor responsible for SHPT in ESRD (6-8).

SHPT induces several forms of renal osteodystrophy, including osteitis fibrosa cystica and mixed osteodystrophy (5-8). However it seems that the importance of SHPT and the possibility of its reduction frequently are neglected issues among HD centers (4-8). On the other hand, evaluation of ESRD patients for SHPT is a very important measure because early detection and treatment of SHPT may slow the progression of bone, cardiac and other complications of this disease (6-10).

Objectives

The aim of the study is to determine the prevalence of SHPT and its relationship in ESRD patients living in the province of Khuzestan, Iran.

Patients and Methods

This cross-sectional study was conducted on ESRD patients undergoing regular hemodialysis (HD) in our HD center in Ahvaz, Iran. The study was conducted between October 2012 to January 2013.

The ESRD was defined as irreversible and advanced loss of renal function requiring renal replacement therapy. A standardized questionnaire was used to collect medical re-

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[1]Chronic Renal Failure Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

***Corresponding author:** Seyed Seifollah Beladi Mousavi, Email: Beladimusavi@yahoo.com

Implication for health policy/practice/research/medical education

Chronic kidney disease-mineral and bone disorder is an important issue because disorders of mineral metabolism including hypercalcemia and hyperphosphatemia are thought to contribute to atherosclerosis and vascular calcification and therefore contribute to high rate of myocardial ischemia and heart failure among end-stage renal disease (ESRD) patients.

cords including cause of ESRD, date of onset of HD, length of time receiving peritoneal or HD services.

In our center, HD was conducted using synthetic (polysulfone) dialyzer membranes and bicarbonate-based dialysis solution at a delivered bicarbonate concentration of 35-40 mEq/l.

Blood samples were obtained prior to a dialysis session from ESRD patients who participated in the study for check of intact PTH level and routine laboratory studies, including serum calcium, phosphorus, and alkaline phosphatase. Serum intact PTH (iPTH) was measured by use of immunoradiometric assays (second generation PTH assays).

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of the Chronic Renal Failure Research Center, affiliated to Ahvaz Jundishapur University of Medical Sciences approved the study. All of the patients provided written informed consent.

Statistical analysis

For statistical analysis, we used the SPSS version 15 software. Chi-square or Fisher exact and *t* tests were performed for evaluation of various risk factors and compare with quantitative variables. Statistical significance in the study was considered at *P* value of <0.05.

Results

In present study 112 HD patients, 49 females (43.7%) and 63 males (56.3%) with mean age of 52.6 ± 15.3 years were enrolled in the study. The main causes of ESRD were diabetes mellitus (41.1%), hypertension (19.6%) and unknown (12.5%) and autosomal dominant polycystic kidney disease (10.7%) (Table 1).

Table 1. Main causes of ESRD in HD patients

Causes	Number	Percent
DM	46	41.1
HTN	22	19.6
Unknown	14	12.5
ADPKD	12	10.7
Congenital	4	3.6
Urologic disorders	4	3.6
GN	2	1.8
Others	8	7.1
Total	112	100.0

Abbreviations: DM, Diabetes mellitus; HTN, Hypertension; ADPKD, autosomal dominant polycystic kidney disease. ESRD, end-stage renal disease; HD, hemodialysis; GN, glomerulonephritis.

The mean level of serum calcium was 8.55 ± 0.59 mg/dl, with a range between 7.10 and 10.40 mg/dl. 55.4% (n = 62) of patients had acceptable levels of calcium according to KDOQI guidelines (8.4 to 9.5 mg/dl), while 7.1% (n = 8) were above and 37.5% (n = 42) were below the values suggested by the guidelines for mineral metabolism (11) (Figure 1).

The mean level of serum phosphate was 7.44 ± 0.71 mg/dl, with a minimum of 5.8 mg/dl and a maximum of 9.40 mg/dl. In all cases, the level of serum phosphate was above the normal range according to KDOQI guidelines (3.5-5.5 mg/dl) (11). Seventy-eight patients had intact PTH levels above 300 ρg/mL (69.6%), 22 patients had intact PTH levels between 150-300 ρg/mL (19.6%) which is in the accepted ranges suggested by K/DOQI guidelines and 12 patients had intact PTH levels below 150 ρg/mL (10.7%) (Figure 2; Table 1) (11). There was no significant difference in prevalence of SHPT between diabetic and nondiabetic HD. Statistical analysis demonstrated that 82.1% of patients had calcium phosphorus product more than 55 mg^2/dl^2.

Discussion

SHPT is a well-recognized complication of ESRD and induces several forms of renal osteodystrophy among these patients (5-9). In addition, alterations in calcium and phosphorus metabolism, as a result of SHPT contribute to a high rate of excess vascular calcification particularly in the form of extensive coronary artery calcification

Table 2. Serum levels of calcium, phosphorus and iPTH

K/DOQI guidelines	Proportion of patients	Mean ± SD	Range
Calcium 8.4-9.5 mg/dl	112	8.55 ± 0.59	7.10-10.4
Phosphorus 3.5-5.5 mg/dl	112	7.44 ± 0.71	5.8-9.40
CA X P 55 mg^2/dl^2	112	63.6 ±8	46.4-89.44
iPTH 150-300 ρg/mL	112	483.3 ± 285.8	41-954

Abbreviation: iPTH, intact parathyroid hormone.

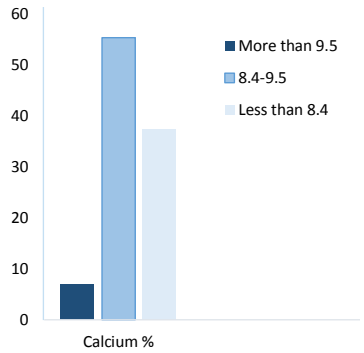

Figure 1. Percentage distribution of patients in accordance with Ca levels.

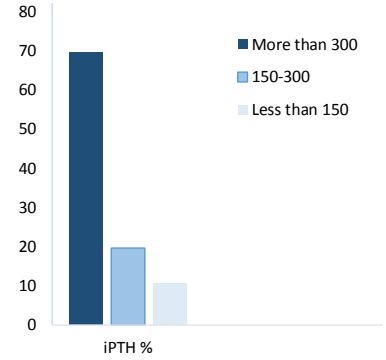

Figure 2. Percentage distribution of patients in accordance with iPTH levels.

(6-8). Moreover, several observational studies have shown that SHPT and disorders of bone and mineral metabolism including hyperphosphatemia and, hypercalcemia may be associated with increased risks of death and cardiovascular events among ESRD patients (7-10). Therefore evaluation of ESRD patients for SHPT should be as an important measure among these patients. However it seems that SHPT is as a neglected issue among HD centers (7-10).

This study provides important information about the epidemiology of SHPT and the other markers of bone and mineral metabolism disorders among ESRD patients. According to data from our study, the percentages of patients on dialysis with intact PTH below 150 ρg/mL, between 150 to 300 ρg/mL and above 300 pg/mL are 10.7%, 19.6% and 69.6%, respectively. It means that a very significant percentage (69.6%) of ESRD patients undergoing maintenance HD in Khuzestan province, Iran have intact PTH levels greater than 300 ρg/mL which significantly differs from that the results of other published study about this issues (12,13).

For example, multinational study of DOPPS which is one of the largest and most representative observational studies among ESRD patients on dialysis about the state of bone and mineral metabolism (BMM) disorders and their management in five European countries, the United States and Japan have showed that only 26.7% of patients on dialysis have levels of iPTH greater than 300 ρg/mL which is very lower compared to the results of our study. According to the results DOPPS study the percentages of patients on dialysis with iPTH levels below 150 ρg/mL and intact PTH higher than 300 ρg/mL in Japan, European countries and United States were 58.6% and 19.0%, 50.1% and 26.9%, and 48.2% and 30.3% for the United States, respectively (14).

The results of our study are approximately similar to the results of the study by Douthat et al, which carried out on 1210 patients on dialysis from 25 dialysis centers in Argentina in 2010. This study described the state of BMM disorders and their management among these patients. According to the results of the study by Douthat et al, the percentages of patients on dialysis with iPTH below 150 ρg/mL and iPTH above 300 ρg/mL was 24% and 54.5%, respectively (13).

The data of our study also shows that a large number of our patients have other BMM markers including the levels of serum calcium and phosphorus, outside the ranges suggested by K/DOQI guidelines (11).

To achieve adequate control of SHPT among ESRD patients on maintenance dialysis or patients with an estimated glomerular filtration rate (GFR) of less than 15 mL/min, the K/DOQI practice guidelines suggested that target plasma levels of iPTH, serum levels of phosphate and serum levels of corrected total calcium should be maintained between 150 to 300 ρg/mL, 3.5 and 5.5 mg/dl (1.13 to 1.78 mmol/l) and 8.4 and 9.5 mg/dl (2.10 to 2.37 mmol/l) respectively (11,14-17).

According to these guidelines, all of our patients have levels of serum phosphorus outside the range suggested by the KDOQI guidelines. In addition more than 40% of our patients have also the levels of serum calcium outside the ranges.

Conclusion

Chronic kidney disease-mineral and bone disorder is an important issue because disorders of mineral metabolism including hypercalcemia and hyperphosphatemia are thought to contribute to atherosclerosis and vascular calcification and therefore contribute to high rate of myocardial ischemia and heart failure among ESRD patients.

Limitations of the study

The major limitation of our study was the relatively small number of patients. To exact evaluation of SHPT in chronic HD patients of Iran, we suggest multi-centric studies.

Authors' contribution

FH and SSBM designed the research. SSBM conducted the research. FH analyzed the data. SSMB and MF prepared the primary draft. SSBM edited the final manuscript. All authors read and signed the paper.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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