Secondary Hyperparathyroidism and Risk Factors in Patients Undergoing Peritoneal Dialysis in a Tertiary Hospital

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Objective: *Secondary hyperparathyroidism (SHPT) can lead to significant morbidity, mortality, and additional healthcare resource utilization in chronic kidney disease. Since the introduction of continuous ambulatory peritoneal dialysis (CAPD) policy for end stage renal disease patients in Thailand, no large studies have been conducted to examine parathyroid dysfunction in these patients. The baseline prevalence data are highly required. The present study was conducted to determine the prevalence of SHPT and the risk factors associated with this dysfunction in CAPD patients.*

Material and Method: *The authors analyzed data of 173 patients who received CAPD at a single center between October 2008 and October 2010. Clinical data and laboratory variables related to parathyroid function were obtained from each patient. Hyperparathyroidism was diagnosed when serum intact parathyroid hormone (iPTH) level was above 300 pg/ml. Variables predicting the development of hyperparathyroidism were calculated by univariate and multivariate logistic regression analysis.*

Results: *Hyperparathyroidism was identified in 29.48% of the CAPD patients. Significantly lower serum calcium levels ($p = 0.037$), significantly higher serum phosphate levels ($p = 0.016$) and significantly greater serum alkaline phosphatase concentrations ($p = 0.029$) were observed in the patients with hyperparathyroidism. By multiple regression analysis, the duration on CAPD showed a significant positive correlation with iPTH ($r = 0.359$, $p < 0.01$) while the total corrected Ca levels had a significant negative correlation with iPTH ($r = -0.176$, $p = 0.023$).*

Conclusion: *There is a high prevalence of hyperparathyroidism in the current Thai CAPD population. Duration on CAPD and hypocalcemia are independent risk factors for the development of hyperparathyroidism.*

Keywords: *CAPD, Secondary hyperparathyroidism*

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In chronic kidney disease (CKD) patients, elevated serum levels of parathyroid hormone (PTH), which is a uremic toxin, are deleterious to the function of many organ system including CKD-mineral bone disorder (CKD-MBD)[1].

Secondary hyperparathyroidism (SHPT) is a frequently observed complication in CKD patients. The prevalence of SHPT increases across declining estimated glomerular filtration rate (eGFR) levels, with about 56% occurring in those with an eGFR of < 60 ml/min/1.73m^2[2] and is around 45% among hemodialysis (HD) patients[3].

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SHPT is characterized by increased secretion of PTH, parathyroid gland hyperplasia, and imbalances in calcium and phosphorus[4]. Decreased kidney function in CKD results in vitamin D deficiency and increased serum phosphate. These changes cause a decline in serum calcium, which in turn stimulates PTH synthesis and secretion. PTH regulates the serum level of calcium by increasing the absorption of calcium from the intestine and the kidney through the action of vitamin D[5]. PTH also increases bone resorption, causing osteitis fibrosa cystica, characterized by the pattern of high bone turnover. Rahimian et al found a positive correlation between an elevated alkaline phosphatase level and conditions with radiologic and histological findings of high bone turnover pattern, as in osteitis fibrosa cystica[3]. The increased PTH, hyperphosphatemia, and dyscalcemia in patients with SHPT are associated with significantly increased

mortality and morbidity. This underscores the importance of PTH management in ESRD patients.

Previous studies demonstrated that one-third of continuous ambulatory peritoneal dialysis (CAPD) patients developed SHPT. There are insufficient data regarding SHPT in Thailand[6,7]. The present study was conducted to examine the current status of parathyroid disease, especially hyperparathyroidism, in the Thai PD population and evaluated the risk factors associated with the development of hyperparathyroidism.

Material and Method

This is a retrospective study of 173 ESRD patients undergoing CAPD at Maharach Nakhon Ratchasima Hospital, Nakhon Ratchasima between October 2008 and October 2010. Acute peritoneal dialysis patients were excluded. Medical records of all CAPD patients were reviewed. The following data were collected: age, sex, duration, creatinine, calcium, phosphorus, albumin, magnesium, and intact PTH. The patients were monitored clinically and biochemically during each follow-up visit and the doses of vitamin D and calcium were adjusted to achieve the desired biochemical and clinical standards. Criteria of acceptable care for PD patients included the followings: maintenance of the corrected total serum calcium level between 8.4 to 9.5 mg/dl, serum phosphate between 3.5 and 5.5 mg/dl, serum calcium-phosphorus product < 55 mg^2/dl^2, iPTH levels between 150-300 pg/ml, and absence of symptoms of bone disease such as bone pain, fatigue, and pruritus. The average of the last two iPTH levels, total corrected calcium, albumin, phosphate, and alkaline phosphatase were determined. Hyperparathyroidism was defined as the iPTH level more than 300 pg/ml according to the National Kidney Foundation's Kidney Disease Outcoms Quality Initiative (NKF-K/DOQI™). Hypercalcemia was defined as a serum total Ca level above 9.5 mg/dl. In the majority of patients, calcium supplements were given to bind phosphate and increase serum calcium. The patients were instructed to take the supplement with meals unless their serum calcium was very low. Vitamin D was added in those who had persistent elevation of iPTH levels and/or hypocalcemia despite good compliance with calcium supplementation.

The preferred PD solution was regular calcium content (3.5 mEq/L). Low calcium dialysate (2.5 mEq/L) was prescribed if high doses of oral calcium were used to alleviate hyperphosphatemia, or when larger doses of vitamin D were given to suppress iPTH. The choice of calcium preparation was at the nephrologist's discretion.

Statistical analysis

All database entries and statistical analyses were performed using SPSS software, version 11.0. All descriptive data were expressed as mean $\pm$ SD or as percentage. Student's t-test was used for comparisons of means between the two groups. Factors influencing iPTH levels were compared using univariate and multivariate regression analysis. Statistical significance was attained when $p < 0.05$.

Results

Baseline clinical and laboratory data

Clinical and laboratory parameters of the 173 CAPD patients were shown in Table 1. Most of the patients (87%) were on calcium supplements and 28% received vitamin D. Six patients were treated with aluminum-containing phosphate binders.

As seen in Table 2, 51 patients (29.48%) had hyperparathyroidism while 122 subjects (70.52%) had serum iPTH levels below 300 pg/ml. CAPD patients in the hyperparathyroidism group had significantly lower serum calcium levels ($p = 0.037$) but significantly higher serum phospharte levels ($p = 0.016$) and greater serum alkaline phosphatase concentrations ($p = 0.029$).

Factors affecting iPTH levels

As illustrated in Table 3, by univariate regression analysis, the serum calcium had a significant negative correlation with iPTH ($r = -0.176$, $p = 0.021$), where phosphate exhibited a significant positive correlation with iPTH ($r = 0.19$, $p = 0.012$). By multivariate regression analysis, serum calcium negatively related with iPTH ($r = -0.176$, $p = 0.023$).the duration on PD showed a significant positive correlation with iPTH ($r = 0.359$, $p < 0.01$).

Discussion

The present study demonstrated that 29.8% of 173 CAPD patients had SHPT. This figure was comparable with a 34% prevalence reported by Sherrard et al in 142 CAPD patient in Toronto area during 1987-1988[6]. Of interest, the patient age and the proportion of diabetic patients were comparable between the two studies but the PD duration in the study by Sherrard et al was longer than the present study (3.2 ± 0.3 yrs vs. 1.47 ± 0.85 yrs).

The CAPD patients with SHPT had lower serum calcium, higher serum phosphate and greater serum alkaline phosphatase levels (Table 2) than those

Table 1. Demographic data of the study population (n = 173)

Sex M:F	83 (47.7%):91 (52.3%)
Age (year)	52.43 ± 14.00
Duration of dialysis (months)	17.67 ± 10.14
Etiology of ESRD	
Hypertensive nephrosclerosis	152 (87.4%)
Diabetes	54 (31%)
Glomerulonephritis	35 (20%)
Gout	18 (10.3%)
Lupus Nephritis	4 (2.3%)
Others	19 (11%)
Laboratory	
Hematocrit (%)	25.08 ± 5.43
BUN (mg/dl)	60.29 ± 37.53
Creatinine (mg/dl)	11.26 ± 5.53
Albumin (g/dl)	3.40 ± 0.49
Bicarbonate (mmol/L)	25.50 ± 5.59
Intact PTH (pg/ml)	283.13 ± 396.37
Serum calcium (corrected total) (mg/dl)	9.24 ± 0.98
Phosphate (mg/dl)	4.80 ± 2.17
Calcium-phosphate product (mg^2/dl^2)	43.85 ± 19.39
Serum alkaline phosphatase (mg/dl)	108.38 ± 134.37
Magnesium (mg/dl)	2.25 ± 0.48

Table 2. Clinical and laboratory profiles of patients on CAPD with and without secondary hyperparathyoridism

	Hyperparathyroidism		
	Yes	No	p-value
Total subjects	51	122	
Age (Year) Mean ± SD	64 ± 11.0	63.1 ± 12	0.35
Sex			
Male	24 (47%)	58 (47.5%)	0.95
Female	27 (53%)	64 (52.5%)	
Duration of dialysis (months) Mean ± SD	19.03 ± 11.24	17.14 ± 9.69	0.265
Laboratory			
Intact PTH (pg/ml)	647.48 ± 575.91	130.82 ± 83.30	< 0.001*
Creatinine (mg/dl)	12.22 ± 6.05	10.85 ± 5.27	0.138
Calcium (mg/dl)	8.68 ± 1.04	10.17 ± 7.60	0.037*
Albumin (g/dl)	3.96 ± 0.42	3.41 ± 0.52	0.084
Calcium-phosphate product (mg^2/dl^2)	46.72 ± 19.66	45.73 ± 39.06	0.87
Phosphate (mg/dl)	5.41 ± 2.24	4.55 ± 2.10	0.016*
Alkaline phosphatase (mg/dl)	159.18 ± 228.86	86.43 ± 43.96	0.029*
Magnesium (mg/dl)	2.29 ± 0.50	2.24 ± 0.47	0.49

without SHPT. As mentioned earlier, these were expected finding. Although previous studies showed that hypermagnesemia had inhibitory effects on PTH secretion[7,8], the present study could not reveal correlation between serum magnesium levels and SHPT.

In the present study, duration of PD had positive correlation with iPTH levels (Table 3). This was in agreement with a previous study by Sherrard et al[6], although the rise was significantly observed only after the third year of PD. Indeed, age itself may negatively influence PTH secretion because of the more biological activity in younger subjects[9]. However, in

Table 3. Regression analysis of clinical and biochemical factors affecting iPTH levels

	Univariate	Multivariate
Total corrected calcium	-0.176*	-0.174*
Phosphate	0.190*	0.134
Bicarbonate	-0.0104	-0.136
Age	-0.148	-0.075
Duration on PD	0.07	0.359*

* $p < 0.05$

the present study, age had no effect on PTH secretion.

In conclusion, there is quite high prevalence of hyperparathyroidism in Thai CAPD patients. Duration of CAPD and hypocalcemia are independent risk factors in developing secondary hyperparathyroidism.

Potential conflicts of interest

None.

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การศึกษาความชุกและปัจจัยเสี่ยงของการเกิดภาวะพาราไทรอยด์ฮอร์โมนสูงในผู้ป่วยที่รับการรักษาด้วยการล้างไตทางช่องท้องในโรงพยาบาลระดับตติยภูมิจำนวน 173 ราย

นิรุธ สุวรรณ

วัตถุประสงค์*: ทำการศึกษาความชุกและปัจจัยเสี่ยงของการเกิดภาวะพาราไทรอยด์ฮอร์โมนสูง (มากกว่า 300 พิโคกรัมต่อมิลลิลิตร) ซึ่งเป็นภาวะแทรกซ้อนที่สำคัญในผู้ป่วยโรคไตเรื้อรังซึ่งอาจส่งผลให้เกิดภาวะแทรกซ้อน การเพิ่มอุบัติการณ์การเสียชีวิต และยังส่งผลต่อค่าใช้จ่ายในการให้การดูแลสภาวะสุขภาพต่อผู้ป่วยโรคไตเรื้อรังระยะสุดท้ายที่เข้ารับการรักษาโดยการบำบัดแทนไตด้วยวิธีล้างไตทางช่องท้อง ในระบบหลักประกันสุขภาพถ้วนหน้าของประเทศไทย*

วัสดุและวิธีการ*: ทำการศึกษาระดับของพาราไทรอยด์ฮอร์โมนข้อมูลทางคลินิก และตัวแปรทางห้องปฏิบัติการที่มีความสัมพันธ์กับระดับของพาราไทรอยด์ฮอร์โมน จากเวชระเบียนของผู้ป่วย 173 ราย ที่มีอายุตั้งแต่ 18 ปี ขึ้นไป ซึ่งป่วยด้วยโรคไตวายเรื้อรังระยะสุดท้ายที่เข้ารับการรักษาโดยการบำบัดแทนไตด้วยวิธีล้างไตทางช่องท้อง ในโรงพยาบาลมหาราชนครราชสีมา ระหว่างตุลาคม พ.ศ. 2551 ถึง ตุลาคม พ.ศ. 2553*

ผลการศึกษา*: พบว่าร้อยละ 29.48 ของผู้ป่วยมีภาวะพาราไทรอยด์ฮอร์โมนสูง โดยผู้ป่วยมีค่าซีรัมแคลเซียมต่ำกว่าซีรัมฟอสเฟตสูงกว่า และซีรัมอัลคาไลน์ฟอสฟาเตสสูงกว่าผู้ป่วยที่ไม่มีภาวะพาราไทรอยด์ฮอร์โมนสูง พบว่าปัจจัยที่ส่งผลต่อระดับของพาราไทรอยด์ฮอร์โมน ได้แก่ระยะเวลาในการเข้ารับการรักษาด้วยวิธีการล้างไตทางช่องท้อง และระดับซีรัมแคลเซียมที่ต่ำ*

สรุป*: พบว่าผู้ป่วยโรคไตวายเรื้อรังระยะสุดท้ายที่เข้ารับการรักษาโดยการบำบัดแทนไตด้วยวิธีล้างไตทางช่องท้องในโรงพยาบาลมหาราชนครราชสีมามีความชุกของการเกิดภาวะพาราไทรอยด์ฮอร์โมนสูงใกล้เคียงกับการศึกษาอื่น โดยมีความสัมพันธ์กับระยะเวลาในการเข้ารับการรักษา และระดับซีรัมแคลเซียมที่ต่ำ*