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International Journal of Pharma Research and Health Sciences

Available online at www.pharmahealthsciences.net

Original Article

Correlation of Long Term Chronic Renal Disease (CKD) With Intact PTH (iPTH) and Biochemical Parameters

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ARTICLE INFO

Received: 04 Apr 2016
Accepted: 27 Apr 2016

ABSTRACT

Alteration in macro-mineral system and abnormal status of parathyroid hormone (PTH) level are common in patients with chronic kidney disease (CKD). It is also documented that hyperparathyroidism is a condition developed secondary to CKD, subsequently causing abnormal mineral metabolism which leads to end stage renal disease (ESRD). The objective of present study is to evaluate intact PTH (iPTH), macro-mineral status and Vit D3 in short and long duration CKD patients from both genders. Current study covers the period of Dec 2013 to Dec 2015 and conducted at Department of Biochemistry Laboratory services and Chemical Pathology, Liaquat National Hospital and Medical college-Karachi and Govt Lyari General Hospital Karachi. Selections of patients were made according to the specialty of nephrology, diabetic, non-diabetic, and those on hemo-dialysis or peritoneal dialysis with males = 50 and females = 30 patients. All biochemical and hormonal parameters were determined by standard methods. Results showed patients of both genders exhibiting similar pattern of PTH concentration and biochemical parameters. In female patients' group, maximum duration of renal disease and process of dialysis was 3.5 ± 2.10 years where as in male patients; it was 5.45 ± 3.25 years. None of the patients assessed from both gender groups exhibited protein to creatinine ratio (P:C ratio) greater than 1, however their creatinine clearance was noted to be way below normal ranges. Intact PTH, Ca, P, uric acid, albumin and Vit D3 were all observed to be altered significantly ($P < 0.01$ to $P < 0.001$). Our data exhibited significant correlation of CKD with biochemical parameters, especially iPTH, cCT, calcium, phosphorus and Vit D3. Moreover, duration of CKD also showed influence on the levels of iPTH, such that longer the duration, higher shall be the iPTH in patients from both genders.

Key Words: Chronic kidney disease (CKD), end stage renal disease (ESRD), intact PTH (iPTH), hyperparathyroidism.

1. INTRODUCTION

Alteration in macro-mineral system, especially calcium and phosphorus concentration, in addition to abnormal status of parathyroid hormone (PTH) level is common in patients with chronic kidney disease (CKD)[1-4]. Eventually, hypocalcemia, Hyperphosphatemia,

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impaired synthesis Vit D3 and stress on parathyroid glands result in excess of PTH concentration[1, 2, 5]. It was reported that hyperparathyroidism is a condition developed secondary to CKD, characterized by abnormal mineral metabolism and complications leads to end stage renal disease (ESRD), osteo-dystrophy and parathyroid hyperplasia[1, 2 , 4, 5].

It is also well documented that PTH and Vit D3 are involved in regulation of bone metabolism and thus deficiency or alteration of either may induce bone loss and mineral mal-absorption[6, 7]. Some earlier studies also suggested aged-dependent changes in Vit D3 status, that ultimately affects bone mineral physiology and PTH secretion[6, 8, 9].

The objective of present study is to evaluate PTH, macro-mineral status and Vit D3 in short and long duration CKD patients from both genders. The study will help in providing biochemical parametric baseline in management of CKD and CKD related renal osteo-dystrophy.

2. MATERIALS AND METHODS

*2.1Research Design and patient's selection:*_Current study covers the period of Dec 2013 to Dec 2015 and conducted at Department of Biochemistry Laboratory services and Chemical Pathology, Liaquat National Hospital and Medical college-Karachi and Govt Lyari General Hospital Karachi. Selections of patients were made according to the specialty of nephrology, diabetes and endocrinology. Initially 250 patients were screened and finally grouped into Male = 50 and female = 30. Patients were further classified into diabetic, non-diabetic, and those on hemo-dialysis or peritoneal dialysis, covering total average duration of dialysis as a group in both genders. Age and gender-matched equal number of healthy individuals were grouped as controls.

*2.2 Analytical methods:*Calcium, phosphorus, albumin, uric acid were determined by methods described earlier[10,11]. Creatinine clearance (cCT) and protein to creatinine ratio (P:C ratio) were analyzed as reported previously[12] and intact PTH (iPTH), Vitamin D3 were determined by methods established y Abdel-Wareth et al.[13] and Monge et al.[14], respectively.

2.3 Statistical analysis: Data were statistically analyzed by SPSS ver 13 (USA), using Pearson's correlation, paired t-test and ANOVA. Data were compared with p value less than 0.05 as significant.

3. RESULTS

Results are summarized in Table 1-4. Both gender groups of male (n = 50) and females (n = 30) patients exhibited similar pattern of PTH concentration and biochemical parameters. In female patients' group, maximum duration of renal disease and process of dialysis was 3.5 ± 2.10 years where as in male patients; it was 5.45 ± 3.25 years (Table 1). Out of 30 female patients, 17 (56.66%) showed diabetes as underlying co-morbid, whereas in males, it was comparatively very high (n = 41, 82.00%). Although none of the patients assessed from both gender groups exhibited protein to creatinine ratio (P:C ratio) greater than 1, however their creatinine clearance was noted to be way below normal ranges (Table 1, 2). Intact PTH, Ca, P, uric acid, albumin and Vit D3 were all observed to be altered significantly ($P < 0.01$ to $P < 0.001$) in both groups when compared with normal healthy controls (Table 1, 2). In our study older age doesn't play any significant role in concentration iPTH. Patients from both gender groups exhibited maximum higher levels at age 45-50 years, which declined after age range of 55-65 years, however remaining elevated from normal cut-off range (Table 3). To assess the correlation of duration of CKD with iPTH, patients were also encouraged for follow-up information. However we were able to trace back only 15 out of 30 in female patient group and 21 out of 50 male patient groups. Our data showed duration of CKD and underlying co-

morbid of metabolic disorders did influence iPTH levels in a way that longer the period of CKD, higher shall be the concentration of iPTH (Table 4).

Table 1: Biochemical characteristics of female renal diseases' patients (n = 30)

Parameters	Patients (n = 30)	Controls (n = 30)	P < 0.05
Age	45.50 ± 13.40	41.25 ± 12.25	NS
Duration of renal disease (yrs)	3.50 ± 2.10 yrs	Not applicable	--
Hemodialysis	n = 21	Not applicable	--
Peritoneal dialysis	n = 9	Not applicable	--
Diabetic	n = 17	Not applicable	--
Non-diabetic	n = 13	Not applicable	--
Intact PTH (pg/ml)	89.45 ± 20.55	25.50 ± 8.90	0.001
Calcium (mg/dl)	6.80 ± 3.40	8.70 ± 2.60	0.02
Phosphorus (mg/dl)	5.35 ± 3.50	3.80 ± 1.50	0.03
Uric acid (mg/dl)	6.55 ± 1.65	4.35 ± 1.75	0.03
Albumin (g/dl)	3.10 ± 1.10	4.10 ± 1.50	0.03
Vitamin D3 (ng/ml)	13.45 ± 3.55	28.25 ± 4.35	0.01
Creatinine Clearance (91-119 ml/min)	61.50 ± 20.20	91.45 ± 15.60	0.01
Protein: creatinine ratio (< 1.0)	0.95 ± 0.20	0.55 ± 0.10	0.01

Results are expressed as mean ± SD, NS = non significant

Table 2: Biochemical characteristics of male renal diseases' patients (n = 50)

Parameters	Patients (n = 50)	Control (n = 50)	P < 0.05
Age	55.35 ± 14.65	50.90 ± 13.65	NS
Duration of renal disease (yrs)	5.45 ± 3.25	Not applicable	--
Hemodialysis	n = 39	Not applicable	--
Peritoneal dialysis	n = 11	Not applicable	--
Diabetic	n = 41	Not applicable	--
Non-diabetic	n = 09	Not applicable	--
Intact PTH (pg/ml)	111.60 ± 22.85	30.65 ± 10.10	0.001
Calcium (mg/dl)	7.20 ± 2.90	8.85 ± 3.15	0.02
Phosphorus (mg/dl)	5.75 ± 3.85	3.65 ± 2.60	0.02
Uric acid (mg/dl)	6.85 ± 2.15	4.05 ± 1.35	0.03
Albumin (g/dl)	3.40 ± 1.10	4.45 ± 2.05	0.03
Vitamin D3 (ng/ml)	12.60 ± 4.50	29.35 ± 5.10	0.01
Creatinine Clearance (91-125 ml/min)	55.65 ± 18.35	92.50 ± 16.45	0.01
Protein: creatinine ratio (< 1.0)	0.89 ± 0.15	0.45 ± 0.15	0.01

Results are expressed as mean ± SD, NS = non significant

Table 3a: iPTH levels according to age groups in female renal diseases' patients (n = 30)

Years	PTH (pg/ml)
35	60.14 ± 10.15 (n = 4)
40	70.25 ± 15.25 (n = 5)
45	95.45 ± 20.40 (n = 7)
50	80.25 ± 18.75 (n = 9)
55	65.40 ± 12.35 (n = 5)

Results are expressed as mean ± SD

Table 3b: iPTH levels according to age groups in male renal diseases' patients (n = 50)

Years	PTH (pg/ml)
45	70.15 ± 14.45 (n = 5)
50	85.30 ± 10.65 (n = 7)
55	120.40 ± 20.70 (n = 8)
60	90.60 ± 14.30 (n = 14)
65	75.80 ± 15.50 (n = 16)

Results are expressed as mean ± SD

Table 4a: Duration of renal diseases vs PTH in female group (data of only 15 patients out of 30)

Years	PTH (pg/ml)	Comparison 0.5 yr vs yrs
0.5 yrs	50.15 ± 10.25 (n = 3)	0.001[a]
1 yrs	65.25 ± 12.45 (n = 4)	0.001[b]
2.5 yrs	75.45 ± 11.60 (n = 5)	0.01[c]
3 yrs	110.55 ± 18.70 (n = 3)	0.001[d]

Results are expressed as mean ± SD; comparison [a]0.5 vs 3, [b]1 vs 3, [c]2.5 vs 3, [d]3 vs 0.5 yrs

Table 4b: Duration of renal diseases vs PTH in male group (data of only 21 patients out of 50)

Years	PTH (pg/ml)	Comparison 1 yr vs yrs
1 yrs	55.40 ± 11.20 (n = 2)	0.001 [a]
2 yrs	68.65 ± 12.70 (n = 5)	0.001 [b]
3 yrs	82.75 ± 14.35 (n = 6)	0.01 [c]
4 yrs	123.85 ± 19.20 (n = 4)	0.02 [d]
5 yrs	145.40 ± 20.25 (n = 4)	0.001 [e]

Results are expressed as mean ± SD; comparison [a]1 vs 5, [b]2 vs 5, [c]3 vs 5, [d]4 vs 5 and [3]5 vs 1 yrs

4. DISCUSSION

Present study described the biochemical characteristics of male and female patients diagnosed with CKD of varying duration. All patients were undergoing either hemodialysis or peritoneal dialysis for different time periods. Our data showed significant correlation of CKD with biochemical parameters, especially iPTH, cCT, calcium, phosphorus and Vit D3. Furthermore, duration of CKD also showed influence on the levels of iPTH, such that longer the duration, higher shall be the iPTH in patients from both genders. However, age doesn't come out as influencing factor on iPTH concentrations, rather inversely proportional to circulating iPTH levels in CKD patients. Our study is in agreement with several previous studies that reported altered iPTH, Vit D3, calcium, phosphorus, uric acid and cCT levels of CKD patients undergoing regular dialysis[1, 5, 7].

Hypocalcemia, hyperphosphatemia, low Vit D3 and high PTH were noted to be few of the significant components that became deficient or elevated either do to chronic inflammation, osteodystrophy or due to long-term hemodialysis[1,5,7,15]. It was also pointed out that long duration CKD might induced secondary hyperparathyroidism, resulting in excess release of PTH and impaired synthesis of Vit D3 or vice versa [1,4,15,16].

Previous studies based on race reported that Caucasian ESRD patients exhibited higher PTH and Vit D3 levels as compared to Afro-Americans[17]. Moreover in Asian population, patients that were undergoing dialysis, 36.2% exhibited Ostetitis fibrosa[18]. A previous study reported a higher threshold of iPTH, which was >130 pg/ml in several CKD patients undergoing dialysis[5]. Recent studies reiterated the fact that hyperparathyroidism and relevant excess values of iPTH is one of the outcomes of long-term CKD[19, 20]. It was also already that prevalence of hyperparathyroidism in patients suffering from stage 5 of CKD exhibited higher level of PTH [20]. Furthermore, patients with long-term CKD and undergoing dialysis were at risk of developing bone disorders, and vascular abnormalities due to altered calcium and phosphorus metabolism[21]. Interestingly, previous work also noted early onset of altered mineral metabolism and elevated PTH in patient where renal disease just started its manifestation[22]. Moreover since PTH is the principal mineral regulatory hormone, a reduction in calcium absorption and concomitant retention of phosphate due to alerted state of kidney function in CKD leads to suppression of Vit D3 synthesis, thus resulting in excess of PTH secretion[19, 23].

5. CONCLUSION

Current study described a significant correlation of CKD with biochemical parameters, especially iPTH, cCT, calcium, phosphorus and Vit D3. Subsequently, duration of CKD also showed influence on the levels of iPTH, which means that longer the duration, higher willl be the iPTH in patients from both genders.

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Conflict of Interest: None

Source of Funding: Nil