Cinacalcet HCL for Treatment of Secondary Hyperparathyroidism (SHPT) in Hemodialysis Patients: A Single Centre Experience

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ABSTRACT

Background: The use of Cinacalcet in hemodialysis patients to treat SHPT has recently been started in Pakistan. Cinacalcet can cause imbalance in Ca and PO4 homeostasis andK/DOQI guidelines suggest regular monitoring of iPTH, Ca and PO4 levels in dialysis patients especially those who are on cinacalcet.
Aim: To determine the effectiveness of Cinacalcet treatment in SHPT.
Methods: Total 34 SHP The modialysis patients were enrolled from dialysis unit of a tertiary care hospital in KSA. All patients received cinacalcet treatment; however three of them refused to continue because of persistent vomiting. The baseline and follow up data collected from 31 patients were analyzed.
Results: The mean age of patients was 50±19 years; and frequency of males and females was 68% and 32%, respectively. Baseline mean iPTH level was decreased from 1068 to 841 pg/ml (p=0.041) with an overall20.0% reduction rate; frequency of patients with iPTH levels (>600 pg/ml) was decreased (96.8 vs. 77.4%, p=0.041);and total 77.4%patientscould achieve at least 30% reduction in baseline iPTH level. Mean PO4 level was decreased from 5.39to 5.01 mg/dl (p=0.021); mean Albumin increased from 3.72to 3.77 g/dl (p=0.754)
Conclusion: Cinacalcet HCL therapy effectively treated secondary hyperparathyroidism in hemodialysis patients and maintained their serum iPTH, Ca and PO4 levels within target range
Key words: Hemodialysis, Secondary hyperparathyroidism, Cinacalcet, Hyperphosphatemia, Hypocalcaemia

INTRODUCTION

Chronic kidney disease (CKD) is characterized by fall in renal function below normal.[1] The risk factors and causes of CKD include being elderly, family history of disease, ethnicity, diabetes mellitus, hypertension, vascular disease.[2] As in early stages of CKD, less phosphate (PO4) is excreted but its serum levels do not rise above normal due to increased secretion of parathyroid hormone (PTH).[3] However, in advanced stages of CKD, decreased renal function results in hyperphosphatemia[4]. This hyperphosphatemia does not convert inactive vitamin D to its active form that affects intestinal absorption of calcium (Ca) and results in hypocalcaemia.[5] Hyperphosphatemia also affects Ca levels by increased Ca-PO4 binding.[6] Secondary hyperparathyroidism (SHPT) is one of the complications of CKD.[7] As PTH function is to increase serum Ca level; so, when Ca level drops, biologically active form of PTH i.e., intact parathyroid hormone (iPTH) is secreted[8]. Thus, hyperphosphatemia and hypocalcaemia independently trigger synthesis and secretion of PTH[9].

Cinacalcet HCL drug used to treat SHPT in CKD patients on hemodialysis also affects their serum Ca and PO4 levels.[10] Whereas National Kidney Foundation K/DOQI guidelines suggest regular monitoring of iPTH, Ca and PO4 levels of CKD patients[11], therefore the study was aimed to determine the effectiveness of cinacalcet treatment in secondary hyperparathyroidism in patients on hemodialysis.

MATERIALS AND METHODS

The participation of subjects in the study was absolutely on volunteer basis. All eligible patients were explained about the purpose, possible hazards and benefits of the study. Those who showed willingness to participate in the study and given informed written consent were enrolled. A quasi experimental study was conducted ata tertiary care hospital located in Southwest area of KSA during October 2018 to April 2019.

Total 34 SHPT patients with CKD on hemodialysis, age≥18 years, both males and females were enrolled by using non-probability purposive sampling method were included. Three patients were later on dropped from the study as they refused to continue cinacalcet therapy due to persistent vomiting.

Treatment and effectiveness of the starting dose of cinacalcet HCL was 30 mg at a frequency of three times per week (at the end of dialysis session). The dose was gradually increased upto 120 mg per day (depending upon the iPTH, Ca and Po4 levels)till the end of study (up to six months). The efficacy of treatment was assessed by at least 30% reduction in serum iPTH level from baseline level.

Venous blood specimen was collected and allowed to clot. Then, the clotted blood was centrifuged at 5000 RPM for 10 minutes to separate serum sample. The level of intact parathyroid hormone (iPTH) was estimated by chemiluminescent microparticle immuno assay (CMIA) method[12]. Normal PTH level ranged from 150-600 pg/ml.Serum calcium level was estimated by NM-BAPTA method[13]. Normal Ca level ranged from 8.4-10.0 mg/dl.

Serum phosphate level was estimated by Molybdate UV method[14]. Normal phosphate level ranged from 2.5-5.5 mg/dl. Serum albumin level was estimated by bromcresol green (BCG) method[15]. Normal Albumin level ranged from 3.5-5.0 g/dl.

After taking informed written consent, all eligible patients were included. A close ended interviewer administered questionnaire was used to record primary and secondary data. The demographic characteristics of the patients such as age and gender were investigated by interview. Whereas, the clinical data were obtained from patients' files. The baseline data upon enrollment in the study and follow up data after 3 & 6 months of cinacalcet HCL treatment were collected.

Data were entered and analyzed by using SPSS version 22. Categorical variables were presented as number (percentage) and numerical variables as mean (standard deviation). Chi square test and ANOVA were used to find the differences between biochemical assays measured before and after cinacalcet therapy. P-value ≤0.05 was considered significant.

RESULTS

The mean age of the patients was 50±19 years. Gender-wise frequency showed that 68% patients were male and 32% female. Comparison of means revealed that baseline mean iPTH, PO4 and Ca levels were significantly improved at the end of treatment. Baseline mean iPTH level was significantly decreased from 1068to 841 pg/ml at 20.0% reduction rate. There were total 17.2% patients who achieved at least 30% reduction in baseline serum iPTH level. Mean PO4 level was also significantly decreased from 5.39to 5.01mg/dl. Whereas, mean Ca level was increased from 8.74to 9.05mg/dl (Patients who developed transient hypocalcemia were treated with Calcium Carbonate 600mg twice daily ,two hours away from meals) and mean albumin increased from 3.72 to 3.77g/dl (Table 1).

Table 1: Mean reduction in biochemical assays before and after treatment

Variable	Baseline (n=31)	3M F/up (n=31)	6M F/up (n=31)	p-value
iPTH* (pg/ml)	1068±387	916±348	841±322	0.041
PO4* (mg/dl)	5.39±0.55	4.96±0.66	5.01±0.73	0.021
Ca*(mg/dl)	8.74±0.70	9.02±0.48	9.05±0.33	0.040
Alb* (g/dl)	3.72±0.34	3.73±0.22	3.77±0.22	0.754

*Ca: Calcium; PO4: inorganic Phosphate; Alb: Albumin, iPTH: intact Parathyroid hormone.

The baseline frequency of patients having elevated iPTH levels (>600pg/ml) was96.8% which was significantly decreased to 77.4% at the end of study. The baseline frequency of patients with hyperphosphatemia was also significantly decreased from 48.4 to 22.6%. The baseline frequency of patients with hypocalcaemia was gradually improved by decreasing from 35.5 to6.5%patientsat 6 months follow up (p=0.012). The baseline frequency of patients with hypoalbuminemia was decreased from 16.1 to 3.2% patients but the change was not significant (Table 2).

Table 2: Frequency comparison of patients' status before and after treatment

Variable	Baseline (n=31)	3M F/up (n=31)	6M F/up (n=31)	p-value
iPTH* (pg/ml)				
High(>600)	30(96.8%)	25(80.6%)	24(77.4%)	0.041
Normal(150-600)	01(3.2%)	06(19.4%)	07(22.6%)	
PO4* (mg/dl)				
High(>5.5)	15(48.4%)	05(16.1%)	07(22.6%)	0.014
Normal(2.5-5.5)	16(51.6%)	26(83.9%)	24(77.4%)	
Ca*(mg/dl)				
Low(<8.4)	11(35.5%)	05(16.1%)	02(6.5%)	0.012
Normal(8.4-10)	20(64.5%)	26(83.9%)	29(93.5%)	
Alb* (g/dl)				
Low(<3.5)	05(16.1%)	01(3.2%)	01(3.2%)	1.000
Normal(3.5-5.0)	26(83.9%)	30(96.8%)	30(96.8%)	

*Ca: Calcium; PO4: inorganic Phosphate; Alb: Albumin; iPTH: intact Parathyroid hormone.

DISCUSSION

Several studies evaluated the efficacy and safety of cinacalcet therapy and reported significant decrease in mean iPTH level from baseline with at least 30% reduction rate. Choulwar et al. reported that mean iPTH level was decreased from 404 to 304pg/mlat24% reduction rate after treatment with cinacalcet HCL.[16] Similarly, Aggarwal et al. also reported decrease in mean basal PTH level from 482to 246pg/mlat 43% reduction rate at the end of treatment[17]. Among SHPT patients with CKD but not on hemodialysis, Perez-Ricart et al. reported mean iPTH level was decreased from 400 to 224pg/ml at 38% reductionrate. Moreover, total 67% patients achieved at least 30% reduction in their PTH levels.[18] Similar significant decrease in mean iPTH level from 1068to 841pg/ml at 20% reduction rate was observed in present study. But comparison with other studies revealed that obtained reduction rate was markedly lower than the rates reported by other studies.[16-19] Noteworthy, mean iPTH levels, both before and after treatment, calculated in the study were much higher than initial mean iPTH level of other studies; and only 17.2% patients could achieve at least 30% reduction in serum iPTH level.

Hypocalcaemia and hyperphosphatemia are consequences of CKD and frequently present in dialysis patients[20]. Also, cinacalcet therapy of SHPT in CKD patients on dialysis decreases serum iPTH, Ca and PO4 levels[10] and require their regular monitoring[11]. Choulwar et al. reported that mean Ca level was decreased from 8.83 to 8.07 mg/dL at 8.6% reduction rate.[16] Similarly, Perez-Ricart et a. also reported decrease in baseline mean Ca level from 9.73 to 9.18mg/dl; but increase in mean PO4 from 3.81to 4.32mg/dl[18]. Opposite to the findings from Perez-Ricart, significant decrease was observed in mean PO4 level from 5.39 to 5.01mg/dl in the study. Surprisingly mean Ca level was significantly increased from 8.74 to 9.05 mg/dl; and baseline frequency of normocalcaemic patients was also increased gradually from 64.5 to 93.5% patients at the end of treatment which was contrary to the trend reported by Choulwar. Hypoalbuminemia is also common in dialysis patients due to the loss of protein.[21] Perez-Ricart also reported decrease in baseline mean albumin from 4.20

to 4.17 g/dl[18]. But an insignificant increase in mean albumin from 3.72 to 3.77 g/dl was observed in the present study. However, it was consistent with the findings of Valle et al. who also reported insignificant increase in baseline mean albumin from 3.9 to 4.0 g/dl[22].

CONCLUSION

Cinacalcet HCL therapy effectively treated secondary hyperparathyroidism patients with chronic kidney disease on hemodialysis and maintained their serum iPTH, Ca and PO4 levels within target range. The patients who develop transient hypocalcemia can easily be treated with calcium carbonate to counter the hypocalcemic side effect of Cinacalcet.

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