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Research Article

Open label study to assess the safety and efficacy of cinacalcet in refractory hyperparathyroidism with chronic renal failure

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ABSTRACT

Background: Secondary hyperparathyroidism a common consequence of chronic kidney disease is associated with many complications like renal osteodystrophy, vascular and soft tissue calcification. This study is to assess the safety and efficacy of Cinacalcet a calcimimetic drug in patients with refractory hyperparathyroidism due to chronic renal failure.
Methods: Patients with chronic kidney disease stage 5 on maintenance haemodialysis diagnosed to have refractory hyperparathyroidism who do not attain the target range for hyper-parathyroid indicators serum PTH ≤300, Serum Ca (8.4-9.5), serum phosphorous (3.5-5.5) with the use of calcitriol and phosphate binders were included in the study. Twenty patients satisfying the case definition of refractory hyperparathyroidism due to chronic renal failure received 30mg Cinacalcet therapy. Total duration of treatment was 6 weeks. Standard serum calcium, serum phosphorous, PTH was assessed before and after 6 weeks.
Results: Cinacalcet significantly reduces serum PTH level when results were compared by paired t test. P=0.016 <0.05 (significant). No statistically significant reduction in serum calcium and phosphorous. Serum calcium P value=0.599>0.05, serum phosphorous P=0.132>0.05. In this study after overall assessment.
Conclusions: Cinacalcet is more efficacious and safe in treating refractory hyperparathyroidism due to chronic renal failure.

Keywords: Hyperparathyroidism, Cinacalcet, Calcitriol, Phosphate binders, Calcimimetic, Parathormone

INTRODUCTION

Chronic kidney disease, a major public health problem is associated with a range of incapacitating complications including secondary hyperparathyroidism.[1] Magnitude of the problem is evidenced by the complications associated with secondary hyperparathyroidism including renal osteodystrophy ,vascular and soft tissue calcification, increased risk of morbidity and mortality.[2] Treatment with vitamin D and calcium (conventional therapy) also lead to hypercalcemia, hypophosphatemia and adverse clinical outcomes.[3] Calcimimetic drugs offer a new approach to the treatment of secondary hyperparathyroidism. They increase the sensitivity of calcium sensing receptor and lower PTH level without causing hypophosphatemia and hypercalcemia. Cinacalcet is the first agent in this new class of drugs currently is undergoing clinical trials in dialysis patients who have uncontrolled secondary hyperparathyroidism.[4,5]

The present study assesses the safety and efficacy of cinacalcet in refractory hyperparathyroidism with chronic renal failure. The objective of this study was to assess the efficacy of cinacalcet in patients with chronic kidney disease stage V-D diagnosed to have refractory hyperparathyroidism who do not attain the target range for hyper parathyroid indicators with the use of calcitriol and phosphate binders and to assess the safety profile of cinacalcet in same group of patients.

Review of literature

Secondary hyperparathyroidism is a common consequence of chronic kidney disease in which low vitamin D, hypophosphatemia and peripheral resistance to PTH calcemic action concurrently act to increase PTH production. This will induce parathyroid gland hypertrophy and hyperplasia. PTH increase early in the course of chronic kidney disease, clinically overt

secondary hyperparathyroidism occurs in advanced CKD stages.[2]

Irrespective of etiology, CKD involves a set of progressive mechanisms, which is a consequence of long term reduction of renal mass. This will cause structural and functional hypertrophy of surviving nephrons eventually predispose to sclerosis of viable nephrons. If this pathophysiologic process last more than 3 months, it is termed as chronic renal disease. Risk factors include family history of heritable renal disease, hypertension diabetes mellitus, autoimmune diseases, older age and past episodes of acute renal failure.[4]

Recently widely accepted International classification divides CKD into 5 stages.[4]

Secondary hyperparathyroidism of CKD

Target range of intact plasma PTH in different stage of Chronic kidney disease- National kidney disease outcome quality initiative (KDOQI 2003).[5]

Patients with CKD Stage V-D diagnosed are diagnosed to have refractory hyperparathyroidism if they do not attain the target range S. PTH (<300), S. Ca- (<8.4-9.5), S. Phos (3.5-5.5) with the use of calcitriol and phosphate binders.[5,8,9]

Patients are considered to have refractory secondary hyperparathyroidism when serum Ca, phosphorous, Ca/P product and intact parathyroid hormone levels can no longer be adequately controlled by conventional therapy with vitamin D and Ca based phosphate binders.[5,8]

Understanding the pathophysiology of the factors involved has been of major significance to the developments of new therapeutic strategies for these patients.

Pathophysiology

The four parathyroid gland lie behind the lobes of the thyroid. They are regulated by changes in ionised calcium concentrations. PTH is a single chain poly peptide of 84 amino acids which is synthesized by the chief cells and released in response to a fall in serum ionised calcium concentration. This hormone interacts with vitamin D and its metabolites in regulating Ca absorption and excretion.[10]

Hypocalcemia, hyperphosphatemia, low (1, 25) $(OH)_2$ Vitamin D_3 (Calcitriol) and high FGF-23 levels are the main drivers of secondary hyperparathyroidism in chronic kidney disease. Their combined action results in abnormalities of parathyroid gland and contributes to the autonomous PTH over production.[6]

Hypocalcemia

Serum calcium level is the main regulator of PTH secretions. It acts via calcium-sensing receptor (CaR), a serpentine membrane protein located on the parathyroid cells membrane.[6] Stimulation of receptor by high serum ionic Ca levels decreases the PTH secretion.

Hypocalcemia has time-dependent effect on parathyroid gland mediated by Ca receptor. The degradation of PTH is reduced and secretion is increased within minutes, PTH gene transcription is thereafter increased in the following hours and parathyroid cells proliferation is accelerated in the subsequent days and weeks.[6,8]

Because of a lower number of CaR, higher levels of calcium would be necessary to suppress the PTH production, and the basal PTH secretion will be higher. Hence a higher calcium concentration is required to decrease PTH secretion by 50% in the abnormal tissue.

Hyperphosphatemia

- Decreased GFR in chronic kidney disease leads to reduced inorganic PO43- excretion and consequent PO43- retention.
- Retained PO43- has a direct stimulatory effect on PTH synthesis and on cellular mass of parathyroid glands.
- Retained PO4 also indirectly causes excessive production and secretion of PTH through lowering of ionized Ca and by suppression of calcitriol production.
- Hyperphosphatemia could also stimulate osteocytes to release FGF-23 and decrease calcitriol.5,6,7,14

To atherosclerosis to which these patients are prone, most severe form is calciphylaxis.[7]

Biochemical features

Assay for parathyroid hormone

Accurate assessment of the activity of the parathyroid gland is essential for the monitoring and management of hyperparathyroidism. A new era of PTH measurement began with the use of 2 site immune radiometric assay.

These assays capture PTH peptides from plasma with a solid phase coupled antibody usually directed toward COOH terminal region of PTH molecule, the captured PTH peptides are detected with a second antibody directed toward a different region of molecule usually NH2 terminus. Such assays are now widely used.[6,7] New assays have been developed in which the detection of antibody recognizes the precise NH2 terminus of PTH molecule, so that only intact PTH (1-84) is measured.[4,7]

Serum phosphorous

The concentration of serum P is maintained between 3-4.5 mg/dl.[13]

Serum P normal to slightly decreased in early stages of CKD, and hyperphosphatemia does not usually become clinically evident until the GFR has decreased to 20% of normal due to the phosphaturic action of PTH.[6] As the GFR decreases phosphate retention occurs control of hyperphosphatemia is a crucial intervention in the setting of CKD.

Serum Calcium

Hypocalcemia in CKD may result from several mechanisms, including increased serum P concentration leading to the formation of Ca-P complexes, impaired calcitriol synthesis resulting in decreased intestinal absorption of Ca and skeletal resistance to action of PTH and calcitriol

The parathyroid glands detect a decrease in ionized Ca via calcium sensing receptor on the cell surface and respond by increasing the secretion of PTH. Severe secondary hyperparathyroidism is also associated with hypercalcemia. The effect of increasing serum Ca may be more pronounced when Ca salts are administered in conjunction with vitamin D compounds because the latter increase Ca transport of the intestinal cells.[14,15]

Prevention and management of secondary hyperparathyroidism. The objectives of this study were to maintain the blood levels of Ca and phosphorous as close to normal as possible, to prevent the development of parathyroid hyperplasia or if secondary hyperparathyroidism has already developed to suppress the secretion of PTH, to prevent extra skeletal deposition of Ca. And to prevent or reverse the accumulation of substances which can adversely affect the skeleton.[15]

KDOQI goals for CKD stage V- D

Serum PTH-150-300 pg/ml.

Serum Ca-8.4-9.5 mg/ml, serum phosphorous 3.5-5.5 mg/ml, specific treatment used and intensity of treatment vary with the stage of kidney insufficiency and with the presence or absence of overt bone disease and cardiovascular calcifications.

Calcium

Impaired Ca absorption exists in patients with advanced renal failure, including those undergoing dialysis. The dietary intake of calcium usually ranges from 400-600 mg/day.[20,21]

Time at which Ca supplements should be added during the course of CKD is uncertain. Werner and colleagues found reduced intestinal Ca absorption in patients with GFRs of 20-50 ml/mt.[7] Ca supplements should be given cautiously to patients with marked hyperphosphatemia because of the risk of increasing Ca XP, predisposing the patient to extra skeletal calcification. Ingestion of Ca supplements with meals that are high in phosphate should be limited

Use of vitamin D sterols

The occurrence of hypercalcemia or aggravation of hyperphosphatemia by the use of active vitamin D sterols may well be detrimental to residual renal function. So these drugs should be used with caution and monitored closely.

Use of calcitriol (vitamin D_3)

Reduction of hyperphosphatemia and restoration of normal intestinal Ca absorption by calcitriol can improve blood Ca levels and reduce manifestations of secondary HPT. Oral calcitriol has short half-life (12-16 hours) and causes marked increase in intestinal Ca absorption, hypercalcemia, and hyperphosphatemia. Episodes of hypercalcemia are corrected usually within 1 week of stopping treatment. Hypercalcemia is more for calcitriol.[16,20,22]

Hypercalcemia toxicity of calcitriol is aggravated by the concomitant use of large doses of calcium containing phosphate binding antacids. The advent of non-calcium containing phosphate binders may facilitate the use of vitamin D sterols. Vitamin D pro-hormones.

Adverse effect of vitamin D derivatives

In some patients hypercalcemia may be seen after significant reduction of serum phosphorous or after ingestion of large amount of calcium containing phosphate binder.

Vitamin D supplementation also enhance Ca absorption.[1,25] Dihydroxy vitamin D_3, increased phosphorous absorption from the gut, thereby potentiate effect of PTH on skeleton. Decreased renal function limit the compensated renal mechanism to excrete increased load of PO4.[23,24]

A novel approach to secondary HPT

A current treatment of secondary hyperparathyroidism is either to reduce serum phosphorous by dietary restriction and phosphate binders or to increase serum calcium by vitamin D administration, which might result in an increase in the Ca/phosphate product with its subsequent complications. These modalities while correcting one aspect of mineral metabolism have a tendency to have adverse effect on others.

In recent years, it has become clear that calcium sensing receptors play a central role in regulating parathyroid

hormone levels and subsequently those of Ca and phosphorous. Cinacalcet is a calcimimetic agent that acts at the CaSR in the parathyroid gland, increasing the sensitivity of these receptors to serum calcium.[23] This action results in a reduction in PTH secretion that is accompanied by a reduction in serum calcium.

Patients are considered to have severe or refractory secondary hyperparathyroidism, when serum Ca, phosphorous, Ca/P product and intact PTH levels can no longer be adequately controlled by conventional therapy (phosphate binders, Ca and vitamin D analogs).

The discovery and cloning of calcium receptor by Brown opened the way for a new class of drugs the calcimimetics. This was approved by FDA in March 2004. It was expected that cinacalcet hydrochloride, the only calcimimetic clinically available, will prove its efficacy even in severe secondary hyperparathyroidism.

Calcimimetics

Cinacalcet

Calcium receptor (CaR) is the main regulator of parathyroid in response to serum calcium. It plays a central role in the pathogenesis of secondary hyperparathyroidism in CKD patients and consequent is an attractive therapeutic target.[26]

The term calcimimetic has been coined for those compounds that can modulate the activity of calcium receptor.[26] Type II calcimimetics are organic compounds that bind to regions within the membrane spanning domain of CaR and have the potential to increase the sensitivity of CaR to calcium, lowering the threshold of receptor activation by calcium. Thus, they are allosteric modulators of the receptors.[24,28,29]

In experimental models, calcimimetics were also shown to up-regulate CaR and Vitamin D receptor expression to inhibit parathyroid cell proliferation and hyperplasia.

These actions could allow calcimimetics

- To maintain effectiveness during long term therapy.
- To maintain enhanced efficacy in patients with severe disease despite decreased CaR and VDR expression and to avoid the development of severe SHPT if initiated early, in patients with mild or moderate sHPT.

Cinacalcet hydrochloride is a potent and selective type II calcimimetic agent, clinically used in primary HPT, secondary HPT and even in a case of pregnancy with hereditary hypophosphatemic vitamin D resistant rickets. Cinacalcet increases the sensitivity of CaRl and directly inhibit PTH secretion.

Pharmacokinetics and pharmacodynamics of cinacalcet It is a hydrophobic compound that is absorbed rapidly from the gastrointestinal tract after oral administration. Peak plasma levels are attained 60-90 minutes after oral doses. Plasma PTH levels thus fall abruptly after single oral doses of cinacalcet in haemodialysis patients with secondary HPT, reaching a nadir after 2-4 hours.[12] Volume of distribution is 1000 litter. It is 93-97% protein bound. The excretion is 8% in urine and 15% in faces. It is metabolised by CYP3A4, CYP2D6, CYP1A2.[23]

Magnitude of initial decrease in plasma PTH is largely dose dependent. Values fall by 60% to 70% from baseline levels after doses of 75 or 100 mg.

Because plasma PTH levels decrease substantially but rise subsequently after oral doses of cinacalcet, variations in the interval between drug administration and collection of blood sample for measurement of plasma PTH level will affect the values obtained.[23]

The pharmacokinetic profile of cinacalcet changes in a linear fashion with doses up to 200 mg. Neither the pharmacokinetics nor pharmacodynamics of cinacalcet is affected by haemodialysis procedures. Half-life of cinacalcet in plasma is 30-40 hours, both in patients with chronic kidney disease and those with normal renal function. Hence single daily oral doses of cinacalcet is used to treat secondary hyperparathyroidism among patients undergoing dialysis.[19,23]

It acts rapidly within 30-60 minutes, effectively lower PTH, Ca, phosphorous and Ca-P product. It allows more patients to reach K/DOQ1 target (S PTH <300, S.Ca 8.4-9.5, S.Phos. 3.5-5.5). It lowers PTH with or without combination with vitamin D making it possible to use as a first line therapy.[23]

Drug safety and side effect.

It is safe to use in patients with intact PTH >300 pgm/ml and serum Ca >8.4 mg/dl. Since it lowers serum Ca, there is possibility for developing hypocalcemia. Patients with h/o seizure disorder may use cinacalcet with careful monitoring of serum Ca. The prominent side effects are nausea and vomiting. Cinacalcet is available in 30, 60, 90 mg tablet, maximum dose is 180 mg. Initial dose is 30 mg/day independent of severity of PTH elevation. After initiation of treatment, serum Ca and P is repeated within 1 week and PTH after 1 month. Taking cinacalcet with meals enhances bioavailability in 50% and improves GI tolerance.[23,24]

Cinacalcet in severe secondary hyperparathyroidism

Control of biochemical abnormalities

A meta-analysis of Strippoli et al examined some of these studies and concluded that the addition of cinacalcet to standard of care significantly improved the control of

serum PTH, calcium, phosphate and Ca-PO4 product level as compared to standard of care alone.

Control of bone disease

In a study on HD patients (PTH >300 pg/ml) using histomorphometry on bone biopsy, Malluche et al failed to prove a significant effect of cinacalcet administered for 52 weeks on bone remodelling as compared to conventional therapy.

Cost utility analysis was conducted in USA by Narayan et al comparing para thyroidectomy with cinacalcet therapy in dialysis patients with severe secondary hyperparathyroidism. Cinacalcet was more advantageous for patients who could expect a brief stay (<16 months) on dialysis therapy.[25,32]

Use of cinacalcet in patients undergoing dialysis

Clinical efficacy

Efficacy of cinacalcet for treating SHPT among patients undergoing haemodialysis has been documented adequately. Plasma PTH level fall invariably within a few hours after the administration of cinacalcet and sustained reduction in plasma PTH are achieved during treatment with daily oral doses for 12-18 weeks. Plasma PTH levels declined by an average of 25-40% from baseline, or pre-treatment values in studies that used maximum daily doses of 100-120 mg. Larger reduction achieved using daily doses as high as 180 mg.[33,34] Serum Ca and phosphorous level were decreased modestly during treatment.

METHODS

The aim of this study is to determine the efficacy and side effects of cinacalcet in those patients with refractory hyperparathyroidism due to chronic renal failure.

Study was designed as an open clinical trial. Patients were recruited from outpatient department and dialysis unit of department of nephrology, medical college, Calicut. The study was approved by institutional research and ethics committee.

Patients with chronic kidney disease stage V on maintenance haemodialysis diagnosed to have refractory hyperparathyroidism who do not attain the target range for hyper parathyroid indicators serum PTH ≤300, Serum Ca (8.4-9.5), serum phosphorous (3.5-5.5) with the use of calcitriol and phosphate binders were included in the study. Patients were told about the study and written informed consent was obtained from all the patients.

Inclusion criteria

- Patients of both sexes
- Age between 30-55years
- Patients refractory to standard therapy (calcitriol±calcium based phosphate binder /non calcium phosphorous binder).

Exclusion criteria

- Patients not willing to participate in the study
- Patients responding to standard therapy
- Pregnancy, lactation, other co-morbid condition requiring concomitant medication.

Trial method

A total of 72 adult patients with chronic kidney disease stage V who had been on maintenance haemodialysis were enrolled in this prospective clinical trial. Patients were recruited from outpatient department and dialysis unit of department of nephrology medical college Calicut. All the patients were already on standard regimen which consists of calcitriol and calcium phosphate binder/noncalcium phosphate binder. Medical charts of all 72 selected patients were reviewed to extract the basic data. Blood samples of all these patients were sending to a single standard laboratory in Calicut. Their base line calcium, phosphorous and PTH values were estimated. The estimation of PTH was done by immunodiametric assay. Among these 72 patients 20 patients (15 males, 5 females) were found to have satisfied the case definition of refractory hyperparathyroidism due to chronic renal failure. These Patients were interviewed in detail and complete history was elicited which covered personal data, duration of illness, and other modalities of treatment. All these details were entered in case report form or proforma. Patients were briefed about the study and written informed consents were obtained. They were also explained about the advantages of cinacalcet therapy. Duration of treatment as per the study protocol was 6 weeks. Cinacalcet 30 mg daily was given for 6 weeks. Majority of the patients were given cinacalcet free of cost. Patients were instructed to report immediately if any untoward effects occurred. All these patients were required to attend nephrology department for review and evaluation after one month. When they came for review the compliance to treatment with cinacalcet were assessed by asking relevant questions. They were also asked about any adverse effect during treatment. Standard serum calcium, serum phosphorous and PTH were again assessed after 6 weeks from the same laboratory. One female patient was dropped from the study due to severe vomiting following administration of cinacalcet. One of the patients unfortunately circum to death during the study. Two patients were lost to follow up.

Analysis of data

Statistical analysis was done using statistical package for social service (SPSS) software 16 version. Mean and standard deviation were used to describe the variables. Paired t test was done for analysis of data. Results were

tabulated and significance was expressed according to the p value≤0.05 (significant) and ≤0.001 (highly significant.

RESULTS

A total of 72 chronic kidney disease stage V-D patients who were already on standard regimen were enrolled in the study. Their base line calcium, phosphorous, PTH, blood urea, serum creatinine, age, sex, duration of illness was recorded.

Twenty patients satisfying the case definition of refractory hyperparathyroidism due to chronic renal failure received cinacalcet therapy. Total duration of treatment was 6 weeks. Standard serum calcium, serum phosphorous, PTH was again assessed after 6 weeks.

Table 1: Comparison of variables (PTH, S. calcium, S. phosphorous) both before and after treatment 1st change of drugs in prescribing pattern.

N=16	Before treatment		After treatment (6 weeks)	
	Mean	Standard deviation	Mean	Standard deviation
PTH	705.125	464.501	517.163	531.517
S. Calcium	8.29	1.23	8.42	1.06
S.Phophosorus	8.031	2.977	7.563	2.125

Table 2: Change in serum phosphorous, serum calcium and PTH both before and after treatment (Paired sample test).

	Mean	Slandered deviation	t	df	Sig. (2-tailed)
Pair 1 PTH 0-6 weeks	187.962	275.860	2.725	15	0.016
Pair 2 S.calcium 0-6 weeks	- .13	0.93	-0.537	15	0.599
Pair 3 S.phosphorus 0-6 weeks	0.469	1.177	1.592	15	0.132

Pair-1= 0.016<0.05 and is significant; Pair-2= 0.599>0.05 and is not significant; Pair -3=0.132>0.05 and is not significant.

Out of twenty patients 15 patients were males and 5 patients were females Among them ten patients belongs to below 40 years and ten patients belongs to 40-55 years. One patient dropped out from study due to severe vomiting, one patient died in between treatment and two patents were lost to follow up. Remaining 16 patients completed the study. Five of them had diabetic nephropathy and two of them had hypertensive nephropathy. Duration of illness, blood urea, serum creatinine, serum calcium, serum phosphorous, serum PTH at 0 week (before treatment). Serum PTH, serum calcium, serum phosphorous after 6 weeks (after treatment). Serum PTH after 12 weeks who showed increased level of PTH (above 1000) after increasing dose to 60 mg and duration of treatment to 12 weeks.

Addition of cinacalcet in refractory hyperparathyroidism with chronic renal failure has produced significant reduction in serum PTH level .No significant changes were observed regarding serum phosphorous and serum calcium level.

DISCUSSION

Secondary hyper parathyroidism is characterised by parathyroid hyperplasia, persistently elevated plasma levels of PTH, abnormal calcium and phosphorous homeostasis. It commonly accompanies chronic kidney disease.

Conventional treatment for secondary hyperparathyroidism includes calcium supplements, dietary phosphate restriction, Ca/non Ca containing phosphorous binders and active vitamin D sterols. This treatment is often associated with significant side effects including hypercalcemia and hyperphosphatemia. Patients who do not attain the target range for hyper parathyroid indicators with the use of calcitriol and phosphate binders were diagnosed to have refractory hyperparathyroidism.[36-39]

Calcimimetics have provided an alternative approach to the treatment of secondary hyperparathyroidism by directly targeting calcium sensing receptor on parathyroid cell surface that regulates secretion of PTH. Cinacalcet is a class 1 calcimimetic. It significantly reduces PTH levels in dialysis patients with refractory hyperparathyroidism, simultaneously bringing about a reduction in serum Ca and phosphorous level. Present study is undertaken to assess the safety and efficacy of cinacalcet in refractory hyperparathyroidism in chronic kidney disease.

All the patients were given 30 mg OD cinacalcet. 2 patients showed higher PTH level (above 1000) even after increasing dose of cinacalcet to 60 mg for 12 weeks. One of the patients unfortunately circum to death during the study. Two patients were lost to follow up. It significantly reduces serum PTH level when results were compared by paired t test. P=0.016 <0.05 (significant).

No statistically significant reduction in serum calcium and phosphorous. Serum calcium P value=0.599>0.05, serum phosphorous P=0.132>0.05. Adverse effect-one female patient stopped cinacalcet after 2 weeks of therapy due to severe vomiting. In this study after overall assessment cinacalcet is more efficacious and safe in the medical management of refractory hyperparathyroidism due to chronic renal failure.

Limitations of study were, it is a single centre study with limited duration of treatment. As the prevalence of patients with refractory hyperparathyroidism with chronic renal failure is less it was difficult to obtain bigger sample

size with in the limited study period. This study is not randomized, so possibility of bias is present. Hence randomized double blind multicentre studies with bigger sample size and extended duration of treatment are required.

CONCLUSION

Secondary hyperparathyroidism is a common consequence of chronic kidney disease which results from abnormal regulation of calcium and phosphate homeostasis.

Refractory hyperparathyroidism is diagnosed in those patients who do not attain the target range of S. PTH<300, S. Ca (8.4-9.5), S. Phosphate (3.5-5) with the use of conventional therapy with calcitriol and phosphate binders. However conventional treatment is often associated with significant side effects including hypercalcemia and hyperphosphatemia.

Therapy with calcimimetic is a new approach in the treatment of secondary hyperparathyroidism. Calcimimetics activates calcium sensing receptors on the surface of chief cells in parathyroid gland which results in a rapid reduction in PTH secretion, simultaneously lowers serum calcium and phosphorous.

Present study is undertaken to assess the safety and efficacy of cinacalcet in refractory hyperparathyroidism with chronic renal failure. The study results showed statistically significant reduction in serum PTH level. No statistically significant reduction in serum calcium and phosphorous level were observed and it has not resulted in hyper calcemia or hyper phosphatemia. Only one patient stopped treatment due to severe vomiting.

Therefore cinacalcet is a potentially highly effective and well tolerated drug for refractory hyperparathyroidism with chronic renal failure. Multicentre randomized controlled studies with longer duration of treatment and bigger sample size are required to confirm the effectiveness of cinacalcet.

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