The Role of Calcitriol in Chronic Kidney Disease Mineral Bone Disorder in Dialysis Patients

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Abstract: Chronic kidney disease-mineral bone disorder (CKD-MBD) is a systemic disorder of mineral and bone metabolism. It is a systemic condition that manifests as abnormalities in parathyroid hormone (PTH), calcium (Ca), phosphorus (P), and vitamin D metabolism, with associated bone abnormalities and ectopic calcification. CKD-MBD is associated with vascular calcification and cardiovascular disease (CVD), and these conditions are closely related to an increased mortality rate. Guidelines for the treatment of CKD-MBD have been published by Disease Outcomes Quality Initiative (DOQI) and Kidney Disease Improving Global Outcomes (KDIGO).

Keywords: CKD-MBD, Calcitriol, calcium, phosphorous

1. Objective

The objective of this observational study is to identifying the role of calcitriol in patients with mineral bone disease-chronic kidney disease in dialysis patients. Identify and normalize the serum calcium and phosphorous levels. To establish the dosage of calcitriol required for patients.

2. Introduction

Mineral bone disorder (MBD) is an important complication of chronic kidney disease (CKD). Chronic kidney disease is defined as a disease characterized by alterations in either kidney structure or function or both for a minimum of 3 months duration. (1) Chronic kidney disease is an international public health problem affecting 5-10% of the world population. (2) Chronic kidney disease mineral bone disorder (CKD-MBD) is a systemic disorder of mineral and bone metabolism due to CKD manifested by either one or a combination of the following: (i) abnormalities of calcium, phosphorus, PTH, or vitamin D metabolism; (ii) abnormalities in bone turnover, mineralization, volume, linear growth, or strength; or (iii) vascular or other soft-tissue calcification. (3,4) The major complications related to CKD include cardiovascular disease, anemia, infectious complications, neuropathy and abnormalities related to mineral bone metabolism. (5)

CKD-MBD, defined as biochemical abnormalities in mineral metabolism, abnormalities in skeletal remodeling, and extra skeletal calcification, is present when the glomerular filtration is reduced by more than 40% within the concept of the CKD-MBD, recent progress related to cardiovascular disease risk factors stimulated by cardiovascular disease risk factors stimulated by kidney disease has uncovered three: Vascular calcification, phosphorus, (FGF23). Vascular calcification particularly poses an increased risk of cardiovascular and all cause mortality, and of the clinical conditions associated with vascular calcification, the most extensive calcifications occur in CKD. In CKD, vascular calcification is stimulated by hyperphosphatemia and positive calcium balance.

Emerging data indicate that the CKD-MBD syndrome may begin early in the course of kidney disease and precede the development of clinically detectable abnormalities in plasma phosphorus (Pi), calcium (Ca), parathyroid hormone (PTH), and calcitriol, which are the hallmarks of the established CKD–MBD. beginning in CKD stage 3. Beginning in CKD stage 3, the ability of the kidneys to appropriately excrete a phosphate load is diminished, leading to hyperphosphatemia, elevated PTH, and decreased 1,25(OH)2D with associated elevations in the levels of FGF-23.

The conversion of 25(OH) D to 1,25(OH)2D is impaired, reducing intestinal calcium absorption and increasing PTH. The kidney fails to respond adequately to PTH, which normally promotes phosphaturia and calcium reabsorption, or to FGF-23, which also enhances phosphate excretion. In addition, there is evidence at the tissue level of a down regulation of vitamin D receptor and of resistance to the actions of PTH. Therapy is generally focused on correcting biochemical and hormonal abnormalities in an effort to limit their consequences. The mineral and endocrine functions disrupted in CKD are critically important in the regulation of both initial bone formation during growth (bone modeling) and bone structure and function during adulthood (bone remodeling). As a result, bone abnormalities are found almost universally in patients with CKD requiring dialysis (stage 5D), and in the majority of patients with CKD stages 3–5.

2.1 Advanced and early stages of CKD-MBD

CKD-MBD starts early in the course of CKD. In advanced stages, blood tests will indicate decreased calcium and calcitriol (vitamin D) and increased phosphate, and parathyroid hormone levels. In earlier stages, serum calcium, phosphate levels are normal at the expense of high parathyroid hormone and fibroblast growth factor-23 levels. X-rays will also show bone features of renal osteodystrophy (subperiosteal bone resorption, chondrocalcinosis at the knees and pubic symphysis, osteopenia and bone fractures) but may be difficult to differentiate from other conditions.
2.2 Bone Biopsy

A bone biopsy is a procedure that removes a piece of bone tissue for examination with a microscope. A health care provider performs the biopsy in a hospital with light sedation and local anesthetic. The health care provider uses imaging techniques such as ultrasound or a computerized tomography scan to guide the biopsy needle into the hip bone. A pathologist—a doctor who specializes in diagnosing diseases—examines the bone tissue in a lab. The test can show whether a person’s bone cells are building normal bone.

2.3 Slowed Bone Growth and Deformities

Damaged kidneys must work harder to clear the phosphorous from the body. High levels of phosphorous cause lower levels of calcium in the blood, resulting in the following series of events:

1) When a person's blood calcium level becomes too low, the parathyroid glands release parathyroid hormone.
2) Parathyroid hormone removes calcium from bones and places it into the blood, raising a persons blood calcium levels at the risk of harming bones.

3. Materials and methods

3.1 Materials

It was prospective observational study. The study will be conducted in the department of Nephrology, Krishna Institute of Medical sciences (KIMS) hospital, Hyderabad, India. All the patients suffering from chronic kidney disease- mineral bone disorder on an ongoing hemodialysis condition who are previously on calcitriol were selected. The selection of subjects above age of 18years with CKD-MBD on hemodialysis were eligible for this study.

3.2 Methodology

During the initial visit the research pharmacist will collect the baseline information of the eligible patients and the collected data will be documented in a suitable designed data collection form. Patients demographic details, other co morbid conditions, the medication details, duration of therapy and all other required data will be collected from various data sources. Patients will be followed up until the next 2 hospital visit i.e. after 12 weeks and 24 weeks of treatment and collects the required information. The data of drug related adverse effects, weight gain or loss and other laboratory tests in next two hospital visits were collected by asking patients and checking prescription. Collection of data include: calcium, phosphorous, HB%, PTH levels. The treatment satisfaction score was assessed by dialysis treatment satisfaction questionnaire and the response given by the patient to the questions.

4. Results and Discussion

The study results demonstrate that There was a significant decrease in plasma PTH, which by the fourth week was 1,036 + 213 pg/mL (P < 0.001), and it decreased continuously thereafter; after 12 weeks it was 639 + 158, and by 24 weeks it was 281 f 66 pg/mL. A mild non significant increase was noted in the second half of the study. Mean serum P before dietary instruction was 7.1 + 0.1 mg/dL. Within 2 to 3 weeks and after dietary P instruction, it decreased to 5.5 + 0.4 mg/dL (P < 0.01). By the third week of IV calcitriol as the PTH decreased SP decreased to 5.1 + 0.2 mg/dL (P < 0.05), and by the end of the study it was 5.3 ± 0.2 mg/dL. The calcitriol dose was progressively decreased, and by the end of the study it was 1.2 + - 0.3 pg per dialysis.

4.1 Age distribution of CKD-MBD cases

A total number of 40 cases were enrolled in study. Out of which 03(10%) were in the group of 20-30yrs, followed by 07(23.3%) were in age group of 30-40 years, 08(26.7%) were in the age group of 40-50 years, 08(26.7%) were in the age group of 50-60 years, 04(13.3%) were in age group of above 60 years old.

4.2 (calcitriol therapy), parameters results of the study

The mean values + SE for all biological parameters throughout the study are shown The average values for biological parameters before the study were determined using atleast three values in each patient serum Ca was 10.4 + 0.2 mg/dL; serum P 7.1+ 0.1mg/L; alkaline phosphatase 563 ± 32; PTH 1,466 + 116 pg/mL. By the time serum P was controlled and IV calcitriol was started, PTH had increased to 1,826+ 146pg/mL and serum P decreased to 5.5 to 0.4mg/dL; and SCa was 10.7.

4.3 Food habits

It was also found that patients following non vegetarian diet were up to 68% and the rest 32% were vegetarian.

4.4 Weight variation

The hemodialysis patients show weight variation before and after dialysis (mean weight gain 2.5kg) where as with weight loss (1.8kg) there was weight variation observed according to the dialysis treatment.

4.5 Pharmaco-Economic Analysis: Cost wise comparision of hemodialysis patients in our study population

The cost for dialysis process have been calculated, the process of hemodialysis cost of treatment per month was found to be Rs.21,600. The average cost of medication per month was found to be Rs.4000 The overall average cost laboratory investigations per visit was observed as Rs.1,330.

4.6 Quality of life measurement

Hemodialysis therapy is time-intensive, expensive, and requires fluid and dietary restrictions. Long-term dialysis therapy itself often results in a loss of freedom, dependence on caregivers, disruption of marital, family, and social life, and reduced or loss of financial income. Hemodialysis alters the life style of the patient and family and interferes with their lives. Due to these reasons, the physical, psychological,
References


5. Conclusion

The results demonstrate that there was no significant change in serum Ca concentration throughout the study. The calcitriol dose was progressively decreased, and by the end of the study it was 1.2 + 0.3 pg per dialysis. The cost of treatment and medication for dialysis is much higher. By the end of the study, the maintenance dose of calcitriol was still 1.2 pg 3 X per week. Serum P was controlled within 2 to 4 weeks of intensive dietary instruction followed by dietary management. Serum P levels were within an acceptable range throughout the study. Treatment satisfaction: patients were on average not more satisfied with their treatment on hemodialysis when compared with peritoneal dialysis.
Changes in weight variation of hemodialysis patients during treatment

Effect of calcitriol on serum calcium, phosphorous, alkaline phosphate and PTH in patients with CKD-MBD

PTH and serum Ca are represented in the vertical axis. Once calcitriol dosage was increased to 6 pQ, PTH decreased dramatically. There was no significant change in serum Ca concentration throughout the Study.