Original Article

Assessment of bone mineral metabolism derangements by K/DOQI guidelines in haemodialysis patients at Rawalpindi

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Abstract

Objective: To assess serum calcium, phosphorus and PTH levels with reference to K/DOQI targets in haemodialysis patients at Rawalpindi. Further more efficacy of calcium carbonate (CaCO3) was compared with calcium acetate (CaAc) for maintaining serum P and Ca levels in our ESRD patients.

Methods: One hundred and ninety patients on haemodialysis receiving calcium phosphate binders (CaCO3 n=128 and CaAc n=62) were selected from a tertiary care hospital at Rawalpindi, Pakistan. Serum Ca and P were assayed on chemistry analyzer. PTH was measured on immulite-1000. Data were compared with K/DOQI targets and analysed by using SPSS-15.

Results: The patients had mean serum Ca 2.34 ± 0.29 mmol/L, Phosphorus 1.76 ± 0.43 mmol/L and Parathyroid hormone (PTH) 38.7 ± 35.6 nmol/L. The patients had achieved K/DOQI target ranges of Ca, P, PTH and Ca x P product in 37.9%, 41.1%, 22.6% and 61.5 % respectively. Patients on CaCO3 had significantly higher serum Ca 2.38 ± 0.31 mmol/L than those on CaAc therapy 2.26±0.22 mmol/L.

Conclusion: Most of patients on maintenance haemodialysis at Rawalpindi, did not achieve the recommended K/DOQI target ranges. Appropriate phosphate binders are required for improvement of mineral metabolism and medical outcome in our patients (JPMA 59:64; 2009).

Introduction

Globally the numbers of patients with end stage renal disease (ESRD) on haemodialysis are increasing.[1] Mineral metabolism abnormalities like hypocalcaemia, hyperphosphatemia and secondary hyperparathyroidism leading to renal osteodystrophy is common in patients on maintenance haemodialysis.[2] These derangements in calcium (Ca) and phosphorus (P) metabolism confer increased risk of musculoskeletal and cardiovascular complications leading to death.[3-4] Keeping this in view, the kidney disease outcome quality initiative (K/DOQI) issued the guidelines on Ca, P, PTH and Ca x P product ranges for quality care of ESRD patients.[5-6] Achieving laboratory values within K/DOQI recommended limits is a real challenge in the management of these ESRD patients.

Studies have been conducted in different countries to assess the Ca, P and PTH abnormalities in the patients on haemodialysis with reference to K/DOQI guidelines.[6-9] Multi centres dialysis outcome and practice pattern studies (DOPPS I and DOPPS II) were conducted at two point intervals in patients on haemodialysis in France, Germany, Italy, Japan, Spain, United States, and the United Kingdom. DOPPS-I provided the baseline information regarding the prevalence of Ca, P and PTH metabolism abnormalities among haemodialysed patients with reference to K/DOQI targets.[7] DOPPS-11 revealed marked improvement in the bone mineral parameters as compared with previous DOPPS-1 study over time.[7-8] DOPPS also confirmed the association between mineral metabolism abnormalities and patient out come i-e morbidity and mortality.[8]

Principal modalities that have been used in an attempt to reverse hyperphosphatemia of renal failure include restricting dietary phosphate intake and use of phosphate binders. Most patients receive either CaCO3 or

CaAc to control hyperphosphatemia during maintenance haemodialysis in our medical set up at Rawalpindi. However, calcium based phosphate binders are not being used in most of the advanced countries in order to avoid hypercalcemia.[10]

In order to prevent the mineral metabolism related complications in our clinical practice, it is necessary to assess serum Ca, P and PTH levels regularly in these patients. There is hardly any data available regarding Ca, P and PTH levels among patients on haemodialysis in Pakistani population. The study was planned to assess the bone mineral metabolism derangements and effectiveness of therapeutic calcium based phosphate binders (CaCO3 vs. CaAc) in achieving the K/DOQI guideline targets in the patients at nephrology unit of tertiary care hospital at Rawalpindi, Pakistan.

Patients and Methods

The study was carried out at nephrology unit of tertiary care hospital at Rawalpindi, Pakistan after approval of institutional review and ethical committee. One hundred and ninety patients with creatinine clearance value < 15 ml/min/ 1.73m^2 of either sex above 12 years of age were included in the study after informed consent. Demographic data, history of illness and detailed physical examination were recorded. They were all on maintenance dialysis twice per week for last three months and taking either CaCO3 or CaAc as phosphate binders to control hyperphosphatemia. Patients of acute renal failure, on peritoneal dialysis, not taking any phosphate binders and having pervious parathyroidectomy were excluded from the study.

Five ml of predialysis blood was collected and plasma separated immediately in refrigerated centrifuge. Total calcium, phosphorous, albumin, urea, creatinine and alkaline phosphatase were assayed by using pioneer diagnostic kits USA on Selectra-E auto analyzer (Vitalab, Netherlands). Total calcium was analyzed by cresolphthalein complexone method.[11] Phosphate was measured with phosphomolybdate reduction reaction.[12] Other biochemical parameters including alkaline phosphatase, creatinine and albumin were measured by P-nitrophenylphosphate DEA method, Jaffe reaction and bromcresol methods respectively. Finally intact PTH was measured on Immulite-1000 by two site chemiluminiscent enzyme labeled immunometric assay.[13] CV for all biochemical parameters and PTH were within 2-5%.

Data was analyzed using SPSS 15 (Chicago, IL). Mean, SD and percentages of all the parameters were calculated and compared by using the K/DOQI guidelines. Independent t-test was applied to evaluate the difference between groups taking CaCO3 and CaAc. Percentages of patients with mineral metabolism abnormalities were compared with DOPPS. The level of significance was taken as <0.05.

Results

Demographic data revealed the mean age of the participants as 47 ± 12 years consisting of 64% males and 36% females. The duration of haemodialysis in these patients varied from 3 to 66 months. The baseline biochemical investigations of ESRD patients are summarized in Table-1. The mean serum Ca was 2.34 ± 0.290 mmol/L and serum P 1.76 ± 0.43 mmol/L which were lower than the reference range while for intact PTH 38.7 ± 35.6 nmol/L was above the reference limits. The majority of the patients had serum Ca (62.1%), P (59%) and PTH (77.4%) outside the K/DOQI recommended range and greater percentages were above the permissible limits in the nephrology unit of tertiary care hospital at Rawalpindi-Pakistan (Table-2).

Table-1: Biochemical parameters in haemodialysis patients at Rawalpindi-Pakistan (n=190).

Parameter	Mean (SD)	Median	Range
Total Calcium (mmol/L)	2.34 ± 0.29	2.3	1.52-3.01
Phosphate (mmol/L)	1.76 ± 0.43	1.79	0.93-3.87
PTH (nmol/L)	38.7 ± 35.55	29.2	1.9-180
Urea (mmol/l)	20.0 ± 7.9	20	1.6-43.0
Creatinine (? mol/l)	882.1 ± 421.05	906	65-1789
Albumin (g/L)	37.4 ± 4.3	37	23-51
Alkaline Phosphate (U/L)	381 ± 244	318	135-1587
Ca x P(mmol2/l2)	4.12 ± 1.07	4.04	1.54-7.78

Table-2: Achievement of K/DOQI guideline targets of bone mineral metabolism parameters in haemodialysis patients at Rawalpindi-Pakistan (n=190).

Parameter	No of Patients	% of Patients
Serum total Calcium (mmol/L)		
<2.10	32	16.8
2.10-2.37 *	72	37.9
>2.37	86	45.3
Serum Phosphate (mmol/L)		
<1.13	10	5.3
1.13-1.78 *	78	41.0
>1.78	102	53.7
Plasma PTH (nmol/L)		
<15.8	57	30.0
15.8-31.6 *	43	22.6
>31.6	90	47.4
Ca x P Product (mmol2/L2)		
<4.4*	43	61.5
>4.4	90	38.5

K/DOQI Guidelines Targets *

One hundred twenty eight patients were taking CaCO3 and 62 patients were on CaAc therapy for lowering serum phosphate levels. Serum Ca levels were significantly high in patients on CaCO3 2.38 ± 0.31 mmo/L as compared to CaAc 2.26 ± 0.22 mmol/l group (P<0.001). However, serum PO4 levels in both groups did not show any significant change (Table-3).

Table-3: Comparison of mineral metabolism parameters in haemodialysis patients taking calcium carbonate and calcium acetate as phosphate binders (n=190).

Parameter	Calcium Carbonate Mean(SD)	Calcium Acetate Mean(SD)	p
Calcium (mmol/L)	2.38 ± 0.31	2.26 ± 0.22	<0.001
Phosphate (mmol/L)	1 .77 ± 0.47	1.74 ± 0.34	0.604
PTH (nmol/L)	37.81 ± 33.82	40.4 ± 39.11	0.634
Ca x P Product (mmol2/L2)	4.23 ± 1.21	4.04 ± 93.12	<0.013

Discussion

This study illustrates the current status of mineral metabolism abnormalities among ESRD patients on haemodialysis as recommended by K/DOQI guidelines.[5] In our study hyperphosphatemia leading to secondary hyperparathyroidism was a main mineral metabolism abnormality noted. The similar difficulty in achieving plasma P and PTH with reference to K/DOQI targets has been reported in Spanish ESRD patients.[14] Maudel and co-workers (2005) also reported hyperphosphatemia (29%) and increased PTH (31%) in haemodialysed patients but lower than our patients.[15] However, Block and co workers (1998) reported more cases of hyperphosphatemia than our patients.[16]

Most dialysis patients have elevated levels of serum P that adversely affects patient's survival.[17] The role of phosphate retention in the pathogenesis of secondary hyperparathyroidism has been established.[18] Secondary hyperparathyroidism causes bone resorption and subsequent calcifications in tissues, a condition known as renal osteodystrophy.[2] It is well known that high and lower PTH levels than K/DOQI guide lines are associated with increased mortality by causing renal osteodystrophy and adynamic bone disease respectively.[7] Hypercalcaemia in some patients could be due to increased intake of calcium based phosphate binders (CaCO3 and CaAc) in our medical setup.

Phosphate binders like CaCO3 and less frequently CaAc have been used in our nephrology units to control hyperphosphatemia in the patients. Patients using CaAc revealed better control over mineral metabolism as compared to CaCO3 in our dialysis units. Hypercalcaemia was more in patients using CaCO3 as compared to CaAc. This corresponds to results from other studies which revealed similar finding of hypercalcemia in patients using CaCO3.[19-21] In addition increase frequency of the vascular tree, mitral and aortic valve calcification had been reported in patients receiving calcium based phosphate binders.[22-23]

New phosphate binders like sevalemer, lanthanum carbonate and cinacelet may be introduced in our country. There are reservations regarding their cost as majority of our patients belong to the less affluent class. Apart from that, large doses for sevalamer hydrochloride make patient compliance difficult.

The Ca, P and PTH in our patients on haemodialysis were somewhat close to DOPPS I. Lesser number of patients had bone parameters in K/DOQI recommended range compared to DOPPS II. The number of patients with no parameters in K/DOQI limits was 22.6% while 6.8% of our population had all the four parameters in K/DOQI limits. Our clinician should put lot of effort to achieve the K/DOQI targets.[7]

Apart from dietary restriction, appropriate phosphate binders are required for achieving Ca and P close to K/DOQI guideline. It will also help in prevention and management of renal osteodystrophy and CVS complications in ESRD patients. Every patient should be managed according to K/DOQI guidelines which will reduce morbidity and mortality and improve the quality of dialysis care in our country.

It is concluded that the current clinical management of ESRD patients' mineral metabolism in our set up is far from achieving the target set by K/DOQI guidelines. Patients on maintenance haemodialysis using CaCO3 revealed more hypercalcaemia and requires appropriate phosphate binders for improvement of medical outcome in our patients.

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