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ORIGINAL ARTICLE

K/DOQI guideline requirements for calcium, phosphate, calcium phosphate product, and parathyroid hormone control in dialysis patients: can we achieve them?

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Abstract *Background* Mineral metabolism has emerged as an important predictor of morbidity and mortality in dialysis patients. Kidney Disease Outcomes Quality Initiative (K/DOQI) clinical practice guidelines for bone metabolism and disease in chronic kidney disease (CKD) recommend that, in Stage 5 CKD, the target levels for calcium (Ca) (corrected for serum albumin), phosphate (P), calcium × phosphate (Ca × P) product and parathyroid hormone (PTH) levels should be maintained at 8.4–9.5 mg/dl, 3.5–5.5 mg/dl, < 55 mg^2/dl^2 and 150–300 pg/ml, respectively. *Objectives* To evaluate our ability to achieve K/DOQI guidelines for bone metabolism and disease targets in our patients and to compare them between patients on hemodialysis (HD) and peritoneal dialysis (PD) and also with those reported in the literature. *Methods* We reviewed bone metabolism laboratory parameters in 57 HD patients and 69 PD patients, who had been on dialysis for more than 9 months. *Results* The percentage of patients whose serum Ca, P, Ca × P product and PTH were within K/DOQI recommended target ranges were 46%, 53%, 77% and 28% in HD patients and 52%, 65%, 77% and 23% in PD patients, respectively. There were no significant differences between HD and PD patients in the percentage of all parameters that were within K/DOQI recommended target ranges. The percentage of our HD patients who had Ca, P, and PTH levels within recommended target range was similar to those in previous reports. *Conclusion* In our unit, the management of bone and mineral metabolism in HD and PD patients is still far short of meeting K/DOQI guidelines. These findings appear similar in HD and PD patients. Our findings resemble those reported in the literature.

Keywords Mineral metabolism · Dialysis · Parathyroid hormone

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Introduction

In dialysis patients, homeostasis of mineral metabolism is important not only for maintaining

musculoskeletal health, but is also associated with mortality [1–4]. Guidelines have been developed for the management of mineral metabolism in HD patients, partly in response to growing evidence about the relationship between vascular calcification and mortality [5]. The National Kidney Foundation K/DOQI clinical practice guidelines for bone metabolism and disease in CKD suggested that, in Stage 5 CKD, the target levels for Ca, P, Ca × P product and PTH levels should be maintained between 8.4–9.5 mg/dl, 3.5–5.5 mg/dl, < 55 mg^2/dl^2 and 150–300 pg/ml, respectively [5]. In terms of these guidelines, some authors have found that current practice for the management of bone and mineral metabolism in HD falls far short of meeting the K/DOQI guidelines. We reviewed the laboratory parameters of bone and mineral metabolism in our HD and PD patients and evaluated our ability to meet the aforementioned targets. Even though these guidelines have been written for patients on HD, we have assumed that these are applicable to patients on PD.

Patients and methods

We studied 57 HD patients and 69 PD (including CAPD and APD) patients who had started dialysis after April 1993 and before Sept 2004 in our unit. None had undergone previous parathyroid surgery. The same 3 physicians (SVJ, JMB, DGO) took care of all the HD and PD patients included in this study and managed the parameters of bone and mineral metabolism according to standard practice. Serum albumin corrected Ca, P and PTH values in recent 3 months were retrieved in patients who were on HD or PD for more than 9 months. PTH measurements were based on an intact molecule assay; Ca and P were measured with standard laboratory techniques. Data are expressed as mean ± SD. Student's *t*-test was used to compare the mean of quantitative variables between groups. The χ^2-test was used to compare the differences in categorical variables. The *P* value less than 0.05 was considered significant.

Results

Mean total weekly KT/V was 2.66 in 57 PD patients in whom it was measured. Of the 69 PD patients, 34 were anuric and mean glomerular filtration rate (GFR) (average of the sum of urea and creatinine clearances) in the remaining 35 patients was 4.52 ± 3.29 ml/min. Mean percentage urea reduction (PUR) in 57 HD patients was 75.1 ± 7.3%. We found no significant differences between HD and PD patients with respect to Ca, P, Ca × P and PTH values. In the two groups the only significant difference among all parameters studied was the average daily dose of $CaCo_3$ that was higher in HD patients than in PD patients (2361.2 ± 1444.9 and 1461.0 ± 810.0 mg/day, respectively) (Table 1). There were no significant differences in the percentage of HD and PD patients whose Ca, P, Ca × P product and PTH were within K/DOQI recommended target ranges, except for serum phosphate—a higher percentage (22.8%) of HD patients had serum phosphate below the recommended target range than did those on PD (7.2%) (Table 2). The percentage of our HD patients who had Ca, P and PTH levels within the recommended target range was similar to those in other reports (Table 3). The percentage of our HD and PD in whom all four-laboratory values were within guideline recommended target ranges was low, and similar to that in other reports (Table 4).

Discussion

Derangements of mineral and bone metabolism in CKD are associated with increased morbidity and mortality [5]. Deaths from all causes and cardiovascular mortality were directly associated with higher concentrations of PTH, phosphorus, calcium, and calcium-phosphorus product [3]. Mortality risk increased above a PTH level of approximately 700 pg/ml, phosphorus of 6.0 mg/dl, and a calcium phosphorus product of 60 mg^2/dl^2 [3, 5]. Therefore, it is important to try to achieve the guideline target ranges. There is increasing concern regarding the risk of mortality associated with hyperphosphatemia and

Table 1 Demographic characteristics of laboratory parameters in HD and PD patients

Parameters	HD (n = 57)	PD (n = 69)
Age (years)	62.9 ± 16.1	62.2 ± 15.7
Gender (male/female)	34/23	41/28
Time on dialysis (months)	46.1 ± 45.4	45.0 ± 34.9
Corrected calcium (mg/dl)	9.52 ± 0.76	9.50 ± 0.56
Phosphate (mg/dl)	4.68 ± 1.55	4.82 ± 1.15
Ca × P products (mg^2/dl^2)	44.9 ± 15.1	46.4 ± 12.4
PTH (pg/ml)	452.5 ± 550	470.9 ± 471.8
Doses of CaCO3 (mg/day) (n_1/n_2 = 44/59)	2361.2 ± 1444.9	1461.0 ± 810.0[a]
Dose of Calcitriol (mcg/week) (n_1/n_2 = 27/27)	1.72 ± 0.84	1.72 ± 0.74
Dose of Sevelamer (mg/day) (n_1/n_2 = 3/6)	7200.0 ± 2400.0	3600.0 ± 2070.7

n_1/n_2: Sample size of HD/PD in using $CaCO_3$, Calcitriol and Sevelamer

[a] $P < 0.001$ (HD group vs. PD group)

elevations in the calcium–phosphorus product [1, 6–9]. Thus, controlling serum phosphorus that involves not only restriction of dietary phosphate intake but also the use of phosphate binders has become an important aspect of the management of ESRD patients. Both of these interventions (diet and phosphate binders) require a great deal of patient education as well as close patient compliance. Furthermore, none of the existing phosphate binding agents is truly satisfactory. Aluminum (Al)-containing agents are highly efficient but they have been abandoned because of their potential toxicity [10–12]. Calcium carbonate (CaCO3) binds phosphorus effectively but often induces hypercalcaemia and a positive calcium balance, especially in patients with low-turnover bone disease; a positive calcium balance has been incriminated in the development of vascular, valvular, cardiac and metastatic calcification [13–17] leading to increased morbidity and mortality [18]. Sevelamer is an effective agent, but large doses are needed and it is expensive [19–25]. Lanthanum carbonate is as effective as calcium carbonate [26] but concerns have been raised regarding its tissue deposition [27–28].

Our study, in accordance with other studies, [3, 29] shows that in less than one-half of our patients did the serum calcium levels fall within the recommend target ranges. Although our patients had good control of the serum P level and Ca × P product (mean serum P: 4.68 ± 1.55 mg/dl, mean Ca × P products 44.9 ± 15.1 mg^2/dl^2 in HD patients and mean serum P 4.82 ± 1.15 mg/dl, mean Ca × P products 46.4 ± 12.4 mg^2/dl^2 in PD patients), only 52.6% of HD patients and 65.2% of PD patients had serum P within the recommended target range; 22.8% of HD patients and 7.2% of PD patients had values below recommended target range, and 24.6% of HD patients and 27.5% of PD patients above recommended target range. Ca × P products within the target range and above the target range was 77.2% and 22.8% in HD patients and 76.8% and 23.2% in PD patients. The percentage of our HD patients who had Ca, P and PTH within the target range was not significantly different from those reported in the literature. The percentage of our patients who had all four criteria (Ca, P, Ca × P product and PTH) within the range simultaneously was very low at 5.3% in HD and 10.1% in PD, which were similar to those in the published reports [3, 29]. In our study, we compared HD patients with PD patients, who were looked after by the same nephrologists, and found no significant differences between HD and PD patients in reaching

Table 2 Laboratory determinations that were within the K/DOQI recommended range in 57 HD and 69 PD patients

Laboratory measurements	Range	Patients (%)		P value
		HD (n = 57)	PD (n = 69)	
Ca (mg/dl)	<8.4	3.5	2.9	>0.05
	8.4–9.5	45.6	52.2	>0.05
	>9.5	50.9	44.9	>0.05
P (mg/dl)	<3.5	22.8	7.2	<0.05
	3.5–5.5	52.6	65.2	>0.05
	>5.5	24.6	27.5	>0.05
Ca × P (mg^2/dl^2)	<55	77.2	76.8	>0.05
	≥55	22.8	23.2	>0.05
PTH (pg/ml)	<150	31.6	24.6	>0.05
	150–300	28.1	23.2	>0.05
	>300	40.3	52.2	>0.05

Table 3 Laboratory parameters in 57 HD patients compared with laboratory parameters in literature

Parameters	Range	Patients (%)			
		DOPP I	DOPP II	SLU	TGH
Ca (mg/dl)	<8.4	9.4	8.9	21	3.5
	8.4–9.5	40.5	42.5	49	45.6
	>9.5	50.1	48.6	30	50.9
P (mg/dl)	<3.5	7.6	9.0	8	22.8
	3.5–5.5	40.8	44.4	36	52.6
	>5.5	51.6	46.7	56	24.6
PTH (pg/ml)	<150	52.9	47.5	8	31.6
	150–300	21.4	26.2	20	28.1
	>300	25.7	26.3	72	40.3

DOPP: Dialysis Outcomes and Practice Patterns

DOPP I: US = 1996, Europe = 1998, Japan = 1999

DOPP II: 2002: Includes data from France, Germany, Italy, Japan, Spain, UK, and US only

SLU: 2003: Saint Louis University, Division of Nephrology, St. Louis, Mo, USA

TGH: 2005: Toronto General Hospital, University Health Network, Toronto University

To convert serum calcium in mg/dl to mmol/l, multiply by 0.2495; serum phosphate in mg/dl to mmol/l, multiply by 0.3229; PTH in pg/ml to ng/l, multiply by 1, to mmol/l multiply by 0.11

K/DOQI target ranges regarding serum Ca, P, Ca × P and PTH.

These findings indicate the difficulties we face with the current management of bone and mineral metabolism in dialysis patients. Management of mineral metabolism requires a complex mix of dialysis therapy, medications, dietary intervention, and patients' adherence. This complexity makes it difficult for providers to successfully manage mineral metabolism with the current therapeutic tools.

Table 4 Percentage of patents in57 HD patients and 69 PD patients within guideline ranges for all four-laboratory values compared to HD patients in other reports

Number of measurements in guideline range	Patients (%)			
	DOPP I	DOPP II	SLU	TGH
All 4	4.6	5.5	7	HD 5.3 PD 10.1

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