# Phosphorus control in peritoneal dialysis patients

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**Hyperphosphatemia is independently associated with an increased risk of death among dialysis patients. In this study, we have assessed the status of phosphate control and its clinical and laboratory associations in a large international group of patients on chronic peritoneal dialysis (PD) treatment. This cross-sectional multicenter study was carried out in 24 centers in three different countries (Canada, Greece, and Turkey) among 530 PD patients (235 women, 295 men) with a mean $\pm$ s.d. age of 55 $\pm$ 16 years and mean duration of PD of 33 $\pm$ 25 months. Serum calcium ($Ca^{2+}$), ionized $Ca^{2+}$, phosphate, intact parathyroid hormone (iPTH), 25-hydroxy vitamin $D_3$, 1,25-dihydroxy vitamin $D_3$, total alkaline phosphatase, and bone alkaline phosphatase concentrations were investigated, along with adequacy parameters such as *Kt/V*, weekly creatinine clearance, and daily urine output. Mean *Kt/V* was 2.3 $\pm$ 0.65, weekly creatinine clearance 78.5 $\pm$ 76.6 l, and daily urine output 550 $\pm$ 603 ml day$^{-1}$. Fifty-five percent of patients had a urine volume of $<$400 ml day$^{-1}$. Mean serum phosphorus level was 4.9 $\pm$ 1.3 mg per 100 ml, serum $Ca^{2+}$ 9.4 $\pm$ 1.07 mg per 100 ml, iPTH 267 $\pm$ 356 pg ml$^{-1}$, ionized $Ca^{2+}$ 1.08 $\pm$ 0.32 mg per 100 ml, calcium phosphorus (Ca $\times$ P) product 39 $\pm$ 19 mg$^2$ dl$^{-2}$, 25(OH)$D_3$ 8.3 $\pm$ 9.3 ng ml$^{-1}$, 1,25$(OH)_2D_3$ 9.7 $\pm$ 6.7 pg ml$^{-1}$, total alkaline phosphatase 170 $\pm$ 178 U l$^{-1}$, and bone alkaline phosphatase 71 $\pm$ 108 U l$^{-1}$. While 14% of patients were hypophosphatemic, with a serum phosphorus level lower than 3.5 mg per 100 ml, most patients (307 patients, 58%) had a serum phosphate level between 3.5 and 5.5 mg per 100 ml. Serum phosphorus level was 5.5 mg per 100 ml or greater in 28% (149) of patients. Serum $Ca^{2+}$ level was $\geqslant$9.5 mg per 100 ml in 250 patients (49%), between 8.5 and 9.5 mg per 100 ml in 214 patients (40%), and lower than 8.5 mg per 100 ml in 66 patients (12%). Ca $\times$ P product was $>$55 mg$^2$ dl$^{-2}$ in 136 patients (26%) and lower than 55 mg$^2$ dl$^{-2}$ in 394 patients (74%). Serum phosphorus levels were positively correlated with serum albumin ($P<0.027$) and iPTH ($P=0.001$), and negatively correlated with age ($P<0.033$). Serum phosphorus was also statistically different ($P$=0.013) in the older age group ($>$65 years) compared to younger patients; mean levels were 5.1 $\pm$ 1.4 and 4.5 $\pm$ 1.1 mg per 100 ml, respectively, in the two groups. In our study, among 530 PD patients, accepted uremic-normal limits of serum phosphorus control was achieved in 58%, Ca $\times$ P in 73%, serum $Ca^{2+}$ in 53%, and iPTH levels in 24% of subjects. Our results show that chronic PD, when combined with dietary measures and use of phosphate binders, is associated with satisfactory serum phosporus control in the majority of patients.**

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End-stage renal disease (ESRD) results in decreased secretion and eventually retention of inorganic phosphorus. Hyperphosphatemia not only stimulates the development of secondary hyperparathyroidism and renal osteodystrophy but also is independently associated with an increased risk of death among dialysis patients.[1] The mechanism by which hyperphosphatemia increases mortality risk is not yet clear, but much clinical and experimental data suggest that it may be through promoting cardiovascular calcification.[2–4]

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Turkish participants of this study were members of Turkish Multicenter Peritoneal Dialysis Study Group (TULIP).

Dietary restriction of phosphorus is an important part of phosphate control treatment in all dialysis modalities. But because of other important risk factors for patient mortality and morbidity, such as malnutrition and hypoalbuminemia, dietary restriction may not be successful alone and cannot be effective without the help of other treatment measures, mainly use of phosphate binders.[5,6] Type of dialysis may also be an important factor in the adequacy of phosphorus control in dialysis patients. Intermittent hemodialysis alone is known to be an ineffective modality in controlling serum phosphorus in most patients.[6] More frequent hemodialysis modalities such as short daily dialysis or long nocturnal hemodialysis are both reported to be more effective in achieving the desired serum levels of phosphorus while nearly eliminating the need for phosphate binders.[7–9] On the other hand, hemodialysis modalities such as short daily dialysis or long nocturnal hemodialysis are still in the experimental stage and have not yet been widely used in chronic ESRD patient care. Therefore, phosphate binders are still routinely prescribed for patients with ESRD to prevent hyperphosphatemia.[10]

In the Dialysis Outcomes and Practice Patterns Study (DOPPS), only 41% of the hemodialysis patients had a serum phosphorus concentration within the range recommended by the US National Kidney Foundation–Kidney Disease Outcomes Quality Initiative (K/DOQI) and European Best Practice Guidelines (3.5–5.5 mg per 100 ml).[11] A retrospective analysis of data from the US Renal Data System Case-Mix Adequacy and the Dialysis Morbidity and Mortality Wave II Studies showed that of the total 6407 prevalent long-term hemodialysis patients, 70% had serum phosphate levels greater than 5.0 mg per 100 ml. Nearly half these patients had serum phosphate levels greater than 5.9 mg per 100 ml and 39% had serum phosphate levels greater than 6.5 mg per 100 ml, indicating a high prevalence of hyperphosphatemia in the ESRD population receiving hemodialysis treatment.[1]

Considering the more liberal diet policy of peritoneal dialysis (PD), learning more about its efficacy in controlling serum phosphorus level is clinically important. Despite that, our current knowledge about the state of phosphorus control in chronic PD patients unfortunately is not satisfactory. Some studies suggest that continuous PD may be better in controlling hyperphosphatemia than intermittent hemodialysis.[12] In a large cross-sectional study among 252 Chinese chronic ambulatory PD patients, hyperphosphatemia was a frequent complication. According to this study, serum phosphorus levels were 5.6 mg per 100 ml or greater in $\geqslant$35.7% of patients, among whom 52.2% had serum phosphorus levels greater than 6.5 mg per 100 ml.[13]

Given the important link between hyperphosphatemia and cardiovascular deaths and the lack of detailed information about the subject, we have performed this cross-sectional, multicenter survey to assess the general status of phosphorus control and its clinical and laboratory associations in a large group of patients on chronic PD treatment.

## RESULTS

Among our 530 chronic PD patients, mean *Kt/V* was $2.3 \pm 0.65$, weekly creatinine clearance $78.5 \pm 76.6$ l, and daily urine output $550 \pm 603$ ml day$^{-1}$ (Table 1). Of the 530 patients, 166 (31%) were on low-calcium (1.25 mmol l$^{-1}$) PD solutions and the rest were on traditional 1.75 mmol l$^{-1}$ calcium-containing PD solutions. Chronic renal failure etiologies can be seen in Table 2.

Serum biochemistry at follow-up and diagnosis of renal osteodystrophy can be seen in Table 3. Mean inorganic phosphorus level was $4.9 \pm 1.3$ mg per 100 ml, $Ca^{2+}$ $9.4 \pm 1.07$ mg per 100 ml, intact parathyroid hormone (iPTH) $267 \pm 356$ pg ml$^{-1}$, ionized $Ca^{2+}$ $1.08 \pm 0.32$ mg per 100 ml, calcium phosphorus (Ca $\times$ P) product $39 \pm 19$ mg$^2$ dl$^{-2}$, 25-hydroxy vitamin $D_3$ ($25(OH)D_3$) $8.3 \pm 9.3$ ng ml$^{-1}$, 1,25-dihydroxy vitamin $D_3$ ($1,25(OH)_2D_3$) $9.7 \pm 6.7$ pg ml$^{-1}$, total alkaline phosphatase $170 \pm 178$ U l$^{-1}$, and bone alkaline phosphatase $71 \pm 108$ U l$^{-1}$. While 14% of patients were hypophosphatemic with a serum phosphorus level lower than 3.5 mg per 100 ml, most of the patients (307 patients, 58%) had a serum phosphorus level between 3.5 and 5.5 mg per 100 ml. Serum phosphorus level was 5.5 mg per 100 ml or greater in 149 patients (28%) (Table 4). Serum $Ca^{2+}$ level was $\geqslant$9.5 mg per 100 ml in 250 patients (49%), between 8.5 and 9.5 mg per 100 ml in 214 patients (40%), and lower than 8.5 mg per 100 ml in 66 patients (12%). Ca $\times$ P product was $>55$ mg$^2$ dl$^{-2}$ in 136 patients (26%) and lower than

**Table 1 | Demographic and clinical data (*n*=530)**

| | |
|---|---|
| Sex (M/F) | 295/235 |
| Age (years) | $55 \pm 16$ |
| Mean dialysis duration (months) | $33 \pm 25$ |
| Weekly total *Kt/V* | $2.21 \pm 0.65$ |
| Body mass index (kg m$^{-2}$) | $25 \pm 4$ |
| Urine output (ml day$^{-1}$) | $550 \pm 603$ |

F, female; M, male.

**Table 2 | Etiology of end-stage renal failure in the study group (*n*=530)**

| | |
|---|---|
| Chronic glomerulonephritis | 85 (15.9%) |
| Diabetic nephropathy | 98 (18.3%) |
| Hypertensive nephrosclerosis | 99 (18.5%) |
| Others and unknown | 248 (46.79%) |

**Table 3 | Serum biochemistries**

| | |
|---|---|
| P (mg per 100 ml) | $4.9 \pm 1.3$ |
| $Ca^{2+}$ (mg per 100 ml) | $9.4 \pm 1.07$ |
| Ca $\times$ P product (mg$^2$ dl$^{-2}$) | $46.75 \pm 14.51$ |
| $iCa^{2+}$ (mg per 100 ml) | $2.16 \pm 0.64$ |
| iPTH (pg ml$^{-1}$) | $267 \pm 356$ |
| $25(OH)D_3$ (ng ml$^{-1}$) | $8.3 \pm 9.3$ |
| $1,25(OH)_2D_3$ (pg ml$^{-1}$) | $9.7 \pm 6.7$ |
| ALP (U l$^{-1}$) | $170 \pm 178$ |
| BALP (U l$^{-1}$) | $71 \pm 108$ |
| Albumin (g per 100 ml) | $3.7 \pm 0.5$ |

ALP, total alkaline phosphatase, BALP, bone alkaline phosphatase; iCa, ionized Ca; iPTH, intact parathyroid hormone.

55 $mg^2$ $dl^{-2}$ in 394 patients (74%). Table 4 shows mean serum levels of phosphorus, calcium, and Ca × P product in patient groups using various phosphate binders. Distribution of patients with respect to their serum phosphorus levels can be seen in Figure 1.

Multivariate analysis was used to determine independent correlations of different parameters with serum phosphorus levels. Serum phosphorus level was positively correlated with serum albumin ($P$=0.027) and iPTH ($P = 0.001$) and negatively correlated with age ($P$=0.033) (Table 5). Mean serum phosphorus levels were also statistically different in the older age group (>65 years) compared to the younger patients, with values of $4.5 \pm 1.1$ and $5.1 \pm 1.4$ mg per 100 ml, respectively, ($P$=0.013) (Table 6). Mean serum phosphorus levels of patients between the second and ninth decades of life are given in Figure 2. Patient distribution with respect to PTH (0–150, 150–300, and >300 pg $ml^{-1}$) can be seen in Table 7.

## DISCUSSION

Inorganic phosphorus, as an intracellular anion, is the source of adenosine triphosphate and controls the level of 2,3-diphosphoglycerate present in red blood cells.[14,15] Phosphate balance in dialysis patients depends on phosphate intake, absorption (minus phosphate binding), and dialysis removal. Therefore, one of the main goals of dialysis therapy is controlling the ESRD patient's serum inorganic phosphorus level within the recommended range of 3.5–5.5 mg per 100 ml.[16,17] In the 1993 USRDS Dialysis Morbidity and Mortality Study, 46.4% of hemodialysis patients had a serum phosphorus level within that desired range.[18] In a more recent study, data from hemodialysis centers across seven countries including France, Germany, Italy, Japan, Spain, United Kingdom, and United States have shown good control of serum phosphorus in 40.8% (DOPPS I, 1996–2001) and 44.4% (DOPPS II, 2002–2004) of patients, and the results were not dramatically different among the countries. The majority of patients not within guideline ranges had high serum phosphorus levels (51.6% in DOPPS I, 46.7% in DOPPS II).[19] Today, the mean serum phosphorus level of the maintenance hemodialysis patient population in the United States is 6.2 mg per 100 ml and an alarming 60% of patients have a serum phosphorus level in excess of the 5.5 mg per 100 ml, which is the upper limit recommended by K/DOQI guidelines.[6] All these data suggest that with standard three times weekly maintenance hemodialysis, despite the use of dietary measures and phosphate binders, our success in maintaining normal serum phosphorus levels in ESRD patients is unsatisfactory. On the other hand, patients with some residual renal function[20] or who are undergoing more frequent hemodialysis such as short daily dialysis or long nocturnal hemodialysis may have a better chance at achieving the desired levels of serum phosphorus.[7–9] Although there are not enough data, chronic PD as a continuous dialysis modality has an expected theoretical superiority over intermittent hemodialysis. Indeed, some early reports have supported the modality-related advantage of PD over hemodialysis.[12] A more recent study performed in 252 Chinese CAPD patients found that 35.7% of patients had serum phosphorus levels of 5.6 mg per 100 ml or greater, among whom 18.6% had a serum phosporus level greater than 6.5 mg per 100 ml.[13] Our relatively larger group of chronic PD patients from 24 centers located in Turkey, Greece, and Canada has shown a comparable performance in phosphorus control with serum phosphorus levels within the desirable limits in 58% of patients. In our patient group of 530 patients, the mean serum phosphorus level was $4.9 \pm 1.3$ mg per 100 ml. We were not able to show any relationship between the type of phosphate binder used and the success of phosphorus control. Patients on calcium

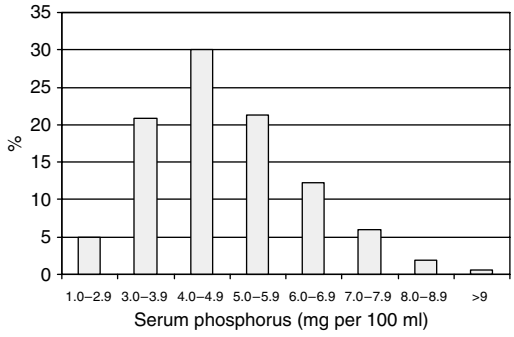


**Figure 1 | Distribution of patients with respect to serum phosphorus level ($n = 530$).**

**Table 4 | Distribution of serum levels of phosphorus, calcium, and Ca × P product in the study group as a whole and when grouped by phosphate binder type or non-phosphate binder user status**

| | P (mg per 100 ml) | | | | $Ca^{2+}$ (mg per 100 ml) | | | | Ca × P product ($mg^2$ $dl^{-2}$) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Patient number | <3.5 | 3.5–5.5 | >5.5 | *P*-value | <8.5 | 8.5–9.5 | >9.5 | *P*-value | <55 | >55 | *P*-value |
| Calcium carbonate | 19 | 84 | 48 | NS | 22 | 53 | 80 | NS | 97 | 56 | NS |
| Calcium acetate | 22 | 93 | 41 | NS | 19 | 58 | 78 | NS | 126 | 28 | NS |
| Sevelamer | | 6 | 24 | NS | | 16 | 16 | NS | 17 | 22 | NS |
| Non-users | 33 | 124 | 36 | NS | 25 | 87 | 76 | NS | 154 | 36 | NS |
| Total (*n*=530) | 74 | 307 | 149 | NS | 66 | 214 | 250 | NS | 394 | 136 | NS |
| Total (%) | 14 | 58 | 28 | | 12 | 40 | 48 | | 74 | 26 | |

NS, statistically not significant.
Non-users: patients who are not on any type of phosphate binder.

**Table 5 | Correlation of serum phosphate levels with relevant clinical and laboratory parameters**

| | Serum phosphorus level | |
|---|---|---|
| | *P*-value | Standardized coefficient-$\beta$ |
| Age | 0.033* | −0.167 |
| Albumin | 0.027* | 0.202 |
| ALP | 0.100 | −0.216 |
| BALP | 0.819 | −0.030 |
| iPTH | 0.001* | 0.266 |
| *Kt/V* | 0.155 | −0.112 |

ALP, total alkaline phosphatase; BALP, bone alkaline phosphatase; iPTH, intact parathyroid hormone. *$P<0.05$.

**Table 6 | Mean serum phosphorus levels in patients older and younger than 65 years**

| Age (years) | *n* | P (mg per 100 ml) |
|---|---|---|
| <65 | 344 | 5.1 ± 1.4* |
| >65 | 185 | 4.5 ± 1.1 |

*$P$=0.013 vs older patients.

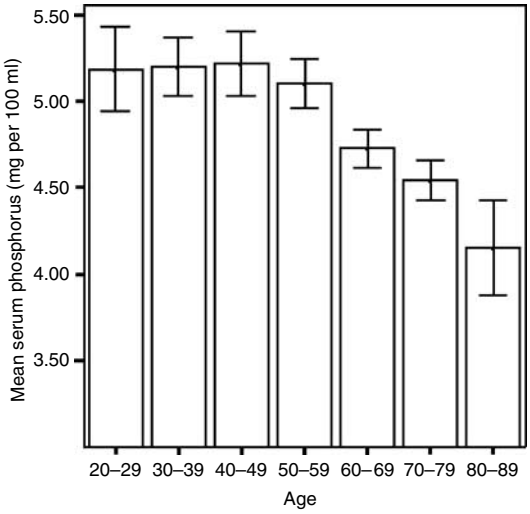


**Figure 2 | Mean serum phosphorus levels by age.**

acetate, calcium carbonate, or sevelamer had equally efficient serum phosphorus control rates with no statistical difference among the three groups.

Our overall group had a total weekly creatinine clearance of 2.21 ± 0.65 l and a mean daily urine volume of 550 ± 603 ml, indicating good dialysis adequacy and residual renal function. But interestingly, serum phosphorus levels in our patient group did not show any statistically significant correlation with either of these parameters. In our study, 72.9% of oligoanuric patients had a serum phosphorus level ⩽5.5 mg per 100 ml. Wang *et al.*[13] have shown that in Chinese CAPD patients, serum phosphorus levels were 5.6 mg per 100 ml or greater in 44.0% of anuric patients versus 28.7% of patients with RRF. As discussed above, in

**Table 7 | Distribution of the study group patients with respect to serum iPTH levels**

| iPTH (pg ml$^{-1}$) | *n* | % |
|---|---|---|
| 0–150 | 256 | 48 |
| 150–300 | 124 | 24 |
| >300 | 150 | 28 |
| Total | 530 | 100 |

iPTH, intact parathyroid hormone.

hemodialysis patients, dialysis adequacy has been an important factor in determining the success of phosphorus control.[7,8,20] But in our study, we were unable to show any correlation between PD adequacy and serum phosphorus levels. This finding may be related to the fact that in the great majority of our patients, weekly creatinine clearance values were within or even above suggested adequacy limits for chronic PD patients.

Another interesting point derived from our data was the negative correlation between serum phosphorus level and age (Table 4). We think that the relationship between age and serum phosphorus levels may originate from age-related changes in nutrition and eating habits. Results of a study performed by Nakamoto *et al.*[21] suggest that elderly CAPD patients may have a lower plasma albumin level compared with younger patients. However, the authors attribute that finding to a higher albumin loss from the peritoneum in elderly patients than in middle-aged and younger patients.[21] A later start in dialysis may affect eating habits through adverse changes in physical abilities due to chronic neuromuscular disorders such as Parkinson's disease or a previous stroke and depression,[22] all contributing in some degree to malnutrition and resulting in lower serum phosphate levels in the elderly. As an important cause of mortality and morbidity in dialysis patients, malnutrition is considered to be an even more important factor in the elderly population.[23] However, data derived from our study did not suggest any age-dependent decrease in serum albumin levels in chronic PD patients. On the other hand, age-related decrease in serum inorganic phosphorus may be a contributing factor in the mechanism of low turnover bone disease known to be more frequent in elderly uremics.[24] Nevertheless, some studies do not support any relationship between age and low turnover bone disease.[25]

Another age-related factor that is known to be important in bone metabolism is the antiaging protein 'klotho'. Besides being an antiaging protein, klotho is also involved in mineral and vitamin D metabolism. Klotho gene mutation leads to a syndrome strangely resembling the symptoms seen in patients undergoing dialysis, including hypoactivity, sterility, skin thinning, muscle atrophy, osteoporosis, vascular calcification, soft-tissue calcification, defective hearing, thymus atrophy, pulmonary emphysema, ataxia, abnormalities of the pituitary gland, hypoglycemia, hyperphosphatemia, and paradoxically high-plasma calcitriol levels.[26] In mice, an increase in dietary phosphorus may modulate and increase

klotho gene expression, and symptoms of klotho deficiency seem to be decreasing most likely through increasing klotho gene expression.[27] Moreover, osteoprotegerin, a secreted factor that inhibits osteoclastogenesis, is upregulated in klotho-deficient mice, suggesting an independent impairment of osteoblast and osteoclast differentiation, which could be the a cause of low bone turnover osteopathy.[26] We believe that we need more studies that have been designed to investigate the relationship among phosphorus balance, bone metabolism, and the effects of klotho in a dialysis patient population.

Efficacy of calcium-based phosphate binders, namely calcium carbonate and calcium acetate, is known to be clinically satisfactory, especially when combined with adequate dialysis and dietary measures. But great concern has been expressed about their effect on raising serum calcium levels and $Ca \times P$ product. Therefore, non-calcium-based phosphate binders have been developed to avoid the unwanted effects of high serum calcium and increased $Ca \times P$ product. Elevated $Ca \times P$ product is associated with increased mortality in hemodialysis patients; especially at levels above $75\,mg^2\,dl^{-2}$, the mortality rate increases significantly.[1] In some studies, all-cause mortality rate increases, even before reaching that point, with significant increases in mortality starting at levels as low as $62.5\,mg^2\,dl^{-2}$.[28] It is also reported that for each $10\,mg^2\,dl^{-2}$ increase in $Ca \times P$ product, a 6% increase in the mortality risk and 7% increase in the risk of sudden death may be expected.[29] In our 530 chronic PD patients, $Ca \times P$ product was below the recommended K/DOQI upper limit of $\leqslant 55\,mg^2\,dl^{-2}$, with an overall mean of $46.75 \pm 14\,mg^2\,dl^{-2}$, indicating that with 31% utilization of low-calcium PD solutions, 73% of our patients were below the recommended upper limit of $Ca \times P$ product despite a predominant 92% use of calcium-containing phosphorus binders (307 versus 30 patients). This result, when compared with DOPPS I data with 68% of $Ca \times P$ products below $55\,mg^2\,dl^{-2}$, may suggest some therapeutic advantage of PD over hemodialysis regarding vascular calcification risk.[11] Indeed, results of a recent study by Sigrist *et al.* (Sigrist *et al. Nephrol Dial Transplant* 2007; **22**: 418; abstract) have shown that PD was associated with less vascular calcification compared with hemodialysis. Moreover, the authors observed that during a 2-year observation period vascular calcification showed less progression in PD patients than in hemodialysis patients.

Because of the regulatory restrictions to its use, we had a relatively small number of patients using sevelamer, which was barely enough for statistical evaluation, and some patients were not using any phosphate binders (Table 4). Patients on various combinations of phosphate binders were excluded from statistical evaluation. Interestingly, unlike earlier reports, we did not observe a higher prevalence of hypercalcemia in patients using calcium carbonate compared with those on calcium acetate as a phosphate binder.[30] Based on our results, the risk of hypercalcemia in both calcium acetate- and calcium carbonate-using PD patients seems to be equal.

In ESRD patients, hypocalcemia, hyperphosphatemia, and reduced vitamin D synthesis result in elevated levels of PTH and secondary hyperparathyroidism. The clinical consequences of increased PTH levels include renal osteodystrophy, and systemic and arterial effects that increase mortality. In contrast, in some situations such as diabetes, treatment with corticosteroids, hypoparathyroidism, immobilization, post-menopausal or age-related osteoporosis, and aluminum toxicity may result in decreased osteoblastic and osteoclastic activity in the bones, namely adynamic bone disease.[31] As a chronic renal replacement therapy, PD, however, especially when performed with traditional $1.75\,mmol\,l^{-1}$ calcium-containing PD solutions,[32] is associated with a tendency for suppression of PTH levels, resulting in adynamic bone histology.[33,34] In our study group of 530 chronic PD patients, mean iPTH level was $267 \pm 356\,pg\,ml^{-1}$, which was close to the upper margin of the acceptable range ($150–300\,pg\,ml^{-1}$) for uremic patients.[16] Forty-eight percent of those patients had a serum iPTH level less than $150\,pg\,ml^{-1}$, supporting the findings above. Only 24% of patients were found to have an iPTH level within the normal uremic level of $150–300\,pg\,ml^{-1}$, Another 28% of our patients were found to have iPTH levels of higher than $300\,pg\,ml^{-1}$.

ESRD patients are known to have low levels of $1,25(OH)_2D_3$ due to diminished conversion of $25(OH)D_3$ secondary to lack of renal 1-α-hydroxylation. On the other hand, hypoalbuminemia and presence of diabetes mellitus may also independently affect serum $25(OH)D_3$ levels, probably because of poor nutritional status associated with diabetes and that $25(OH)D_3$ is actively catalyzed to $24,25(OH)_2D$ in CRF, probably largely via extrarenal 24-hydroxylase(s).[35] Recently, $25(OH)D_3$ *per se* has attracted more attention because of the emerging literature suggesting that $25(OH)D_3$ itself exerts important and independent effects on PTH, renal bone disease, and muscle function.[36] Although 33% of our patients were on some form of vitamin D supplementation, either as $1,25(OH)_2D_3$ or 1-α-$(OH)D_3$, mean $1,25(OH)_2D_3$ and $25(OH)D_3$ levels were found as low as $9.7 \pm 6.7\,pg\,ml^{-1}$ (normal range: $15–75\,pg\,ml^{-1}$) and $8.3 \pm 9.3\,ng\,ml^{-1}$, respectively. In uremic patients, 25-hydroxyvitamin D levels within the range of $15–30\,ng\,ml^{-1}$ are considered as insufficiency, and levels below $< 15\,ng\,ml^{-1}$ indicate an important vitamin D deficiency. Based on that information, both mean $25(OH)D_3$ and $1,25(OH)_2D_3$ levels in our chronic PD patients were well below the recommended limits, and 67% were left untreated. We believe that to avoid hypercalcemia, we have been insufficient in appropriately supplementing vitamin D to our PD patients.

In conclusion, findings derived from this study show that chronic PD, when combined with dietary measures and phosphate binders, is associated with more satisfactory serum phosphate control in the majority of patients compared with comparative HD cohorts. On the other hand, vitamin D levels in our chronic PD patients were below the recommended limits and, probably for the sake of avoiding

hypercalcemia and high Ca × P products, we have been insufficient in appropriately supplementing vitamin D in our chronic PD patients.

## MATERIALS AND METHODS

This cross-sectional, multicenter study was carried in 24 centers in three countries (Canada, Greece, and Turkey) among 530 PD patients (mean age: 55 ± 16 years; mean duration of PD: 33 ± 25 months; 235 women and 295 men). iPTH (chemiluminescence method; DPC, Diagnostic Product Corporation, Los Angeles, CA, USA), $25(OH)D_3$ ($^{125}I$ radioimmunosorbent assay, DiaSorin Inc., Stillwater, MN, USA), $1,25(OH)_2D_3$ ($^{125}I$ radioimmunosorbent assay, DiaSorin Inc.), serum calcium ($Ca^{2+}$), ionized $Ca^{2+}$, phosphate ($PO_4$), total alkaline phosphatase, and bone alkaline phosphatase levels were measured by standard clinical laboratory techniques.

Patients were selected through one basic inclusion criterion: chronic PD patients who had been on PD for more than 1 year and were able to give their written informed consent in the presence of a witness. Exclusion criteria included patients being on HD for longer than 1 month during their renal replacement therapy, having a history of peritonitis within the past month, history of parathyroidectomy, and use of aluminum-containing medications longer than 3 months during the past 1 year.

### Statistical analysis

SPSS 10.0 statistical package program was used. All results are expressed as mean ± s.d. and range where appropriate. Fisher's exact test, *t*-test, or $\chi^2$ test were used for determining the differences in demographics. Pearson's coefficients were used to describe correlations between non-normal and Gaussian-distributed variables, respectively. Multivariate analysis was used to determine the independent correlations of the different parameters with serum phosphorus levels.

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