CME

clinical medicine

The Effect of a Predialysis Calcitriol Administration Protocol on Postdialysis Parathyroid Hormone Levels

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Abstract

Patients with chronic kidney disease often develop secondary hyperparathyroidism because of decreases in 1,25$(OH)_2$-vitamin D (calcitriol) levels. These changes may be ameliorated with appropriate administration of oral calcitriol during the predialysis period. A calcitriol administration protocol was used with patients beginning on June 1, 2001. Mean serum intact parathyroid hormone (iPTH), calcium, and phosphorous levels from the three months preceding and three months following initiation of dialysis were measured. A significant difference in iPTH levels between patients treated under the calcitriol protocol and patients in the control group was observed. In addition, patients treated under the protocol were more likely to receive calcitriol than those who were not. No significant difference in serum calcium or phosphorous levels was observed. Administration of calcitriol via a protocol in predialysis patients reduced iPTH levels among patients after the initiation of dialysis.

Introduction

Patients with end-stage renal disease (ESRD) frequently develop secondary hyperparathyroidism because of decreased production of 1,25$(OH)_2$-vitamin D (calcitriol) in the kidneys. As a result, patients may develop osteomalacia or osteodystrophy. The onset of secondary hyperparathyroidism occurs early in chronic renal failure. Patients with glomerular filtration rates (GFRs) as high as 60 mL/min/1.73 m^2 may begin to produce decreased levels of calcitriol, resulting in increased intact parathyroid hormone (iPTH) and increased serum phosphorous levels.[1]

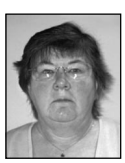
Prevention of secondary hyperparathyroidism with either oral or intravenous administration of calcitriol has been recommended for dialysis patients.[1,2] The use of calcitriol among patients with chronic kidney disease has been suggested, though evidence for its use is limited. The demonstrated benefits of predialysis calcitriol administration include a decrease in serum parathyroid levels.[3–5] The primary risk of calcitriol administration is an elevated serum calcium level. In addition, concern exists regarding the development of adynamic bone disease, which occurs with overzealous suppression of parathyroid hormone.[6]

The National Kidney Foundation has created guidelines, on the basis of expert opinion,[7] that recommend 25-hydroxyvitamin D repletion for patients with low 25-hydroxyvitamin D levels and GFRs between 15 and 60 mL/min/1.73 m^2. The guidelines further recommend the use of an active vitamin D sterol (such as calcitriol) for patients with a GFR <15 mL/min/1.73 m^2. They do not address the use of calcitriol in patients with elevated parathyroid levels and GFRs >15 mL/min/1.73 m^2.

The onset of secondary hyperparathyroidism occurs early in chronic renal failure.

A potential benefit of predialysis calcitriol administration is decreased secondary hyperparathyroidism after institution of hemodialysis. Because the development of secondary hyperparathyroidism is variable, a coordinated program of monitoring and administration would seem relevant. To examine this issue, we constructed a predialysis calcitriol administration protocol and began applying it to patients with chronic



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kidney disease preparing for dialysis. We compared patients who were treated with the protocol with those whose treatment preceded the institution of the protocol.

Methods

Beginning on June 1, 2001, our group initiated a pre-ESRD calcitriol administration protocol (Figure 1). Patients with chronic renal failure were referred by their nephrologists to our case management dietitians before starting dialysis. Levels of iPTH were assessed at the time of referral by case management dietitians, who then initiated oral calcitriol administration if indicated. Serum calcium and phosphorous levels were measured and monitored as well, and patients were observed until the initiation of dialysis. On dialysis initiation, the pre-ESRD calcitriol protocol was stopped and patients were given either intravenous calcitriol or paracalcitol with dialysis.

Before June 1, 2001, patients were monitored by individual nephrologists who monitored iPTH, calcium, and phosphorous levels with no specific coordination. The level of predialysis calcitriol was determined and adjusted by individual physicians. Patients initiating dialysis (and thus enrolled in the calcitriol protocol) after June 1, 2001 were designated a study group. Patients initiating dialysis prior to June 1, 2001 were designated a control group. Serum levels of iPTH, calcium, and phosphorous were determined for both groups before and after dialysis initiation (Table 1).

Patient records from three dialysis units were reviewed. Patients older than aged 18 years were included in the review if they had had an iPTH level checked within three months before the onset of dialysis and a level within three months after the onset of dialysis. Patients who received prior renal replacement therapy (transplantation, peritoneal dialysis, hemodialysis) or who had parathyroid disease unrelated to renal failure were excluded.

Variables collected included pre- and postdialysis serum calcium, phosphorous, and iPTH levels. Age, sex, and calcitriol dose were re-

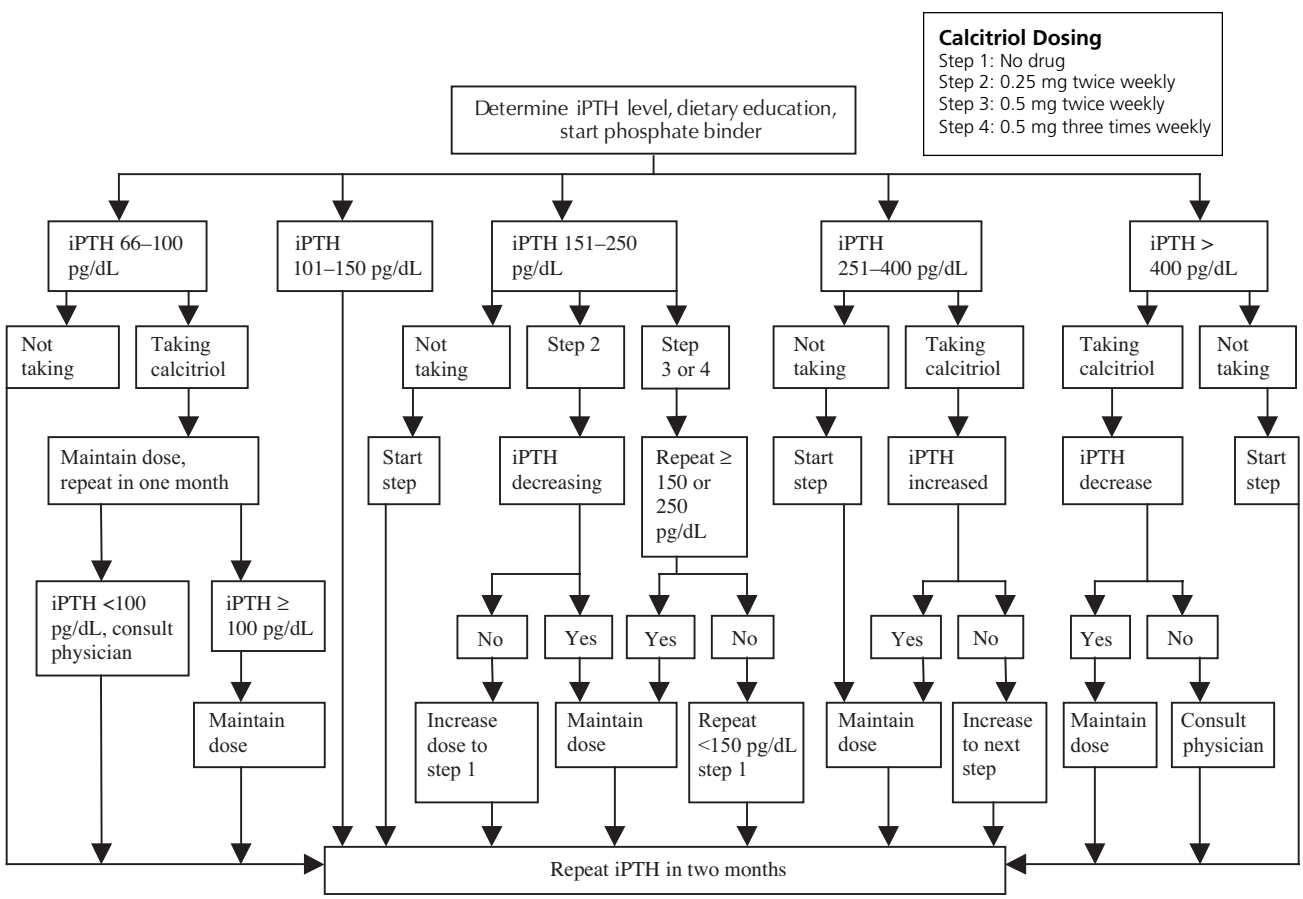

Figure 1. Calcitriol protocol, iPTH, intact serum parathyroid hormone

corded as well. Control group and study group pre- and postdialysis serum iPTH, calcium, and phosphorous levels were compared using one-way analysis of variance.

Results

Forty patients were included in the study, 24 in the control group and 16 in the study group. Fifty percent of patients (20) in the total population were male, and 50% patients in both control and study groups were male as well. The mean age of the overall population was 61.8 years, and the mean ages of study group and control group patients were 60.6 years and 62.6 years, respectively. Mean estimated GFR at the beginning of the study for the study group was 19.2 mL/min per 1.73m^2 and for the control group was 18.7 mL/min per 1.73m^2.

There was no significant difference in the mean iPTH between the study and control groups during the three-month period preceding the initiation of dialysis. After starting dialysis, patients in the study group had lower mean iPTH levels than those in the control group. The difference was significant during the first month after dialysis but not during the second month (Figure 2).

There was no significant difference between mean serum calcium and phosphorous levels in the study and control groups. Patients in both groups had little overall change in serum calcium levels throughout the course of the study (Figure 3). Patients in both groups had an overall increase in mean serum phosphorous levels from the predialysis to postdialysis periods (Figure 4).

Twenty-two patients within the total population received calcitriol during the three months before the initiation of dialysis. A majority of patients in the study group received calcitriol and a minority of patients

Table 1. Characteristics and serum calcium, phosphorous, and intact parathyroid hormone levels for 40 adult hemodialysis patients before and after dialysis initiation

	Study	Control	P value
Age in years Mean (± SD)	60.7 (19.1)	62.6 (15.3)	.72
Sex Male n (%) Female n (%)	12 (50) 12 (50)	8 (50) 8 (50)	1.00
Intact parathyroid hormone levels (mg/dL) Mean (minimum–maximum)			
90–60 days before dialysis	462 (86–1,426)	368 (26–1,130)	.34
59–30 days before dialysis	426 (101–968)	405 (76–1,096)	.80
29–0 days before dialysis	278 (93–635)	606 (128–1,190)	.06
1–30 days of dialysis	268 (106–623)	609 (331–935)	.02
31–60 days of dialysis	335 (222–553)	547 (156–939)	.56
Calcium levels (mg/dL) Mean (minimum–maximum)			
90–60 days before dialysis	8.7 (7.8–10.3)	8.7 (7.3–9.8)	.72
59–30 days before dialysis	8.7 (7.3–10.0)	8.8 (7.7–9.9)	.59
29–0 days before dialysis	8.6 (7.6–10.2)	8.2 (4.6–9.7)	.19
1–30 days of dialysis	8.2 (7.6–11.3)	8.8 (8.0–9.6)	.15
31–60 days of dialysis	8.3 (7.0– 9.3)	8.7 (5.1–10.0)	.35
Phosphorous levels (mg/dL) Mean (minimum–maximum)			
90–60 days before dialysis	5.1 (2.7–7.1)	5.1 (3.7–7.3)	.96
59–30 days before dialysis	5.3 (2.7–9.1)	5.5 (3.2–7.6)	.62
29–0 days before dialysis	5.9 (3.3–10.2)	5.7 (4.6–7.9)	.55
1–30 days of dialysis	5.4 (3.3–7.8)	5.8 (3.6–8.7)	.49
31–60 days of dialysis	6.6 (5.3–7.5)	5.6 (3.4–7.8)	.14
Calcitriol prescription before dialysis n (%)			
Yes	12 (54.5)	4 (22.0)	.04
No	10 (45.5)	14 (88.0)	

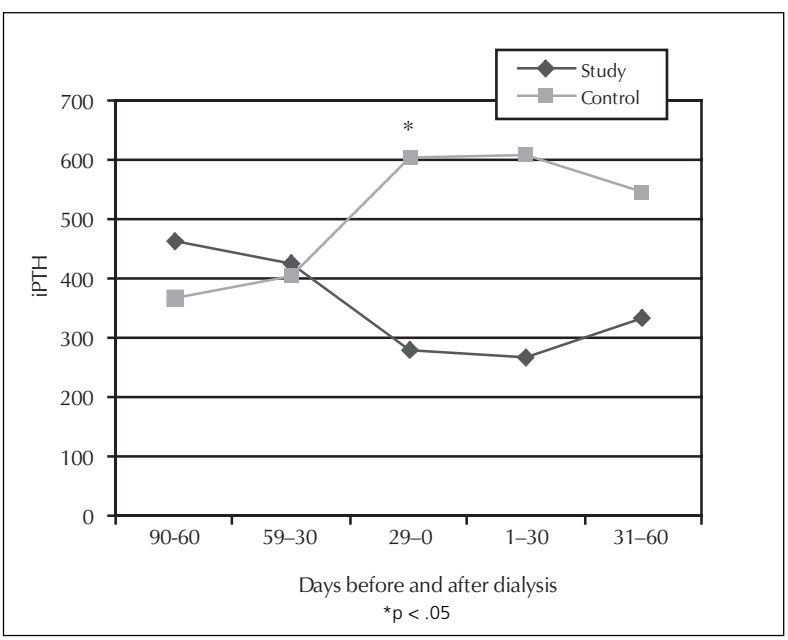

Figure 2. Mean intact parathyroid hormone (iPTH) levels.

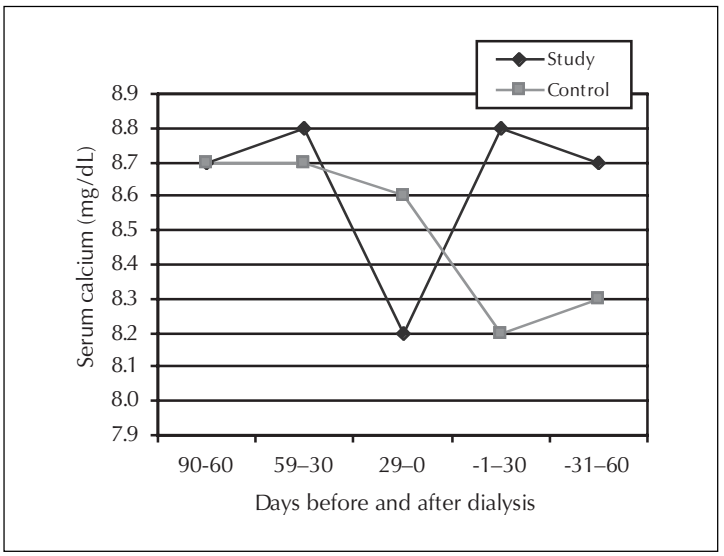

Figure 3. Mean serum calcium (mg/dL). There was no statistically significant difference between the groups.

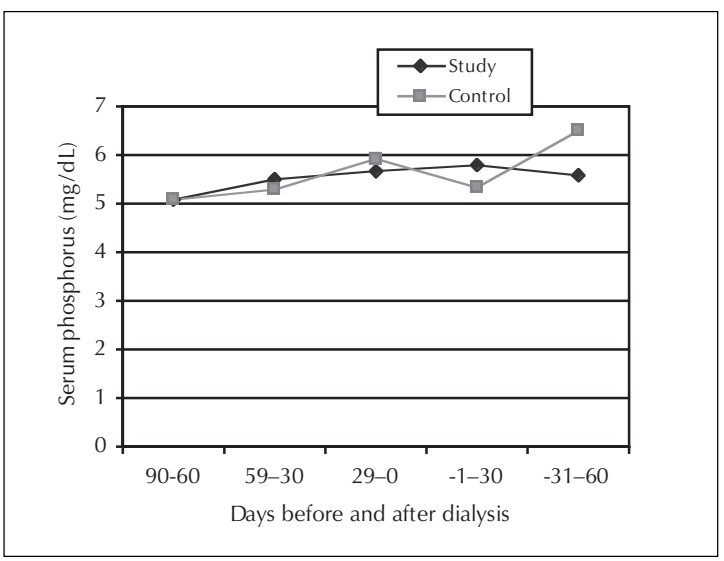

Figure 4. Mean serum phosphorus levels (mg/dL). There was no statistically significant difference between the two groups.

Table 2. Mean serum intact parathyroid hormone, calcium, and phosphorous levels 1 to 30 days after hemodialysis initiation

	iPTH[a] (mg/dL)	Calcium (mg/dL)	Phosphorous (mg/dL)
Calcitriol			
Study group	313	8.8	6.0
Control group	520	9.0	6.2
No calcitriol			
Study group	128	8.6	4.7
Control group	428	9.1	5.0

[a] iPTH, intact parathyroid hormone.

in the control group received it. Patients in the study group who received calcitriol had a lower mean iPTH level than those in the control group within the first month after the initiation of dialysis. Patients in the study group who did not receive calcitriol had a lower mean iPTH level than those in the control group. Patients in both control and study groups who received calcitriol had lower mean serum calcium levels than those who did not receive calcitriol during the month after initiation of dialysis (Table 2).

Discussion

This study examined the benefit of applying systematic monitoring of serum iPTH, calcium, and phosphorous levels and systematic administration of calcitriol in a pre-ESRD population. Patients referred to case management dietitians had significantly lower iPTH levels after the initiation of dialysis than those not monitored under the protocol. There was no significant difference in serum calcium and phosphorous levels between the two groups. The most obvious explanation for the difference would seem to be careful monitoring and the administration of calcitriol when appropriate.

The difference in iPTH levels at the onset of dialysis did not seem to reflect the indiscriminate use of calcitriol (as evidenced in Table 2), although patients monitored under the protocol were much more likely to receive calcitriol than those who were not. Patients in the study group who did not receive calcitriol appear to have had low average iPTH levels (mean iPTH within the first 30 days after initiation of dialysis was 128 mg/dL) mitigating against its use. The reason for the lack of patients in the control group who did not re-

ceive calcitriol seems likely to reflect oversight, or a lack of realization of the potential importance of predialysis calcitriol administration. The fact that there was a better outcome (lower postdialysis iPTH levels) despite less calcitriol being administered in the study group suggests that careful monitoring and appropriate administration are at least as important as simply prescribing calcitriol to a population with chronic kidney disease.

The lack of significant differences in mean calcium or phosphorous levels may have resulted from the use of phosphate binders in both groups. We could not adequately assess the predialysis use of phosphate binders in the control group, because a prescription is not required for many kinds of phosphate binders, leaving no evidence in the medical records of phosphate binder use.

When managing the treatment of patients with chronic kidney disease, nephrologists confront a variety of issues, ranging from dietary education to placement of access and medication changes. Monitoring bone disease and secondary hyperparathyroidism may be considered less of a priority than other issues during the period leading up to dialysis. Oversight of bone disease management with the use of a protocol to monitor serum calcium, phosphorous, and iPTH levels may be a means for avoiding this problem. Dietitians familiar with bone disease issues, patient education, and calcitriol use seem an appropriate group to help in this endeavor. Our experience confirms this assertion.

Prior studies have compared different regimens of calcitriol administration and have found benefits in decreasing the use of multiple oral boluses and single weekly boluses of calcitriol. Our protocol was derived from a review of other studies as well as clinical experience. Other protocols may be effective as well.

Limitations

This study is retrospective, includes patients from only three dialysis units, and excludes patients for whom there were not predialysis iPTH measurements, which may have led to selection bias. There might have been a significant difference in calcium and phosphorous levels between the study and control groups that was not evidenced because of insufficient numbers of patients. Parathyroid hormone levels are an indirect measurement of future bone disease, potentially a more relevant clinical outcome. Finally, we studied iPTH, calcium, and phosphorous levels within a fairly short period preceding dialysis. Variation in the outcomes of patients monitored very early in the course of their disease may be markedly different than for those monitored at later stages.

Future Directions

It is surprising how little clinical literature is available regarding the administration of predialysis calcitriol. Long-term studies need to be conducted of patients with chronic kidney disease, examining when, how often, and how much calcitriol should be administered to prevent bone disease. In addition, the role of phosphate binder administration warrants study. ❖

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When managing the treatment of patients with chronic kidney disease, nephrologists confront a variety of issues, ranging from dietary education to placement of access and medication changes.

Hope

Hope is necessary in every condition.

— Samuel Johnson, 1709-84, English poet, essayist, biographer, and lexicographer