
Management of Bone Disease, Calcium, Phosphate and Parathyroid Hormone

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Vitamin D in dialysis patients

Date written: August 2005
Final submission: January 2006
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GUIDELINES

- a. Oral calcitriol, either daily or intermittent “pulsed”, is effective at lowering Parathyroid hormone (PTH) levels in patients on peritoneal dialysis. (Level II evidence)
- b. Vitamin D and its analogues, either given orally daily, orally intermittently or intravenously, are effective at lowering PTH levels in patients on haemodialysis. (Level I/II evidence)

SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on Level III and IV evidence)

- Vitamin D therapy should be avoided when serum phosphate and/or calcium levels are significantly elevated, in order to reduce the risk of further elevation of calcium x phosphate product and excess vascular and extravascular calcification.
- Patients on vitamin D therapy must have regular monitoring of serum calcium, phosphate and PTH levels.
- Oral calcitriol is effective for the prevention or treatment of hyperparathyroidism in most patients on haemodialysis (HD) or peritoneal dialysis (PD).
- Oral calcitriol can be effectively used either daily or less frequently as pulsed therapy, although there is insufficient evidence to say that the latter is superior to the former, either in terms of lowering PTH or reducing adverse effects.
- Intravenous calcitriol may be more effective at lowering PTH levels and be less likely to cause hypercalcaemia, but the lack of well-designed studies of sufficient size prevent a more definitive statement.
- Consideration may be given to using intravenous calcitriol when high PTH levels are resistant to oral calcitriol, or if patient compliance with self-administered oral calcitriol is in doubt.
- Vitamin D analogues are effective at lowering PTH, but human studies proving their effectiveness with fewer side-effects (hypercalcaemia and/or

hyperphosphataemia) are either lacking or are not definitive. On the basis of current evidence, there is little reason to recommend their use over either conventional oral calcitriol or intravenous calcitriol.

- Use of alternatives to oral calcitriol (intravenous or the vitamin D analogues) needs to be balanced against their significantly higher costs

Background

Active vitamin D is a cornerstone for the prevention and treatment of hyperparathyroidism in patients on dialysis. It chiefly works by directly inhibiting the production and release of PTH from the parathyroid glands, as well as increasing serum calcium levels by stimulating calcium absorption from the gut. In parallel, it stimulates phosphate absorption, and so its adverse effects include hypercalcaemia, hyperphosphataemia, and oversuppression of PTH levels.

There is a clear and important place for the use of vitamin D in patients on both PD and HD. Unfortunately, the literature while relatively large, is dominated by poorly designed or insufficiently large studies to accurately define the ideal ways to use vitamin D. Despite this deficiency, certain patterns of use have evolved, often without clear evidence supporting them.

The objectives of this guideline are to summarise the evidence in favour of the use of vitamin D in patients on dialysis, and 2 make recommendations about the relative merits of the various types and modes of administration of vitamin D therapy.

Search strategy

Databases searched: MeSH terms for chronic kidney disease were combined with MeSH terms and text words for bone disease, then combined with MeSH terms and text words for vitamin D, and then combined with the Cochrane highly sensitive search strategy for randomised controlled trials. The search was carried out in Medline (1966 – January Week 2 2005). The Cochrane Renal Group Trials Register was also searched for trials not indexed in Medline.

Date of searches: 8 February 2005; 16 February 2005.

What is the evidence?

Peritoneal dialysis

Most publications about vitamin D therapy in dialysis patients are descriptions of studies conducted in the haemodialysis (HD) population. This in part reflects the fact that HD is more common than peritoneal dialysis (PD) in most countries (particularly in the USA, from where most of the literature comes). The literature skewing has also to some degree occurred because it is impractical to use intravenous vitamin D or vitamin D analogues in PD patients.

Despite the limited literature in PD, there is sufficient to make some recommendations. These have obvious similarities to those guidelines proposed for predialysis patients, with more emphasis on treatment rather than prevention of renal bone disease (assuming it is established to some degree when a patient commences PD).

There is also a higher incidence of low bone turnover/low PTH levels/dynamic bone disease in PD patients compared to haemodialysis patients. This needs to be taken into account when recommending vitamin D therapy in this group.

One study specifically in PD patients, compared pulsed and daily oral calcitriol (Moe SM et al 1998), and concluded that they were equally efficacious at suppressing PTH levels. A further study by Gadallah MF et al (Adv Perit Dial 2000) compared pulse oral and pulse intraperitoneal calcitriol, and concluded that the latter was marginally superior in terms of lower PTH levels and less bone disease.

A firm recommendation regarding the optimal route and frequency of administration of calcitriol in PD patients is not possible based on these two studies alone, but the evidence is consistent with advocating vitamin D therapy in this patient group for management of hyperparathyroidism and renal bone disease. The need for careful monitoring and dose adjustments is comparable to the recommendations in predialysis patients.

Haemodialysis

The regular and convenient intravenous (IV) access intrinsic to HD allows the option of using IV vitamin D and IV vitamin D analogues that is not practical for other patients with renal impairment. The options for vitamin D therapy on HD therefore are daily oral calcitriol, pulse oral calcitriol, pulse IV calcitriol, and pulse IV vitamin D analogues.

The popularity of pulse IV vitamin D or analogues in the USA is also partly cost-driven, in that it qualifies for a financial reimbursement as a procedure. Oral vitamin D (whether daily or pulse) does not, despite the fact that it is considerably cheaper than the IV alternatives.

A further potential advantage of pulse vitamin D therapy (oral or IV) in HD patients is that it can be given under supervision at the end of a dialysis session, which should improve patient compliance.

The key question however, is whether there are medical advantages with any of the forms of vitamin D therapy in HD patients. While it cannot be disputed that each is effective at reducing PTH levels and treating renal bone disease, it is less clear from the published literature whether one approach is more efficacious than others. Based on the less than ideal information available, a reasonable approach may be to use the less expensive oral vitamin D (daily or pulse) for most patients, and reserve the more expensive IV options for resistant cases.

Daily versus pulsed oral calcitriol in haemodialysis

Three randomised, controlled trials have compared daily oral and intermittent oral calcitriol in dialysis patients (HD and PD) (Moe et al 1998, Herrmann P et al 1994, Nephron 1994, Caravaca F et al 1995). A meta-analysis failed to show superiority of either therapy. Unfortunately, two of the studies (Herrmann and Moe) mainly included patients with only mild hyperparathyroidism (PTH < 66.0 pmol/L), and so the potential role of intermittent oral therapy in severe hyperparathyroidism is unclear.

Oral versus Intravenous calcitriol in haemodialysis

There have been more studies comparing intermittent IV calcitriol with oral calcitriol (either daily or intermittent), although variations in trial design, dosage and intervals make comparison between them difficult. Initial enthusiasm for IV calcitriol was based on small, non-randomised, inadequately controlled studies.

A meta-analysis of 4 trials of randomised, controlled or cross-over design comparing intermittent IV with oral therapy (Bacchini G et al, Nephron 1997; 77: 267–272; Indridason OS et al, Kidney Int 2000; 57: 282–292; Fischer ER et al, Clin Nephrol 1993; 40: 216–220; Liou HH et al, Miner Electrolyte Metab 1994; 20: 97–102) concluded that IV was more effective at suppressing PTH levels (K-DOQI guidelines, AJKD 2003; 42, number 4, supplement 3: page 96). However, two of the trials only included patients with mild hyperparathyroidism (average PTH at entry < 44.0 pmol/L). Two other trials enrolling patients with more severe hyperparathyroidism (Quarles LD et al 1994, Levine BS et al 1996) had too few patients to complete the study to qualify for meta-analysis.

Another meta-analysis published in 2003 (Mazess RB et al 2003) examined 21 trials comparing IV with oral calcitriol in HD patients. Most studies had severe limitations, most commonly being small numbers. In 10 of the 15 studies that efficacy was assessed, there was no difference between IV and oral dosing. IV produced faster and/or greater suppression of PTH levels in 5 studies, but in 2 of these, the IV dose was substantially greater than the oral dose. In 19 of the 21 articles the oral dose used was only half or less than the IV dose due to the lower bioavailability of oral calcitriol. The authors concluded that meaningful comparison requires larger, longer studies with therapeutically equivalent dosing.

The uncertainty about clinical advantages of IV vs oral calcitriol needs also to be balanced against the significantly higher costs (several fold) of the IV preparation.

Despite these differences in interpretation of the literature, the KDOQI guidelines state: “The intermittent, intravenous administration of calcitriol is more effective than daily oral calcitriol in lowering serum PTH levels (EVIDENCE)”. An alternative (and less costly) interpretation could be phrased: “Oral calcitriol is effective for lowering PTH levels in the majority of patients. A trial of IV calcitriol may be warranted in those patients resistant to the effects of oral calcitriol”.

Vitamin D analogues in haemodialysis

Important limitations of vitamin D therapy are hypercalcaemia and worsening hyperphosphataemia due to stimulation of calcium and phosphate absorption from

the gut. This is particularly important in the light of the increasingly clear data showing that an elevated calcium/phosphate product is associated with a higher mortality rate. For this reason, considerable effort has gone into developing analogues of vitamin D that retain the inhibitory effect on PTH production and release, while diminishing or even abolishing the calcaemic and phosphataemic effects.

Several such analogues are now available and in use – paricalcitol and doxercalciferol (predominantly in the USA), and maxicalcitol and falecalcitol (predominantly Asia). In animal models they effectively suppress PTH levels while having less calcaemic and phosphataemic effects than calcitriol.

Placebo-controlled human studies with the vitamin D analogues have shown that they effectively suppress PTH levels. Of concern, though, is that they were no different to calcitriol in terms of phosphataemic effect (Martin KJ et al 1998, Frazao JM et al 2000, Morita A et al 1996, Shimamatsu K et al 1981).

There is also a notable paucity of studies in humans comparing vitamin D analogues with each other or with calcitriol.

There has been one published study comparing IV paricalcitol (19-nor-1 α , 25-dihydroxyvitamin D₂) with IV calcitriol for suppression of PTH levels in HD patients (Sprague SM et al 2003). A total of 263 patients were randomised to a dose-escalating protocol of either treatment for up to 32 weeks. While those in the paricalcitol arm reached the primary end point (50% reduction of baseline PTH) faster, by the end of the study there was no significant difference in the proportion of patients achieving that mark. There was also no difference in the proportion of patients who developed hypercalcaemia or an elevated calcium/phosphate product (secondary endpoints), although those in the paricalcitol group had less sustained hypercalcaemia or elevated product. There was no difference in hyperphosphataemia between the two groups. Those in the calcitriol arm had a greater reduction in alkaline phosphatase levels. The study was conducted in 1995 and 1996, but not published until 2003. Criticisms include that there was a low PTH level for eligibility (> 33 pmol/L) and that there was a fixed dose ratio of the two agents that favoured paricalcitol by 4:1.

There is no outcome data from this or other randomised studies with which to assess the clinical impact of vitamin D analogues. A widely quoted retrospective analysis of survival of HD patients in the USA concluded that those who received paricalcitol appeared to have a significant survival advantage over those receiving calcitriol (mortality rate 0.180 per person-year vs. 0.223, $p < 0.001$) (Teng M et al 2003). Of note, the mortality rates in both groups (16% and 20% at 1 year) were both higher than that calculated by the ANZDATA database (13.6% at 1 year, 2003 report), despite the almost complete lack of use of either agent in Australia and New Zealand. This historical cohort study was not randomised, and a prospective, randomised study is needed to explore this important observation.

The lack of good studies comparing vitamin D analogues with calcitriol prevent formulation of clear guidelines about the place of these agents in current dialysis practice. The KDOQI guidelines state: "In patients with corrected serum calcium

and/or phosphorus levels above the target range, a trial of alternative vitamin D analogs, such as paricalcitol or doxercalciferol may be warranted (OPINION)". This uncertainty needs to be balanced against the higher costs of these agents.

Summary of the evidence

There is no doubt that vitamin D or its analogues, regardless of the route of administration or frequency of dosing, are all effective at lowering parathyroid hormone levels in patients on dialysis. Unfortunately the current literature does not permit definitive statements about the advantages or otherwise of the multiple possible ways of using these agents.

What do the other guidelines say?

Kidney Disease Outcomes Quality Initiative: Extensive recommendations, refer to— guideline 8B, pages S92 to S99.

UK Renal Association: No recommendation.

Canadian Society of Nephrology: No recommendation.

European Best Practice Guidelines: No recommendation.

International Guidelines: No recommendation.

Implementation and audit

No recommendation.

Suggestions for future research

No recommendation.

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Appendices

Table 1 Characteristics of included studies

Study ID (author, year)	N	Study Design	Setting	Participants	Intervention (experimental group)	Intervention (control group)	Follow up (months)	Comments
Bacchini et al, 1997	20	Randomised controlled clinical trial	Hospital, Italy	20 chronic HD patients	Pulse oral calcitriol	IV calcitriol	4	
Caravaca et al, 1995	33	Randomised controlled clinical trial	University Hospital, Spain	33 secondary hyperparathyroidism patients with basal serum intact PTH over 4 x upper normal limit	Daily oral calcitriol	Intermittent oral calcitriol	10 wk	Third arm of IV calcitriol
Fischer et al, 1993	11	Prospective crossover randomised controlled clinical trial	Hospital, Australia	11 HD patients on maintenance calcitriol	IV calcitriol	Oral calcitriol	8	
Frazao et al, 2000	211	Randomised controlled clinical trial	18 HD units , US	138 HD patients with moderate to severe secondary hyperparathyroidism	Intermittent oral doxercalciferol	Placebo	8	
Gadallah et al, 2000	76	Randomised controlled clinical trial	University Hospital, US	76 CCPD patients	Intraperitoneal calcitriol	Oral calcitriol	48	

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Herrmann et al, 1994	45	Randomised controlled clinical trial	6 dialysis centres, Germany	45 dialysis patients with elevated 1,84-iPTH	0.75 µg calcitriol, daily continuous	Twice weekly calcitriol, intermittent	3	
Indridason et al, 2000	52	Randomised controlled clinical trial	5 dialysis units, US	52 patients (PTH 150 – 600 pg/mL)	Daily oral calcitriol	Calcium carbonate	10	Three arm parallel trial, with third arm intervention of intermittent IV calcitriol
Liou et al, 1994	10	Randomised crossover controlled clinical trial	Hospital, Taiwan	10 HD patients with secondary hyperparathyroidism	IV calcitriol	Oral calcitriol	3	
Martin et al, 1998	78	Randomised controlled clinical trial	11 dialysis centres, US	78 ESRD patients on HD	Paricalcitol	Placebo	3	
Moe et al, 1998	21	Randomised controlled clinical trial	University Hospital and Veterans Administration Hospital, US	18 CAPD patients with mild to moderate secondary hyperparathyroidism	Pulse oral calcitriol	Daily oral calcitriol	6	
Quarles et al, 1994	19	Randomised controlled clinical trial	Hospital, US	19 HD patients with severe hyperparathyroidism	IV calcitriol with oral placebo	Pulse oral calcitriol and IV placebo	9	
Sprague et al, 2003	266	Randomised controlled clinical trial	27 centres, US, Netherlands, Spain, Switzerland	263 ESRD patients on chronic HD	Paricalcitol	Calcitriol	8	

Table 2 Quality of randomised trials

Study ID (author, year)	Method of allocation concealment	Blinding			Intention-to-treat analysis	Loss to follow up (%)
		(participants)	(investigators)	(outcome assessors)		
Bacchini et al, 1997	Not specified	No	No	Not stated	Unclear	0.0
Caravaca et al, 1995	Not specified	No	No	Not stated	No	21.2
Fischer et al, 1993	Not specified	No	No	Not stated	Unclear	0.0
Frazaio et al, 2000	Not specified	Yes	Yes	Yes	Yes	28.3
Gadallah et al, 2000	Alternating, based on date of enrolment into PD programme	No	No	Not stated	No	66.3
Herrmann et al, 1994	Random numbers	No	No	Yes	No	84.4
Indridason et al, 2000	Permuted block	No	No	No	No	19.2
Liou et al, 1994	Not specified	No	No	Not stated	Unclear	0.0
Martin et al, 1998	Not specified	Yes	Yes	Not stated	Unclear	0.0
Moe et al, 1998	Random numbers	No	No	Not stated	No	14.3
Quarles et al, 1994	Random numbers	Yes	Yes	Yes	Unclear	10.5
Sprague et al, 2003	Not specified	Yes	Yes	Not stated	Unclear	1.1

Table 3 Results for continuous outcomes

Study ID (author, year)	Outcomes	Intervention group (mean [SD])	Control group (mean [SD])	Difference in means [95% CI]
Bacchini et al, 1997	Calcium (mmol/L) at 4 mo	1.38 (0.08)	1.31 (0.10)	0.07 (95%CI: -0.01, 0.15)
	Phosphorus (mmol/L) at 4 mo	1.72 (0.40)	1.54 (0.34)	0.18 (95%CI: -0.15, 0.51)
	Mean serum PTH mild / moderate	136 (88)	80 (58)	56.0 (95%CI: -14.15, 126.15)
Caravaca et al, 1995	Daily oral vs intermittent oral			
	Ionized Ca (mmol/L) after treatment	1.18 (0.06)	1.11 (0.11)	0.07 (95%CI: -0.01, 0.15)
	Total Ca (mmol/L) after treatment	2.64 (0.11)	2.48 (0.14)	0.16 (95%CI: 0.03, 0.29)
	Phosphorus (mmol/L) after treatment	2.32 (0.23)	2.20 (0.36)	0.12 (95%CI: -0.18, 0.42)
	Alkaline Ph (IU/mL) after treatment	595 (659)	551 (378)	44.00 (95%CI: -510.02, 598.02)
	1,25(OH) ₂ vitamin D ₃ (pg/mL) after treatment	26.7 (13.8)	15.0 (10.7)	11.70 (95%CI: -0.93, 24.33)
	Basal PTH (pg/mL) after treatment	651 (361)	861 (455)	-210.00 (95%CI: -623.43, 203.43)
	Maximal PTH (pg/mL) after treatment	1669 (977)	1445 (639)	224.00 (95%CI: -624.47, 1072.47)

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	Minimal PTH (pg/mL) after treatment	348 (269)	283 (268)	65.00 (95%CI: -207.39, 337.39)
	Ca Max PTH (mmol/L) after treatment	0.93 (0.09)	0.89 (0.07)	0.04 (95%CI: -0.04, 0.12)
	Ca Min PTH (mmol/L) after treatment	1.39 (0.06)	1.32 (0.09)	0.07 (95%CI: -0.01, 0.15)
Intravenous vs intermittent oral				
	Ionized Ca (mmol/L) after treatment	1.10 (0.06)	1.11 (0.11)	-0.01 (95%CI: -0.09, 0.07)
	Total Ca (mmol/L) after treatment	2.48 (0.09)	2.48 (0.14)	0.00 (95%CI: -0.11, 0.11)
	Phosphorus (mmol/L) after treatment	2.10 (0.44)	2.20 (0.36)	-0.10 (95%CI: -0.46, 0.26)
	Alkaline Ph (IU/mL) after treatment	307 (206)	551 (378)	-244.00 (95%CI: -532.84, 44.84)
	1,25(OH) ₂ vitamin D ₃ (pg/mL) after treatment	27.6 (26.3)	15.0 (10.7)	12.60 (95%CI: -4.62, 29.82)
	Basal PTH (pg/mL) after treatment	569 (363)	861 (455)	-292.00 (95%CI: -673.35, 89.35)
	Maximal PTH (pg/mL) after treatment	1123 (691)	1445 (639)	-322.00 (95%CI: -924.34, 280.34)
	Minimal PTH (pg/mL) after treatment	201 (168)	283 (268)	-82.00 (95%CI: -292.58, 128.58)

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	Ca Max PTH (mmol/L) after treatment	0.83 (0.07)	0.89 (0.07)	-0.06 (95%CI: -0.12, 0.00)
	Ca Min PTH (mmol/L) after treatment	1.35 (0.05)	1.32 (0.09)	0.03 (95%CI: -0.04, 0.10)
Fischer et al, 1993	Metabolic bone activity EDTA/MDP	3.1 (1.66)	2.7 (1.66)	0.40 (95%CI: -0.99, 1.79)
Gadallah et al, 2000	PTH (pg/mL) at follow up	162 (271.53)	384 (584)	-222.00 (95%CI: -534.44, 90.44)
	Alkaline phosphatase (IU/L) at follow up	72 (89.10)	178 (148)	-106.00 (95%CI: -189.39, -22.61)
	Phosphorus (mg/dL) at follow up	4.7 (5.94)	6.8 (9.2)	-2.10 (95%CI: -7.38, 3.18)
	Ca x P (mg/dL) at follow up	42.1 (24.61)	63.4 (33.2)	-21.30 (95%CI: -41.15, -1.45)
	Serum Ca (mg/dL)	9.6 (6.79)	9.8 (8.4)	-0.20 (95%CI: -5.37, 4.97)
Indridason et al, 2000	PTH (pg/mL) at end of study (Oral)	125 (105.99)	160 (147.59)	-35.00(95%CI: -133.82, 63.82)
	PTH (pg/mL) at end of study (IV)	65 (45.83)	160 (147.59)	-95.00 (95%CI: -184.39, -5.61)
	BAP conc (µg/L) at end of study (Oral)	17.8 (20.12)	27.5 (23.22)	-9.70 (95%CI: -26.01, 6.61)
	BAP conc (µg/L) at end of study (IV)	10.6 (5.04)	27.5 (23.22)	-16.90 (95%CI: -30.79, -3.01)

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	Serum calcium (mg/dL) at end of study (Oral)	9.2 (1.21)	9.0 (0.93)	0.20 (95%CI: -0.56, 0.96)
	Serum calcium (mg/dL) at end of study (IV)	9.4 (0.82)	9.0 (0.93)	0.40 (95%CI: -0.16, 0.96)
	Serum phosphorus (mg/dL) at end of study (Oral)	4.9 (1.43)	3.5 (1.39)	1.40 (95%CI: 0.37, 2.43)
	Serum phosphorus (mg/dL) at end of study (IV)	5.2 (1.25)	3.5 (1.39)	1.70 (95%CI: 0.71, 2.69)
	Serum aluminium (µg/L) at end of study (Oral)	15.7 (13.68)	11.0 (4.51)	4.70 (95%CI: -1.86), 11.26)
	Serum aluminium (µg/L) at end of study (IV)	21.9 (14.44)	11.0 (4.51)	10.90 (95%CI: 4.17, 17.63)
	Serum 1,25 (OH) ₂ D ₃ conc (pg/mL) (Oral)	13.2 (12.07)	6.5 (2.12)	8.2 (95%CI: 3.09, 13.31)
	Serum 1,25 (OH) ₂ D ₃ conc (pg/mL) (IV)	15.9 (12.65)	6.5 (2.12)	9.40 (95%CI: 3.85, 14.95)
Liou et al, 1994	Ca (mg/dL) after treatment	10.2 (1.58)	10.5 (0.32)	-0.30 (95%CI: -1.30, 0.70)
	Serum phosphate (mg/dL) after treatment	5.0 (0.63)	5.3 (0.32)	-0.30 (95%CI: -0.74, 0.14)
	Alkaline phosphatase (U/l) after treatment	172 (41.11)	201 (72.73)	-29.00 (95%CI: -80.78, 22.78)

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	Intact PTH (pg/mL) after treatment	141 (132.82)	400 (101.19)	-259.00 (95%CI: -362.49, -155.51)
	C-PTH (ng/mL) after treatment	11.9 (6.64)	25.0 (10.12)	-13.10 (95%CI: -20.60, -5.60)
	Serum albumin (g/dL) after treatment	3.85 (0.22)	3.84 (0.28)	0.01 (95%CI: -0.21, 0.23)
	Magnesium (mg/dL) after treatment	2.94 (0.35)	3.08 (0.22)	-0.14 (95%CI: -0.40, 0.12)
Martin et al, 1998	iPTH (pg/ml) wk 12	406 (670.40)	592 (252.74)	-186.00(95%CI: -408.75, 36.75)
	Serum Ca (mg/dL) wk 12	9.56 (0.95)	9.02 (0.92)	0.54 (95%CI: 0.12, 0.96)
	Serum P (mg/dL) wk 12	6.35 (2.02)	5.48 (1.66)	0.87 (95%CI: 0.05, 1.69)
Moe et al, 1998	% change PTH/time	7.2 (4.2)	8.4 (4.2)	-1.20 (95%CI: -5.10, 2.70)
	Serum Ca (mmol/L)	2.59 (0.25)	2.65 (0.30)	-0.06 (95%CI: -0.32, 0.20)
	Serum P (mmol/L)	1.68 (0.58)	1.52 (0.29)	0.16 (95%CI: -0.25, 0.57)
	Serum 1,25(OH) ₂ vitamin D (pg/mL)	85.1 (49.9)	42.5 (13.7)	42.60 (95%CI: 10.25, 74.95)
	Total body Ca (DEXA) (g)	3060 (788)	2913 (550)	147.00 (95%CI: -610.08, 904.08)

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Quarles et al, 1994	Parathyroid gland size, gland number (#/patient)	3.1 (1.13)	3.0 (1.96)	0.10 (95%CI: -1.65, 1.85)
	Gland volume (cm ³ /patient)	3.3 (2.26)	2.3 (1.96)	1.00 (95%CI: -1.22, 3.22)
	Min PTH (pg/mL)	379 (316.78)	319 (226.27)	60.00 (95%CI: -209.76, 329.76)
	Ca EC ₅₀ (mmol/L)	1.24 (0.08)	1.22 (0.03)	0.02 (95%CI: -0.04, 0.08)