



Vitamin D Supplementation Dose as The Prevention of Fragility Fracture In Chronic Kidney Disease Patient: A Systematic Review

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ABSTRACT

Keywords:

Vitamin D; Supplementation;
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CKD affects more than 10% of the global population. It can cause osteoporosis and increase the risk of fractures, especially as CKD becomes more serious. In CKD, mineral and bone disorders (CKD-MBD) cause abnormalities in how the body processes vitamin D, calcium, phosphorus, or parathyroid hormone (PTH). It can also affect bone strength and cause calcium build-up in the soft tissues. Treatment usually starts with correcting the chemical abnormalities that occur in the body due to CKD-MBD before focusing on osteoporosis and fractures. A study review spanning 2010 to 2023 investigated optimal vitamin D supplementation doses in CKD patients, indicating varied outcomes influenced by factors like dosage, duration, and population characteristics. Doses ranged from 800 to 8,000 IU/day of cholecalciferol, with recommendations contingent on serum 25(OH)D levels.

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Introduction

Chronic kidney disease (CKD) is a degenerative disorder that affects more than 10% of the general population worldwide, or over 800 million people (Kovesdy, 2022). Patients with chronic renal illness are more prone to osteoporosis and fractures than the general population. The increase in fractures in people in general and those with CKD is due to bone mass loss associated with ageing (Pimentel et al., 2021). The metabolic imbalances found in CKD affect both the restructuring and mineralization processes. These imbalances are now acknowledged to manifest in the initial stages of renal disease, even when kidney function appears normal. This occurs prior to the onset of biochemical signs indicating CKD mineral and bone disorder (CKD-MBD), which typically emerges as the kidney's condition decreases. This condition affects the majority of CKD patients in stages 4 and 5 (Evenepoel et al., 2021; Khairallah & Nickolas, 2018).

CKD-MBD is a condition marked by abnormalities in the metabolism of vitamin D, calcium, phosphorus, and parathyroid hormone (PTH). It also results in problems with bone strength, bone growth, and bone mineralisation, as well as calcium build-up in soft tissues such as blood vessels (Tinawi, 2022). Lack of active vitamin D, phosphate build-up, decreased calcium absorption from the gut, as well as insufficient production of a substance called alpha

klotho by the kidneys, and increased levels of fibroblast growth factor 23 (FGF23) all contribute. All these factors together lead to secondary hyperparathyroidism and structural changes in the bones, resulting in decreased bone mineral density and increased risk of fractures (Jean et al., 2017; Kuřma et al., 2021).

In CKD, the levels of circulating 25(OH)D start declining from the initial stages due to various factors. These include skin hyperpigmentation, decreased synthesis of cholecalciferol in the skin, dietary limitations, impaired absorption in the intestines, heightened catabolism of vitamin D, and significant urinary excretion of vitamin D-binding protein (DBP) and vitamin D metabolites, particularly in cases of severe proteinuria (Ketteler et al., 2017). When there's a deficiency in vitamin D, the reduction in calcium absorption is offset by a rise in PTH. This hormone promotes the conversion of 25(OH)D into 1,25(OH)2D (Ureña Torres et al., 2022).

Treatment for people with chronic kidney disease (CKD) should start by addressing the chemical abnormalities in the body associated with bone and mineral problems, before trying specific treatments for osteoporosis or fractures. The 2017 KDIGO guidelines recommend the first step to address the mineral and metabolic imbalances that occur within the body due to CKD. One of the main problems associated with CKD is secondary hyperparathyroidism, which means that the parathyroid glands in the body become overactive. This often occurs early in CKD and gets worse over time as the kidneys become less functional. The guidelines also suggest treatment for mineral balance issues such as phosphate and calcium, as well as vitamin D deficiency in stage 3-5 CKD patients who have persistently high or above-normal parathyroid hormone (PTH) levels. (Ketteler et al., 2017). We also provided the results of a study that looked at whether supplementing with vitamin D could help improve the outcome of such treatment.

Research Methods

Trial Design

Our study was conducted as an international cohort study, incorporating expertise-based control measures along with randomized controlled trial methodologies. Further details regarding eligibility criteria, interventions, outcomes, and statistical analyses were provided.

Search Strategy

To investigate the optimal dosage of vitamin D supplementation for preventing osteoporosis in CKD patients, we conducted a comprehensive review. This review encompassed the KDIGO 2017 clinical practice guideline update, PubMed, and Springer publications spanning from 2010 to 2023. Additionally, we scrutinized the reference lists of identified articles to uncover further relevant studies. Our search terms included "bone fragility fractures in chronic kidney disease patients," "management of osteoporosis in CKD patients," "Vitamin D supplementation for mineral and bone disease in CKD patients," "Vitamin D and renal disease," and "vitamin D as treatment of secondary hyperparathyroidism."

Following the PICOS (participants, interventions, comparisons, outcomes, and study design) principle, we focused on (P) patients with CKD, particularly those exhibiting signs of secondary hyperparathyroidism; (I) the dosage of vitamin D supplementation; (C/O) the outcome of serum PTH levels; and (S) randomized controlled trials (RCTs) and cohort studies.

Inclusion And Exclusion Criteria

The eligible article should have the following inclusion criteria (1) RCTs about the management of osteoporosis or mineral and bone disease in CKD patients (2) CKD patients

given Vitamin D supplementation statistical outcomes on PTH level;(3) RCTs years published from 2010 until 2023. Studies were excluded if any of the following characteristics, (1) RCTS published before years of 2010; (2) no interest outcomes reported.

Results and Discussion

The studies resumed on the following table:

Table 1 The studies resumed

Study	Population	Intervention	Result
Moe SM, Saifullah A, LaClair RE et al; (2010)	This was a study conducted over 3 months, using a randomised and double-blind method, in stage 3 and 4 CKD patients who were vitamin D deficient and had problems with parathyroid hormone (PTH).	cholecalciferol (4000 IU/d × 1 month	In the cholecalciferol group, parathyroid hormone (PTH) decreased by 10% ± 31% (P = 0.16).
Marckmann P, Agerskov H et al; (2012)	We conducted a parallel double-blind intervention study in CKD patients undergoing haemodialysis (HD) and CKD patients not undergoing haemodialysis.	40,000 IU of cholecalciferol orally per week for 8 weeks	In patients not undergoing haemodialysis, a significant increase in 1,25-diOHD (n = 13, P < 0.01) and a decrease in parathyroid hormone (PTH) (n = 13, P < 0.001) could be observed.
Cupisti A, Egidi MF, Vigo V et al; (2015)	There were 405 pre-existing patients with chronic kidney disease (CKD) stages 2-4.	10,000 IU once-a-week for 12 months	25-hydroxyvitamin D levels increase and parathyroid hormone (PTH) levels decrease.
Sprague SM, Crawford PW, Melnick JZ et al. (2016)	There were 429 subjects balanced between the studies, with stage 3 or 4 CKD, secondary hyperparathyroidism, and vitamin D deficiency.	calcifediol (30 or 60 µg) equal to 1200 IU or 2400 IU/ day for 26 weeks	The reduction of iPTH by ≥30% increased gradually with treatment duration, reaching 22%, 40%, and 50% at 12, 26, and 52 weeks, respectively.
Yadav AK, Vivek K et al; (2018)	There were 120 subjects with stable stage G3-G4 chronic kidney disease (CKD), non-diabetics, both male and female, with ages ranging between 18 and 70 years.	oral dose of 300.000 IU of cholecalciferol for 16 weeks	Intact parathyroid hormone (iPTH) levels decreased in the group receiving cholecalciferol.

Westerberg A, Sterner G, Ljunggren O et al; (2018)	There were 95 patients with stage 3-4 CKD.	cholecalciferol 8000 IU/day for 12 weeks	Calcidiol levels increased to 162 ± 49 mmol/L in patients receiving cholecalciferol, while parathyroid hormone (PTH) levels remained stable.
Omrani HR, Daraizade A; 2018 ¹⁴	There were 80 patients undergoing haemodialysis with ages ranging from 30 to 85 years.	cholecalciferol (50000 units, 3 times a week) and calcitriol (0.25 µg, once a day) for 3 months	There was no significant difference between the two treatment groups. Both groups reduced iPTH levels and thus improved secondary hyperparathyroidism.

Conclusion

Our review showed that the dose of vitamin D affecting PTH concentrations which leads to treating CKD-MBD remains inconsistent between studies. This is due to various durations, dose, and population characteristics. The range dose of vitamin D(cholecalciferol) starts from 800 IU up to 8.000 IU/day. As a result, the suggested dose is based on the annual assessment's serum 25(OH)D level.

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