INPLASY

Effects of vitamin D supplements on bone metabolism in kidney transplant recipients: a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 January 2024 and was last updated on 10 January 2024.

INTRODUCTION

Review question / Objective Physicians are reluctance to prescribe vitamin D supplements among kidney transplant recipients for fear of hypercalcaemia, hyperphosphatemia or hypoparathyroidism in patients with chronic kidney disease. Aside from the general recommendations about regulating serum calcium, phosphate, and parathyroid hormone for those with chronic kidney disease, there are no specific recommends for vitamin D supplementation for kidney transplant recipients. Overall, the effects of vitamin D supplements on the prevention and treatment of abnormal bone metabolism in kidney transplant recipients are largely unproven.

In this systematic review and meta-analysis, we aimed to analysis the effects of vitamin D supplements on bone metabolism in kidney transplant recipients, for providing ideas to clinical treatment.

Condition being studied Kidney transplantation (KTx) is the effective treatment of choice for the majority of patients with end-stage renal disease (ESRD) because it can improve survival and quality of life1. Attention is increasingly focused on preventing the longer-term complications of transplantation by addressing factors that affect long-term morbidity, including weight gain, cardiovascular risk, post-transplantation diabetes mellitus, cancer, and mineral and bone disorder (MBD).

The risk of MBD in patients with chronic kidney disease(CKD) and ESRD have substantially elevated, mainly due to alterations in vitamin D, parathyroid hormone (PTH), calcium, phosphorus, and fibroblast growth factor 23. Successful KTx corrects many metabolic abnormalities related to the development of renal osteodystrophy. However, kidney transplant recipients (KTRs) can still experience persistent and complex MBD, including MBD due to long-term kidney failure, de-novo MBD, bone metabolic changes related to transplant immunosuppression (especially corticosteroids), age-related bone loss and

persistently impaired kidney function resulting in ongoing raised parathyroid gland activity. Among these factors, calcium and phosphorus metabolism disorders, secondary hyperparathyroidism (SHPT), vitamin D deficiency, bone loss and osteoporosis are common. Vitamin D deficiency may lead to decrease calcium absorption, aggravate SHPT, and bone loss eventually. Study report that one year after KTx, up to 50% of KTRs continue to have SHPT. Post-transplantation SHPT is also related to bone disease, adverse cardiovascular outcomes and poorer graft function over time8. Post-transplantation bone disease can result in fractures. The risk of fracture for KTRs is four times higher than in the general population and is increased when compared with haemodialysis patients. The fracture event in KTRs is associated with higher rates of hospitalization, increased health care costs and higher all-cause mortality. Therefore, prevention and treatment of abnormal bone metabolism in KTRs are essential to long-term high-quality survival.

METHODS

Participant or population Participants were adults (≥18 years of age) of kidney transplant recipients. Participants of any transplant other than a kidney transplant, including kidney-pancreas transplants, were excluded.

Intervention Intervention group was given vitamin D supplements.

Comparator The comparator group was given placebo or no treatment.

Study designs to be included Randomized controlled trials.

Eligibility criteria Studies that met the following criteria were included for analysis: (1) randomized controlled trials, (2) study involving recipients of a kidney transplant, (3) participants were adults (≥18 years of age), (3) study intervention was vitamin D therapy after transplantation, and comparator was placebo or blank control, and (4) study reported outcomes included one or more of the following: fracture, bone mineral density, serum intact parathyroid hormone, 25-hydroxyvitamin D, serum calcium, serum phosphate, bone alkaline phosphatase, serum alkaline phosphatase, calciuria, hypercalcaemia, proteinuria, estimated glomerular filtration rate and acute graft rejection. Studies if they met the following criteria were excluded: (1) trial of recipients of any transplant other than a kidney transplant, including kidney-pancreas transplants, (2) trial on animals or a non-human study, (3) study was an abstract, case report, review, letter, editorial, expert opinion, or (4) full text was not available or lack of sufficient data.

Information sources We searched the PubMed, EMBASE, Web of Science, and the Cochrane Library from inception through September 30, 2023 for randomized controlled trials about vitamin D's effect on bone metabolism after kidney transplantation. The reference lists of systematic reviews and included studies were also searched.

Main outcome(s) Fracture, bone mineral density, serum intact parathyroid hormone, 25-hydroxyvitamin D, serum calcium, serum phosphate, bone alkaline phosphatase, serum alkaline phosphatase, calciuria, hypercalcaemia, proteinuria, estimated glomerular filtration rate and acute graft rejection.

Quality assessment / Risk of bias analysis The risk of bias of the included RCTs were independently evaluated by two authors using the Cochrane Risk Assessment Tool. The studies were assessed on selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias. The disagreement in risk of bias assessment was resolved by discussion among the authors.

Strategy of data synthesis Vitamin D supplements group were compared with control according to the PRISM guideline for systematic reviews and meta-analysis. For dichotomous outcomes, the pooled effect size of outcomes were expressed using relative risk (RR) with 95% confidence interval (CI). If continuous outcomes were used to assess the effects of treatment, the standardised mean difference (SMD) with 95% CI was used. Heterogeneity of results among included studies were evaluated by using Q (heterogeneity X2) and I2 statistic. Values of $P \leq 0.10$ and I2≥50 % was considered to represent significant heterogeneity. When heterogeneity was present, a random effect model was used to estimated pooled RR or SMD and its 95% CI; otherwise, a fixed effect model was used. Datas were showed graphically using forest plots. In the forest plots, the differences of outcome measures were indicated statistically significant if the 95% CI of RR did not cross 1, or if the 95% CI of SMD did not cross 0.

Subgroup analysis No subgroup analysis.

Sensitivity analysis The sensitivity analysis was performed by removing one study at a time to

examine the effect of each single study on the pooled result.

Country(ies) involved The study was carried out in China.

Keywords vitamin D, kidney transplantation, bone metabolism, bone mineral density, systematic review.

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