

Embargoed until June 14, [13:15](#)

Budapest, June 14, 2019

Benefits beyond fracture risk reduction? Results of the VITALE study

Kidney transplantation is the treatment of choice for most people with kidney failure, as it will improve their survival while increasing their quality of life compared to remaining on dialysis. However, while a kidney transplant can restore healthy kidney function, recipients remain at increased risk of fractures, heart disease, diabetes and some cancers. Observational studies have suggested that vitamin D may reduce the risk of these important post-transplant complications. The VITALE study shows that, compared with currently recommended doses, high doses of oral vitamin D₃ (cholecalciferol) safely and effectively lower the risk of fractures, but have no effect on the risks of heart disease, diabetes or cancer after a kidney transplant [1].

Lead VITALE investigator Dr Marie Courbebaisse (Paris, France), commented: "Our study shows that currently recommended doses of vitamin D are not sufficient to protect patients from the risk of fracture after kidney transplantation. This challenges advice in the current international KDIGO guidelines, which recommend using low doses of cholecalciferol similar to those recommended for the general population."

Kidney transplant recipients are at increased risk of fracture due to a combination of factors. As the kidneys fail, they are no longer able to maintain normal levels of parathyroid hormone, vitamin D, and blood levels of calcium and phosphate, which are important for bone health. As a result, patients are likely to have renal bone disease—known as chronic kidney disease-mineral bone disease (CKD-MBD) at the time of their transplant; or they may develop the condition if their transplanted kidney has suboptimal function. Some immunosuppressant drugs, given to prevent organ rejection, also have adverse effects on bone health. Current guidelines recommend correction of vitamin D deficiency or insufficiency to help improve bone health, based on guidelines in the general population [2]. However, high-grade evidence to support this recommendation has been lacking [3].

Vitamin D₃ (cholecalciferol) is the form of vitamin D that is naturally made by the body through exposure to direct sunlight. The aim of the VITALE study was to compare the

skeletal and non-skeletal effects of high versus low doses of cholecalciferol after kidney transplantation. A prospective, multicenter, double-blind, controlled trial, VITALE randomly assigned 536 kidney transplant recipients (mean age 50.8 years, 335 males) to either 100,000 IU (high dose) or 12,000 IU (low dose) cholecalciferol every two weeks for two months, then monthly for 22 months. In the study, 'low dose' corresponded to a minimum recommended intake of 400 UI/day.

After 24 months, vitamin D levels were significantly greater in the high-dose group compared to the low-dose group: 43.1(12.8) ng/mL versus 25.1(7.4) ng/mL compared with 20.2(8.1) versus 19.2(7.0) ng/mL at study inclusion ($p < 0.0001$). The incidence of fractures was significantly lower in the high-dose group (1% versus 4% in the low-dose group; $p = 0.02$). There were, however, no differences between the two groups in the risks of diabetes, major cardiac events (e.g. heart attack), new cases of cancer, or death. High-dose treatment was well tolerated, with no increased risks of vascular calcification or abnormal blood levels of calcium and phosphate (hypercalcemia and hyperphosphatemia, respectively).

Professor Carmine Zoccali, ERA-EDTA President concluded: "The VITALE study is important for nephrologists and their patients, because it shows that high-dose vitamin D is an effective way of lowering the rate of fractures after kidney transplantation, with a very low risk of any side effects. More broadly, we see yet again that other benefits for vitamin D seen in observational studies are not reflected when supplementation is tested in randomized controlled trials."

[1] Courbebaisse M, et al. Non-skeletal and skeletal effects of high doses versus minimum recommended intake of vitamin D3 in renal transplant recipients in a prospective, multicenter, double-blind, randomized study. LBCT Abstract ERA-EDTA Congress 2019, Budapest

[2] KDIGO clinical practice guideline for the care of kidney transplant recipients. Am J Transplant 2009; 9(Suppl) 3

[3] Palmer S, et al. Interventions for preventing bone disease in kidney transplant recipients: Cochrane systematic review. Nephrol Dial Transplant 2018;33 (suppl 1): 321

About ERA-EDTA

With more than 7,000 active members, the ERA-EDTA is one of the biggest nephrology associations worldwide leading European nephrology and one of the most important European Medical Associations. It organises annual congresses and a Scientific Education Interactive Day (SEID), it produces guidelines, it collects data and performs epidemiological studies through its Registry. It supports fellowships and research projects. Its publications are NDT and CKJ (this last journal is Open Access). The ERA-EDTA also has an online Educational platform: the European Nephrology Portal (ENP) which includes NDT-Educational@ENP. The 2020 Congress will be held June 6-9 in Milan (Italy). Visit the booth to receive more information!

Web site: www.era-edta.org