JOURNAL FÜR MENOPAUSE

FRANCIS RM
Prevention and treatment of osteoporosis: vitamin D supplementation or treatment with active vitamin D metabolites?

Journal für Menopause 2000; 7 (Supplementum 2) (Ausgabe für Deutschland), 24-25

ZEITSCHRIFT FÜR DIAGNOSTISCHE, THERAPEUTISCHE UND PROPHYLAKTISCHE ASPEKTE IM KLIMAKTERIUM

Indexed in EMBASE/ Excerpta Medica

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R. M. Francis

Prevention and treatment of osteoporosis: vitamin D supplementation or treatment with active vitamin D metabolites?

Summary

There is a decline in serum 25 hydroxyvitamin D (25OHD), 1,25 dihydroxyvitamin D (1,25$(OH)_2$D) and calcium absorption with advancing age, which leads to secondary hyperparathyroidism and bone loss. Calcium and vitamin D supplementation in this age group improves calcium absorption, suppresses parathyroid hormone (PTH) and decreases bone loss. Supplementation also reduces the incidence of hip and other non-vertebral fractures, particularly in the frail elderly who are likely to have vitamin D deficiency.

In contrast, women with vertebral fractures have lower calcium absorption than age-matched control subjects, which does not usually respond to treatment with physiological doses of vitamin D. A randomised controlled study showed that low dose alfacalcidol improved calcium absorption, decreased serum PTH and reduced alkaline phosphatase in elderly women with radiological evidence of vertebral osteoporosis, whereas vitamin D_2 500–1,000 IU daily had no effect. Studies of the effect of active vitamin D metabolites in the management of elderly women with established vertebral osteoporosis have yielded conflicting results, but suggest that alfacalcidol and calcitriol might decrease spine bone loss and reduce the incidence of vertebral fractures. Further studies are required to evaluate the efficacy of vitamin D and its metabolites in the treatment of elderly women with vertebral fractures.

The effect of advancing age on vitamin D metabolism and calcium absorption

Serum 25OHD concentration declines with advancing age, mainly due to decreased cutaneous production of vitamin D. There is also a reduction in serum 1,25 $(OH)_2$D, related to impaired renal function and diminished activity of the 1α hydroxylase enzyme. These changes in vitamin D production and metabolism may contribute to the decline in calcium absorption, the increase in PTH and continuing bone loss with advancing age [1].

Effects of vitamin D supplementation

Increasing serum 25OHD in the elderly raises serum 1,25$(OH)_2$D, improves calcium absorption and decreases serum PTH, although this response may be attenuated in the presence of renal impairment [1]. A French study in 3,270 women (mean age 84 years) living in nursing homes and apartment blocks for the elderly, showed that 800 IU vitamin D_3 and 1.2 g elemental calcium daily decreases PTH, increases femoral neck BMD and reduces the risk of hip fracture by 27 % [2]. An American study of 389 men and women (mean age 70 years) living at home demonstrated that 700 IU vitamin D_3 and 500 mg elemental calcium daily had a modest beneficial effect on bone density and decreased the incidence of non-vertebral fractures by 54 % [3].

It is unclear if the benefits of treatment seen in these studies were due to vitamin D, calcium or the combination of both, but a Finnish study showed that an annual IM injection of 150,000 or 300,000 IU vitamin D decreases the risk of fractures in elderly people by 25 % [4]. In contrast, a Dutch study showed a small increase in hip bone density with 400 IU vitamin D_3 daily, but no effect on the incidence of hip fractures in elderly people [5].

The UK Medical Research Council has now funded a multi-centre study of the secondary prevention of osteoporotic fractures in elderly people. Over 6,000 men and women over the age of 70 years presenting with an osteoporotic fracture will be randomised to receive calcium, vitamin D, calcium and vitamin D or double placebo. This study should establish if vitamin D reduces the incidence of subsequent fractures in this group and confirm if supplementation with calcium is also required.

Vitamin D metabolism in established osteoporosis

Women with vertebral crush fractures have lower calcium absorption than age-matched control subject, which may be due to impaired production of 1,25$(OH)_2$D or relative resistance to the action of the vitamin D metabolites on the bowel [1]. In a study using increasing doses of vitamin D in women with vertebral crush fractures, Gallagher found that 50 % required doses of at least 20,000 IU daily to correct the malabsorption of calcium [6]. Subsequent work from Leeds showed that

treatment with 25OHD$_3$ increased serum 25OHD and 1,25(OH)$_2$D to the same extent in elderly women with vertebral fractures and age-matched control subjects, but calcium absorption only increased significantly in the control subjects [7]. Although this suggests that there is relative resistance to the action of vitamin D in women with vertebral fractures, the malabsorption of calcium may be overcome by the use of active vitamin D metabolites such as calcitriol or alfacalcidol [1].

A recent randomised, controlled study has compared the effects of treatment with alfacalcidol 0.25 µg twice daily and vitamin D$_2$ 500–1,000 IU daily on calcium absorption and bone resorption in 46 elderly women with radiological evidence of vertebral osteoporosis [1] Vitamin D$_2$ was given in a dose of 500 IU daily for the first three months, followed by 1,000 IU daily for the second period of three months. Calcium absorption increased significantly on treatment with alfacalcidol, but not with vitamin D$_2$ [1]. Serum intact PTH and alkaline phosphatase decreased significantly with alfacalcidol, but were unchanged with vitamin D$_2$ treatment.

Treatment of established osteoporosis with vitamin D metabolites

Although the malabsorption of calcium seen in elderly women with osteoporosis and vertebral crush fractures may be overcome by treatment with low dose calcitriol and alfacalcidol, studies of their effect on bone mass and fractures have yielded conflicting results [1]. Some studies have shown a significant reduction in spinal bone loss and vertebral fractures in women with vertebral osteoporosis treated with active vitamin D metabolites, but this has not been a universal finding [1]. Patients on treatment with alfacalcidol or calcitriol also require monitoring of serum calcium and creatinine, because of the risk of hypercalcaemia and renal impairment

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After graduating in Medicine from the University of Leeds in 1975, Dr. Francis worked in Leeds and Harrogate, before being appointed a member of the Clinical Scientific Staff at the MRC Mineral Metabolism Unit in Leeds General Infirmary in 1980. Whilst working in the MRC Unit he developed a major clinical and research interest in osteoporosis and vitamin D metabolism. In 1983 he was awarded a Smith and Nephew Travelling Fellowship, which allowed him to spend a year working on the cellular mechanisms of bone resorption in St. Louis, USA. On returning to the United Kingdom, he worked in Leeds and London, before moving to Newcastle in 1986. Dr. Francis is now Reader in Medicine (Geriatrics) at the University of Newcastle upon Tyne and Consultant Physician at Freeman Hospital. He runs a large Bone Clinic and supervises a research programme examining the pathogenesis, sequelae and treatment of osteoporosis in men and women. He writes and speaks extensively on osteoporosis and is a Trustee and Member of the Council of Management of the National Osteoporosis Society in the UK.

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