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Calcium, vitamin D, vitamin K2, and magnesium supplementation and skeletal health

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Abstract

Supplementation with calcium (Ca) and/or vitamin D (vitD) is key to the management of osteoporosis. Other supplements like vitamin K2 (VitK2) and magnesium (Mg) could contribute to the maintenance of skeletal health. This narrative review summarizes the most recent data on Ca, vitD, vitK2 and Mg supplementation and age-related bone and muscle loss. Ca supplementation alone is not recommended for fracture prevention in the general postmenopausal population. Patients at risk of fracture with insufficient dietary intake and absorption could benefit from calcium supplementation, but it needs to be customized, taking into account possible side-effects and degree of adherence. VitD supplementation is essential in patients at risk of fracture and/or vitD deficiency. VitK2 and Mg both appear to be involved in bone metabolism. Data suggest that VitK2 supplementation might improve bone quality and reduce fracture risk in osteoporotic patients, potentially enhancing the efficacy of Ca ± vitD. Mg deficiency could negatively influence bone and muscle health. However, data regarding the efficacy of vitK2 and Mg supplementation on bone are inconclusive.

Introduction

The loss of bone quality and/or density is a para-physiological phenomenon observed in perimenopause and postmenopause, as well as in other conditions involving ageing, inflammatory and/or autoimmune diseases, chronic drug consumption (e.g. glucocorticoids, chemotherapies, etc) and/or nutritional deficiencies [1]. Data extensively agree with the key role of calcium (Ca) and vitamin D (vitD) supplementation for the prevention of osteopenia/osteoporosis in subjects at a higher risk of fragility

fractures and for the treatment of bone strength reduction in association with antiresorptive [bisphosphonates (BPs), denosumab (Dmab)] and anabolic agents [teriparatide (TPTD), i.e. recombinant human parathyroid hormone (PTH) (1–34)] [2]. Emerging evidence suggests the possible involvement of other supplements, like vitamin K2 (VitK2) and magnesium (Mg), in the achievement and maintenance of bone integrity [3,4].

In this article, we shall review and discuss principal options of supplementation to preserve the skeleton, both the most recognised ones (Ca and vitD) and those that seem to be promising, (VitK2 and Mg). More specifically, we will synthesize the mechanism of action, the metabolism and the most relevant data about the efficacy and safety of Ca, VitD, VitK2 and Mg. Our main objective is to provide a detailed review of the currently available principal supplements for the management of bone loss and/or sarcopenia, so that clinicians may have a better awareness of actual benefits and potential limits of all these supplements and encourage an adequately personalized choice for each patient.

Section snippets

Materials and methods

A systematic search of the PubMed and Medline databases was conducted, including systematic reviews, meta-analyses, randomized controlled trials (RCTs) and consensus of expert opinions reporting data regarding Ca, vitD, VitK2 and Mg supplementation on bone mineral density (BMD), bone quality, fracture risk and muscle strength in adults until March 2020. Our review excluded papers published in non-peer-reviewed supplements....

Metabolism

Calcium is involved in many bodily activities, for instance cellular differentiation, enzymatic activation, neuronal and immune responses [5]. However, the most well-known role of Ca is the regulation of muscle contraction and maintenance of skeletal integrity. Extracellular Ca homeostasis is due to three main processes: intestinal absorption, renal reabsorption and bone remodelling [5]. Specifically, Ca intestinal uptake is mostly related to both transcellular and paracellular mechanisms. In...

Metabolism

VitD is a pro-hormone whose active form 1, 25(OH)2D3 – resulting from hepatic and renal hydroxylation - binds cellular membrane and nuclear VDRs [29]. VitD is mostly involved in intestinal Ca absorption, since 1, 25(OH)2D3 enhances TRPV6 synthesis and permeability of tight junctions. 1, 25(OH)2D3 and Ca are inversely associated with PTH which, if persistently higher than normal, might directly affect the skeleton, by increasing bone resorption, negatively influencing bone homeostasis and...

Metabolism

VitK2 is a fat-soluble compound [46], also called menaquinone (MK), recognized as safe and effective in bone loss management. VitK2 contributes to regulate the function of osteocalcin (OC) - the main bone non-collagenous protein - improving bone quality. Specifically, VitK2 increases OC gamma-carboxylation with greater efficacy compared to other types of VitK (VitK1 and K3) [46]: gamma-carboxylated OC (cOC) is the active form of OC, binding Ca to bone hydroxyapatite [46]. VitK2 is also involved ...

Metabolism

Mg is one of the most important bodily elements (~50–60 % in bone tissue; ~1 % in extracellular compartment) and the second most abundant intracellular cation [68]. One third of skeletal Mg resides in cortical bone, either on the surface of hydroxyapatite or on the area surrounding crystal structures [69]. Mg deficiency might affect bone directly (by reducing bone stiffness, increasing osteoclasts and decreasing osteoblasts) and indirectly (by interfering with PTH and vitD, promoting...

Conclusion

Osteoporosis is a systemic skeletal disorder with important negative consequences on general health and quality of life in postmenopause and in old age [1]. Besides specific pharmacological and/or hormonal treatments, supplementation strategies seem to be very important [2]. In this field, vitD supplementation, alone or combined with Ca, appeared fundamental to strengthen the positive effects of any specific therapy in frailer patients, at higher risk of vertebral and non-vertebral fragility...

Contributors

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