Maturitas 107 (2018) 7–12

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Calcium in the prevention of postmenopausal osteoporosis: EMAS clinical guide

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ARTICLE INFO

Keywords:
Calcium
Postmenopausal osteoporosis
Prevention
Diet
Excess-calcium risk

ABSTRACT

Introduction: Postmenopausal osteoporosis is a highly prevalent disease. Prevention through lifestyle measures includes an adequate calcium intake. Despite the guidance provided by scientific societies and governmental bodies worldwide, many issues remain unresolved.
Aims: To provide evidence regarding the impact of calcium intake on the prevention of postmenopausal osteoporosis and critically appraise current guidelines.
Materials and methods: Literature review and consensus of expert opinion.
Results and conclusion: The recommended daily intake of calcium varies between 700 and 1200 mg of elemental calcium, depending on the endorsing source. Although calcium can be derived either from the diet or supplements, the former source is preferred. Intake below the recommended amount may increase fragility fracture risk; however, there is no consistent evidence that calcium supplementation at, or above, recommended levels reduces risk. The addition of vitamin D may minimally reduce fractures, mainly among institutionalised people. Excessive intake of calcium, defined as higher than 2000 mg/day, can be potentially harmful. Some studies demonstrated harm even at lower dosages. An increased risk for cardiovascular events, urolithiasis and even fractures has been found in association with excessive calcium intake, but this issue remains unresolved. In conclusion, an adequate intake of calcium is recommended for general bone health. Excessive calcium intake seems of no benefit, and could possibly be harmful.

1. Introduction

Osteoporosis is a chronic disease with a growing prevalence due to the increase in life expectancy [1]. It is far more common in women than in men, and its prevalence increases markedly after the menopause. Approximately 30% of all postmenopausal women have osteoporosis in the United States and Europe, and at least 40% of these women will suffer one or more fragility fractures [2]. As with other chronic diseases affecting modern societies, such as cardiovascular disease and cancer, risk reduction is a preferred strategy.

There are several options for the reduction of osteoporosis risk. Lifestyle is pivotal, as the use of anti-osteoporotic drugs, at least in

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http://dx.doi.org/10.1016/j.maturitas.2017.10.004

Europe, has been limited by governmental agencies for treatment only [3]. Physical activity and nutrition are two crucial lifestyle measures aimed at reducing osteoporosis risk [4]. Nutrition, including an adequate calcium intake, has been shown to be an excellent approach for the maintenance of a healthy bone status at all life stages, starting from early infancy [5].

The aim of the present clinical guide is to aid health professionals, when advising women regarding calcium intake for the prevention of postmenopausal osteoporosis. The recommendations have been graded to provide evidence-based guidance. Systematic reviews, meta-analyses and randomized controlled trials (RCTs) have been given priority. PubMed was searched from January 2007 through to June 2017 to obtain the most up-to-date evidence.

These recommendations do not apply to women already receiving anti-osteoporotic drugs, since their efficacy has been proved in clinical trials in which the participants were supplemented with calcium and vitamin D.

2. The rationale for calcium supplementation

Calcium plays a key role in human physiology. As a second messenger, calcium has a central role in mediating a wide array of functions, including muscle contraction, and metabolic pathways [6]. Moreover, it is a basic constituent of hydroxyapatite crystals, the mineral component providing stiffness to the collagen network of mature bone. Insufficient calcium accrual, leading to a sub-optimal bone mass peak and low bone mineralisation, is an important factor favouring osteoporosis and fracture [7].

The rationale for recommending an adequate calcium supply is simple; calcium is crucial for bone mineralisation, hence its intake has to be sufficient.

2.1. Biochemical mechanisms of calcium metabolism

There are still unresolved questions regarding the biochemical mechanisms involved in calcium metabolism. Current evidence suggests that the intestine absorbs a low percentage only, which does not generally exceed 35%, of the calcium present in food. Two mechanisms are operative: passive diffusion, which acts only when the luminal concentration of calcium is sufficiently high; and active absorption, a saturable transport pathway involving vitamin D receptors that operates when calcium concentrations are low [8,9]. Parathyroid hormone (PTH) acts as a sensor that, in the event of a decrease in calcium levels, stimulates the production of calcitriol, the active metabolite of vitamin D.

2.2. Adolescence and menopause

While maintaining an adequate calcium intake is important throughout life, it is even more so during childhood and adolescence and after the menopause. Bone density increases during the growth periods of the teenage years reaching a peak soon after the cessation of linear skeletal growth. While bone mass is genetically determined, some clinical studies have suggested a key modulatory role for physical activity and nutrition. A Swiss study detected a synergistic interaction between physical activity and high protein intake on parameters related to bone structure and strength development in a population of children followed-up for 8 years up to mid-adolescence [10] (Evidence level IIa).

The bone density peak is sustained for some years and thereafter begins to decline, the process being stimulated during the mid-40s, when menopause transition commences. After the menopause, an accelerated period of bone loss occurs, which lasts for 6–10 years. Thereafter, bone loss continues until the end of life.

3. The daily intake of calcium

For clinical practice, it is important to know how much calcium needs to be ingested. The answer to this question is presently unknown, because intestinal absorption is subject to many variables, including age, gender, gonadal function, ethnic group, other dietary components and even the pattern of calcium intake (i.e. variation of ingested amounts throughout the day).

Recommended dietary intake levels vary throughout life, being higher during the time of bone formation and in older people. Most health agencies recommend higher requirements in those specific life periods, which may increase up to 1000–1300 mg/calcium per day, as detailed below. As the main source of dietary calcium is derived from dairy products, people with low intake (i.e. vegans or those with lactose intolerance) should have their intake re-assessed. The prevalence of lactose intolerance has been estimated at around 25% among US adults [11]. Furthermore, coeliac disease and previous bariatric surgery may impair absorption.

The importance of vitamin D was shown in a study of 9961 US adults that found that 25-hydroxyvitamin D status seems to be the dominant predictor of bone mineral density (BMD) relative to calcium intake [12].

Recommendations on calcium intake vary worldwide. For example, those from the US National Institutes of Health are based on recommended dietary allowances (RDA); i.e. the average daily intake sufficient to meet the requirements of 97–98% of healthy individuals [11]. RDA for women are 1300 mg between 9 and 18 years of age, 1000 mg between19 and 50 years and 1200 mg thereafter. The National Osteoporosis Society (NOS) in the UK uses the term reference nutrient intake. In the case of calcium, it is set at a daily requirement of 700 mg. This lower daily calcium intake is considered sufficient to meet the daily requirements of 97.5% of the adult population. This amount is increased to 1000 and 800 mg in peripubertal and adolescent boys and girls, respectively [13]. The NOS recommendation is consistent with balance data from metabolic studies in which individuals had their intake and output of calcium (stool, sweat, urine) measured. The authors concluded that neutral calcium balance, defined as calcium output equal to input, was achieved at an intake of 741 mg/day [14]. The NOS also defines 400 mg/day as a lower reference nutrient intake (LRNI), i.e. the lowest amount of calcium required to maintain a healthy skeleton [13].

3.1. Calcium intake at the population level

Data exist on the average calcium intake at the population level. One US study analysing data from NHANES (2003–2006) [15] showed that less than one third of women aged 9 to71 had an adequate intake of calcium (or the level assumed to ensure nutritional adequacy) from their diet alone; the proportion improved among supplement users but, still, less than 50% achieved age-specific recommendations. In this population, two thirds of women aged over 51 years took calcium supplements.

Information from Europe shows differences between countries. The Mediterranean diet, for example, often contains inadequate amounts of calcium. One Spanish study using dietary questionnaires found that the mean daily calcium intake of a group of 2009 adults from the general population was 698 mg [16]. However, low rates of fragility fracture are found in that country [1]. In contrast, intake averaged 1250 mg/day in a cohort of Finnish women [17].

4. Calcium for the prevention of postmenopausal osteoporosis

Daily calcium intake should be estimated before deciding on a management strategy and this can be undertaken using online calculators [see for example 18]. Alternatively, a basic dietary anamnesis may offer information on the amounts of consumed dairy products and