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Mini Review

The effect of weight loss programs on bone mineral density in early postmenopausal women

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Abstract

Menopause is an important milestone for the bone mineral density (BMD) of women. During postmenopausal period, levels of estrogen in the body reduce rapidly. Loss of excess weight at this age is important in order to reduce co-morbidities, but it can also deteriorate bone mass and boost the development of osteoporosis. The positive association between body weight or BMI and bone mineral density is well documented. Weight loss can possibly increase bone resorption through various mechanisms. During weight loss in early postmenopausal women, the usual Ca intake (1g/day) is insufficient, as increase the Ca-PTH axis through the reduction of Ca absorption. In cases where weight loss induced by diet is combined with resistance exercise, it can possibly prevent bone loss, since BMD is more closely related to muscle mass rather than to adipose tissue. Last but not least, the history of weight loss at middle age may be an indicator of the risk of hip fracture at a later stage of life, under conditions.

Keywords: Early postmenopausal women, Weight loss, Bone mass, Diet, Exercise training

Introduction

According to the World Health Organization (WHO), menopause is the period in which reduced production of estrogen can be observed[1]. Based on the literature, in the US, Europe and much of the developed world, menopause occurs on average during the fifth decade of a woman's life[1,2]. Over the last century, the percentage of postmenopausal women has increased by three times and is expected to further rise. On annual basis it is estimated that approximately 25 million women are going into menopause[2]. The progressive loss of ovarian function results in estrogen depletion, which has significant effects on the body of women in postmenopausal age[3]. The immediate effects are directly related to vasomotor symptoms, whilst mid-term effects including skin atrophy (decreased dermal collagen production, elastin, proteoglycans, and reduced capacity of water absorption), loss of muscle mass (sarcopenia, decreased protein synthesis), atrophy of the urogenital system (urinary incontinence, vagina vulnerable to infections and inflammation), and long-term effects are related to osteoporosis and cardiovascular disease (CVD)[3-5]. Aging induces bone fragility and this results into loss of BMD[6]. Alteration in bone structures may also affect bone strength. After menopause, the observed estrogen deficiency accelerates bone loss[6]. Permanent bone losses mainly come from trabecular and endocortical bone (bone next to marrow), and not from subperiosteal or intracortical bone[7,8].

Obese individuals (including postmenopausal women) are being recommended to have a reduction of 5-10% of initial body weight, as this may reduce risk factors like diabetes type 2 and heart disease[9]. However, there are studies arguing that a weight reduction of 10% in combination with a poor diet and sedentary behavior in obese or overweight population with BMI=28-42 Kg/m^2, can lead to 1-2% loss of bone mass at various sites of bones[9-13]. Similarly, there are studies that also highlighted the reduction in BMD after weight loss[14,15]. In addition, data from NHANES I epidemiologic follow up study[16], reported that weight loss ≥10% of the maximum body weight, is an important risk factor for hip fracture among middle-aged women. Specifically, the study observed that the risk of hip fracture was increased by 2.5-fold in women

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during middle-age (50-64 years), who lost the most weight (≥10%) and where thinnest at maximum body weight (~62 Kg), as compared to women, who had maximum weight ~76 Kg and had ≤5% weight lost. Also, according to the follow up NHANES study, the landmark age for hip fracture among the majority of women (aged at baseline 50-64 years) was 65 years and over. Langlois et al., suggest that history of weight loss that occurred in middle-age may indicate decline in health that increase hip fracture risk in old age[16].

Body weight is a significant determinant of BMD in women[17]. In general, it is considered that low BMI (less than 16,5 Kg/m^2) is associated with low BMD and increased risk of verdebral fracture[17,18], whereas normal body weight or overweight act protectively against low BMD and fractures[19,20]. Exercise training is an important factor that could protect skeletal muscle mass during the phase of losing weight and it may also protect the relative bone mineral density, as BMD is closely related to muscle mass[21].

This review concerns non-osteoporotic women in the early years after menopause and aims to firstly study the influence of weight loss on BMD in this population and secondly determine whether dietary energy intake and exercise affect bone loss during weight reduction.

The role of weight loss programs induced by diet on bone mineral density of early postmenopausal women

As previously mentioned, ovarian estrogen production reduces at menopause and this has as result the decrease of intestinal capacity of Ca absorption and the deterioration of renal conservation. This may lead to increased calcium requirements[22].

The target of calcium intake for this population is 1200 mg/day in combination with adequate vitamin D status (30 ng/mL)[22]. However, it is believed that estrone production in obese women is greater than in non-obese women and its action is protective against bone loss[23]. Estrone is produced by the aromatization of androgens in peripheral fat and it is converted to 17β-estradiol. Studies show that, obese post-menopausal women have higher concentrations of sex hormone, as well as, higher BMD compared to non-obese women[24,25]. The reduced ability of the gonads to produce estrogens induces bone loss while obesity prevents it. This suggests that gonadal function, body weight and bone mineral density might be regulated by common pathways[26].

Leptin is another hormone which increases in accordance with fat mass and body weight, and declines with weight reduction[27,28]. This hormone can determine osteoblast differentiation and act as a potent inhibitor of bone formation, which then may control bone mass and its disorders. Its reduction through weight loss could possibly affect the rate of bone turnover[26].

However, environmental factors, like dietary intake and body weight may have an effect on BMD, as well as, they could become important regulators of bone balance[29,30]. There are studies, over the last decade concerning obese postmenopausal women, indicating that weight loss of 5-10% is correlated with a decreased bone mass and an increased bone resorption[10,13,14,31]. Von Thun et al., mentioned that dietary - induced weight loss can result in a significant loss of BMD, which even after regaining the weight lost, it does not return to its original levels[32]. Energy-restricted diet can reduce Ca-absorption, as well as, the consumed amount of Ca and vitamin D. This type of diet negatively affects the intake of macronutrients, that usually promote Ca-absorption (e.g. protein, fat, lactose) and it limits the absorption of Ca which then results to increased cortisol levels. In overweight postmenopausal women (including early postmenopausal women), that began losing weight (~0,7 Kg/wk), the intake of 1 g Ca/day increased the calcium-PTH axis. This possibly occurs secondary to a reduction in Ca absorption in the first weeks of weight loss[33]. Specifically, the consumption of 1g Ca/d, led to a reduction of calcium absorption at a time point before six weeks, thus activating the Ca-PTH axis and restoring Ca absorption levels back to baseline values. Because of these, Cifuentes et al. observed that the PTH is responsible for the 22% of the variance of Ca absorption during weight loss. The aforementioned study also shown that the total absorbed Ca is sufficient, when Ca intake is 1,8 g/day[33]. In a randomized, double-blind, placebo-controlled study by Ricci et al. which included 43 obese postmenopausal women (3 years since menopause), it was observed that 1 g calcium supplementation in combination with a behavior-modification nutrition-education weight loss program, can decrease PTH level by 13% at the end of weight loss period (6 months), as a result to diminish the accelerated bone turnover after moderate weight loss[10]. In agreement with previous studies, Jensen et al. randomized control study (included 17 postmenopausal women) suggested that the total body BMD was not protected when participants attempted to lose weight by formula diet (58 g protein, 800 mg Ca, 800 mg phosphate, 200 IU VitD). Instead, bone loss was partially inhibit when the same diet formula was combined with supplementation of 1g calcium/day[14].

Additionally, in a study by Ricci et al., which involved 27 obese post-menopausal women of age of 55.9±7.9 years, it was observed that moderate energy restriction may had an effect on bone turnover, that could be partially regulated by alterations in estrone and serum PTH[31].

According to the findings above, we may argue that the usual recommended calcium intake might be insufficient in early post-menopausal women who adhere to an energy restricted diet. On the other hand, a calcium supplement may decrease PTH serum levels and prevent a high rate of bone turn over.

Concerning protein diet and BMD, it has been previously hypothesized that nutrition with high levels of protein (>1.2 g/kg/day or over thirty percent of energy from protein), may result in metabolic acidosis and hypercalciuria. This can adversely affect bone health and reduce BMD and thereby

increase the likelihood of fracture[34,35]. However, recent data in the literature suggests that a high protein diet can help maintain muscle mass and thus, maintain bone density during dietary-induced weight loss[36]. Regarding postmenopausal women, studies[37,38] shown that high dietary protein intake (1 scoop of a powder= 6 g prot/d combined with diet (dairy, lean meat, fish, legumes) or usual protein diet (0,85 g/d) combined with food supplement with 0,75 g/kg body weight) helps to reduce the loss of BMD, however other findings[39-41] do not show any effect or harmful repercussion of dietary protein intake on bone mass during weight reduction caused by energy restriction. Based on the previous results, we can argue that further studies are needed to determine whether there is a limit of protein consumption that can change BMD and bone function.

The role of weight loss programs induced by diet and exercise on BMD of early postmenopausal women

Lifestyle change, which includes increased physical activity and low-calorie diet, is the basic therapeutic approach for overweight and obese people[42]. One of the most basic functional benefits of exercise during the weight loss process is to maintain the skeletal muscle mass (SMM). As mentioned, maintaining and possibly increasing SMM is important, as BMD is more closely related to muscle mass than to adipose tissue and body weight. It has been observed that bone mineral density can be maintained during the process of losing weight, when such process is the result of a well-balanced diet in combination with exercise[21]. In a study including 30 overweight 57±3-year post-menopausal women, it was observed that a weight loss of 10%, caused by energy restriction rather than exercise, was associated with a decrease in BMD at clinically important sites of the fracture. In the same study, women who had a weight loss of 8.4% due to exercise only (>twenty minutes of exercise, >twice per week) did not show a decrease in BMD at any site[15]. In addition, a study of 51 post-menopausal women, who had been in menopause for at least 2 years, showed that adding aerobic exercise three times a week to their life/schedule could result in risk reduction of bone loss[11]. However, studies that investigated the role of exercise on BMD during moderate loss of weight in post-menopausal women, have shown that regional BMD loss can be prevented by exercise at some[11,43-44], but not at all sites[43,44], as, it appeared that BMD decreased by 1-2%, with a weight loss of 2-9 Kg through exercise and a daily calcium intake of 700-900 mg[12,11,43-44].

Also, in the Gozansky et al. study of post-menopausal women, it was demonstrated that weight loss through exercise, even if such loss was of moderate size (0.8 Kg - 4 Kg), it was associated with a decrease in BMD, especially in women who did not receive osteoporosis medication (raloxifene or estrogens)[43].

Nevertheless, the majority of studies in existing literature highlighted the resistance exercise as the appropriate strategy for protection of lean tissue during weight loss through energy restriction, whilst aerobic exercise seemed to have little effect on the maintenance of the lean tissue[45].

Recent studies evidenced that, moderate weight loss in early postmenopausal women did not necessarily endanger health of bone mass when anti-estrogen therapy and exercise took place.

Possible mechanisms of action of weight loss and obesity on BMD

Weight reduction decreases glucagon-like peptide-2[46] (GLP-2), leptin[47], insulin-like growth factor (IGF-I), growth hormone and estrogen[48]. Additionally, moderate weight loss can increase cortisone levels in serum, especially when there are low levels of estrogen in the body (post-menopausal age), which results in increased osteoclastic activity and reduced absorption of calcium[49,50]. The reduction of calcium absorption activates the Ca-PTH axis and these changes are expected to negatively affect the bone mass, as they affect the normal function of osteoblasts and osteoclasts. Moreover, low/normal Ca (0,8-1 g/d) consumption during weight loss leads to a rise in the Ca-PTH axis. GLP-2 reduces bone resorption and increases bone mineralization[46]. IGF-I is known for its anabolic action[48]. Leptin, directly acts on osteoblasts and indirectly to osteoclasts, having as a central effect the inhibition of bone formation[47,51,52]. Finally, the decrease in estrogen levels observed in both weight reduction and menopause, results in the direct or indirect promotion of osteoclastic activity due to the increase in cytokine levels (i.e., interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor-a(TNF-a))[50].

The balance of hormonal changes and their effect on BMD during weight loss in early postmenopausal women is also dependent on other factors such as physical activity, initial body weight and diet conditions (extent and duration of energy restriction or nutrient intake levels).

Conclusion

The relationship between BMD and weight loss is crucial for maintaining the quality of bones in early postmenopausal women. Considering that postmenopausal women experience increased requirements of calcium, because of the deterioration of Ca absorption efficiency and renal conservation, emphasis should be given in calcium adequate intake during weight loss. Dairy products are the best sources of calcium content and absorption, and should be included in the diet of early postmenopausal women who want to lose weight in combination with adequate vitamin D status (30 ng/mL). Energy restricted diets containing 0,8-1 g/d Ca, seem to be insufficient of the Ca needs in overweight early postmenopausal women. This has as result the reduction of Ca absorption and the activation of Ca-PTH axis, which they may lead to deterioration of the bone mineral density.

Weight loss diet programs containing 1,8 g/d Ca seem to reduce PTH levels and can be partially inhibit bone loss. The role of protein diets (>30% of energy from protein >1.2 g/kg/day) in maintaining bone mass and its protective effect on bone health is supported by several studies, mentioned in the official bibliography, but not all.

Training strategies, which include resistance exercises during weight loss caused by energy restriction, consider as the appropriate method for maintaining lean tissue. The suggestion that history of weight loss that occurred in middle-age may is an important risk factor for hip fracture in old age, it would be very interesting to confirm with further epidemiologic and clinical studies which involve early postmenopausal women.

There have been several steps in recent years to understand the changes in BMD during weight loss, but there are many questions remained unanswered. Such questions concern the frequency and intensity of exercise, as well as, the optimal modes for maintaining BMD during weight loss. Definitely, there is need for future longitudinal prospective studies and well-designed randomized controlled trials, which will enables us to clarify and analyze the role model of nutrition, supplementation of vitamin D and the exact rate of weight loss, which a postmenopausal woman needs to follow in order to protect her bone health and metabolic profile.

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