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Review

The relationship between calcium and obesity

Çayan Kuytak, Jale Çatak

Department of Nutrition and Dietetics, Istanbul Sabahattin Zaim University, Faculty of Health Sciences, Istanbul, Turkey

ABSTRACT

Dietary and behavioral approaches to obesity, a serious public health problem worldwide, have not prevented the progression of obesity. Scientists have explored the mechanisms of adipose tissue and intracellular calcium to find different therapeutic methods for obesity. Although the first step in the treatment of obesity is energy restriction, studies have shown that dietary calcium can play an important role not only in the regulation of skeletal integrity but also in energy metabolism. The anti-obesity effect of calcium has been demonstrated by animal studies, observational population studies and randomized clinical studies. However, some studies have failed to explain the effect of calcium in obesity treatment. Although the protective effects of calcium against obesity and comorbidities are promising, larger studies are needed. This review investigates the anti-obesity mechanisms of action of dietary calcium in animal studies, observational population studies, and randomized clinical trials.

Keywords: Calcium metabolism, calcium, obesity.

Obesity is defined as excessive fat accumulation that may be harmful to health.[1] Economic growth, industrialization, ease of transportation, urbanization, sedentary lifestyle, processed foods, and transition to diets with high energy intake, in many countries, the prevalence of obesity has doubled, or even quadrupled.[2] Obesity greatly increases the risk of chronic diseases such as type 2 diabetes, cardiovascular diseases, certain cancers, depression and injuries, which lead to mortality and morbidity.[2,3]

Today, dietary and behavioral approaches regarding obesity, which is a serious public health problem worldwide, have been unable to prevent the progression of obesity.[4] The scientific community has investigated the mechanisms that effect adipose tissue in order to discover different therapeutic methods for obesity.[4,5]

Mechanisms of the underlying pathophysiology of obesity and comorbid diseases may be factors related to intracellular and extracellular calcium.[6] Calcium is the most abundant micronutrient in the human body.[6] Calcium plays a role in many biological functions, especially in skeletal mineralization, as well as in muscle contraction and cell division in glycogen metabolism.[7] Calcium metabolism in the human body can be controlled by negative feedback mechanisms such as intestinal absorption, renal reabsorption, and bone storage.[8] Various hypotheses have been proposed regarding the metabolic effect of calcium on adipose tissue in the treatment of obesity.[9]

STUDIES SUPPORTING CALCIUM ASSOCIATION IN OBESITY

The effect of calcium on body weight and body fat distribution has been confirmed by recent studies.[10] The relationship between body weight and calcium intake was first reported by McCarron[11] While the purpose of their study was to investigate the relationship between nutrients and blood pressure, the increased calcium intake with food was found to have a negative correlation

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Correspondence: Çayan Kuytak. İstanbul Sabahattin Zaim Üniversitesi, Sağlık Bilimleri Fakültesi, Beslenme ve Diyetetik Bölümü, 34303 Küçükçekmece, İstanbul, Türkiye. Tel: +90 536 - 853 05 64 e-mail: cayankuytak@hotmail.com

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with body weight. Zemel et al.[12] examined triglyceride accumulation and lipolysis activity of adipose tissue in low and high calcium intake in mouse models, and as a result, found that there was an inverse correlation between calcium intake and adipose tissue accumulation. In the NHANES III study of over 7,000 men and women, low calcium intake was associated with fat mass.[13] Another study of 283 participants between the ages of 18-64 reported that low calcium intake was a risk factor for being overweight and obesity.[14]

A cross-sectional epidemiological study of 1,259 participants conducted in Poland reported there was a negative correlation between dietary calcium and body mass index (BMI).[15] Suhett et al.[16] conducted a study on 350 eight and nine-year-old children found that children with low calcium intake had increased waist circumference and reported that low calcium intake was associated with abdominal obesity. Another study indicated that people who take less than 600 mg of calcium per day with nutrients had BMI in the category of >25 kg/m^2.[17]

Lu et al.[18] observed children and adolescent for a period of three years, and divided them into two groups according to high and low dairy intake, in which 38% of the low dairy intake group were found overweight and this finding was related to calcium's potential effect on weight control. One study found that calcium intake increased fat oxidation in participants who lost weight.[19]

Despite these studies, other studies reported there was no clear relationship between calcium intake and body weight.[10-12] One two-year study found that overweight and obese individuals had no significant difference in body weight after daily 1,500 mg calcium supplementation.[10] Another study assigned obese and overweight women into two groups, the placebo group and the group receiving 500 mg daily calcium supplement; despite restrictions on energy intake, there was no significant difference in weight change between the groups.[20]

In a study by Jones et al.,[21] 49 people received diets containing 700-1,400 mg calcium for 12 weeks; at the end of this study, although participants were given a calcium-rich diet and a diet restricted in energy intake, it was reported that calcium did not impact weight loss. One study on 2,267 people examined the relationship between calcium intake via dairy consumption and body weight and waist circumference; at the end of this six-year study, the relationship between calcium intake through dairy products and anthropometric changes could not be explained.[22]

One randomized controlled study examined the body weights of 323 healthy males who received calcium supplements for two years and reported that calcium supplements did not have significant effect on body composition.[23] In a cross-sectional study conducted on 236 healthy female students between the ages of 18-30 selected randomly among the students of Isfahan University of Medical Sciences, no significant relationship was found between calcium intake and excess weight and obesity.[24] Larsen et al.[25] reported in a study that there was a weak relationship between dietary calcium loss and weight loss.

PROPOSED MECHANISMS IN CALCIUM-OBESITY RELATIONSHIP

Various mechanisms have been proposed to explain the effects observed in studies on the effect of calcium intake on obesity.[11] One anti-obesity action mechanism of calcium is related to the amount of intracellular Ca^{2+} in the adipocyte cell. This mechanism is regulated by 1,25-dihydroxyvitamin D (1.25-$(OH)_2$-D) which plays a role in inducing lipogenesis and stimulating intracellular Ca^{2+} in the adipocyte, leading to lipolysis.[26,27] In high calcium diet, while 1,25-dihydroxyvitamin D (1.25-$(OH)_2$-D) is suppressed, concentration of intracellular Ca^{2+} in adipose tissue decreases, which results in increased lipolytic activity and reduced lipogenesis, explaining the fat loss model in adipose tissue. This process has been used to explain the anti-obesity effect.[9]

In recent years, studies have reported that the activity of the calcium sensitive receptor may play a role in the modulation of adipocyte cell function.[27] Increase in intracellular calcium in the adipocyte cell following low calcium intake is explained as follows: according to this model, activation of calcium-sensitive receptors found in adipose tissue results in increased vitamin D in circulation. This can be attributed to the potential effect of greater activation of lipogenic markers as well as decreased activation of lipolytic enzymes (Figure 1).[28]

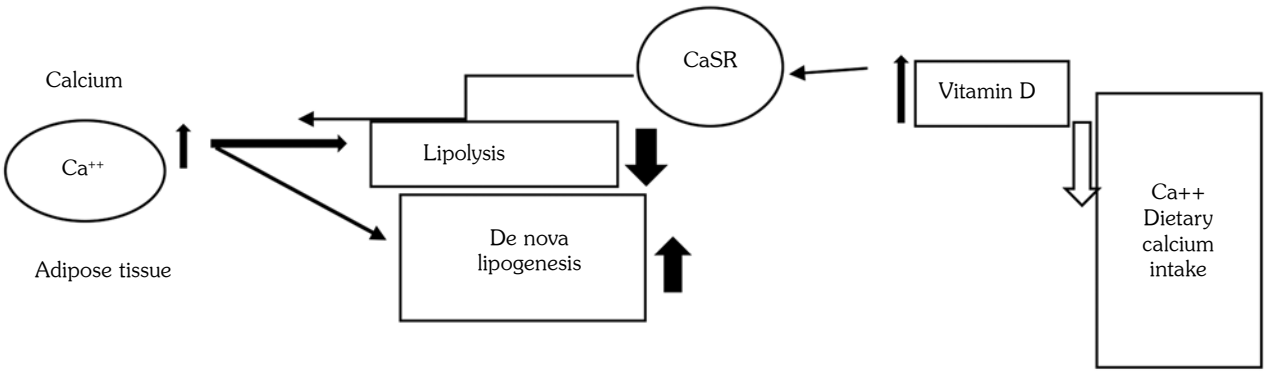

Figure 1. Model showing the role of increased intracellular calcium in fat synthesis within adipose tissue, during low calcium intake.[28]
Ca: Calcium; CaSR: Calcium sensitive receptor.

Another mechanism that may allow calcium to decrease body weight is by decreasing intestinal fat absorption and increasing fecal fat excretion. Calcium forms insoluble calcium soaps with fatty acids in the intestinal tract, therefore increasing the amount of fecal fat removal, with the potential effect of regulating body weight.[29]

One meta-analysis compared 1,241 mg daily calcium intake to low-calcium intake (<700 mg) and reported 5 g/day increase in fecal fat levels with high calcium intake.[30] Another study demonstrated a positive correlation between increased calcium intake and fecal fat amount.[31] In the period following the increase of calcium intake from 500 mg/day to 1,800 mg/day, 8.2 g increase in fecal fat loss was detected.[32] In a similar study, total fecal fat excretion doubled by increasing calcium intake by 1,600 mg for seven days (Figure 2).[29]

In a randomized controlled study by Soerensen et al.,[33] 15 young male subjects were administered 500 mg calcium without dairy products as a control diet, 1,700 mg calcium based on milk, and 1,700 mg calcium based on cheese, respectively. At the end of the study, it was found that those who were on control diet had significantly less amount of fecal fat excretion compared to those with milk or cheese-based diet.

At the same time, animal studies have also shown that calcium affected sense of appetite and it was observed that calcium was an effective micronutrient in regulating appetite.[32]

In conclusion calcium is a micronutrient that has recently gained significance in regulating body weight or body fat distribution. While it is not a silver bullet in the struggle against obesity, it plays a large role despite being a small mineral.

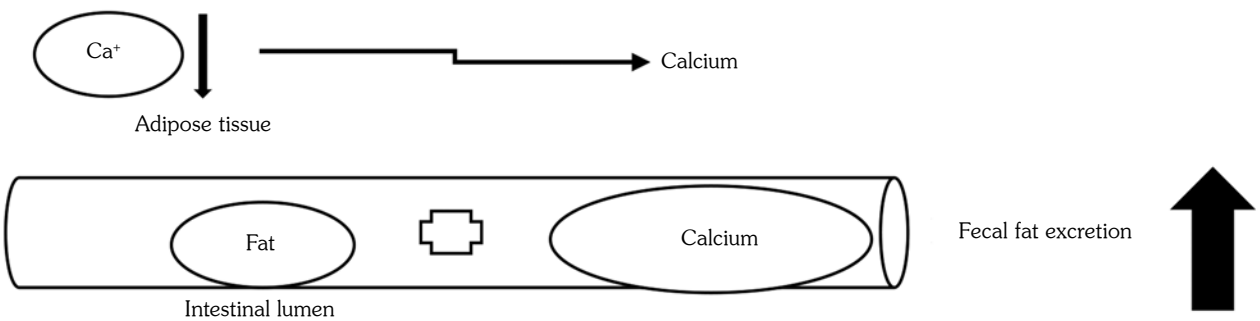

Figure 2. Mechanism showing increase in fecal fat excretion with decreased intracellular calcium in adipose tissue of within the intestinal system.[29]
Ca: Calcium.

The anti-obesity effect of calcium has been demonstrated in animal studies, observational population studies, and randomized clinical trials. However, some studies were unable to explain the effect of calcium in obesity treatment. While the protective effects of calcium against obesity and comorbidities seem promising, there is a need for studies of larger scope.

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