

EVIDENCE-BASED CLINICAL PRACTICE

Dietary Calcium Intake and Obesity

Sarina Schrager, MD

Obesity is increasing in the United States in epidemic proportions. Epidemiologic data suggest that people with high calcium intake have a lower prevalence of overweight, obesity, and insulin resistance syndrome. Studies in transgenic mice have demonstrated that calcium influences adipocyte metabolism. High calcium intake depresses levels of parathyroid hormone and 1,25-hydroxy vitamin D. These decreased hormone levels cause decreases in intracellular calcium, thereby inhibiting lipogenesis and stimulating lipolysis. High dietary calcium intakes also increases excretion of fecal fat and may increase core body temperature. Calcium from dairy products seems to have more of an impact than calcium from dietary supplements. Primary care providers should include recommendations about adequate calcium intake in standard dietary counseling about weight management. (J Am Board Fam Pract 2005; 18:205–210.)

The prevalence of obesity is increasing dramatically in the United States. Current data estimate that more than 60% of the adult population between the ages of 20 and 74 are obese or overweight.¹ The estimated annual direct and indirect costs of obesity in the United States are close to \$100 billion.² Obesity prevalence has increased dramatically in children as well.^{3,4} Overweight and obesity in children is directly associated with being overweight in adulthood. Obesity is related to multiple disease outcomes and has been shown to be related to increased mortality rates. In fact, obesity will soon overtake smoking as the most important modifiable cause of mortality in this country. Low calcium intake has been identified as a potential contributing factor to obesity.⁵

Many diet studies have found the average dietary calcium intake in people in the United States to be much lower than the current recommendations.⁶ Dietary calcium is important in building bone mass in children as well as in preventing osteoporosis in the elderly. Only 30% of children in the United States currently meet the recommended daily allowance (RDA) for calcium. The majority of dietary calcium consumed in the United States comes

from dairy products. The upper limit recommended for calcium is 2500 mg per day.

Low levels of dietary calcium and dairy products increase the risk of hypertension and insulin resistance syndrome (IRS).^{7–9} The Coronary Artery Risk Development in Young Adults (CARDIA) study⁹ found that dairy product consumption was inversely proportional to all components of the IRS, including obesity. In this study, each daily serving of a dairy product was associated with 21% lower odds of developing IRS.

Epidemiologic studies have found an association between dietary calcium intake and obesity. Animal research has demonstrated a plausible physiologic mechanism for such an association, and some human clinical trials have produced suggestive results. The National Dairy Council has promoted the association between eating dairy products and obesity prevention in a national advertising campaign titled “The Weight Is Over.”

This article will review the epidemiologic data supporting a relationship between dietary calcium intake and obesity, explain the physiologic basis for such a relationship, and present some supportive recent data in humans. The article will conclude with implications for primary care providers.

Epidemiologic Data Supporting the Obesity-Dietary Calcium Relationship

Several epidemiologic studies relate obesity prevalence and dietary calcium intake (Table 1). Zemel et al¹⁰ reanalyzed National Health and Nutrition

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From the Department of Family Medicine, University of Wisconsin–Madison. Address correspondence to Sarina Schrager, MD, Department of Family Medicine, University of Wisconsin–Madison, 777 S. Mills St., Madison, WI 53715 (e-mail: sbschrag@wisc.edu).

Table 1. Human Studies of Calcium and Weight

Author	Type of Study	Population	Results
Zemel et al ¹⁰	Reanalysis of NHANES III data set (SORT C)	380 women 7114 men	RR of being in the highest quartile for body fat was reduced as calcium intake increased. RR in second quartile of Ca ²⁺ intake was 0.75, in third RR quartile was 0.40, and in highest quartile of Ca ²⁺ intake RR was 0.16 (<i>P</i> < .0009 for women, <i>P</i> < .0006 for men)
Davies et al ¹³	Reanalysis of 5 clinical studies (2 cross-sectional, 2 longitudinal, 1 RCT) of calcium and bone density (SORT C)	Total sample size among all studies: 780 women in 3rd, 5th, 8th decades	Negative associations between calcium and body weight found in all studies for all 3 age groups. OR for being overweight (BMI >26) was 2.25 for young women who were in the lower half of calcium intakes. In RCT, calcium-treated women had significant weight loss over 4 years. Authors estimate that a 1000-mg difference in calcium intake may be responsible for an 8-kg difference in body weight.
Heaney et al ¹¹	Extension of reanalysis of above studies (SORT C)	Young women (3rd decade) n = 348 Midlife women (5th decade) n = 216	Young women: at 25% for calcium intake, there was a 15% prevalence of overweight and a 1.4% prevalence of obesity. At a calcium intake equal to the current RDA, the prevalence of overweight was only 4% and obesity 0.2%. In midlife women, there was a significant decrease in yearly weight gain with increasing calcium intakes.
Skinner et al ¹⁴	Prospective cohort study examining children's body fat and calcium intake from 2 months old to 8 years old (SORT B)	52 white child-mother pairs completed entire study (25 boys, 27 girls)	Dietary calcium was negatively related to body fat percentage in both boys and girls (<i>P</i> = .02 to 0.04). Models including dietary calcium predicted 28% to 34% of variability in body fat percentage.
Drapeau et al ¹⁵	Prospective cohort study (Quebec Family Study) measured twice (between 1989 and 1994 and also between 1995 and 2000) (SORT B)	248 volunteers between 18 and 65 years old (112 men, 136 women)	Increases in consumption of fruit and lowfat milk were associated with lower body fat and lower body weight.
Loos et al ¹⁶	Cross-sectional study within a larger prospective cohort study (the HERITAGE Family Study) (SORT B)	362 men (109 black, 253 white) and 462 women (201 black, and 261 white)	Significant inverse associations were found for all men and white women between calcium intake and percentage of body fat. There was no significant association seen in black women.
Zemel et al ¹⁷	Randomized, placebo-controlled trial for 24 weeks. (SORT B, RCT but small sample size)	32 obese adults (27 women, 5 men)	All subjects were placed on a calorie-deficient diet. Then participants were randomized to 1 of 3 arms: standard diet, 400 to 500 mg calcium with a placebo; high-calcium diet, standard diet supplemented with 800 mg of calcium; and high-dairy diet, 1200 to 1300 mg of dietary calcium with placebo supplemented. Participants on the high-dairy diet lost the most weight and the most truncal fat. The participants on the high calcium diet lost the second highest amount and the participants on the standard diet lost the least amount.
Shapses et al ¹⁸	Randomized placebo-controlled trial for 25 weeks. Data combined from 3 separate trials. (SORT B, RCT with larger sample size, but not powered to detect differences)	100 premenopausal and postmenopausal women	Subjects were randomized to receive either 1000 mg of calcium in a supplement or a placebo. Weight loss was encouraged with behavior modification and nutrition education. Women participated in support groups and a subset of postmenopausal women was encouraged to consume one third of their calories with a meal replacement drink. There were no significant differences in body weight or change in body fat between the 2 groups.

NHANES III, National Health and Nutrition Examination Study III; RCT, randomized control trial; BMI, body mass index; SORT, strength of recommendation; RDA, recommended daily allowance; OR, odds ratio; RR, resistance ratio.

Examination Study III (NHANES III) data and found that after controlling for energy intake and physical activity, body fat was lower in people with the highest calcium intake. There was a reduction in risk for obesity with each increasing quartile of calcium intake. At the highest quartile of calcium intake (an amount approximately equal to the current RDA for calcium), the risk of being in the highest body mass index quartile was reduced by 85%.

Heaney et al¹¹ reanalyzed data from 2 cohorts of women studied from 1984 to 1985 and 1995 through 1997. These 348 women were enrolled in studies examining calcium intake and bone density. The young women at the 25th percentile of calcium intake for the group had a 15% prevalence of overweight. Women in the group whose calcium intake was equivalent to the current RDA for calcium had only a 4% prevalence of overweight. In the second cohort of midlife women, a reduction in average yearly weight gain was associated with increasing calcium intake.

Heaney et al¹² also reanalyzed 6 observational studies and 3 clinical trials that were originally exploring dietary calcium intake and either bone density or blood pressure as outcome measures. This reanalysis found a consistent effect of higher dietary calcium intake and either body fat, body weight, or reduced midlife weight gain. In this pooled data set, each 300-mg increase in daily calcium intake was associated with a 1-kg decrease in body fat among children and a 2.5- to 3-kg decrease in body weight in adults.

Davies et al¹³ reanalyzed 5 clinical studies of calcium intake and bone density. The pooled data set included 780 women in their 30s, 50s, or 80s. Four of the studies were observational, and one was a randomized controlled trial. There were significant negative associations between calcium intake and body weight. The odds ratio for being overweight in the young women was 2.25 for those below the 50th percentile for calcium intakes. In the controlled trial, women who received calcium had a significant weight loss over 4 years compared with the placebo group. The authors extrapolated that a 1000-mg difference in calcium intake is associated with a 8-kg difference in body weight and that dietary calcium intake may explain approximately 3% of the change in weight.¹³

Several problems exist with data from reanalysis of previous trials such as those above. First, some of

the same studies were included in both of the above reviews, which makes it hard to evaluate the results.^{12,13} Second, none of the trials were designed with body weight as an endpoint. Therefore, unknown confounding factors may exist that effect the data. Third, because the associations are derived from observational studies, no evidence of causality can be ascertained. For instance, it may be that the people who ingested more calcium were also less likely to eat at fast-food restaurants and were therefore less likely to be overweight or obese. In that case, the calcium intake was caused not by the lower risk of overweight or obesity but by another factor entirely. It is also unclear whether calcium itself has a major impact on body weight or whether the impact comes from some other component of dairy products.

Skinner et al¹⁴ demonstrated a negative relationship between dietary calcium intake and body fat in a group of 8-year-old children in his prospective study. In the author's statistical model, children could reduce their body fat by 0.4% simply by drinking an extra 8-oz glass of skim milk or 8 oz of low-fat yogurt each day. The CARDIA prospective study examined dairy consumption and several outcome variables associated with the IRS⁹ and found an inverse relationship between dairy consumption and all the components of the IRS, including obesity. The Quebec Family Study observed that calcium and dairy product intake induced changes in body composition (ie, decreased abdominal circumference) in a long-term observational study.¹⁵ The Health, Risk Factors, Exercise, Training, and Genetics (HERITAGE) Family Study, another long-term prospective study, found significant associations between low calcium intake and high levels of adiposity in white and black men and white women. These associations were not found in black women.¹⁶

Prospective Studies in Humans

The epidemiologic evidence suggests a strong relationship between dietary calcium intake and weight. However, there have been only 2 prospective controlled trials in humans using calcium supplementation as a variable and body weight as an outcome. One of the studies found a significant relationship between calcium supplementation and weight loss in people on a calorie-restricted diet¹⁷ whereas the other did not.¹⁸

In their 2004 study, Zemel et al¹⁷ randomized 32 obese adults to a standard calorie-deficient diet alone, a calorie-deficient diet supplemented with calcium, or a calorie-deficient diet supplemented with dairy products. Participants lost 6.4% body weight with the calcium-supplemented diet, 8.6% with the standard diet, and 10.9% with the high dairy diet ($P < .01$). It is interesting that truncal fat loss was significantly augmented with calcium and augmented even more by the high dairy diet (19% of all fat lost on standard diet vs 50% of all fat lost on calcium-supplemented diet vs 66% of all fat lost on high-dairy diet, $P < .001$).

Shapses et al¹⁸ performed 3 separate, randomized, placebo-controlled trials of 1000-mg calcium supplementation in 100 premenopausal and postmenopausal women. There were no significant differences between the calcium-supplemented group and the placebo group in body weight or body fat. Baseline calcium intakes ranged from 600 to 1000 mg per day in both groups. The calcium-supplemented group's calcium intakes averaged 1000 mg more than the placebo group. Calcium supplementation in this trial did not accelerate weight loss. There was, however, a small nonsignificant difference between the supplemented and placebo groups in their mean total weight lost and the proportion of weight lost as fat, with the supplemented group losing more weight and a higher proportion of weight as fat.

Proposed Mechanisms of Action

There are 2 main physiologic mechanisms proposed to explain how calcium intake can affect body weight or body fat. The first is the effect of dietary calcium on intracellular calcium levels in adipocytes, and the second is the effect of dietary calcium on fatty acid absorption from the gastrointestinal tract.

Effect of Dietary Calcium on Adipocytes

Ninety-nine percent of a body's calcium content is stored in the extracellular space. The majority of extracellular calcium is stored in bones and teeth. Intracellular cytosolic soluble calcium mediates many metabolic pathways, including platelet aggregation and insulin resistance. Calcitropic hormones, such as parathyroid hormone (PTH) and 1,25-hydroxy vitamin D, regulate intracellular calcium. Low dietary calcium intake stimulates high

levels of PTH and 1,25-hydroxy vitamin D, which in turn stimulate high levels of intracellular calcium in adipocytes stimulating lipogenesis and inhibiting lipolysis. High dietary calcium intake depresses the levels of PTH and 1,25-hydroxy vitamin D, thereby causing lower levels of intracellular calcium and inhibiting lipogenesis and stimulating lipolysis.^{19,20} Therefore, calcium intake may directly affect whether adipocytes store or break down fat.

Results of studies in transgenic mice are consistent with the preceding observations. High-calcium diets were associated with a 51% decrease in adipocyte fatty acid synthase expression and activity and a 3- to 5-fold increase in lipolysis in mice.²⁰ In mice subjected to calorie restriction, low-calcium diets impeded body fat loss, and high-calcium diets accelerated fat loss.²⁰ All the mice on calcium-supplemented diets exhibited increased core temperature as well, whereas the mice on the plain energy-restricted diet did not. A specific protein (uncoupling protein 2) is up-regulated in the calcium-supplemented mice, which may cause increased core temperature, although the mechanism of action is not clear.²¹

Change in Fat Absorption

The second proposed mechanism by which calcium may impact body weight is that increased dietary calcium seems to bind more fatty acids in the colon, thereby inhibiting fat absorption. Welberg et al,²² in a small 1994 study, showed that calcium supplementation increased the percentage of excretion of total fat as related to fat intake. The calcium supplementation in this study was either 2 or 4 g. Denke et al²³ supplemented 13 men with approximately 2 g of calcium per day in a 1993 study. The percentage of dietary fat excreted per day increased from 6% to 13% with calcium supplementation. The Nestle Company supplemented chocolate with 900 mg of calcium and tested the fecal fat content of 10 men in a double-blind crossover study. Calcium supplementation of chocolate increased fecal fat from 4.4 to 8.4 g per day ($P < .0001$).²⁴ These studies show a small effect of calcium on fat absorption that probably contributes to the antiobesity effects but does not explain it entirely. The degree of fecal fat loss in these studies of high calcium supplementation is only approximately 3% of that induced by medications such as orlistat.²⁵

Dairy versus Calcium Supplements

Several of the previously reviewed studies suggest that calcium from dairy products affects weight loss more than calcium derived from dietary supplements.¹⁷ Preliminary data point to some other component in dairy products, possibly whey protein, effecting the weight-loss effect of calcium.²⁶ Whey protein provides a multitude of bioactive substances that may work synergistically with the calcium to alter lipid metabolism.

Implications for Primary Care Providers

Calcium is not a magic bullet in the battle against obesity, although it may play a small, but significant, role. The affect of dairy products or calcium is probably greatest in those people whose adipocyte status is changing, such as during weight loss, age-associated weight gain, and growth.²⁷ Women, in particular, are at high risk for age-associated weight gain after menopause. Calcium contributes to maintenance of strong bones and may modulate weight gain in postmenopausal women. As such, primary care providers can target postmenopausal women and overweight or obese adults and children for extra counseling about calcium intake. (Strength of Recommendation level C: expert opinion.²⁸) An important concept to remember is that calcium does not seem to be effective unless a calorie restriction is already in place. Replacing other sources of protein with low-fat dairy products may help augment weight loss. Adequate calcium intake, preferably from dairy products, may be especially important in people who have hypertension or components of the IRS. All patients should be encouraged to consume 3 to 4 servings of low-fat dairy products every day. Primary care providers should include recommendations about calcium intake in standard dietary counseling about weight management.

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