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Introduction

Obesity is an increasingly common problem, both in the United States and in Europe, as well as in developing countries (1, 2). Studies show that 65% of American adults are overweight (BMI 25-29.9) or obese (BMI >30), and 31.0% of children and adolescents are at risk for being overweight or are overweight (3). In addition to social stigma, obesity is also strongly associated with diabetes, hypertension, dyslipidemias, coronary heart disease, pulmonary disease, osteoarthritis, and other disorders (4).

The disease's increasing prevalence highlights the importance of finding effective interventions for obesity and its associated diseases. There is a growing body of evidence, both in mouse models and in human studies, that—through regulation of vitamin D—high calcium consumption may contribute to low body weight, may enhance weight loss in conventional energy restricted diets, and may reduce visceral adiposity.

The association of calcium and adiposity

There have been several strong studies noting lower levels of adiposity in people consuming high levels of calcium and dairy products. In a 10 year prospective study, Pereira *et al.* examined the associations of diet and obesity in 3,157 black and white young adults, ages 18-30. Comparing the highest to the lowest quintile in terms of dairy consumption the odds of obesity were found to be reduced 19.7% ($P < 0.001$) in a dose dependent manner, the odds of elevated blood pressure were reduced 14.2% ($P < 0.001$), and the odds of abnormal glucose homeostasis were also reduced 13.6% ($P < 0.01$). Overall, obese people with the highest dairy intake relative to those with the lowest intake had a 71% reduction in their odds of having insulin resistance syndrome (also known as the metabolic syndrome). Interestingly, when the groups were examined based on calcium consumption, rather than on dairy consumption, the results were not significant, suggesting that there may have been an additional factor in dairy products which contributed to the observed effects (5).

Data from The National Health and Nutrition Examination Survey (NHANES III) also demonstrated a significant inverse relationship between dietary calcium and body fat. The odds of being in the highest quartile of body fat were reduced from 1.0 for the first quartile of calcium intake, to 0.75, 0.5, and 0.16 for the second, third and fourth quartiles of calcium intake respectively (6).

Calcium's effect on body fat does not appear to be limited to adults. A longitudinal study of children from 2 months to 8 years of age showed an inverse relationship between calcium intake and body fat. Predictive equations demonstrated that of the 26-34% variation in body fat between the children, dietary calcium consumption explained 7-9% of the variability (7).

A study by Lin *et al.* found that dietary calcium, not the energy in the diet, predicted weight loss. In this secondary analysis of a prospective study looking at the effect of exercise on bone composition, Lin found that although energy consumption predicted percent weight change in women consuming more than 1876 kcal/day, in women who consumed less, only calcium, not energy, was found to be a negative predictor of change in body weight and in body fat. This study also found that while dairy calcium was a negative predictor of weight change, non-dairy calcium was not (8).

Davies *et al.* reviewed data from 5 clinical studies (4 observational studies and 1 double-blind, placebo controlled, randomized trial) of calcium intake, all of which were primarily designed to study the effect of dietary calcium on bone mineral. 780 women in their third, fifth, and eighth decades were studied. Those whose diet put them in the lower half of calcium intake were found to have an odds ratio of 2.25 ($P < 0.02$) for being overweight. In the randomized trial, although both the placebo group and the calcium supplemented group lost weight, the calcium supplemented group lost 0.671 kg/year, whereas the placebo group which lost 0.335 kg/year, a 0.346 kg/y difference ($P < 0.025$) (9).

Taken in concert, these studies provide strong evidence that high intakes of calcium predict lower levels of adiposity.

High calcium diets in controlled trials

There have been several studies looking at the effect of dietary calcium in controlled trials, and the results have been somewhat mixed. One randomized controlled study which measured weight and bone density during an energy restricted diet over a three month period found no significant difference between the control and calcium supplemented groups. This may be partly attributable to the non-dairy source of the calcium. However, the group that was not supplemented lost bone mass during the study while the supplemented group did not (10).

A longitudinal study by Phillips *et al.* also found no relationship between calcium and adiposity. Phillips enrolled 196 non-obese pre-menarcheal girls, and followed them from ages 8-12 years old until 4 years post-menarche. They found no relationship between dietary calcium or dairy products and BMI or percent body fat (11). However, it was noted that the control group had an unusually high level of dietary calcium and that the high calcium group reported modest intakes of calcium, totaling 827 mg of Calcium per day (12), less than the recommended 1300 mg per day.

However, other controlled trials did see a benefit for those who had high calcium diets. Zemel *et al.* studied 32 women who were placed on energy restricted diets for 24 weeks and were assigned to either a diet low in Calcium (400-500 mg/d), or to one of two diets of 1300 mg/d achieved either through supplementation or dairy products. The women assigned to the high calcium group via supplementation had a 26% (8.58 kg) greater weight loss than did the low calcium diet group, and the women assigned to the high calcium group via dairy products showed a 70% (11.07 kg) greater weight loss ($P < 0.01$) than did the low calcium diet group. Fat loss for the two high calcium groups was 38%

and 64% greater than the low calcium diet group respectively ($P < 0.01$). Notably, those on the low calcium diet lost 19% of the fat from their trunk, while those on the high calcium and high dairy diets lost 50% and 66% of the fat from their trunks respectively ($P < 0.001$) (12, 13). This is especially significant because truncal adiposity has been shown to correlate highly with obesity related morbidity (14).

The observed changes in weight and body fat modulation shown above was mirrored in another study published as an abstract, in which 34 obese subjects on a 500 kcal/day energy deficient diet were assigned to either 3 servings of yogurt (attaining 1100 mg/day of Calcium) or a calcium intake of 400-500 mg/day, which was consistent with the US average. Both groups lost weight, -4.43 ± 0.47 kg vs. -2.75 ± 1.25 kg in the yogurt and control groups respectively ($p < 0.005$). The yogurt group lost a greater percentage of the weight from their trunk than did the control group, 60% vs. 26.4% ($P < 0.005$) (15).

The modulation of the distribution of fat may be achieved even without a caloric deficit. Isocaloric substitutions of 3 servings of dairy a day for 6 months resulted in a 5.4% reduction in total body fat and a 4.6% reduction in truncal fat in the absence of any weight change, suggesting a preservation of lean body tissue. The control group experienced no change in body composition (12).

The mechanisms of calcium's effect.

The association between calcium consumption and lower levels of obesity was first noted in the 1980s but was largely dismissed because no mechanism was known linking calcium and obesity. However, recently, several mechanisms have been proposed and tested. One study demonstrated that, compared to controls, men fed chocolate fortified with calcium had an increase in fecal fat (16). Thus, part of calcium's anti-adiposity effect may be through the sequestering of fatty acids as salts in the intestine.

However, this seems to be only part of the picture. Much work has been done to assess the effect of calcium and calcitropic hormones on adipocytes. Dietary calcium has been shown to raise intracellular calcium, which in turn suppresses PTH and Vit D (17). Vitamin D has been shown to increase fatty acid synthase expression and activity in human adipocytes by 50%-100%, and to inhibit lipolysis by 80%, effectively promoting the synthesis of fat and inhibiting its break down (18). Furthermore, physiologic doses of Vit D have been shown to be an inhibitor of apoptosis via down regulation of caspase-1 and caspase-3 gene expression in human adipocyte (19). As a result of these and other modulatory effects, vitamin D and PTH lead to an expansion of adipocyte lipid storage and adipocyte number (12).

The greater effect of dairy calcium compared to other sources of dietary calcium has yet to be fully explained. It may be that calcium has better bioavailability in dairy foods. Another hypothesis is that there is a bioactive molecule found in whey, a fraction of milk that contributes to the modulatory effect of calcium (20).

How much is too much Calcium

The NIH defines the Upper Limit (UL) as the highest level of daily intake of calcium from food, water, and supplements that is likely to pose no risk of adverse health effects for individuals in the general population. For children older than 1 year and adults (including pregnant and lactating women), the UL for Calcium is 2,500 mg/day (21) which is equivalent to just over half a gallon of 1% milk per day (300 mg Ca per cup of milk) (22). For the general population the risks of exceeding the UL for calcium include hypercalcemia (although this extremely rare in healthy people), and the potential for deficiencies in other divalent cations such as Zn, Fe, Mg, and Phosphorus. Calcium can interact with medications such as digoxin, antibiotics, phenytoin, thiazides, glucocorticoids, levothyroxine, and others drugs, so care should be taken in persons with medical conditions (21). As always, moderation should be used when planning a diet, and a physician should be consulted before beginning a new diet.

The average person in the United States does not have a problem, however, with consuming too much calcium. In the United States, 55% of men and 78% of women ages 20 or older are not meeting their recommended daily intake of calcium (21). The estimated mean calcium intake of girls aged 6-11 years is 865 mg per day, for girls aged 12-19 consumption is around 773 mg per day (23), and for adults aged 50 -85 years the mean consumption ranged from 814-1142 mg per day (including supplements) (24). These levels fall well below the 1300 mg Adequate Intake (AI) level of calcium for girls and boys 9 through 18 years, and below the 1200 mg AI recommended for adults 50 years and older (25). Therefore, for most people increasing calcium and dairy intake would help them meet their AI, rather than surpass the UL, and therefore decrease their risk of osteoporosis (26, 27).

Conclusion

Obesity is a growing problem in the United States and elsewhere, and is associated with a social stigma and with many diseases. Diets high in calcium and dairy products may help combat this disease. However, despite a growing body of evidence, there is still need for large-scale prospective clinical trails to confirm previous findings and to demonstrate the scope of calcium's and dairy's effects. Furthermore, more research needs to be conducted to determine why dairy seems to have a greater effect than does supplemental calcium.

Physicians should feel comfortable recommending that a patient increase his or her consumption of a low-fat dairy product, such as milk, or use supplements in order to achieve the AI of calcium, reduce the risk of obesity, and to enhance weight loss. Although high calcium diets and dairy products are not magic bullets for obesity, they do offer distinct benefits. In addition to reducing one's risk for osteoporosis, a high calcium and high dairy diet offers a way to specifically reduce truncal obesity, and augment the weight loss achieved with a low-calorie diet and exercise .

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