



Literature Review & Commentary

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Vitamin K, Crohn's disease, and osteoporosis

Vitamin K status and rate of bone resorption were measured in 44 patients (mean age, 36.9 years; mean disease

duration, 10.5 years) with Crohn's disease in clinical remission and 44 age- and sex-matched healthy controls. Vitamin K status was determined by measuring the serum concentration of undercarboxylated osteocalcin, and rate of bone resorption was determined by measuring urinary excretion of N-telopeptides of type I collagen [NTx]). Vitamin K status was significantly lower in patients than in controls, and there was a significant inverse correlation between vitamin K status and rate of bone resorption, even after controlling for vitamin D status, calcium intake, and other potential confounding variables.

Comment: There is a high prevalence of osteopenia and osteoporosis in people with Crohn's disease. Bone loss may result from many factors, including nutritional deficiencies and glucocorticoid use. Deficiencies of magnesium, zinc, vitamin D, and B vitamins are common in patients with Crohn's disease, and a deficiency of any one of these nutrients could increase the risk of bone loss.

Vitamin K is required to manufacture osteocalcin, a unique protein found in bone that attracts calcium to bone tissue. Without adequate vitamin K, normal bone mineralization is impaired. Vitamin K has also been shown to inhibit bone resorption, although the mechanism is not clear. Vitamin K status has been found to be lower in people with osteoporosis than in age-matched healthy controls. While the degree of deficiency is typically not great enough to compromise the blood-clotting system, it appears that bone health can be adversely affected by even marginal vitamin K deficiency. The results of the present study suggest that people with Crohn's disease, even those in remission, should increase their vitamin K intake, perhaps by several hundred milligrams per day. The main dietary sources of vitamin K are dark green vegetables and soybean oil. Vitamin K is also present in some multiple-vitamin preparations.

Duggan P, et al. Vitamin K status in patients with Crohn's disease and relationship to bone turnover. *Am J Gastroenterol* 2004;99:2178-2185.

Antioxidants: some good news finally

Some 13,017 French men and women (aged 35-60 years) were randomly assigned to receive, in double-blind fashion, a daily nutritional supplement or placebo for a median of 7.5 years. The supplement provided daily 120 mg of ascorbic acid, 30 IU of vitamin E, 6 mg of beta-carotene, 100 mcg of selenium (as selenium-enriched yeast), and 20 mg of zinc (as zinc gluconate). Among the group as a whole there were no significant differences in incidence of total cancers, ischemic heart disease, or all-cause mortality. When total cancer

incidence was analyzed according to gender, however, a protective effect of antioxidants was seen in men (relative risk [RR] = 0.69; 95% CI, 0.53-0.91) but not in women (RR = 1.04; 95% CI, 0.85-1.29). A similar trend was observed for all-cause mortality in men (RR = 0.63; 95% CI, 0.42-0.93) and women (RR = 1.03; 95% CI, 0.64-1.63).

Comment: The results of this study indicate that a low-dose antioxidant supplement taken for a median of 7.5 years reduced the incidence of cancer by 31% and all-cause mortality by 37% in men. In contrast, no beneficial effect was seen in women. The different results seen in men and women may be due to the fact that men have lower baseline levels of certain antioxidants, especially beta-carotene, than women do.

These findings are encouraging, considering the spate of bad news that has recently appeared regarding antioxidant supplementation. The most widely publicized negative study, reported in the *Annals of Internal Medicine* (2005;142:37-46), suggested that high-dose vitamin E supplementation (400 IU/day or more) increases all-cause mortality. As I pointed out in an editorial about that study (see Healthnotes Newswire, at <http://www.emersonecologics.com>), important flaws render the study's conclusions questionable. Furthermore, if long-term use of high-dose alpha-tocopherol does have a small negative effect in some people, the same is probably not true of mixed tocopherols (the form in which vitamin E occurs naturally in food).

Herberg S, et al. The SU.VI.MAX Study: a randomized, placebo-controlled trial of the health effects of antioxidant vitamins and minerals. *Arch Intern Med* 2004;164:2335-2342.

Glutamine for childhood diarrhea

One hundred twenty-eight (128) otherwise healthy children (aged 6-24 months; mean, 12.6 months) with acute diarrhea were randomly assigned to receive, in double-blind fashion, oral glutamine (0.3 g per kg of body weight per day) or placebo for 7 days, in addition to standard therapy. The mean duration of diarrhea was significantly shorter in the glutamine group than in the placebo group (3.40 vs. 4.57 days; 25.7% reduction; $p = 0.004$). Compared with placebo, glutamine had no effect on serum interleukin-8 and salivary IgA levels, suggesting that its effects on the gastrointestinal mucosa, rather than on immune function, were responsible for the improvement in diarrhea.

Comment: Glutamine is known to protect the structure and function of the intestinal mucosa in various catabolic states. The present study demonstrates that glutamine supplementation can decrease the duration of acute diarrhea in children. While the dose used was relatively large (equivalent to 21 g/day for a 70-kg person), even larger doses of glutamine have been given to humans without producing any apparent deleterious effects. Glutamine should, therefore, be considered for the treatment of young children with acute diarrhea.

Yalcin SS, et al. Effect of glutamine supplementation on diarrhea, interleukin-8 and secretory immunoglobulin A in children with acute diarrhea. *J Pediatr Gastroenterol Nutr* 2004;38:494-501.

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