

High Blood Levels of Vitamin D May Lower MS Risk

BOSTON, Dec. 19 -- Higher circulating levels of 25-hydroxyvitamin D have been associated with a lower risk of multiple sclerosis among Caucasians, researchers here reported.

There was a 41% decrease in MS risk for every 50-nmol/L increase in serum 25-hydroxyvitamin D levels, a good marker for tissue vitamin D tissue, found Alberto Ascherio, M.D., Dr.PH, of the Harvard School of Public Health here, and colleagues.

These results converge with a growing body of evidence supporting a protective role for sun exposure and vitamin D supplements in MS development, they reported in the Dec. 20 issue of the *Journal of the American Medical Association*.

However, for blacks and Hispanics, who had lower vitamin D levels than whites, there was no significant association between vitamin D and multiple sclerosis,

The prospective, nested case-control study of 257 MS patients came from analysis of more than seven million U.S. military personnel whose serum samples are stored in the Department of Defense Serum Repository.

MS cases were identified through army and navy physical disability databases for 1992 through 2004, and diagnoses were confirmed by medical-record review.

Each case was matched to two controls by age, sex, race/ethnicity, and dates of blood collection. Vitamin D status was estimated by averaging 25-hydroxyvitamin D levels of two or more serum samples collected before the date of initial multiple sclerosis symptoms.

Among whites (148 cases, 296 controls), the risk of multiple sclerosis significantly decreased with increasing levels of 25-hydroxyvitamin D. For a 50-nmol/L increase in 25-hydroxyvitamin D, the odds ratio (OR) was 0.59 (95% confidence interval, 0.36-0.97). There was no significant difference by sex, the investigators said.

In an analysis by quintile, those in the top quintile had a 62% lower MS risk compared with those in the bottom quintile (OR for top vs bottom quintile, 0.38; CI, 0.19-0.75, $P=0.006$). Risks in quintiles two through four were intermediate and not significant, but the overall trend across quintiles was significant.

Using the lowest quintile (63.3 nmol/L) as the reference, the ORs for each subsequent quintile were 0.57, 0.57, 0.74, and 0.38 ($P=0.02$ for trend across quintiles). Only the OR for the highest quintile, corresponding to 25-hydroxyvitamin D levels higher than 99.1 nmol/L, was significantly different from 1.00 (OR, 0.38; CI, 0.19-0.75; $P=0.006$).

Adolescence appears to be a crucial exposure period for MS, Dr. Ascherio said. Therefore his team analyzed whether serum concentrations of circulating vitamin D before age 20 predicted MS risk and found the inverse relationship particularly strong. Only one of 39 cases and 16 of 76 controls had levels

of 100 nmol/L or higher, resulting in an OR of 0.09 (CI, 0.01-0.75; $P=0.03$) compared with levels less than 100 nmol/L.

Among blacks and Hispanics (109 cases, 218 controls), whose levels were lower than those of whites, the researchers reported finding no significant associations between vitamin D and MS risk. However, they said, the smaller sample size for these individuals and their substantially lower vitamin D levels may have reduced the power to detect an association in this group.

Because circulating levels of 25-hydroxyvitamin D are sensitive to sunlight and are affected by dietary vitamin D, an important still unanswered question is whether 25-hydroxyvitamin D has a role in regulating immune responses. On the other hand, the researchers speculated that MS itself might affect vitamin D levels, possibly by changes in behavior, such as avoiding the unpleasant heat of sun exposure.

Another potential explanation, they suggested, is the possibility that some other exposure to UV light, rather than vitamin D production, contributes to protection.

In addition, the authors pointed out that although unlikely, a genetic predisposition to both MS and circulating low 25-hydroxyvitamin D levels could appear as a protective effect of vitamin D on MS in the study.

If the association between vitamin D and MS reported in this study reflects a true protective influence of vitamin D, which is known to be a potent immunomodulator, then increasing vitamin D levels in adolescents and young adults could lead to an important reduction in MS, the investigators suggested.

According to the Institute of Medicine, an adequate intake of vitamin D is 200 U/d for adults younger than 50 years, and the highest dose considered safe is 2,000 U/d. Adverse effects have been reported only at intakes several-fold higher, they said.

However, the researchers cautioned, "a broad recommendation for a several-fold increase in vitamin D intake among adolescents and young adults requires stronger evidence than that provided by observational studies alone."

First-degree relatives of individuals with MS are at a higher risk of developing MS, and a prevention trial in this population would be "possible and timely," Dr. Ascherio said

"Meanwhile, use of vitamin D supplements for MS prevention should not be undertaken until efficacy is proven," the researchers concluded.

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