Vitamin B Didn't Cut Poststroke Vascular Events

BY SHARON WORCESTER

FROM THE LANCET NEUROLOGY

Daily B vitamin supplementation is no more effective than is placebo for reducing the incidence of major vascular events in patients who have had a recent stroke or transient ischemic attack, according to findings from the Vitamins to Prevent Stroke (VITATOPS) trial.

Among 8,164 patients enrolled in the multicenter, parallel, double-blind trial, major vascular events (nonfatal stroke, nonfatal myocardial infarction, or death from any vascular cause) occurred in 15% of patients randomized to B vitamin supplementation and in 17% randomized to placebo after a median follow-up period of 3.4 years. This translated into a nonsignificant relative risk of 0.91, Dr. Graeme J. Hankey of Royal Perth (Australia) Hospital and his colleagues from the VITATOPS Trial Study Group reported.

When each type of vascular event was analyzed separately, B vitamin supplementation was not associated with a significant reduction in the relative risk for nonfatal or fatal stroke, nonfatal or fatal MI, or death from any cause. However, there was a slight, but statistically significant, reduction in the risk of death from vascular causes (relative risk, 0.86).

Dr. Hankey and his associates wrote that the findings suggest that B vitamins, while safe in poststroke and post-TIA patients, should not be recommended to prevent recurrent stroke (Lancet Neurology 2010 Aug. 4 [doi:10.1016/S1474-4422(10)70187-3]).

Study participants were enrolled between Nov. 19, 1998, and Dec. 31, 2008, within 7 months of experiencing stroke or TIA and were randomized to receive placebo or 2 mg of folic acid, 25 mg of vitamin B_6, and 0.5 mg of vitamin B_{12} daily in addition to usual medical care.

No unexpected adverse events occurred during follow-up, and no significant differences were seen between the treatment and placebo groups in regard to common adverse events, the investigators noted.

Although prior cross-sectional and observational epidemiological studies have suggested that raised plasma concentrations of total homocysteine are associated with increased risk for major vascular events, and that B vitamin supplementation can lower total homocysteine—as it did in this study—this did not translate to a reduced incidence of subsequent vascular events in the study, they said.

Fasting blood tests performed at the end of follow-up in 1,164 patients showed that the B vitamin group had 3.8 micromol/L lower homocysteine than in the placebo group (10.5 vs. 14.3 micromol/L). An analysis of a subset of 925 patients with fasting blood levels of homocysteine available from baseline and follow-up indicated that each 1.0-micromol/L decrease in total homocysteine was associated with only a nonstatistically significant 2% reduction in risk of the primary outcome.

The study is limited by incomplete adherence to trial drugs and by incomplete follow-up, as well as by a relatively short duration of follow-up, the investigators said.

To control for random error, the researchers added their data to those from other randomized controlled trials of homocysteine-lowering therapy in patients with or without preexisting cardiovascular disease. This "updated meta-analysis" also showed that B vitamins are not significantly more effective than placebo for reducing the risk of the composite outcome of stroke, myocardial infarction, or vascular death (RR, 0.99).

In a subgroup analysis, B vitamins were shown to possibly reduce the risk of stroke, myocardial infarction, or vascular death in patients with symptomatic small vessel disease of the brain causing lacunar infarction or intracerebral hemorrhage—a reduction that has also been suggested by other investigators who have reported that homocysteine is a risk factor for cerebral small vessel disease, they noted.

Dr. Hankey and some other authors of the study reported receiving payments and honoraria for various duties from companies that manufacture stroke therapies, including Johnson and Johnson, Sanofi-Aventis, and Schering Plough, Boehringer Ingelheim, and Pfizer.

The study was funded by the Australia National Health and Medical Research Council, the U.K. Medical Research Council, the Singapore Biomedical Research Council, the Singapore National Medical Research Council, the Australia National Heart Foundation, the Royal Perth Hospital Medical Research Foundation, and the Health Department of Western Australia. ■

MY TAKE

Don't Give Up on B Vitamins Yet

The VITATOPS trial indicated that there is still weak evidence for a small relative risk reduction in fatal or nonfatal stroke with B vitamin supplementation. This is one reason why B vitamins might still be potentially worthwhile in stroke and TIA patients. A much larger global trial would be needed to confirm or refute such moderate effects.

Indeed, there are numerous examples of treatments that required an accumulation of data from large, sufficiently powered trials along with meta-analyses of the data from those trials before the benefits of the treatments were appreciated. Examples include antiplatelet treatment with aspirin, cholesterol reduction with drugs, and tamoxifen for breast cancer.

While the VITATOPS trial does not provide sufficiently robust evidence in support of B vitamin supplementation for secondary prevention of vascular events after stroke or TIA, there is still a place for further trials of homocysteine-lowering treatment.

PETER SANDERCOCK, M.D., *is with the department of clinical neurosciences, Western General Hospital, Edinburgh. His comments are paraphrased from an editorial (Lancet Neurology 2010 Aug 4 [doi:10.1016/S1474-4422(10)70188-5]). He reported that he has no conflicts of interest.*

Hearing Loss Among 12- to 19-Year-Olds Is on the Rise

BY DENISE NAPOLI

FROM JAMA

Roughly 20% of 12- to 19-year-olds in the United States have some form of hearing loss, up from 15% of adolescents surveyed between 1988 and 1994, a study has shown.

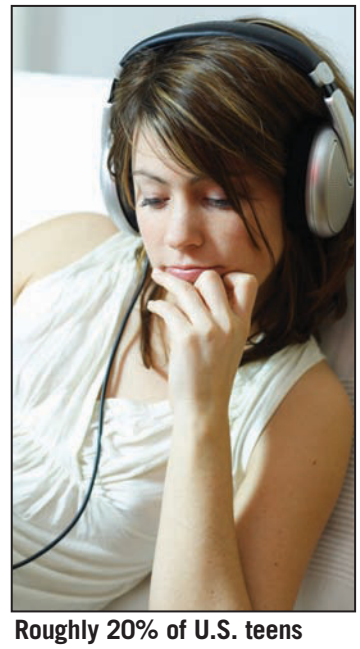
That represents a significant 31% jump that is likely underestimated, according to Dr. Josef Shargorodsky of the Brigham and Women's Hospital in Boston and his associates.

Dr. Shargorodsky, who is also of the Massachusetts Eye and Ear Infirmary, Boston, and his associates looked at data from the National Health and Nutrition Examination Survey (NHANES) 2005-2006 and compared them with data from NHANES III, conducted between 1988 and 1994. Both surveys provide nationally representative data on U.S. civilians aged 12-19 years, and both surveys included audiometry testing of both high- and low-frequency hearing (JAMA 2010; 304:772-8).

A total of 2,928 NHANES III participants who had full data from a complete audiometry exam were included for analysis in the more recent study; there were 1,771 participants from NHANES 2005-2006 who had complete data.

There were no differences between the groups in terms of age, race, sex, or poverty-income ratio, although NHANES III participants were more likely to have had a history of three or more ear infections.

Dr. Shargorodsky and his associates found that among NHANES III participants, surveyed between 1988 and 1994, the prevalence of any hearing loss greater than 15 dB among 12- to 19-year-olds was 15%. By the 2005-2006 survey, in contrast, that number had jumped to 20%, representing roughly 6.5 million individuals.



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Roughly 20% of U.S. teens have some form of hearing loss.

The increases persisted when the data were stratified by type of hearing loss. For example, 11% of NHANES III participants had unilateral hearing loss; by 2005-2006, that number had jumped to 14%. The same increase was repeated when looking only at bilateral hearing loss, with a prevalence of 4% during NHANES III and 5.5% in 2005-2006.

The investigators also found that high-frequency hearing loss (13% in 1988-1994, vs. 16% in 2005-2006) was more prevalent than low-frequency loss (6% in 1988-1994, vs. 9% in 2005-2006) in both time periods.

However, only the change in high-frequency loss was significant.

Even more significant—and more troubling—was the increased prevalence of mild or worse hearing loss (25 dB or greater) in the 2005-2006 survey (as opposed to "slight" hearing loss of between 15 and 25 dB). That figure jumped from 3.5% to 5%—or more than 1 in 20 adolescents.

Dr. Shargorodsky and his associates pointed out some limitations to their study. For one, they wrote, "children whose hearing aids could not be removed, who could not tolerate earphones, or who had cochlear implants were not tested," although this likely contributed to underestimation of hearing loss, if anything.

Additionally, the study's cross-sectional design could not assess causality.

"Interval factors between surveys, such as vaccination against *Haemophilus influenzae* and *Streptococcus pneumoniae*, as well as greater awareness of music-induced hearing loss, may have led to the expectation of no change or a reduction in the prevalence of hearing loss, but this was not observed," the researchers said.

Dr. Shargorodsky and his associates reported having no disclosures relevant to this study, which was funded by the Massachusetts Eye and Ear Infirmary Foundation and the Vanderbilt University. ■