

Benefits of Multivitamins Unclear, Panel Finds

Members call for legislation that would expand the FDA's role in addressing oversight of multivitamins.

BY JEFF EVANS
Senior Writer

BETHESDA, MD. — Evidence of the effectiveness and safety of multivitamin and mineral supplements to prevent chronic diseases is too sparse and ambiguous to recommend for or against their use, according to a panel of experts at a conference on multivitamin and mineral supplements and chronic disease prevention sponsored by the National Institutes of Health.

But the fact that half of all American adults take some form of multivitamin and/or mineral (MVM) supplement indicates that more efficacy and safety data should be gathered and greater industry oversight is needed to ensure supplement quality and adequate reporting of adverse events, the 13-member panel agreed.

The panel targeted its recommendations specifically toward disease prevention in adults and not in children, pregnant women, or those with vitamin or mineral deficiencies.

The panelists found evidence generated by randomized, controlled trials that supports the use of certain individual or specific combinations of vitamins and minerals for reducing the progression of macular degeneration, reducing bone loss and fracture risk, and preventing esophageal and gastric cancers.

But in many other cases, firm conclusions could not be reached on the benefit of particular vitamins and minerals or combinations of the two for other types

of cancer, cardiovascular disease, and cataracts.

In particular, the panel recognized the following supportive evidence:

► Vitamin D and calcium supplements taken together have been shown to increase bone mineral density and prevent hip and nonvertebral fractures in postmenopausal women (Cochrane Database Syst. Rev. 2004;1:CD004526; Cochrane Database Syst. Rev. 2001;1:CD000227).

► In another trial, people who took vitamins C and E, β -carotene, and zinc had less progression of age-related macular degeneration than those who did not receive such supplements (Acta Ophthalmol. Scand. 1998;76:224-9).

► In a Chinese trial, a combination of vitamin E, β -carotene, and selenium significantly reduced the incidence and mortality of esophageal and gastric cancer (Cancer Epidemiol. Biomarkers Prev. 1994;3:161-6).

► Recommendations made by the Centers for Disease Control and Prevention urge women of childbearing age to take folic acid supplements to prevent neural tube defects in infants.

Yet in two separate cancer prevention trials, researchers found that β -carotene actually increased lung cancer incidence and mortality in smokers and male asbestos

workers (J. Natl. Cancer Inst. 1996;88:1550-9; N. Engl. J. Med. 1994;330:1029-35).

If a patient is an active smoker, "I would urge doctors to discourage them from taking β -carotene supplementation," said panel member Audrey F. Safflas, Ph.D., professor of epidemiology at the University of Iowa, Iowa City. In addition, "I would urge physicians to inquire about their patients' vitamin and supplement intake," she said.

Panel members expressed concern over the lack of regulatory oversight of the

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production and labeling of multivitamin/mineral supplements, and they made a plea for legislation that would expand the role of the Food and Drug Administration to address such issues. If the FDA required

specific safety data from dietary supplement manufacturers and/or distributors, the agency could then:

► Inform consumers and health professionals about the tolerable upper limit of MVM supplements and the risks and benefits of exceeding those limits.

► Develop a mandatory adverse event reporting system for dietary supplements.

► Require product labeling to display the MedWatch toll-free telephone number and Web site address to facilitate the reporting of adverse events.

Depending on the vitamin or mineral, anywhere from 1% to 11% of users consume particular supplements at levels above the tolerable upper limit, said panelist Patsy M. Brannon, Ph.D., who is a

professor in the division of nutritional sciences at Cornell University, Ithaca, N.Y. Evidence suggests that such high-intake use occurs most often with vitamins A, B₃, and E, as well as zinc, selenium, and iron, she added.

Given the large numbers of people taking an MVM, the panel acknowledged that relatively little is known about supplements.

Over the past 8 years, only about 30,000 adverse events associated with MVMs have been reported to MedWatch, and the majority of these have been reported with concomitant use of other medications, said panelist Robert D. Gibbons, Ph.D., director of the Center for Health Statistics at the University of Illinois, Chicago.

"Given the huge number of individuals who are taking these substances, there are a relatively small number of reports, so it was our opinion that probably this was not as well publicized as it could be," said panel member Dr. Douglas B. Kamerow, who is a professor of clinical family medicine at Georgetown University, Washington.

In addition, uncertainties in the measurement of vitamin and mineral intake in studies and in real-world practice make it difficult to determine the effect of supplementation on chronic disease and any adverse events associated with their use, the panel noted.

The panel members proposed building a detailed national database of MVM supplements, and developing a strategy aimed at identifying the possible interactions of MVM supplements with nutrients or prescribed and over-the-counter medications. ■

Obesity Appears to Be a Stronger Asthma Risk Factor in Women

BY BRUCE JANCIN
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KEYSTONE, COLO. — Obesity appears to be modestly associated with subsequent development of asthma, particularly in women, Dr. David A. Beuther reported at a meeting sponsored by the National Jewish Medical and Research Center.

His metaanalysis of data from the Nurses' Health Study and six other large prospective studies totaling well over 200,000 subjects with 2- to 10-year follow-up concluded that women who became overweight or obese were 68% more likely to develop asthma within 1 year than those who maintained a body mass index (BMI) below 25 kg/m².

In men, a BMI greater than 25 was associated with a 46% increase in incident asthma in 1 year, according to Dr. Beuther of the Denver center.

All seven of the prospective studies showed a positive relationship between obesity and asthma. In many of the studies, the relationship didn't achieve statistical significance; however, when the data were pooled, the results became highly significant.

A major caveat regarding the putative

obesity-asthma link is that most studies to date have relied on self-reported asthma or physician-diagnosed asthma without confirmatory pulmonary testing. The question arises: Do these heavy patients truly have asthma, or do they merely develop asthmalike symptoms of wheezing and shortness of breath because of obesity-induced chest wall restriction?

Dr. Beuther is conducting a bronchoscopic study designed to answer this question, as well as to

better characterize the airway inflammation present in obese asthmatic patients. He has found that many obese patients who carry the diagnosis of asthma do not actually have the disease upon rigorous testing.

And yet the obesity-asthma relationship certainly has biologic plausibility. Obesity is at its essence a systemic inflammatory state.

Receptors for leptin, a proinflammatory cytokine produced by adipocytes, are found in the lungs. It is possible that the upregulated systemic inflammatory state of obesity spills over to contribute to airway inflammation and asthma.

A couple of relatively small studies in asthmatic children are supportive. In one, 23 asthmatic children were found to have higher leptin levels than controls—and their leptin levels dropped to that of controls

within several weeks after going on inhaled corticosteroid therapy (Ann. Allergy Asthma Immunol. 2004;93:277-80). And in a study of 102 asthmatic children, elevated leptin was associated with a twofold increased prevalence of asthma. Atopic asthmatics had far higher leptin levels than nonatopic asthmatics (J. Allergy Clin. Immunol. 2004;114:254-9).

In addition, recent

preliminary data suggest obesity and asthma share four chromosome loci, Dr. Beuther continued.

If obesity is assumed to be an independent risk factor for asthma, it is reasonable that obese asthmatics who lose weight should experience improvement in their respiratory disease. The single randomized, controlled, 38-patient study of medical weight loss and asthma performed to date showed a positive correlation.

More physicians are recognizing the advantages of bariatric surgery for losing substantial weight and keeping it off. Published studies show patients average 30% weight loss maintained at 10 years, compared with a typical 5% short-term weight loss with medical therapy that fades away by 1 year.

Bariatric surgery could be a key but underused tool for understanding obesity and asthma. Most bariatric surgery studies are observational, lack a control group, and do not define asthma rigorously. For example, in a study of 298 morbidly obese patients, 30% were classified as asthmatic at the time of their bariatric surgery. Two years post surgery, 79% of the asthmatics had subjectively improved asthma symptoms (Obes. Surg. 2004;14:1381-8). ■

