Folate, Vitamin B_{12} Cut Fracture Risk After Stroke

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SAN FRANCISCO — Preliminary evidence suggests that it's reasonable to give poststroke patients supplements of folate and vitamin B_{12} to prevent fractures, Steven R. Cummings, M.D., said at a meeting on osteoporosis sponsored by the University of California, San Francisco.

Supplementation also might reduce fracture risk in patients who are housebound or elderly, who might be deficient in these vitamins. "I don't yet think you can rely on this as a treatment for osteoporosis in other settings until we have more data," added Dr. Cummings, professor emeritus of epidemiology and biostatistics at the university and director of clinical research at the California Pacific Medical Center Research Institute.

He has applied for a grant to study whether these safe and inexpensive supplements might reduce fracture risk in all kinds of people, but results will not be available for at least 2 years, if he gets the grant.

Stroke doubles to quadruples the risk of subsequent hip fracture. A high homocysteine level is a risk factor for stroke and for osteoporosis in the elderly, even though it is not associated with decreased bone density, several large cohort studies have shown. Vitamin B_{12} commonly is used with folate to suppress homocysteine concentrations.

In a Dutch study of more than 1,100 people in two cohorts, those with homocysteine levels in the highest quartile had nearly double the risk for hip fracture or nonspine fractures over a 6- to 8-year period compared with those with the lowest-quartile levels (N. Engl. J. Med. 2004;350:2033-41).

In a separate, double-blind study, approximately 559 Japanese patients who had had a stroke were randomized to 2 years of dietary supplementation with placebo or 5 mg folate/day and 1,500 mcg B_{12}/day. Homocysteine levels decreased by 38% in the treatment group and increased by 31% in the placebo group. The treatment group had 78% fewer hip fractures, compared with the placebo group (JAMA 2005;293:1121-2).

"That is the biggest fracture reduction that I have seen yet in the field of osteoporosis. That is impressive," Dr. Cummings said. The results are even more impressive considering that both groups showed about a 3% loss in metacarpal bone mineral density, and patients physically fell at similar rates (two per year in each group).

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DR. CUMMINGS

"These kinds of numbers make me think that this is almost too good to be true," he added. Because folate and vitamin B_{12} are so safe and inexpensive, though, it's reasonable in the meantime to offer them to select groups of patients.

No one knows how these agents might work to decrease fracture risk. "We assumed that all of the effect would be in bone density, but it's not," he said.

Dr. Cummings and other researchers also have their eyes on another safe and inexpensive agent that might prevent and treat osteoporosis—nitrates.

A 1998 observational study found that women who took nitrates intermittently had 3%-5% higher bone mineral densities in hips and heels, compared with women who did not take nitrates or took them continuously.

A separate study reported by investigators at the University of Toronto randomly assigned postmenopausal women with osteopenia or osteoporosis to take 5 mg or 20 mg of nitrates or placebo each day. After 4-6 months, measures of bone resorption decreased by 36% in the 5-mg group and by 45% in the 20-mg group, compared with placebo.

"That's sort of like what you get from estrogen, and close to what you get with some bisphosphonates," he said. Estrogen and bisphosphonates do not affect bone formation, but nitrates increased markers of bone formation by 16% and 23%, compared with placebo in this study.

Raising the funding needed for studies is difficult, however, because no pharmaceutical company stands to profit from sales of nitrates, Dr. Cummings said. ■

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