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Folic Acid Fortification May Have Lowered Stroke Deaths

• By Lisa Drayer, MA, RD

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NEW YORK (CBS) You could be reducing your risk for a stroke without even knowing it. And you may have the government to thank.

Fortifying enriched grain products with folic acid in the 1990s appears to have been followed by a decline in stroke and ischemic heart disease deaths, according to research presented Friday at the American Heart Association's 44th annual Conference on Cardiovascular Disease Epidemiology and Prevention.

"We found evidence of a three-fold acceleration in the decline of stroke-associated mortality that is temporally related to fortification of flour with folic acid," said study investigator Lorenzo D. Botto, M.D., a medical epidemiologist with the Centers for Disease Control and Prevention's National Center on Birth Defects and Developmental Disabilities in Atlanta. "If folic acid fortification is responsible for the improvement in stroke-associated mortality, the public health benefits are substantial."

In 1998, the FDA published a final rule requiring enriched bread and grain products to be fortified with folic acid, because of its role in protecting against birth defects in a growing fetus. At the time, researchers hypothesized that fortification might offer a secondary benefit of reducing serum homocysteine concentrations in the population as a whole, which might lead to a decline in death rates due to cardiovascular disease and stroke.

Indeed, after analyzing national death certificate data among individuals of all genders and racial groups, aged 40 or older, from 1990 to 2001, researchers found that overall stroke mortality rates declined by 4.5 percent per year after 1997, as compared to about 1 percent per year, before 1997. Overall, this was associated with a 10 to 15 percent lowered risk of stroke-associated mortality in the three years after fortification (1999-2001), compared with the three years before fortification (1994-96), and was most likely related to the prevention of 31,000 stroke-associated deaths, as well as 17,000 deaths related to ischemic heart disease.

How Folic Acid Protects Us

Folic acid lowers levels of homocysteine, an amino acid in the blood. High levels of this amino acid are associated with increased risk for heart disease, specifically heart attacks and strokes. Researchers think high homocysteine somehow causes an insult

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on the vascular wall, weakening the vessel and making it more prone to damage. In the study, fortification of flour with folic acid was shortly followed by a 14 percent reduction of the serum homocysteine concentration, from 9.6 ìmol/L to 8.3 ìmol/L.

A clinical trial published last month in the Journal of the American Medical Association known as the Vitamin Intervention for Stroke Prevention (VISP) revealed that high dose folic acid supplementation among a group of stroke patients with abnormally high homocysteine levels resulted in a moderate reduction of homocysteine, but this did provide protection against recurrent stroke.

Both groups were given a multivitamin in addition to B vitamin supplementation, and over a 2-year period, researchers found that there was no significant difference seen in risk of recurrent stroke among individuals who experienced at least a 2 ìmol/L drop in homocysteine after taking 2.5 mg of folic acid (in addition to other B vitamins), as compared to the group that supplemented their diet with 20 ug of folic acid, which experienced a 0.3 ìmol/L drop in homocysteine.

But researchers say this study does not discount the value of folic acid in providing protection against cardiovascular disease. "In the VISP trial, those with baseline high levels of homocysteine did have a higher risk of stroke over the 2 years," says Dr. Quanhe Yang, lead researcher in the fortification study. He also points out the fact that a 2 ìmol/L difference in homocysteine was still associated with reduced overall mortality and cardiovascular events.

James Toole, MD, lead author of the VISP trial, agrees that his own study does not downplay the importance of folic acid in any way, and that the results seen in his study could possibly be due to the fact that his population was older, and therefore they may have not been consuming folic acid-fortified foods for most of their adult life. "Their population was a younger group who hadn't experienced a stroke, and so they were looking at primary prevention. It might be that you have to start consuming more folic acid before you have a stroke or heart attack in order to be protected."

Both Toole and Yang agree that for a specific population at high risk for cardiovascular disease, the amount of folic acid needed to reduce homocysteine levels to a therapeutic level may be higher than that for an average population, which was studied in this latest research. But confusing the issue is the fact that we still don't know what level of homocysteine is ideal. "Right now, all we're able to do is to look at the average homocysteine level, and compare that to cardiovascular disease risk" says Toole.

Folic Acid Requirements

If you are at high risk for heart disease, experts say it is a good idea to take a multivitamin with 400 ug of folic acid. In fact, just last month, as part of their new guidelines for cardiovascular disease prevention in women, the American Heart Association recommended folic acid supplements for high risk women with high levels of homocysteine, as an adjunct to a heart healthy diet, although they emphasize that you should check with your doctor first.

"For individuals at high risk for heart disease who maintain high homocysteine levels despite consuming a heart healthy diet, I give folic acid supplements," says Dr. Robert H. Eckel, Chair of the Council on Nutrition, Physical Activity, and Metabolism, of the American Heart Association.

Additionally, all women of childbearing age should consume 400 ug of folic acid, to prevent neural tube defects in a growing fetus, such as spina bifida. Since the damage

can occur during the first trimester (before a woman may be aware she is pregnant), it is important for all women of childbearing age to consume this vitamin.

Just last week, a Swedish study suggested that natural folate (the form found in foods) may help to reduce the risk of ovarian cancer in women who consume alcohol. This finding is consistent with previous research on folic acid and reduced risk of breast and colorectal cancer among individuals who consume alcohol.

Since too much folic acid can mask a deficiency of vitamin B12, however, a problem seen in older adults, experts say it's a good idea to get tested for B12 levels if you take folic acid supplements. High amounts (over 1000 ug) may lead to nerve damage as well.

More Ways than One to Get Your Folate

The Institute of Medicine, in setting the Daily Recommended Intakes for folate, defined Dietary Folate Equivalents (DFEs):

1 ug of DFEs = 1 ug of food folate = 0.5 ug of folic acid taken on an empty stomach = 0.6 ug of folic acid with meals.

Thus, the RDA for folate for adults is 400 ug DFEs and may be met with 400 ug of food folate or 240 ug folic acid from enriched food products.

According to Dr. Martha H. Stipanuk, Professor in the Division of Nutritional Sciences and Director of Graduate Studies in the Field of Nutrition at Cornell University, the requirements were based on currently-available estimates folate bioavailability. "Food folate is about 50% available, whereas folic acid, taken with food is about 85% available. Thus folic acid taken with a meal is 1.7 times as available as food folate; folic acid taken on an empty stomach is twice as available as food folate."

One thing to keep in mind: Although synthetic folic acid is better absorbed than the natural folate in foods, this does not ensure that a fortified food is a healthier option than a non-fortified food (and that you can't get your folate with simple additions).

For example, a 3/4 cup of Frosted Flakes (1 serving) has 20% of the Daily Value of folic acid (80 ug or 160 ug DFE). But it also is low in fiber and protein (It contains 1 gram of each). Kashi Go Lean is not fortified, but contains 10 grams of fiber and 8 grams of protein for the same sized serving. Add just a cup of orange juice (109 ug folate or 109 ug DFE) to your Kashi and you will get 25% of your daily folic acid requirement.

Likewise, enriched bread is fortified with about 40 ug of folic acid (80 ug DFE or 20% of your daily requirement), but is low in protein and fiber. Whole wheat bread has 2 fiber, and 3 grams of protein, and you can add spinach to your sandwich to boost folate intake – 1 cup of chopped spinach has 108 ug folate, or 27% of your daily requirements.

Here is a meal that would allow you to meet your daily folate needs, or 400 ug DFE:

¼ cup Special K cereal (25%)
½ cup of orange juice (12.5%)
½ cup of cooked lentils (45%)
1 cup raw spinach (27%)

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