Folate scores a win in animal studies: Brief, high doses of B vitamin blunt damage from heart attack

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Long known for its role in preventing anemia in expectant mothers and spinal birth defects in newborns, the B vitamin folate, found in leafy green vegetables, beans and nuts has now been shown to blunt the damaging effects of heart attack when given in short-term, high doses to test animals.

In a new study, an international team of heart experts at Johns Hopkins and elsewhere report that rats fed 10 milligrams daily of folate, also known as folic acid or vitamin B9, for a week prior to heart attack had smaller infarcts than rats who took no supplements. On average, researchers say, the amount of muscle tissue exposed to damage and scarred by the arterial blockage was shrunk to less than a tenth.

The team's findings, set for publication in the April 8 edition of the journal Circulation, come just weeks after other international studies in humans suggested that low-dose folic acid supplements may prevent dementia in the elderly and premature births.

"We want to emphasize that it is premature for people to begin taking high doses of folic acid," says senior study investigator David Kass, M.D., a professor at The Johns Hopkins University School of Medicine and its Heart Institute.

"But if human studies prove equally effective, then high-dose folate

could be given to high-risk groups to guard against possible heart attack or to people while they are having one," says Kass.

The more likely and most practical advantage to ingesting supplements, he says, lies in folic acid's potential to act as a short-term buffer for people who may be having a heart attack and who rush to their local emergency room complaining of chest pain.

Clinical trials are expected in the near future, although Kass says a major challenge in testing is that a high dose of folic acid for humans comparable to that given the rats would require an average-size adult to swallow more than 200 one-milligram pills per day, "an impractical and unrealistic regimen, even if the body excretes the excess."

In addition, he cautions, "we do not yet know if folate is safe to consume in this high a dose, or how much or how little of it is needed to be effective," citing 25 milligrams per day as the highest dose previously tested safe to consume in adults as.

Kass says that such large amount of folate may also yield unpredictable side effects. Some studies have linked the nutrient supplement to increased rates of colon and prostate cancer.

Each year, an estimated 565,000 first-time heart attacks occur in the United States, with an additional 300,000 recurrent heart attacks.

Results from the new study, conducted in rats - dozens were fed supplements and dozens more did not receive any - showed that overall pumping function during heart attack remained strong in vitamin B9-fortified animals.

The amount of blood pumped by the treated hearts during a 30-minute window when blood flow to the heart was restricted to simulate a heart attack stayed near normal for rodents, at an average ejection fraction of 73 percent. Meanwhile, it fell in the untreated group to 27 percent.

Similarly, the muscle wall at the front of the heart kept contracting during heartbeats, thickening by 37 percent in the supplement-fed group, but the muscle could barely compress, thickening by 5 percent, in the untreated group. (Sixty percent would be the normal amount of thickening in a healthy rat heart.)

Moreover, researchers found that an injection of folic acid into the bloodstream of rats that had never before taken supplements, within the first 10 minutes of a heart attack, was almost equally as effective as preventive therapy in reversing muscle damage, and in lowering infarct size by a factor of 10.

“Folic acid is already well known to be safe to consume in high doses in the short term, and it is very inexpensive, costing pennies per milligram, so its prospects look promising,” says Kass.

Researchers plan further tests to determine precisely why folate protects the heart, and to determine how effective it is in not-as-high doses. But they point out that it has long been known for its role in the normal workings of the cell’s principal energy source, the mitochondria, whose function is essential to maintaining healthy blood vessels.

It was this evidence that led to the latest study, which, says lead investigator An Moens, M.D., suggests that folate acts as an energy reserve in the heart, “providing much needed energy for muscle contraction, in the form of ATP, at the same time the heart is being starved for oxygen-carrying blood by a blocked artery.”

According to Moens, a postdoctoral cardiology research fellow at Johns Hopkins, study results showed that high-energy phosphate levels went down 43 percent in the blood of treated rats, but levels dropped by one-third more (by 66 percent) in untreated rats.

“With more fuel, the heart kept pumping even though its blood flow was reduced,” says Moens, now a cardiologist at the University of Antwerp in Belgium. “The smaller heart attacks seemed related to this better energy balance in the heart produced by the folate.”

In the study, heart function was monitored by more than two dozen key tests, such as echocardiogram and magnetic resonance imaging, as well as by blood analysis before, during and after the heart attack, when blood flow was allowed to resume in the coronary artery that had been blocked.

Among the team’s other findings that backed up the protective effects of folate on the heart were mild, slight dips in systolic blood pressure during heart attack in treated rats, while pressure fell in untreated animals by 25 percent. Similarly, blood flow was stable in the treated group, but dropped by 40 percent in untreated animals. Post-heart attack buildup of dangerous chemicals, known as reactive oxygen species, was halved in treated rats. And fatal arrhythmias, unstable heartbeats that can immediately follow a heart attack, also went down from 36.7 percent to 8.3 percent in the supplement-fed group.

“In future, we might just pop in an I.V., and give people high-dose folate while they are waiting for their catheterization or CT scans to search for blockages,” says Moens.

Source: Johns Hopkins Medical Institutions