B Vitamin Therapy Doesn’t Trim MI, Stroke Risks

No patient subgroup gained from the therapy, and those with high baseline homocysteine fared worse.

BY BRUCE JANCIN
Denver Bureau

STOCKHOLM — Lowering plasma homocysteine with B vitamin therapy does not prevent subsequent MI and strokes in patients who have had an MI — to the contrary, it may even be harmful, according to the results of the first large randomized treatment trial to examine the issue.

“The homocysteine hypothesis is dead. Homocysteine is not a causal risk factor. It is an innocent bystander,” Kaare Harald Bonaa, M.D., told this news service at the annual congress of the European Society of Cardiology.

Homocysteine’s relationship to cardiovascular disease has been a topic of intense investigation in the past decade. The homocysteine story would now appear to illustrate the hazards of extrapolating from epidemiologic association to clinical practice in the absence of favorable treatment outcome studies.

“The strength of considerable epidemiologic evidence linking high plasma homocysteine to increased MI and stroke rates, many American and European physicians have in recent years suggested B vitamin therapy to reduce homocysteine levels in their patients at high cardiovascular risk. The rationale was that since such therapy was inexpensive, it was thought safe, and could have turned out to have a big payoff in reduced clinical events, it might have been a reasonable strategy to use while awaiting results of randomized treatment outcome studies.

But now the Norwegian Vitamin Trial (NORVIT), has shown that such therapy does not prevent cardiovascular events; indeed, it may even increase the risk. And there was also a disturbing trend, albeit not statistically significant, for an increase in cancer, said Dr. Bonaa, professor of cardiology at the University of Tromso (Norway).

Dr. Bonaa was the principal investigator in NORVIT, a randomized, double-blind, multicenter trial in which 3,749 Norwegian patients were followed for 3.5 years after assignment to 0.8 mg/day of vitamin B6; 40 mg/day of vitamin B12; both, or placebo during their hospitalization for an acute MI. Participants also received all of the standard drugs given post MI.

Patients in the two folate acid arms of NORVIT experienced a rapid and sustained mean 28% decrease in homocysteine. The rationale for including the vitamin B12 arms in the trial came from epidemiologic studies showing that people with low dietary intake of this nutrient also have increased risks of stroke and MI.

The primary end point in NORVIT was a composite of fatal and nonfatal MI and stroke. It occurred in 18% of the placebo group and in a similar percentage of those who got folate acid or vitamin B12 alone. However, the incidence in patients randomized to both folate acid and vitamin B12 was 20% higher, a highly significant difference. (See box.)

In a multivariate analysis, combination therapy was associated with statistically significant 20% increased relative risks of three study end points — MI, MI and stroke, and death — compared with the other three study groups, along with a more than 30% increase in cancer, which was not statistically significant.

No patient subgroup benefited from B vitamin therapy. Those with a high baseline homocysteine — that is, in excess of 13 mcg/L — fared worst, with a 27% increase in cardiovascular events regardless of whether they received B vitamins.

Studies are being planned to learn whether folate acid accelerates cancer cell growth. Discussant Ian Graham, professor of epidemiology and public health at the Royal College of Surgeons, and a cardiologist at Trinity College, Dublin, agreed that the NORVIT cancer findings warrant further study. While epidemiologic data suggest a diet rich in folate protects against cancer, there is also evidence from in vitro studies to support the argument that folate promotes cancer cell growth.

NORVIT was sponsored by the Norwegian Research Council, the Norwegian Council on Cardiovascular Research, and other nonprofit institutions, with no industry support.

Device May Improve Outcomes of In-Hospital Cardiac Arrest

BY BRUCE JANCIN
Denver Bureau

VANCOUVER, B.C. — The tradition al “code blue” strategy of handling in-hospital cardiac arrests has remained essentially unchanged for 30 years, a period during which — in sharp contrast — massive resources have been devoted to improving public access defibrillation for out-of-hospital cardiac arrest, Antoni Martinez-Rubio, M.D., said at a meeting of the International Academy of Cardiology.

“We [cardiologists] have spent lots of money and done lots of reports looking at what happens outside our hospitals, but we have not looked hard enough at what happens inside our hospitals,” according to Dr. Martinez-Rubio, a cardiologist at Sabadell Hospital, Barcelona.

Thirty percent of all sudden cardiac deaths occur in-hospital. The literature indicates that the acute survival rate following attempted resuscitation of in-hospital cardiac arrest is 40%-45%. Only 15%-20% of patients are discharged alive and with only a modest improvement in neurologic impairment.

Given the inefficiencies and generally poor outcomes of the code blue approach, it is time for a major change in how in-hospital cardiac arrests are managed. And the necessary tool is already at hand in the form of the Food and Drug Administration-approved Powerheart Cardiac Rhythm Module (CRM), Dr. Martinez-Rubio added.

The CRM continuously monitors a patient’s heart at the bedside, detects onset of a life-threatening arrhythmia, and automatically delivers a shock for external cardioversion. In the multicenter European trial headed by Dr. Martinez-Rubio and sponsored by Cardiac Science Inc., the mean lapsed time between arrhythmia onset and delivery of a defibrillatory shock was 15 seconds.

Contrast that to the traditional code blue scenario, in which a patient is monitored by telemetry in a high-cost ICU or in an intermediate care unit. In that setting, a detected arrhythmia triggers an alarm, which has to be recognized by the nursing staff, which then calls for the crash cart and physicians to come to the bedside. All of this takes time. And, as a recent American Heart Association report emphasized, the earlier cardiac resuscitation can be performed, the better. Indeed, survival rates decrease by 7%-10% for every minute defibrillation is delayed, the cardiologist continued.

In addition to the 117-patient European multicenter study led by Dr. Martinez-Rubio (J. Am. Coll. Cardiol. 2003;41:627-32), there has also been a favorable single-center Brazilian study of the CRM (Resuscita
cion 2004;63:11-6). In another example, physicians at Mount Sinai Medical Center in Brooklyn, N.Y., reported that the response time to study patients with cardiac arrest in their ICU and CCU averaged nearly 3 minutes, compared with just 38 seconds for the CRM to charge up and deliver a shock (Resuscitation 2004;68:48).

“In my opinion, this should be the new standard of care,” Dr. Martinez-Rubio declared.

He provided an update on an ongoing study he is directing in which patients at risk for arrhythmic death are being randomized to traditional monitoring and code blue response in the CCU or to a stay in a regular hospital ward while connected to the Powerheart.

With 95 patients randomized to date, during 3,540 hours of monitoring outside the CCU there have been 122 arrhythmic events, including 36 cases of ventricular arrhythmia. There are as yet no significant differences in clinical outcome; however, the cost savings achieved by using the CRM on a regular ward instead of traditional monitoring in the CCU amounts thus far to $89,000. And that’s assuming a $400 per day difference in the cost of staying in a regular ward, compared with the CCU, which is probably a considerable underestimate.

In addition, an ongoing prospective study at the University of Michigan, Ann Arbor, is comparing the effectiveness of the traditional code blue emergency response protocol with the CRM in patients staying in the university hospital’s cardiac ICU. The study is being led by Kim A. Eagle, M.D., clinical director of the university’s cardiovascular center.