All NSAIDs Increase Mortality in MI Survivors

BY BRUCE JANCIN
Denver Bureau

DALLAS — The use of NSAIDs—whether cyclooxygenase-2–selective or not—in patients who've had an acute MI increases their risk of mortality, especially in higher doses, according to data from the Danish National Patient Registry.

To patients with ischemic heart disease, "I would say that you should try to avoid these drugs, but if you need to take them, use lower doses," Dr. Gunnar H. Gislason said at the annual scientific sessions of the American Heart Association.

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DR. GISLASON

The widely publicized prior studies that revealed the increased risks of MI and death associated with NSAID use—and that resulted in some COX-2-selective agents being taken off the market as well as an across-the-board black box label warning for all NSAIDs—were based largely on patient populations with an average background cardiovascular risk. Dr. Gislason and his coinvestigators sought to learn whether the increased cardiovascular risk associated with NSAID use also applied to patients at very high cardiovascular risk: namely, those who've already had an MI. Funding for their study was provided by the Danish Heart Foundation.

Dr. Gislason reported on all 58,432 patients discharged from Danish hospitals following a first acute MI during 1995-2002. A centralized national prescription database revealed that more than 40% of these first-MI survivors subsequently filled at least one prescription for an NSAID. Nearly 10% of all patients used a COX-2 inhibitor after having their MI.

The two most widely used, older, nonselective NSAIDs in Denmark are ibuprofen (used by 17.5% of the post-MI patients), and diclofenac (used by 10.6%). Rofecoxib was taken by 5.2% of the patients, whereas celecoxib was used by 4.3%.

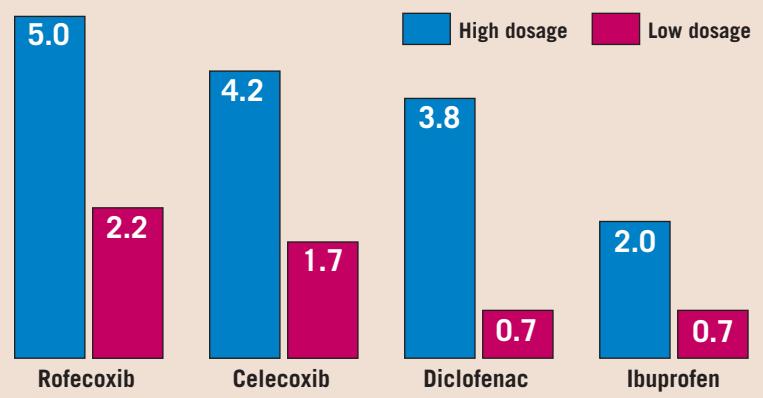
The use of a COX-2 inhibitor in high doses—that is, more than 25 mg/day for rofecoxib or 200 mg of celecoxib—was associated with a four- to fivefold increased mortality risk during the time a patient was on the drug, compared with NSAID nonusers. Lower-dose therapy with a COX-2 inhibitor was associated with a lesser—albeit significantly increased—mortality risk. (See box.) The risk calculations were adjusted for comorbid illnesses, age, gender, and socioeconomic status, according to Dr. Gislason of Bispebjerg University Hospital, Copenhagen.

High-dose therapy with the nonselective NSAIDs was also associated with increased mortality risk.

The rate of out-of-hospital deaths was unusually high in the NSAID users. The Danish investigators are still sorting out the causes using death certificate data. One possibility, as yet unconfirmed, is that NSAID users experienced an excess of arrhythmic deaths outside the hospital. In addition, hospitalization for heart failure following an MI was more common among users of COX-2 inhibitors.

There was no significant difference in the rates of readmission for a second MI between NSAID users and nonusers, possibly because more than 90% of the Danes were on low-dose aspirin post MI, a therapy that could have blunted any pro-MI adverse effect of NSAIDs, he said. ■

Adjusted Risk of Mortality of Post-MI Users of NSAIDs, Compared With Nonusers



Note: Based on all 58,432 patients discharged from Danish hospitals after their first acute MI during 1995-2002.
Source: Dr. Gislason

Proteinuria Boosts Mortality After Myocardial Infarction

BY MITCHEL L. ZOLER
Philadelphia Bureau

STOCKHOLM — Patients with proteinuria following a myocardial infarction had significantly worse outcomes than did patients without proteinuria, Powell O. Jose reported in a poster presentation at the annual meeting of the European Society of Cardiology.

"Assessing proteinuria in patients following an MI may improve their risk stratification," said Mr. Jose, a researcher at Brigham and Women's Hospital in Boston.

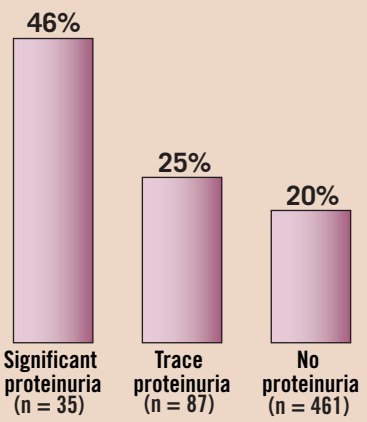
The analysis used data collected in the Survival and Ventricular Enlargement (SAVE) trial, one of the first studies to establish the efficacy of an ACE inhibitor in patients with left ventricular dysfunction after an MI (N. Engl. J. Med. 1992;327:669-77).

The post hoc analysis by Mr. Jose and his associates focused on 583 of the 2,231 patients in the SAVE trial who were assessed for proteinuria with a dipstick test when they entered the study. The urine tests showed that 122 patients had proteinuria and 461 did not. During an average follow-up of 42 months, patients with proteinuria had a 31% total mortality and a 27% incidence of cardiovascular mortality, compared with a 20% total mortality and a 17% cardiovascular mortality in the patients without proteinuria.

In a multivariate analysis that controlled for demographic and clinical measures, patients with proteinuria were 73% more likely to die from any cause and 81% more likely to die from cardiovascular disease, compared with MI patients without proteinuria. Both of these differences were statistically significant.

The link between proteinuria and mortality was most dramatic in the 35 patients who had significant proteinuria. In this subgroup, the all-cause mortality during follow-up was 46%, whereas in the 87 patients with trace proteinuria, the all-cause death rate was 25%. In patients without proteinuria, mortality during follow-up was 20%. ■

All-Cause Mortality in Patients With Proteinuria



Source: Mr. Jose

Subclinical Hypothyroidism Linked to CHF in Elderly

BY MARY ANN MOON
Contributing Writer

Elderly patients with subclinical hypothyroidism have a higher rate of congestive heart failure than do those who are euthyroid, according to Dr. Nicolas Rodondi, of the University of California, San Francisco, and associates.

Overt hypothyroidism is known to be associated with cardiovascular disease (CVD), but studies evaluating a possible link between subclinical hypothyroidism and CVD have produced conflicting results. Dr. Rodondi and his associates conducted what they described as the first prospective study to assess the risk of congestive heart failure (CHF) events in subjects with subclinical hypothyroidism.

The investigators assessed thyrotropin levels in 2,730 men and women aged 70-79 years who were participating in a large cohort study of aging. The subjects were followed for 4 years to determine whether these hormone levels were related to CHF or other cardiovascular disease events.

A total of 338 subjects (12.4%) were found to have subclinical hypothyroidism, defined as an elevated level of thyrotropin and a normal level of free thyroxine (T_4). During follow-up, 178 subjects had CHF events (Arch. Intern. Med. 2005;165:2460-6).

Subjects with moderately to severely elevated thyrotropin levels (7.0 mIU/L or greater) had more CHF events (35.0 per 1,000 person-years) than did those who were euthyroid (16.5 per 1,000 person-years). Each standard deviation increase of 4.0 mIU/L was associated with a 30% increase in CHF events.

This link was even stronger among subjects known to have had previous CHF events. The rate of recurrent CHF events was seven times higher in those with subclinical hypothyroidism than in those who were euthyroid.

In contrast, subjects with mildly elevated thyrotropin (4.5-6.9 mIU/L) did not have higher rates of CHF events. Subclinical hypothyroidism was not found to be associated with other coronary heart disease events, stroke, peripheral arterial disease, CVD-related mortality, or total mortality.

In an editorial accompanying this report, Dr. Lawrence M. Crapo, of Santa Clara Valley Medical Center, San Jose, Calif., noted that these findings "certainly support the idea that the treatment of severe subclinical hypothyroidism with levothyroxine in patients younger than 80 years may be beneficial, but this remains to be proved in a randomized prospective therapeutic trial."

The results further indicate that patients with mild hypothyroidism probably would not benefit from such treatment, Dr. Crapo said (Arch. Intern. Med. 2005;165:2451-2). ■