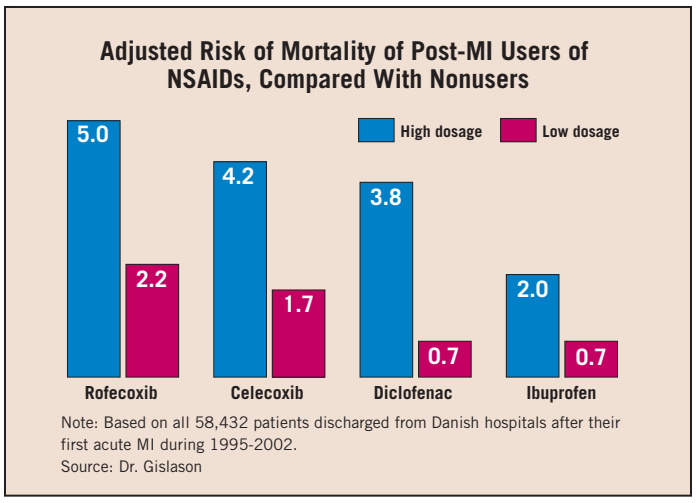

High Doses of NSAIDs After Acute MI Increase Mortality

BY BRUCE JANCIN
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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.

Widely publicized prior studies revealed that the increased risks of MI and death associated with NSAID use were based largely on populations with an average background cardiovascular risk. The studies resulted in some COX-2-selective agents being taken off the market and a black box label warning for all NSAIDs.

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 have already had an MI. Their study was funded by the Danish Heart Foundation.

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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 patients used a COX-2 inhibitor after having their MI.

In Denmark, the two most widely used, older, nonselective NSAIDs 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—although 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. One possibility for this, 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, which could have blunted any pro-MI adverse effect of NSAIDs, he said. ■

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