NSAIDs During a Heart Attack Raise Death Rate

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CHICAGO — Being on a nonsteroidal anti-inflammatory drug when an ST-elevation MI strikes is associated with markedly worse 30-day outcomes in fibrinolytic-treated patients, Dr. C. Michael Gibson said at the annual scientific sessions of the American Heart Association.

This new observation, coupled with the recent report that patients placed on an NSAID after MI had worse outcomes, indicates the peri-infarct period "should be a nonsteroidal-free time," according to Dr. Gibson, director of the Thrombolysis in Myocardial Infarction (TIMI) data coordinating center at Brigham and Women's Hospital, Boston.

"I think if someone [with an MI] is on an NSAID, you probably need to be very vigilant in your antiplatelet therapy," he added.

The increased risk of developing an MI while on nonaspirin NSAIDs has received enormous publicity, with some cyclo-oxygenase-2–selective NSAIDs being withdrawn from the market for that reason. Dr. Gibson and his TIMI coinvestigators asked a different question: What's the impact of being on an NSAID when an MI occurs?

They conducted a retrospective secondary analysis of the prospective Enoxaparin and Thrombosis Reperfusion for Acute Myocardial Infarction Treatment, TIMI 25 (EXTRACT-TIMI 25) study, in which more than 20,000 patients undergoing thrombolysis for ST-elevation MI were randomized to enoxaparin or unfractionated heparin. Within 7 days prior, 572 had taken an NSAID, whereas 19,907 had not.

The incidence of recurrent MI within 30 days was 6.5% in the NSAID group, compared with 4.1% in patients who had not been on an NSAID. The rate of death or MI was 15.9% in NSAID users and 10.8% in nonusers. Incorporating indicators of pump failure into the outcome, the rate of death, recurrent MI, severe heart failure, or shock was 18.2% in NSAID users and 12.6% in nonusers. Most of these end points occurred within the first 7-10 days post MI, Dr. Gibson noted.

The two groups differed at baseline in several key ways. NSAID users were older, were more likely to have hypertension, had slightly worse renal function, and had a 20% prevalence of diabetes, compared with 15% in NSAID nonusers. Thus, NSAID users were a higher cardiovascular-risk cohort, and hence more likely to be on aspirin and other cardiac drugs.

After researchers adjusted for these and other potential confounders in a multivariate logistic regression analysis, NSAID use at the time of MI was associated with a 44% greater relative risk of recurrent MI and a 29% increased risk of death, MI, severe heart failure, or shock; both relative risks were statistically significant.

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Dr. Gibson stressed that as a retrospective analysis of a study in which patients weren't randomized to NSAID use, these data must be considered hypothesis generating. There is no information as to which specific NSAIDs patients were on or what doses were used. It's possible that the worse outcomes in NSAID users were due to unidentified confounders.

Nevertheless, several biologically plausible potential mechanisms exist for the observed association between NSAID use at the time of a major MI and worse outcomes, he continued. It's known that many over-the-counter NSAIDs interfere with access of aspirin's binding site to cyclo-oxygenase-1, which might lessen aspirin's cardioprotective effect.

NSAID inhibition of prostaglandin E2 may also lead to hypertension and increased afterload, which could account for the high rates of heart failure and shock. NSAID inhibition of prostaglandin E1 can cause hyperkalemia, increasing the risk of sudden arrhythmic death. And, as is well known, cyclo-oxygenase-2inhibition may increase the risk of thrombosis. Audience members were surprised at the trend for more TIMI-grade major and minor bleeding in NSAID nonusers: 3.8%, compared with 3.5% in NSAID users. Dr. Gibson agreed, adding "if these drugs are prothrombotic, that might explain it in part." ■