NSAIDs During a Heart Attack Raise Death Rate

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CHICAGO — Being on a nonsteroidal anti-inflammatory drug (NSAID) at the time of a heart attack increases the likelihood of death within 30 days, according to Dr. C. Michael 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 antplatelet therapy," he added.

The increased risk of developing an MI while on nonaspirin NSAIDs has received enormous publicity, with some cycle-oxygenase-2–selective NSAIDs being withdrawn from the market for that reason. Dr. Gibson and his TIMI co-investigators 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 thrombolytic 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. In overall mortality in survivors, however, there was not a significant difference. In the TIMI-25 study, patients with diseases, including diabetes, exacerbations, and even intracranial bleeding did not experience a difference in death or recurrent MI.

Dr. Gibson noted 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 cyclooxygenase-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, cyclooxygenase-2 inhibition may increase the risk of thrombosis.

The results of the study and others’ finding suggest that being on an NSAID at the time of an MI results in death and that cyclooxygenase inhibition may be a trigger for cardiovascular events, suggesting a potential for cyclooxygenase inhibition prophylaxis.

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