Correspondence

Letter by Alla et al Regarding Article, "Duration of Treatment With Nonsteroidal Anti-Inflammatory Drugs and Impact on Risk of Death and Recurrent Myocardial Infarction in Patients With Prior Myocardial Infarction: A Nationwide Cohort Study"

To the Editor:

We read with interest the article by Schjerning Olsen et al[1] on the risk of myocardial infarction (MI) and the duration of nonsteroidal anti-inflammatory drug (NSAID) use. Using a national database, the authors elegantly demonstrate that even short-term use of NSAID carries an increased risk of death and recurrent MI in patients with prior MI. Although we agree with the authors' conclusions, a few issues require further clarification. First, competitive inhibition of aspirin binding at the platelet cyclooxygenase-1 receptor is 1 of the proposed mechanisms contributing to the adverse effect of nonselective NSAIDs in patients with MI.[2] Considering the critical need for effective dual-antiplatelet therapy in the first few months to a year after MI (particularly those receiving coronary stents), the risks associated with NSAIDs use are likely to be significantly greater within this time frame after MI. Were the authors able to assess the effect of time between the index MI and initial exposure to NSAIDs on the risk of recurrent MI in their study?

Second, even short-term NSAIDs can cause/aggravate gastrointestinal problems (dyspepsia/gastrointestinal bleeding) and result in premature discontinuation of aspirin.[3] Could this be 1 of the contributors to the risk of recurrent MI with NSAIDs apart from inhibition of endothelial cyclooxygenase -2 and aspirin antagonism at the cyclooxygenase-1 receptor? Furthermore, there is an increased risk for MI following antiplatelet therapy cessation (occurring on average ≈8–11 days following cessation).[4] Would the authors be able to assess the impact of NSAID prescription on adherence with antiplatelet therapy (refill interval/frequency of aspirin, clopidogrel, or both)? Finally, it is well known that inflammatory disorders like rheumatoid arthritis independently increase risk of MI. Although the authors performed a sensitivity analysis excluding patients with known rheumatologic disorders, an important caveat needs to be highlighted. Rheumatologic disorders are often difficult to diagnose because of their nonspecific symptoms, and there frequently is a significant time lag between the onset of symptoms and diagnosis (as long as 10 years).[5] Therefore, it is conceivable that some patients in the current study had an underlying rheumatologic disorder that was not yet diagnosed at the time of initial NSAID prescription (ie, prescription use of NSAIDs could long antedate the diagnosis of rheumatoid arthritis). Whereas this proportion is unlikely to be large, it could be a potential confounder biasing the results of the current analysis.

In summary, irrespective of the mechanisms, the current study adds to accumulating evidence supporting the association between NSAID use and recurrent MI. We agree with the authors' conclusion that even short-term use can have an adverse cardiovascular impact, although we believe that the magnitude of risk is higher in the first few months to a year after the index MI. Health agencies, media, and professional societies must work together to enhance physician and patient awareness and hopefully limit prescription and nonprescription use of NSAIDs in patients with established coronary artery disease.

Disclosures

None.

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