

Inhibition of Clinical Benefits of Aspirin on First Myocardial Infarction by Nonsteroidal Antiinflammatory Drugs

Tobias Kurth, MD, ScD; Robert J. Glynn, PhD, ScD; Alexander M. Walker, MD, DrPH;
K. Arnold Chan, MD, ScD; Julie E. Buring, ScD;
Charles H. Hennekens, MD, DrPH; J. Michael Gaziano, MD, MPH

Background—There is clear evidence from numerous randomized trials and their meta-analyses that aspirin reduces risks of first myocardial infarction (MI). Recent data also suggest that other nonsteroidal anti-inflammatory drugs (NSAIDs) may interfere with this benefit of aspirin.

Methods and Results—We performed subgroup analysis from a 5-year randomized, double-blind, placebo-controlled trial of 325 mg aspirin on alternate days among 22 071 apparently healthy US male physicians with prospective observational data on use of NSAIDs. A total of 378 MIs were confirmed, 139 in the aspirin group and 239 in the placebo group. Aspirin conferred a statistical extreme ($P < 0.00001$) 44% reduction in risk of first MI. Among participants randomized to aspirin, use of NSAIDs on 1 to 59 d/y was not associated with MI (multivariable adjusted relative risk [RR], 1.21; 95% confidence interval [CI], 0.78 to 1.87), whereas the use of NSAIDs on ≥ 60 d/y was associated with MI (RR, 2.86; 95% CI, 1.25 to 6.56) compared with no use of NSAIDs. In the placebo group, the RRs for MI across the same categories of NSAID use were 1.14 (95% CI, 0.81 to 1.60) and 0.21 (95% CI, 0.03 to 1.48).

Conclusions—These data suggest that regular but not intermittent use of NSAIDs inhibits the clinical benefits of aspirin. Chance, bias, and confounding remain plausible alternative explanations, despite the prospective design and adjustment for covariates. Nonetheless, we believe the most plausible interpretation of the data to be that regular but not intermittent use of NSAIDs inhibits the clinical benefit of aspirin on first MI. (*Circulation*. 2003;108:1191-1195.)

Key Words: myocardial infarction ■ aspirin ■ prevention ■ epidemiology