NSAID Use Linked to Elevated Risk of Stroke

VITALS

Major Finding: People taking an NSAID – ibuprofen, diclofenac, rofecoxib, or celecoxib – had a significantly increased risk for fatal or nonfatal stroke on days taking the drug in a multivariate analysis. The risk ranged from about 30% higher in ibuprofen users to about twofold higher in diclofenac users. People taking naproxen did not have a significantly increased stroke risk.

Data Source: A million people from the general Danish population aged 10 or older as of January 1997, followed for 9 years.

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STOCKHOLM – Treatment with various types of nonsteroidal anti-inflammatory drugs was linked with a significantly higher risk for strokes in a review of a million people from the Danish general population during 1997-2005.

"Commonly used NSAIDs such as diclofenac and ibuprofen were associated with an increased risk of hemorrhagic and ischemic stroke," and the link showed a dose-response relationship, reported Dr. Gunnar H. Gislason. The public needs "increased awareness about the cardiovascular risk of NSAIDs, even in healthy people," said Dr. Gislason, a cardiologist at Gentofte Hospital in Hellerup, Denmark.

The study focused on three nonselective NSAIDs, ibuprofen, diclofenac, and naproxen; and on two COX-2 selective NSAIDs, rofecoxib (Vioxx) and celecoxib (Celebrex). The results showed significant links between use of all of these drugs except naproxen and an increased risk for fatal and nonfatal strokes.

The study used data collected in Danish national prescription, patient, and mortality records. In Denmark, all five NSAID formulations are available only by prescription. The database included 4.6 million people as of Jan. 1, 1997, the entire population of Danish citizens aged 10 or older as of that date. The study included follow-up data through the end of 2005.

The analysis focused on the 1.5 million people who had no hospitalizations during the 5 years prior to January 1997, and further focused on the 1 million people with one or more filled prescriptions for a selected list of drugs during the 2 years before January 1997. The median age of these 1 million people was 39 years in January 1997, and 58% were men.

During the 9 years of follow-up, 55% of the study group never used an NSAID, 17% filled one prescription, 14% filled two or three prescriptions, and 14% filled four or more prescriptions for NSAIDs. Ibuprofen was the most commonly prescribed NSAID, used by 29% of the study population, followed by diclofenac (17%), and naproxen (4%). Rofecoxib and celecoxib were each used by about 2% (total exceeds 45% because some people used more than one NSAID). The total, average duration of use for each drug was small, ranging from a mean of 13 days for rofecoxib to 24 days for naproxen.

In an analysis controlling for age, gender, comorbidities, and concomitant medications, people treated with ibuprofen, diclofenac, rofecoxib, or celecoxib had a significantly increased risk for fatal or nonfatal stroke. The increased risk ranged from about 30% higher among all ibuprofen users to about double in all diclofenac users. The two coxibs each linked with about an 80% increased risk. The only NSAID without a significantly linked risk was naproxen.

In general, the risk increased at higher dosages. For example, ibuprofen users who averaged 1,200 mg/day or less had about a 20% increased risk of fatal or nonfatal stroke on the days they took the drug. People who took more than 1,200 mg a day had an average increased risk of about 80%. Both increases were significant.

Analysis also showed significantly increased risks for ischemic stroke with ibuprofen and diclofenac, but not with the other NSAIDs. Again, the risk was greater at dosages of more than 1,200 mg/day of ibuprofen or at least 100 mg/day of diclofenac. ■