

AHA Statement
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AHA statement recommends doctors change approach to prescribing pain relievers for patients with or at risk for heart disease

American Heart Association Scientific Statement

DALLAS, Feb. 27 — Many doctors should change the way they prescribe pain relievers for chronic pain in patients with or at risk for heart disease based on accumulated evidence that nonsteroidal anti-inflammatory drugs (NSAIDs), with the exception of aspirin, increase risk for heart attack and stroke, according to an American Heart Association statement published today in *Circulation: Journal of the American Heart Association*.

“We believe that some physicians have been prescribing the new COX-2 inhibitors as the first line of treatment. We are turning that around and saying that, for chronic pain in patients with known heart disease or who are at risk for heart disease, these drugs should be the last line of treatment,” said Elliott M. Antman, M.D., FAHA, lead author of the American Heart Association scientific statement and professor of medicine at Harvard Medical School and Brigham and Women’s Hospital.

“We advise physicians to start with non-pharmacologic treatments such as physical therapy and exercise, weight loss to reduce stress on joints, and heat or cold therapy. If the non-pharmacologic approach does not provide enough pain relief or control of symptoms, we recommend a stepped-care approach when it comes to prescribing drugs. Take into account the patient’s health history and consider acetaminophen, aspirin and even short-term use of narcotic analgesics as the first step. If further relief is needed, physicians should suggest the least selective COX-2 inhibitors first, moving progressively toward more selective COX-2 inhibitors, which are at the bottom of the list, only if needed. All drugs should be used at the lowest dose necessary to control symptoms and prescribed for the shortest time possible.”

Drugs in the NSAIDs class inhibit cyclooxygenase (COX), an enzyme system that comes in two major forms: COX-1, which the body produces constantly in most tissues, and COX-2, produced during the body’s inflammatory response. Because COX-1 is also protective of the gastrointestinal (GI) tract, long-term use of drugs that suppress COX-1, such as aspirin, have been associated with gastrointestinal complications, including ulcers. “Selective” COX-2 inhibitors were developed to avoid the GI complications of traditional NSAIDs, not because they had advantages in terms of pain relief, Antman said.

However, multiple studies have indicated an increased risk of cardiovascular disease (CVD) complications from COX-2 selective NSAIDs, particularly in patients with prior CVD or risk factors for CVD.

“Recent studies indicate that the cells lining the blood vessels have more of the COX-2 enzyme than initially thought. So it’s possible that inhibiting the COX-2 pathway can make a person’s blood more likely to clot. There is also an increase in sodium and water retention, which in turn could worsen heart failure and produce high blood pressure,” Antman said. “The more you inhibit COX-1, the greater the increase in GI risk; the more you inhibit COX-2 the greater the cardiovascular risk.”

The scientific statement comes two years after the association released the last one on the issue. It was prompted, in part, by new analyses indicating that the increased cardiovascular risk associated with COX-2 selective NSAIDs may also extend to less selective traditional NSAIDs.

The statement includes details from a meta-analysis indicating that, compared with placebo, COX-2 selective drugs seem to increase the risk of a heart attack by about 86 percent. The statement also points out that two common NSAIDs traditionally thought of as non-selective – diclofenac and ibuprofen – appear to increase the relative risk of cardiovascular disease. In the last two years, the U.S. Food and Drug Administration (FDA) added warning statements to NSAIDs, other than aspirin, pointing out the increased risk for cardiovascular events.

One non-selective NSAID, naproxen, did not seem to increase CVD risk in these analyses. However, Antman pointed out that although naproxen appeared safer than the other NSAIDs, relatively few studies have been done with naproxen and doctors should continue to be cautious about prescribing it as well, pending more information.

"This is a fast-moving field with new information available from multiple sources," Antman said. "We feel the most important thing the American Heart Association can do is to give practical advice to clinicians who treat cardiac patients with pain every day."

Because there are so many drugs in the NSAID class and because they can affect either COX-1 or COX-2 or both, it is very important to know where a given drug falls in the range of selectivity, particularly when evaluating the results of head-to-head comparisons of different drugs, Antman said. The statement contains guidance that helps doctors see where individual drugs lie on the continuum of COX-1 versus COX-2 selectivity.

Selective COX-2 inhibitors have been in the news since the FDA removed the selective COX-2 inhibitor, rofecoxib, from the market in 2004. Since then, other COX-2 selective drugs have been removed from the market in the United States and other countries. One selective COX-2 inhibitor, celecoxib, remains on the market, but warnings on it were strengthened and the FDA advised that patients with a history of CVD or risk factors for CVD should be informed of the possibility of increased risks from long-term use, Antman said.

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