

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs): A lesson in unexpected adverse cardiovascular effects.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) have become one of the most popular and widely used medications in existence. For many years, athletes around the world have used these agents to relieve the pain and suffering associated with bone, joint, and muscle pain.

While all medications have side effects, the most common side effects from NSAIDs is stomach or gastrointestinal (GI) discomfort or bleeding. Musculoskeletal pain relief is effective with the use of NSAIDs, but the first generation of a newer drug formulation inhibited COX-1 receptors in the body that are more likely to also stimulate conditions that favored abdominal pain and GI bleeding. These newer drugs tended to cause "blood thinning" by disrupting normal blood clotting. Examples of COX-1 inhibitors are Advil, Aleve, Motrin, and Relafen. These drugs, in small doses, are available as over-the-counter medications. Aspirin and Tylenol, while different types of NSAIDs, are other commonly used anti-inflammatory pain relievers. Fortunately, all these earlier available drugs do not appear to be associated with a high incidence of cardiovascular (CV) complications.

Around 1990, medical science advanced the idea that selective inhibition of COX-2 enzymes in the body might still permit pain relief, but markedly decrease GI side effects, including bleeding. In 1999, the Food and Drug Administration (FDA) approved this newest class of drugs. Subsequently, the public became familiar with the beneficial effects of COX-2 inhibitors like Vioxx, Celebrex, and Bextra. This newest class of drugs was associated with excellent pain relief, but what appears to be an unacceptable incidence of adverse CV outcomes, mainly the increased occurrence of heart attack and stroke. The mechanism of damage seems to be an enhanced prothrombotic state favoring the formation of blood clots in some people.

Several controlled scientific studies provide the data to show an unacceptable CV complication rate associated with usage of COX-2 inhibitors. Before the recent FDA led withdrawal of these COX-2 inhibitors, combined yearly sales exceeded \$5 billion in the United States. Within the past month, a jury awarded an individual COX-2 inhibitor individual user a major financial award related to the use and CV complications associated with Vioxx, a Merck pharmaceutical company product. This company was thought to be less than forthright with its release of information related to possible CV toxicities associated with its particular COX-2 pain relief product. Merck plans a legal appeal concerning this judgement.

What are the lessons learned from this ongoing controversial story related to drug safety that individuals in the general public can consider ?

1. All drugs have side-effects; some more and some worse than others.
2. Ask your health-care practitioner what signs and symptoms you should be watching for while taking a given drug.
3. Access the internet to gain general information about any drug you take. Use this information to help organize your questions when you talk with your physician.
4. While the FDA, pharmaceutical companies, and physicians are trying to help protect people to maximize health, while reducing pain and suffering, competing interests and priorities make our present healthcare delivery system less than ideal.
5. Support unbiased medical research and government initiatives to foster and create evidence based analysis and improved systems of checks and balances in drug development, safety, and long-term health consequences.