Cox-2 Inhibitors and Cardiovascular Risks

The controversy over the cardiovascular risks of cox-2 inhibitors stems from 2 main trials: VIGOR and CLASS. These two trials were designed to assess the gastrointestinal safety of rofecoxib (Vioxx) and celecoxib (Celebrex), respectively. From these trials, it was observed that the cox-2 inhibitors had a higher number of cardiovascular events than the NSAIDS that they were paired against. For example, in VIGOR, there were 4 fold more myocardial infarctions in the rofecoxib group than in the naproxen group.

There are a few possible mechanisms for increased CV risks in cox-2 inhibitors. First, since cox-1 is not inhibited, thromboxane (promotes platelet aggregation) is not inhibited. Cox-2 inhibits prostacyclin (inhibits platelet aggregation). This combination effect would theoretically increase platelet aggregation. Second, cox-2 inhibitors have been observed to increase blood pressure and cause edema.

There are also a few arguments on why cox-2 inhibitors do not increase CV risks. First, VIGOR used naproxen, which inhibits platelet aggregation (reversibly) longer than other NSAIDs. Therefore, Merck© has argued that naproxen is cardioprotective (however, studies have also shown that naproxen is NOT cardioprotective). Second, the VIGOR trial used patients with rheumatoid arthritis, who are already at a higher risk for cardiovascular events. Third, VIGOR did not allow patients to use low dose aspirin for cardioprotection.

Conclusion: we aren’t certain that cox-2 inhibitors increase CV risks. However, it would be wise to use caution when prescribing cox-2 inhibitors to patients, especially if they are at risk for cardiovascular events.

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