

Cardiovascular Effects of Nonsteroidal Antiinflammatory Drugs

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Aspirin has been on the market for 115 years. Beginning with the marketing of indomethacin for the treatment of rheumatoid arthritis in 1963, over twenty nonsteroidal antiinflammatory drugs (NSAIDs) with aspirin-like actions have been developed over the past half century, culminating with the introduction of a new class of selective inhibitors of cyclooxygenase (COX)-2, the coxibs, about fifteen years ago.

Although nuances in tolerability of various NSAIDs had been described in the pre-coxib era (based on clinical trials of a few hundred patients treated for up to a few months), important differences in safety were subsequently demonstrated in head-to-head randomised comparisons of individual coxibs and one or more traditional NSAIDs; these comparisons were based on clinical trials of tens of thousands of patients treated for up to a few years.

As a result of these more extensive trials, new light has been shed on the whole field of NSAID research during the past decade. The coxib trials added to information provided by epidemiological studies that had previously associated regular use of NSAIDs with increased blood pressure and enhanced risk of congestive heart failure, and identified an increased risk of myocardial infarction as a class effect of COX-2 inhibitors. This risk was largely unexpected and paradoxical, given that aspirin, the prototypic COX inhibitor, had been clearly shown to be cardioprotective, over a wide range of doses up to 1,500 mg daily.

I will discuss the mechanisms underlying the cardiovascular effects of low-dose aspirin, traditional NSAIDs, and coxibs, in an attempt to reconcile the pharmacology of COX-isozyme inhibition with the contrasting results that have emerged from randomised clinical trials.