PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

COX-2 inhibitors and risks for cardiovascular events

ArticleInfo		
ArticleID	:	57
ArticleDOI	:	10.1186/ar-2001-71150
ArticleCitationID	:	71150
ArticleSequenceNumber	:	14
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2001–9–12 Received : 2001–9–12 Accepted : 2001–11–2 OnlineDate : 2001–11–5
ArticleCopyright	:	Biomed Central Ltd2001
ArticleGrants	:	

ArticleContext	:	130753311

Kazuki Takada,[Aff1]

Aff1 NIH, Bethesda, MD, USA

Keywords

COX-2 inhibitors, cardiovascular events, arthritis

Context

Generous use of NSAIDs for arthritis is limited by their gastrointestinal toxicity. Identification of a second form of cyclooxygenase (COX-2), and of the association of the gastrointestinal toxicity to COX-1, generated a hope for safer anti-inflammatory agents via selective COX-2 inhibition. Consequently, rofecoxib and celecoxib were introduced in 1999, and their advantage of gastrointestinal safety over NSAIDs was demonstrated. However, selective COX-2 inhibitors (coxibs) may reduce prostacyclin production without affecting thromboxane-A2 production, thus potentially leading to an increased cardiovascular disease (CVD) risk. Mukherjee *et al* undertook a systematic review on CVD risks of coxibs compared with that of NSAIDs.

Significant findings

Systematic search yielded two major (VIGOR and CLASS) and two small randomized controlled trials. Published data of the VIGOR and the CLASS studies were supplemented by the data subsequently submitted to the FDA by sponsors. The VIGOR study showed an increased CVD risk (relative risk [RR] = 2.38) in the rofecoxib group compared to the naproxen group. This increased risk would result in one additional cardiovascular event in every nine months in ~200 patients treated with rofecoxib compared to an equal number treated with naproxen. Aspirin was not allowed in the study, but the risk was more pronounced in aspirin-indicated patients (RR = 4.89) than others (RR = 1.89). No significant differences in CVD risks were found in the CLASS study (celecoxib 400 mg twice daily versus diclofenac or ibuprofen) or in two small trials (rofecoxib 12.5 mg/day versus nabumetone), all of which allowed aspirin use. However, predicted annual myocardial infarction rates in both the VIGOR (0.74%) and the CLASS (0.80%) studies were higher than that in the large cohort in the placebo group (0.52%) in a meta-analysis of primary cardiovascular prevention trials.

Comments

An effort to evaluate CVD risks of coxibs like Mukherjee's is necessary and welcome in order to elucidate their true advantage over NSAIDs. Although this systematic review is valid in estimating a relative risk of each coxib against its parallel control agent, it does not evaluate a "class effect" between coxibs and NSAIDs for the following reasons: firstly, control NSAIDs differ in their antiplatelet and antithrombotic capacities; secondly, the use of aspirin in the CLASS study could have abrogated a true difference in CVD risks between experimental and control agents, particularly in patients with higher baseline CVD risks; thirdly, a comparison of CVD risks of coxibs from these studies with that in historical placebo cohorts is of virtually no use due to significant differences in known and unknown confounding conditions, such as the increased risk of CVD inpatients with rheumatoid arthritis. Given the remarkable popularity and exposure of coxibs, CVD risks and renal effects of coxibs should be elucidated and carefully balanced against their GI advantages.

Methods

Systematic review of relevant randomized controlled trials via MEDLINE and the World Wide Web

Additional information

References

1. Mukherjee D, Nissen SE, Topol EJ: Risk of cardiovascular events associated with selective COX-2 inhibitors. JAMA. 2001, 286: 954-959.