

Do selective cyclo-oxygenase-2 inhibitors and traditional non-steroidal anti-inflammatory drugs increase the risk of atherothrombosis? Meta-analysis of randomised trials

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FROM ABSTRACT

Objective

To assess the effects of selective cyclo-oxygenase-2 (COX 2) inhibitors and traditional non-steroidal anti-inflammatory drugs (NSAIDs) on the risk of vascular events.

Design

Meta-analysis of published and unpublished tabular data from randomised trials, with indirect estimation of the effects of traditional NSAIDs.

Review methods

Eligible studies were randomised trials that included a comparison of a selective COX 2 inhibitor versus placebo or a selective COX 2 inhibitor versus a traditional NSAID, of at least four weeks' duration, with information on serious vascular events (defined as myocardial infarction, stroke, or vascular death).

Results

In placebo comparisons, allocation to a selective COX 2 inhibitor was associated with a 42% relative increase in the incidence of serious vascular events.

This was chiefly attributable to an increased risk of myocardial infarction.

Among trials of at least one year's duration, the rate ratio for vascular events was 45% increased risk.

The incidence of serious vascular events was similar between a selective COX 2 inhibitor and any traditional NSAID. **[Very Important]**

Conclusions

Selective COX 2 inhibitors are associated with a moderate increase in the risk of vascular events, as are high dose regimens of ibuprofen and diclofenac [Voltaren, Cataflam].

THESE AUTHORS ALSO NOTE:

“Traditional non-steroidal anti-inflammatory drugs (NSAIDs) are widely used to treat pain, but their long term use is limited by serious gastrointestinal side effects.”

It was hypothesised that selective COX 2 inhibitors would provide a safer alternative to traditional NSAIDs.

However, recent concerns about the cardiovascular safety of selective COX 2 inhibitors have limited their use.

“The accumulating evidence suggests that selective COX 2 inhibitors are associated with an increased risk of vascular events.”

This meta-analysis reviewed 138 randomised trials that included 145,373 participants.

The analysis showed a 42% increase in the incidence of a first serious vascular event in individuals taking COX 2 inhibitors as compared to those taking a placebo.

In this study, about two thirds of the vascular events had occurred in the nine long-term trials. [This implies that the longer one takes NSAIDs the higher the chances of having a vascular event.]

These authors “found no significant difference in the incidence of a serious vascular event between participants allocated to a selective COX 2 inhibitor and those allocated to a traditional NSAID.” **[Important]**

DISCUSSION

“When we considered all the randomised trial data, selective COX 2 inhibitors were associated with a highly significant 40% increased risk of serious vascular events, largely due to a 100% increased risk of myocardial infarction.”

“As traditional NSAIDs inhibit the COX 2 enzyme, these drugs might also be associated with an increased risk of vascular events.”

“Results indicated that high dose ibuprofen (800 mg three times daily) and high dose diclofenac [Voltaren, Cataflam] (75 mg twice daily) were each associated with an increased risk of vascular events, but that the risks of high dose naproxen (500 mg twice daily) were substantially smaller.”

CONCLUSIONS

"This meta-analysis has shown that selective COX 2 inhibitors are associated with a moderate increase in the risk of vascular events, as are high dose regimens of ibuprofen and diclofenac [Voltaren, Cataflam]."

"Selective COX 2 inhibitors are associated with a moderately increased risk of vascular events, largely attributable to a twofold increased risk of myocardial infarction."

KEY POINTS FROM DAN MURPHY

- 1) In this study, a selective COX 2 inhibitor was associated with a 42% relative increase in the incidence of serious vascular events, which was primarily an increased risk of myocardial infarction.
- 2) The longer one consumed NSAIDs, the greater the risk for serious vascular events and myocardial infarction.
- 3) The incidence of serious vascular events was similar between a selective COX 2 inhibitor and any traditional NSAID. **[Very Important]**
- 4) The traditional NSAIDs with the greatest risk of a serious vascular event, including myocardial infarction were ibuprofen and diclofenac [Voltaren, Cataflam].
- 5) The NSAID with the smallest risk of a serious vascular event, including myocardial infarction, was naproxen [naproxen: over-the-counter = Aleve; prescription = Naprosyn]
- 6) "Traditional non-steroidal anti-inflammatory drugs (NSAIDs) are widely used to treat pain, but their long term use is limited by serious gastrointestinal side effects."
- 7) This study showed a 42% increase in the incidence of a first serious vascular event in individuals taking COX 2 inhibitors as compared to those taking a placebo.
- 8) "Selective COX 2 inhibitors were associated with a highly significant 40% increased risk of serious vascular events, largely due to a 100% increased risk of myocardial infarction."

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