

All Seven NSAIDs Tied to Cardiovascular Risk

BY SHERRY BOSCHERT

FROM BMJ

Each of seven NSAIDs was associated with significantly increased risk for MI, stroke, or death from cardiovascular disease, compared with placebo, in the most comprehensive meta-analysis of the subject so far.

The relative risks with any individual NSAID, compared with placebo, often were double, triple, or quadruple the risk with placebo, the study found. The absolute numbers of MIs and other cardiovascular outcomes were small, but the network meta-analysis design of the study “provides the best available evidence on the safety of this class of drugs,” Dr. Sven Trelle and his associates reported.

Contrary to some previous reports, the current study also found no suggestion that this increased cardiovascular risk is specific to cyclo-oxygenase-2 (COX-2) inhibitors. Therefore the use of all NSAIDs – and the over-the-counter availability of some of them – should be reconsidered, Dr. Trelle stated (BMJ Jan. 11, 2011;342:c7086[doi/10.1136/bmj.c7086]).

The meta-analysis included any large, randomized controlled trials comparing any NSAID with other NSAIDs or placebo. Data were available for naproxen, ibuprofen, diclofenac, celecoxib, etoricoxib, rofecoxib, and lumiracoxib. The risk for a cardiovascular event had to increase by more than 30% to be considered significant.

Overall, naproxen appeared to be the least harmful NSAID in terms of cardiovascular outcomes. Risks were greatest with ibuprofen, diclofenac, etoricoxib, and lumiracoxib.

Four NSAIDs were associated with significantly increased risk for MI (the primary outcome in the current analysis) in 29 of the trials that reported 554 MIs. The relative risk for MI doubled with rofecoxib or lumiracoxib, was 35% higher with celecoxib, and was 61% higher with ibuprofen, compared with placebo. Evidence was lacking for increased MI risk with the other three NSAIDs.

Twenty-six trials reported 312 deaths from cardiovascular disease, accounting for 46% of all deaths in the trials. All NSAIDs except naproxen were associated with higher risk for cardiovascular death, which increased by 58% with rofecoxib, roughly doubled with ibuprofen, celecoxib, or lumiracoxib, and increased approximately fourfold with diclofenac or etoricoxib, compared with placebo.

All the NSAIDs were linked with increased risk for death from any cause, compared with placebo, and the increase was significant for all except naproxen. There were 676 deaths from any cause in 28 trials, and the risk of death roughly doubled with any of the other six NSAIDs.

Looking at a composite of nonfatal MI, nonfatal stroke, or cardiovascular death in 30 trials that reported 1,091 composite events, the risk increased with all the NSAIDs and increased significantly with all but naproxen. The odds for the composite outcome increased

43% with celecoxib, 44% with rofecoxib, 53% with etoricoxib, 60% with diclofenac, and more than doubled with lumiracoxib or ibuprofen.

An estimated 5% of all visits to U.S. physicians are related to prescribing NSAIDs, which are considered the cornerstone for managing the pain of osteoarthritis and other painful

conditions. Rofecoxib, a COX-2 inhibitor, was withdrawn from the market in 2004 after a randomized, placebo-controlled trial found its use was associated with increased cardiovascular risk. The Food and Drug Administration has since denied approval of etoricoxib because of an inadequate risk-benefit profile. ■

VITALS

Major Finding: Each of seven NSAIDs was associated with significantly increased risk for MI, stroke, or death from cardiovascular disease, compared with placebo.

Data Source: Network meta-analysis of 31 large, randomized controlled trials comparing any NSAID with other NSAIDs or placebo in 116,429 patients with 117,218 patient-years of follow-up.

Disclosures: The Swiss National Science Foundation funded the study. The investigators reported having no conflicts of interest.

Reliable angina relief – Nitrolingual® Pumpspray (nitroglycerin lingual spray)



Fire extinguisher image does not depict actual product.



Stability & Potency



Rapid Pain Relief



Ease of Use

Not actual size



Indications and Usage Nitrolingual® Pumpspray is indicated for acute relief of an attack or prophylaxis of angina pectoris due to coronary artery disease.

Important Safety Information Nitrolingual Pumpspray should not be used while taking phosphodiesterase inhibitors which are used for the treatment of erectile dysfunction. Nitrolingual Pumpspray should be used with caution if patients have low systolic blood pressure, are undergoing diuretic therapy, or show hypersensitivity to this and other nitrates or nitrites. Headache is the most commonly reported side effect with nitroglycerin. Patients may also experience episodes of dizziness, weakness, and other related side effects.

Nitrolingual®
Pumpspray
(nitroglycerin lingual spray)
0.4 mg nitroglycerin per spray



WWW.NITROLINGUAL.COM

© 2010 Arbor Pharmaceuticals, Inc. All rights reserved.

The following trademarks are either registered trademarks or trademarks of Pohl-Boskamp in the United States and/or other countries: Pohl-Boskamp word mark; Pohl-Boskamp logo; Nitrolingual word mark; Peppermint flavor of nitroglycerin; Peppermint scent of nitroglycerin; Nitrolingual Pumpspray shapes; Nitrolingual Pumpspray colors; and the sound of Nitrolingual Pumpspray. Arbor Pharmaceuticals' use of Nitrolingual is under license from G. Pohl-Boskamp GmbH & Co. KG.

Please see full Prescribing Information on next page.

NL.001.01