A bit of a cox-update: NSAIDS old, new and newer

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In the peri-operative setting, nonsteroidal anti-inflammmatory drugs (NSAIDs) and coxibs are often used in multimodal regimens to reduce patients' opioid requirements and opioid related symptoms. Gastrointestinal complications attributed to the traditional non-selective NSAIDs drove the development of COX-2 selective inhibitors (coxibs)[1], however cardiovascular (CVS) and cutaneous safety concerns led to withdrawal of rofecoxib and valdecoxib respectively, and safety warnings.[2,3] Non-selective NSAIDs have subsequently, also become the subject of CVS safety concerns. Additional safety issues are aspirin sensitive asthma and perioperative concerns regarding bone healing and renal function.

Studies in patients undergoing coronary artery surgery showed more thrombo-embolic events in the coxib groups than those receiving placebo, and resulted in coxibs being contraindicated in CABG surgery. By contrast, in a safety study of non-cardiac major surgery patients, the coxib group did not differ from the placebo patients in cardiovascular, renal, wound or gastrointestinal complications.[4,5,6] Meta-analyses also suggest a satisfactory profile in non-cardiac surgery.[7] Although parecoxib is the pro-drug of valdecoxib, it has only very rarely been associated with cutaneous reactions, probably due to very short-term use and uncommon re-exposure, and hence was not withdrawn from use.

The non-selective NSAIDs are still the most widely used anti-inflammatory analgesics peri-operatively, though parenteral options for nil-by-mouth or anaesthetised patients are limited to ketorolac and diclofenac.

COX-1 blockade in platelets reduces thromboxane production. Ketorolac is no longer recommended for intra-operative use because of bleeding problems and NSAIDs confer a small but measurable added risk of haemorrhage in airway surgery,[8,9] and diclofenac formulations are by slow, buffered intravenous infusion, or rectal route with slow onset of action. A potentially useful development is the new diclofenac formulation for bolus injection using cyclodextrin HPβCD to increase the aqueous solubility of the poorly water-soluble diclofenac, thereby improving its bioavailability and stability.

The effect of NSAIDs on bone healing remains a controversial issue in orthopaedic surgery involving bone fusion. Initial retrospective clinical audits and animal studies led to suspicions that NSAIDs may impede osteogenic activity in spinal fusion or fracture healing. The animal studies of bone healing are conflicting and difficult to interpret due to species differences in COX expression. Adequately powered randomised controlled trials designed to address this issue are required to address the concerns regarding NSAIDs in bone healing, and to examine whether COX-1 and COX-2 blockade have different profiles. Recent reviews suggest that short-term use is acceptable.[10,11]

Non-selective NSAIDs and coxibs reduce pain safely and effectively in many patients, however they are not as safe as initially thought. Both have similar cardiorenal profiles, and should be reserved for patients at low risk for cardiac failure, thromboembolic events or renal dysfunction.

References

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