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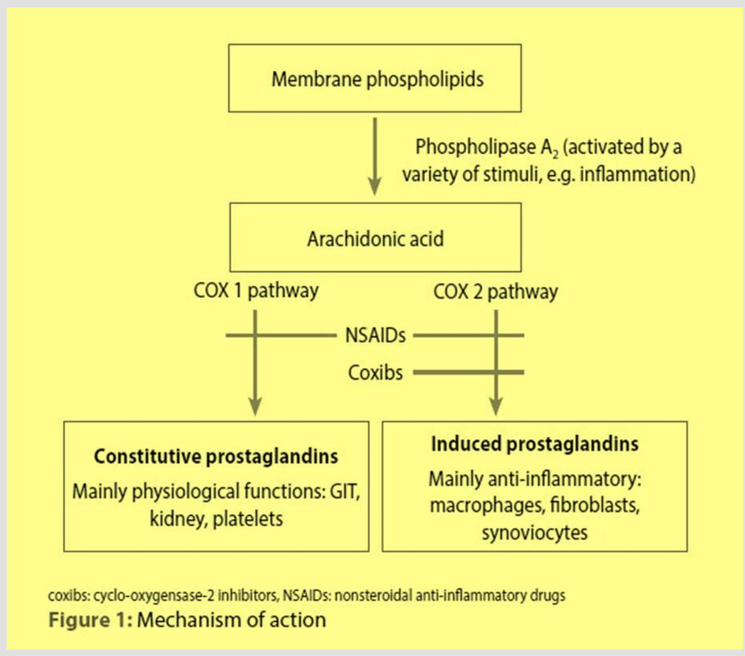
EVIDENCE-BASED PRESCRIPTION FOR CYCLO-OXYGENASE-2 INHIBITORS IN SPORTS INJURIES

Introduction:

Healthcare professionals are increasingly under pressure to return athletes to play in the shortest possible time. There is limited choice in providing treatment that speeds up tissue repair, while simultaneously maintaining good quality of healing. Although inflammation forms a fundamental part in the process of tissue repair, it may cause more pain, and limit functional restoration. Anti-inflammatory treatment with a cyclo-oxygenase-2 inhibitor (coxibs) differs in its mechanism of action (Fig.1), and has been widely recognised as being effective. Its potential detrimental effect on tissue repair, as described mainly in animal model studies, needs to be taken into account. Although the side-effects profile on the gastrointestinal tract favour coxibs over traditional NSAIDs, possible effects on the renal and cardiovascular systems also need to be considered. The prescription of coxibs should be pathology and situation specific. No clear guidelines are available on the correct time of administration and course duration, however literature is in agreement that administration should be for a limited time at the lowest effective dose possible.



coxibs: cyclo-oxygensase-2 inhibitors, NSAIDs: nonsteroidal anti-inflammatory drugs

Figure 1: Mechanism of action

Systemic adverse effects of coxibs:

While effective for pain relief & reducing inflammation, the side-effect profile of coxibs needs to be considered before they are prescribed to athletes.

- Gastrointestinal tract: Coxibs selectively blocks the induced prostaglandin pathway (pain and inflammation), but the potential exists for peptic ulceration, nausea, dyspepsia, constipation, erosion, perforation and bleeding, since COX-2 selectivity is not complete. However, reduced incidence of gastrointestinal tract side-effects are seen with the use of coxibs, compared to that of traditional NSAIDs.
- Renal: Although not deemed to influence normal renal physiology, an increased risk of hyponatraemia in endurance athletes exists due to impaired free water clearance. Factors contributing include: inexperience, a slow running pace, female athletes and a high availability of liquid on the course.
- Cardiovascular: Coxibs is associated with an increase in cardiovascular events. Thromboxane generated in platelets (via COX-1) is responsible for platelet activation, smooth muscle proliferation & vasoconstriction. Prostacyclin generated in vascular endothelial cells (via COX-2) leads to the inhibition of platelet aggregation & vasodilation. Coxibs selectively blocking the COX-2 pathway, results in Thromboxane being unopposed, and the anti-atherothrombotic effects of Prostacyclin removed. This implies a class phenomenon, rather than a specific drug effect, however pharmacodynamics & pharmacokinetic profiles have to be considered.

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Effect on different tissues:

Recent research, mainly on animal models, has shown some detrimental effects on tissue repair:

- Muscle: Healing is a 3-phase process: destruction, repair & remodelling. Reducing the destruction phase allows for faster pain relief & healing. Although anti-inflammatory treatment may limit this phase, it can also limit the repair and remodelling phase.
- Tendons: Injury is generally not an inflammatory process, and coxibs is therefore not indicated for anti-inflammatory actions in degenerative injury.
- Bone: Prostaglandins play an important role in osteogenesis. The effect of coxibs on osteogenesis may impair bone healing, especially when used more than 3-12 weeks.
- Ligaments: A similar healing process to muscle injury. Improved pain levels & return-to-play time has been demonstrated in human studies after ankle sprains. Commencement of treatment post-injury is still being debated, and its effect on long-term ligament repair after early use remains unclear.

Recommendations for use in sports injuries

- Coxibs decrease pain, swelling and loss of function.
- Coxibs efficacy, compared to NSAIDs, has been reported in ankle sprains, lower back pain & acute shoulder pain.
- Studies on its negative effect on tissue healing, were mostly performed on animal models, and remains a subject for debate.
- Prescription of coxibs should be pathology & situation specific. A pure analgesic drug should be considered if analgesic treatment is the primary aim - a NSAID might not be the best choice.
- On clinical examination revealing excessive inflammation, a coxib may be administered for a limited period at the lowest effective dose. Bursitis, synovitis & nerve impingement, due to soft tissue proliferation, responds best to anti-inflammatory treatment.
- Basic POLICE principles (protection, optimal loading, ice, compression & elevation) & other non-pharmaceutical modalities (physiotherapy), should be introduced in the treatment plan to minimise dependence on medication and expedite return to play.
- No rationale for the prophylactic use of NSAIDs in the prevention of pain during sport participation or for sore muscles after exercise. The regular intake of these drugs before exercise may lead to reduced tissue adaptation and delayed healing of musculoskeletal injuries.
- Adequate time for recovery is of the utmost importance.