Review

The future of traditional nonsteroidal antiinflammatory drugs and cyclooxygenase-2 inhibitors in the treatment of inflammation and pain

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Abstract:
Prostanoids act leading roles in a myriad of physiologic and pathologic processes because these autacoids participate in the amplification of biological responses induced by innumerable stimuli. The formation of prostanoids is operated by two synthases named cyclooxygenase (COX)-1 and COX-2. Traditional nonsteroidal antiinflammatory drugs (tNSAIDs) and COX-2 inhibitors (coxibs) give rise to antipyretic, analgesic, and antiinflammatory actions, through their reversible clogging of the COX channel of COX-2 – apart from aspirin which modifies irreversibly the catalytic activity of COX-2. tNSAIDs and COX-2 inhibitors resulted clinically equivalent for the relief of acute pain and symptoms of arthropathies but they failed to modify disease progression. Clinical evidence of the possible contribution of COX-1 in inflammation and pain in some occasion – as suggested by experimental and pharmacology studies – is orphan because none efficacy trial with COX inhibitors was designed to establish it. COX-2 inhibitors were developed with the aim to reduce the incidence of serious gastrointestinal (GI) adverse effects associated with the administration of tNSAIDs ensued as a consequence of the inhibition of cytoprotective COX-1-derived prostanoids. However, the reduced incidence of serious GI adverse effects compared to tNSAIDs demonstrated for 2 COX-2 inhibitors (e.g. rofecoxib and lumiracoxib) has been countered by an increased incidence of myocardial infarction and stroke detected in 5 placebo controlled trials involving the COX-2 inhibitors celecoxib, rofecoxib and valdecoxib. The future of COX-2 inhibitors will be an example of personalised medicine as their use will be restricted to patients who do not respond to tNSAIDs or with increased risk of GI complications.

Key words:
cyclooxygenase, nonsteroidal antiinflammatory drugs, coxibs, prostacyclin, thromboxane