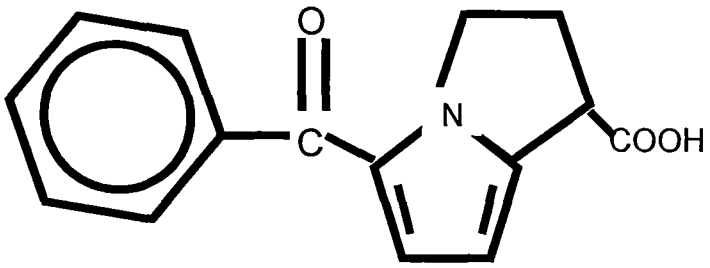
PHARMACOLOGY OF KETOROLAC



Ketorolac is a non steroidal anti inflammatory drug(NSAID) that exhibits potent analgesic effects but only moderate anti-inflammatory activity when administered IM or IV. This drug is useful for providing postoperative analgesia both as the sole drug (less painful ambulatory procedures) and to supplement opioids. It is likely that Ketorolac potentiates the antinocicepetive actions of opioids. In contrast to dose-dependent analgesic effects of opioids, Ketorolac and other NSAIDs appear to exhibit a ceiling effect with respect to postoperative analgesia. The use of Ketorolac as the sole intraoperative analgesic drug may be associated with an increased incidence of purposeful movement on surgical incision. Ketorolac, 30 mg IM, produces analgesia that is equivalent to 10 mg of morphine or 100 mg of Meperidine. An important benefit of Ketorolac-induced analgesia is the absence of ventilatory or cardiovascular depression. Also unlike opioids, Ketorolac has little or no effect on biliary tract dynamics, making this drug a useful analgesic when spasm of the biliary tract is undesirable.

Pharmacokinetics

After IM injection, maximum plasma concentration of Ketorolac is achieved within 45 to 60 minutes, and the elimination half time is about 5 hours. Protein binding exceeds 99% and clearance of this drug is decreased compared with that of opioids. Clearance is decrease further in elderly individuals, and the dose of Ketorolac should be less than that given to younger patients. Ketorolac is metabolised principally by glucuronic acid conjugation.

Side Effects

In common with other NSAIDS, Ketorolac inhibits platelet thromboxane production and platelet aggregation by reversible inhibition of prostaglandin synthetase. Bleeding time may be increased by a single IV dose of Ketorolac administered to patients with spinal anaesthesia. This modest prolongation of bleeding time and marked decrease in platelet aggregation lasts until the drug is eliminated from the body. The difference between platelet responses to Ketorolac during general versus spinal anaesthesia may reflect a hypercoagulable stage produced by the neuroendocrine response to surgical stress that normally occurs during general anaesthesia but not spinal anaesthesia. Conceptually, this stress response effect on coagulation could offset Ketorolac-induced effects on bleeding time, whereas the absence of this effect during spinal anaesthesia would permit the effect of Ketorolac on platelet aggregation to manifest. Increased postoperative blood loss attributed to administration of Ketorolac is consideration, but the clinical significance remains unproved.

Life threatening bronchospasm may follow the administration of Ketorolac to patients with nasal polyposis, asthma, and aspirin sensitivity. Cross-tolerance between aspirin and other NSAIDs occurs regularly. Although the molecular structures of these drugs may be very different, all share the common mechanism of cyclo oxygenase inhibition. Ketorolac appears to have little potential for producing renal toxicity when adequate fluid balance is maintained and renal function does not depend on renal prostaglandin. Patients with congestive heart failure, hypovolaemia, or hepatic cirrhosis release vasoactive substances, in these circumstances, prostaglandins are important for preventing renal arteriolar constriction, which may decrease renal blood transaminase enzymes may occur in some patients treated with Ketorolac. Gastrointestinal irritation, nausea, sedation, and peripheral oedema may accompany the administration of this NSAID.