# Pharmacology of Acetaminophen, Nonsteroidal Antiinflammatory Drugs, and Steroid Medications: Implications for Anesthesia or Unique Associated Risks

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**KEYWORDS**

• Analgesia • NSAIDs • Perioperative • Intraoperative • Steroids • Anesthesia • Acetaminophen

**KEY POINTS**

- Acetaminophen, nonsteroidal antiinflammatory drugs (NSAIDS) and corticosteroids have useful perioperative and intraoperative indications.
- Acetaminophen has shown to be effective to decrease opioid consumption and the incidence of postoperative nausea and vomiting (PONV). Coadministration with NSAIDs results in superior analgesia.
- NSAIDs significantly decrease postoperative pain and the need for opioids. The use of NSAIDs does not increase the risk of bleeding. Their effect on PONV is unclear.
- Corticosteroids can be used for analgesia, PONV, and prolonged duration of sensory and motor block when added to the local anesthetics in peripheral nerve blockade.
- No increased incidence of side effects is noted with short-term use.

Providing analgesia is fundamental for health care providers when treating patients undergoing different surgical procedures. Preventing pain, instead of treating the pain once it has started, is a challenging goal in everyday anesthesiology practice. Whether providing analgesia before (preemptive analgesia[1]), during, or after surgery,

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it is particularly important to know which drug to choose, considering not only its indication and effectiveness, but also the pharmacologic profile, dosing, route, and potential side effects, as well as patients' comorbidities.

Acetaminophen, nonsteroidal antiinflammatory drugs (NSAIDs), corticosteroids, and opioids are 4 major types of nonopioid drugs considered in perioperative pain management. Intraoperatively, nonopioid analgesics have been used to decrease anesthetic and opioids requirements and to reduce the hemodynamic changes related to painful stimuli.[2]

We conducted a literature review regarding the main nonopioid analgesics used in anesthesiology practice beginning with a review of their pharmacologic characteristics. We are reporting their efficacy in the perioperative setting, essentially based on published systematic reviews and metaanalyses.

The use of analgesics has historically proven to decrease the risks related to severe pain,[3] such as myocardial ischemia, thrombosis, and thromboembolisms associated with immobilization, atelectasis, and pulmonary complications correlated with decreased tidal volume and shallow breathing, impaired wound healing and rehabilitation.[4,5] However, opioids have been linked to numerous adverse effects, especially when used alone. These effects include nausea, vomiting, pruritus, urinary retention, constipation, and respiratory depression. The risks of adverse effects can be lowered by the use of multimodal analgesia. Multimodal analgesia involves the use of different medications and techniques to produce analgesia through different mechanisms.[3] It has been proposed since the 1990s, so that the dose of opioids can be restricted or even avoided.[4–7] Nevertheless, multimodal pain management also includes approaches to regional anesthesia, peripheral nerve blocks and local infiltration techniques, and neuraxial analgesia,[3,5] discussions of which are outside of the scope of this review.

## ACETAMINOPHEN

Acetaminophen (also known as paracetamol) has been clinically used since 1887 and was not marketed worldwide until the 1950s owing to concerns regarding toxicity.[8] Acetaminophen is the active metabolite of phenacetin. It has analgesic and antipyretic effects similar to those of aspirin. However, its antiinflammatory properties are weak, presumably owing to poor effectiveness when the concentration of peroxides is high (at the inflammatory site). The analgesia provided by acetaminophen is induced by an inhibition of the cyclooxygenase (COX) pathway, decreasing the production of prostaglandins. Other recently described possible mechanisms of action include an endocannabinoid effect[9] and a modulatory effect on the descending serotoninergic inhibitory pathways.[10]

Acetaminophen can be administered orally or per rectum and, since 2010, an intravenous form was approved in the United States. Oral and rectal administrations have excellent bioavailability but undergo first-pass hepatic metabolism. Oral plasma peak concentration is noticed within 1 hour, and in approximately 30 minutes with the intravenous formulation.[8] The therapeutic dose in adults is up to 1000 mg every 6 hours, with a maximum of 4 g/d. Conjugation with glucuronic and sulfuric acid are the principal pathways of its metabolism. However, a small proportion of acetaminophen is metabolized to NADPI, a product related to the toxic effect of overdose. This byproduct is highly reactive and hepatotoxic, and can lead to a potentially fatal hepatic failure, renal tubular acidosis, and hypoglycemia with very high doses of acetaminophen. It can be detoxified with the use of *N*-acetylcysteine therapy. The elimination half-life of acetaminophen is 2 to 3 hours and the analgesic effect is 4 to 6 hours.[2,11]