Ketorolac tromethamine: A nonsteroidal anti-inflammatory analgesic used as an adjunct for general anesthesia

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This case report describes a general anesthetic where ketorolac tromethamine was used instead of a narcotic. The patient was a 37-year-old male, ASA II category, who underwent general anesthesia for a cholecystectomy. The drug is discussed in terms of preoperative, intraoperative, and immediate postoperative effects.

During the preoperative phase, no effect was demonstrated. Intraoperatively, the drug performed poorly to attenuate responses to intense stimulation as noted by an increase in pulse and blood pressure of greater than 20% during intubation, incision, and abdominal wall retraction. During the immediate postoperative phase, the drug performed well to provide analgesia related to incisional pain.

Ketorolac has not been previously discussed in terms of intraoperative uses. The mechanism of action by which it provides analgesia is through the inhibition of prostaglandin synthesis. It is similar in structure to the other nonsteroidal anti-inflammatory drugs and may offer certain advantages over traditional agents used to provide analgesia, including the absence of respiratory depression, addictive potential, euphoria, a decrease in gastric motility, and cardiovascular effects. These properties may help in the management of certain types of patients who are at risk for respiratory depression or in those who have a contraindication to narcotics.

Key words: Analgesia, anesthesia, ketorolac tromethamine, nonsteroidal anti-inflammatory drug.

Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) act peripherally by inhibiting the cyclo-oxygenase enzyme from converting arachidonic acid to endoperoxides, a crucial step in prostaglandin synthesis. By virtue of these properties, NSAIDs have been used as analgesics, anti-inflammatory agents, and antipyretics. Until recently, they have been available only in oral preparations, with the exception of indomethacin for treating patent ductus arteriosus in infants. Now that ketorolac has been introduced in a parenteral form, NSAIDs can be added to augment other forms of anesthesia.

Ketorolac tromethamine is the first injectable NSAID drug with potent analgesic, moderate anti-inflammatory, and antipyretic properties. It was approved for use by the U.S. Food and Drug Administration on November 30, 1989, as an intramuscular injectable preparation for the short-term management of acute pain. Recent clinical trials have been performed to describe the analgesic properties of ketorolac for the management of postoperative surgical pain. In these trials, ketorolac has been compared to more
traditional analgesics such as morphine and meperidine. There have been no reports on the efficacy of ketorolac used as an adjunct to general anesthesia.

This case report will describe the performance of ketorolac in the immediate perioperative arena (preoperative holding area, intraoperative, and recovery room) when used as a supplement to general anesthesia.

Case summary
A 37-year-old, 67-inch, 83-kilogram Hawaiian male presented to the operating room for a cholecystectomy with intraoperative cholangiograms. His past medical history was significant only for tobacco use, and the patient was classified as ASA II. He reported no drug allergies and was currently taking no medications.

Upon arrival in the preoperative holding area, an 18-gauge intravenous (IV) catheter was placed in his left hand, and an infusion of Ringer’s solution was started at a maintenance rate of 125 mL/hr. The patient was then given an intramuscular (IM) injection of ketorolac 60 mg into the left gluteal muscle. The patient received no other preoperative medication. After 30 minutes the patient was asked to evaluate any change in sensorium, and none could be detected. At this time an anxiolytic dose of midazolam 2 mg was given IV.

Approximately 50 minutes after the administration of ketorolac, the patient was taken to the operating room. Following the application of routine monitors (ECG, precordial stethoscope, pulse oximeter, blood pressure, and end-tidal CO₂) baseline vital signs were obtained—blood pressure (BP) 134/74, pulse (P) 45, and O₂ saturation 98%. Glycopyrrolate 0.2 mg was administered as an antispasmodic, and a priming dose of vecuronium 1 mg was given IV. After preoxygenation, the patient was induced with 400 mg of thiopental IV.

When loss of lid reflex was verified, the airway was tested, and an intubating dose of vecuronium 7 mg was given IV. Postinduction vital signs were BP 130/76 and P 44. With muscle relaxation confirmed by a peripheral nerve stimulator, the patient was intubated. The endotracheal tube cuff was inflated, and placement was confirmed by auscultation of bilateral breath sounds and by the presence of an appropriate end-tidal CO₂ waveform. Postintubation vital signs were BP 172/112, P 80, and O₂ saturation 98%. The end-tidal concentration of isoflurane was measured at 0.6%. An additional 100 mg of thiopental was given IV, and the isoflurane concentration was increased to 1.5%. The next vital sign readings were BP 142/92, P 72, and O₂ saturation 98%.

Maintenance of anesthesia was achieved with a two-to-one mixture of nitrous oxide and oxygen and titration of isoflurane. End-tidal concentrations of isoflurane ranged from 0.9% to 1.5% throughout the anesthetic. Vecuronium was used for surgical relaxation. An oral gastric tube was passed to evacuate stomach contents. Ventilation was maintained with a mechanical ventilator, and minute ventilation was adjusted to keep the end-tidal CO₂ at 34 mm of mercury. The intraoperative course was uneventful.

As the surgical incision was closed, the isoflurane was discontinued. Neuromuscular blockade was reversed with neostigmine 2.5 mg and glycopyrrolate 0.5 mg IV. After determination of a complete reversal of neuromuscular blockade, the patient was placed on 100% O₂ and extubated when he was spontaneously ventilating and following verbal commands. Postextubation vital signs were BP 179/94, P 80, and O₂ saturation 98%. The patient experienced some shivering during emergence. Total anesthesia time was 2 hours and 5 minutes. The patient transferred himself to the stretcher and was taken to the recovery room. He stated at this time that he was not experiencing pain.

When the patient was admitted to the recovery room, the head of his bed was elevated and oxygen was administered to him by face mask at 6 L/min. Admission vital signs were BP 136/78, P 75, and O₂ saturation 98%. His respiratory rate was 22 breaths per minute and his temperature was 97.3°F.

The patient responded appropriately to verbal commands and was able to deep breathe and cough. He assessed his level of surgical pain as zero on a scale of 0 to 10. The recovery room course was uneventful, and the patient was transferred to the ward after 1 hour. No analgesics were required in the recovery room, and the patient assessed his level of pain upon discharge as a 5 on the same scale of 0 to 10. When asked to evaluate the injection site where the ketorolac was given, he reported no pain or tenderness.

Patient-controlled analgesia was begun on the ward, utilizing morphine sulfate. The total morphine requirement 4 hours after admission to the ward was 2.5 mg IV. When asked to evaluate his anesthetic at this time, the patient described it as satisfactory.

Discussion
In this case study, ketorolac was substituted for a narcotic in a general anesthetic. It was administered 1 hour before induction to take advantage of its peak plasma concentration (Table 1). Ketorolac’s performance during laryngoscopy and intubation was poor, as determined by the significant (greater than 20%) rise from baseline in blood pres-
sure and pulse. Ketorolac was also felt to perform poorly in response to other periods of intense surgical stimulation during the procedure, such as skin incision, abdominal wall retraction, and abdominal cavity exploration, as demonstrated by similar elevations in pulse and blood pressure.

This appraisal is based on a comparison by the author of similar induction sequences and maintenance of general anesthetics when 0.1 mg/kg of morphine was given IM preoperatively. Higher end-tidal concentrations of isoflurane were required to attenuate responses to intense stimulation when ketorolac was the parenteral agent used for analgesia. Ketorolac performed well during emergence, as evidenced by the lack of ventilatory depression and gastrointestinal upset. Based on the patient’s responses to graded pain questions, it was concluded that ketorolac performed adequately in the immediate postoperative period. The patient’s sensorium was very clear, as demonstrated by his awareness of his surroundings and appropriate conversations.

Although ketorolac may not provide sufficient analgesia to replace narcotics in certain anesthetics, it may prove useful in the anesthetic armamentarium as an adjunct to other agents or in clinical situations where concerns for ventilatory depression are great and the use of opioid-type agents should be minimized. Such scenarios might include its use in ambulatory surgery; emergence phases of general anesthetics; in patients with myasthenia gravis, chronic obstructive pulmonary disease, sleep apnea disorders, and gall bladder surgery, where spasm of the sphincter of Oddi is a concern. Ketorolac may also prove useful in patients who have demonstrated a low tolerance for opioid-based analgesics, mask inductions, or anesthetics where spontaneous ventilation is desired.

Other advantages of ketorolac include the absence of tolerance, addictive properties, euphoria, or changes in sensorium. It also does not inhibit gut motility and has no cardiovascular effects. Ketorolac has been shown to provide a morphine-sparing effect when used in conjunction with morphine administered by a patient-controlled analgesia system, reducing morphine requirements up to 33% as compared to a placebo control group. A final advantage is ketorolac’s potential to reduce hospital personnel costs associated with the control of narcotics.

Disadvantages of ketorolac include inhibition of platelet aggregation, which may increase operative blood loss. This may be a relative contraindication for using ketorolac in conjunction with regional anesthesia, coagulopathies, or surgical procedures where large blood losses are expected.

There have been various reports of somnolence, gastrointestinal upset, sweating, and pain at the injection site. Other studies have demonstrated a ceiling effect related to the degree of analgesia provided, suggesting that increasing the dosage of ketorolac does not provide increased analgesia. Caution should be used in using ketorolac in the patient with liver or renal impairment, since these are the routes of metabolism and elimination (see Table I).

**Table I**

| Pharmacokinetics of ketorolac tromethamine after 30-mg intramuscular injection |
|---------------------------------|-----------------|-----------------|-----------------|
|                                 | Young adult     | Elderly1        | Hepatic disease2 | Renal disease3  |
|                                 | Healthy adult   | 1.03            | 0.61            | 0.83            |
| Tmax (hours)                    | 0.75            | 4.45            | 7.01            | 5.43            | 9.62            |

Tmax = time to peak plasma concentration.
T0.5 = plasma half-life.
1. Data from Montoya-Iraheta et al.
2. Data from Pages et al.
3. Data from Martinez et al.

Dose adjustment may be required with the elderly and in patients with impaired renal function, since elimination of the drug may be prolonged. Ketorolac is not recommended for use in pediatrics, pregnancy, obstetrics, or in nursing mothers. One final disadvantage of ketorolac is that it is only approved for intramuscular use, although a recent study demonstrated its stability and compatibility in various intravenous solutions, and it was not absorbed into glass or polyvinyl chloride.

**Conclusion**

Ketorolac did not perform well during the preoperative and intraoperative phases of this particular case, but its ability to provide analgesia without respiratory depression was felt to be satisfactory during emergence and recovery.

As with any drug, the risk/benefit ratio must be critically analyzed for the selection of ketorolac in the anesthetic care plan. Ketorolac is an exciting new drug that offers many possible uses. However, its perioperative uses are still undefined. Nurse anesthetists should take an active role in establishing ketorolac’s potential use in anesthetic practice by conducting controlled, prospective trials of use and by critically evaluating its efficacy in their clinical practice.

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