



# Less is more when it comes to ketorolac for pain

It's time to review our dosing with ketorolac for acute pain management.

## PRACTICE CHANGER

Use a low dose (10 mg) of intravenous ketorolac for moderate to severe acute pain in adults because it is as effective as higher doses (15-30 mg).<sup>1</sup>

## STRENGTH OF RECOMMENDATION

**B:** Based on a single, good-quality randomized controlled trial.

Motov S, Yasavolian M, Likourezos A, et al. Comparison of intravenous ketorolac at three single-dose regimens for treating acute pain in the emergency department: a randomized controlled trial. *Ann Emerg Med.* 2017;70:177-184.

## ILLUSTRATIVE CASE

A 46-year-old man with no significant past medical history presents to the emergency department (ED) with right flank pain and nausea. A computed tomography scan reveals a 5-mm ureteral stone with no obstruction or hydronephrosis. You are planning on starting him on intravenous (IV) ketorolac for pain. What is the most appropriate dose?

**K**etorolac tromethamine is a highly effective nonsteroidal anti-inflammatory drug (NSAID). As a non-opiate analgesic, it is often the optimal first choice for the treatment of acute conditions such as flank, abdominal, musculoskeletal, and headache pains.<sup>2</sup> While it is not associated with euphoria, withdrawal effects, or respiratory depression (like its opiate analgesic counterparts), ketorolac carries a US Food and Drug Administration black box warning for gastrointestinal, cardiovascular, renal, and bleeding risks.<sup>3</sup>

NSAIDs are known to have a “ceiling dose,”

a dose at which maximum analgesic benefit is achieved; higher doses will not provide further pain relief. Higher doses of ketorolac may be used when anti-inflammatory effects of NSAIDs are desired, but they are likely to cause more adverse effects.<sup>4</sup> Available data describe the analgesic ceiling dose of ketorolac as 10 mg across dosage forms.<sup>4,5</sup> Yet, the majority of research and the majority of health care providers in current practice use higher doses of 20 to 60 mg. The US Food and Drug Administration label provides for a maximum dose of 60 mg/d.<sup>3</sup>

In one recent study, ketorolac was prescribed above its ceiling dose of 10 mg in at least 97% of patients who received IV doses and in at least 96% of patients receiving intramuscular (IM) doses in a US emergency department.<sup>6</sup> If ketorolac 10 mg is an effective analgesic dose, current practice exceeds the label recommendation to use the lowest effective dose. This study sought to determine the comparative efficacy of 3 different doses of IV ketorolac for acute pain management in an ED.

## STUDY SUMMARY

### Though often used at higher doses, 10 mg of ketorolac is enough for pain

This randomized double-blind trial evaluated the effectiveness of 3 different doses of IV ketorolac for acute pain in 240 adult patients, ages 18 to 65 years, presenting to an ED with acute flank, abdominal, musculoskeletal, or headache pain.<sup>1</sup> Acute pain was defined as onset  $\leq$ 30 days.

Patients were randomized to receive either 10, 15, or 30 mg of IV ketorolac in 10 mL of normal saline. A pharmacist prepared the medica-

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tion in identical syringes, and the syringes were delivered in a blinded manner to the nurses caring for the patients. Pain (measured using a 0 to 10 scale), vital signs, and adverse effects were assessed at baseline and at 15, 30, 60, 90, and 120 minutes. If patients were still in pain at 30 minutes, IV morphine 0.1 mg/kg was offered. The primary outcome was numerical pain score at 30 minutes after ketorolac administration; secondary outcomes included the occurrence of adverse events and the use of rescue medication.

The groups were similar in terms of demographics and baseline vital signs. The mean age of the participants was 39 to 42 years. Across the 3 groups, 36% to 40% of patients had abdominal pain, 26% to 39% had flank pain, 20% to 26% had musculoskeletal pain, and 1% to 11% had headache pain. Patients had pain for an average of 1.5 to 3.5 days.

Baseline pain scores were similar for all 3 groups (7.5-7.8 on a 10-point scale). In the intention-to-treat analysis, all 3 doses of ketorolac decreased pain significantly at 30 minutes, but there was no difference between the groups; for the 10- and 15-mg groups, the mean pain scores post-intervention were 5.1 (95% confidence interval [CI] 4.5-5.7 and 4.5-5.6, respectively); and for the 30-mg group, the mean pain score was 4.8 (95% CI, 4.2-5.5). No *P* values were provided. There was no difference between the groups at any other time intervals. There was also no difference in the number of patients who needed rescue medication (morphine) at 30 minutes between the groups (4 patients in the 10-mg group, 3 patients in the 15-mg group, and 4 patients in the 30-mg group; no *P* values were provided). In addition, adverse events (eg, dizziness, nausea, headache, itching, flushing) did not differ between the groups.

#### WHAT'S NEW

##### 10 mg is just as effective as 30 mg

This trial confirms that a low dose (10 mg) of IV ketorolac is just as effective for acute pain control as higher 15- and 30-mg doses.

#### CAVEATS

##### A 2-hour time limit and no look at long-term effects

The ketorolac dose of 10 mg IV was specially

prepared by the study pharmacist; it is unlikely this will be readily available in clinical settings. However, the 15-mg IV dose is also as effective as the higher 30-mg dose based on study results and is readily available.

It isn't known whether the higher dose would have provided greater pain relief beyond the 120 minutes evaluated in this trial, or if alternative dosage forms (oral or IM) would result in different outcomes. This study was not designed to compare serious long-term adverse effects like bleeding, renal impairment, or cardiovascular events. Additionally, this study was not powered to look at specific therapeutic indications or anti-inflammatory response.

#### CHALLENGES TO IMPLEMENTATION

##### A 10-mg single-dose vial is not readily available

Ketorolac tromethamine for injection is available in the United States in 15-, 30-, and 60-mg single-dose vials. Because a 10-mg dose is not available as a single-dose vial, it would need to be specially prepared. However, this study should reassure providers that using the lowest available dose (eg, 15 mg IV if that is what is available) will relieve acute pain as well as higher doses.

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A 10-mg dose of IV ketorolac is just as effective for acute pain control as a 15- or 30-mg IV dose.