

# Less Is More When It Comes to Ketorolac for Pain

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

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## PRACTICE CHANGER

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

## STRENGTH OF RECOMMENDATION

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

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

**K**etorolac tromethamine is a highly effective NSAID. As a nonopiate analgesic, it is often the first choice for the treatment of acute pain in the flank, abdomen, musculoskeletal system, or head.<sup>2</sup> While it is not associated with euphoria, withdrawal effects, or respiratory depression (like its opiate analgesic counterparts), ketorolac carries an FDA black-box warning for gastrointestinal, cardiovascular, renal, and bleeding risks.<sup>3</sup>

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

In one recent study, ketorolac was prescribed above its ceiling dose in at least 97% of patients who received

IV doses and at least 96% of those who received intramuscular (IM) doses in a US ED.<sup>6</sup> If 10 mg of ketorolac 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

### 10 mg of ketorolac is enough for pain

This randomized double-blind trial evaluated the effectiveness of ketorolac in 240 adult patients (ages 18 to 65) presenting to an ED with acute flank, abdominal, musculoskeletal, or headache pain.<sup>1</sup> Acute pain was defined as onset within the past 30 days.

Patients were randomly assigned to receive either 10, 15, or 30 mg of IV ketorolac in 10 mL of normal saline. A pharmacist prepared the medication in identical syringes, which 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 a numerical pain score at 30 minutes after ketorolac administration; secondary outcomes included the occurrence of adverse events and the use of rescue medication (morphine).

The treatment groups were similar in terms of demographics and baseline vital signs. Mean age was 39 to 42. 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 experienced 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, with no difference between the groups: mean pain scores postintervention were 5.1 for the 10- and 15-mg group and 4.8 for the 30-mg

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group. There was no difference between the groups at any other time intervals. There was also no difference between groups in the number of patients who needed rescue medication at 30 minutes (4 patients in the 10-mg group, 3 patients in the 15-mg group, and 4 patients in the 30-mg group). 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 of IV ketorolac is just as effective as higher doses for acute pain control.

## CAVEATS

### 2-hour limit; no look at long-term effects

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 such as 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

### 10-mg single-dose vial 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 (as it was in this study). 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 will. **CR**

## ACKNOWLEDGEMENT

The PURLs Surveillance System was supported in part by Grant Number UL1RR024999 from the National Center For Research Resources, a Clinical Translational Science Award to the University of Chicago. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center For Research Resources or the National Institutes of Health.

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