

# Anaphylactic reaction after intravenous injection of ketorolac for colicky pain: a case report and review of literature

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## Abstract

Ketorolac has wider clinical use in acute pain management due to cost-effectiveness and safety. We report a case of anaphylaxis to intravenous ketorolac to manage ureteric colic. Health professionals should be aware of the anaphylactic reaction, which is rare yet potentially fatal.

## Introduction

Ketorolac, a Non-Steroidal Anti-Inflammatory Drug (NSAID), is commonly used in pain management. It is considered superior to opiates in cost-effectiveness and safety. Ketorolac inhibits stretch-induced ureteral contractility associated with ureteric colic. Therefore, it is a commonly used analgesic in colic pain. Like other NSAIDs, ketorolac has benign side effects, mainly in gastrointestinal, hematological, and renal systems. However, anaphylaxis is rarely observed following the use of ketorolac(1). We report a rare case of anaphylaxis to ketorolac during pain management for ureteric colic with no prior history of any drug allergy, including NSAIDs.

## Case report

A previously healthy 26-year-old male presented to the emergency room (ER) with a complaint of left flank pain for three hours. The pain was acute on the onset, intermittent type, radiating to the testicle, with no aggravating and relieving factors. It was not associated with nausea or vomiting and burning micturition. He denied a history of asthma, drug allergy, especially to NSAIDs, or allergy to any environmental factors.

On examination, he was afebrile, pulse rate was 76 beats per minute, blood pressure 110/70 mm of Hg, and oxygen saturation was 97% in room air. On examination of the abdomen, it was soft, non-distended, and with tenderness in the left flank. Renal angle tenderness was absent. Normal bowel sounds were present. Other systemic examinations were within the normal limit.

His routine blood investigations revealed an increased total leukocyte count of 14,600/mm<sup>3</sup>, normal blood glucose, and renal and liver function test. Abdomen ultrasonography (USG) showed mild distention of the left ureteropelvic junction and proximal ureter. A radio-opaque ureteric calculus was identified on the proximal ureter. Other abdominal organs were normal, as per USG findings. With this, the working diagnosis of mild left hydroureteronephrosis with ureteric calculi was made.

A rapid bolus of intravenous (IV) ketorolac 30mg (manufactured by Asian pharmaceuticals) was administered. After one minute of IV ketorolac administration, he developed generalized swelling and erythema starting from the face, tongue, and neck and progressing to the trunk and lower limb. There was no shortness of breath or hoarseness of voice. He was then transferred to the red area of the emergency department, and

his vitals were immediately checked. His pulse rate was 58/min, respiratory rate was eight breaths/min, oxygen saturation was 74% (in room air), for which oxygen supplementation was provided, and blood pressure was 60/40 mm Hg.

Given these findings, anaphylaxis to ketorolac was suspected. Oxygen was administered through a face mask at the rate of 8 liters per minute, improving the respiratory rate and oxygen saturation. The patient was given 30ml/kg intravenous normal saline within 10 minutes. The anaphylactic reaction was managed by epinephrine 0.1 mg (1:10000) IV slowly over 5 minutes, 100 mg of IV hydrocortisone, and 22.75 mg IV pheniramine. Cardiac function, respiratory condition, and blood pressure were closely monitored.

Spontaneous recovery of swelling without further complications with a pulse rate of 87/min and blood pressure of 120/80 mm Hg was achieved within 2 hours of the onset of symptoms. After managing the anaphylactic reaction, 1gm of intravenous acetaminophen diluted in 100cc of normal saline was used to control the pain. The patient was then discharged after 24 hours of observation in ER.

## Discussion

Ketorolac is the first injectable non-steroidal anti-inflammatory (NSAID) drug developed by the company Syntex, which gained Food and Drug Administration (FDA) approval. Ketorolac inhibits the formation of prostaglandins, which are involved in pain and inflammation, by inhibiting cyclo-oxygenase enzymes (COX-1 and COX-2). Intramuscular (IM) and Intravenous (IV) routes are commonly chosen for their administration in case of emergency settings where immediate pain relief is of utmost priority. Although morphine has a faster onset of action, ketorolac is commonly used to manage pain in emergency conditions due to cost-effectiveness and fewer side effects while achieving the same level of anesthesia. Ketorolac is frequently indicated in adult patients experiencing moderate to severe pain, especially for colicky pain such as renal colic, spinal surgery, migraine, musculoskeletal pain, etc. There are specific contraindications for using ketorolac, such as ischemic cardiac pain, active gastric ulcer, third trimester of pregnancy or active labor, breastfeeding, active major bleeding, concurrent use with other NSAIDs or lithium, allergy to ketorolac or its ingredients(1).

Anaphylaxis is an acute, potentially life-threatening reaction involving Immunoglobulin E (IgE) and less commonly through non-immunological mechanisms (2). Faria et al. conducted a study on drug induce anaphylaxis survey in Portuguese allergic departments taking 313 patients with a clinical history of drug-induced anaphylaxis. Results showed that 47.9% of those patients had drug-induced anaphylaxis to NSAIDs, out of which the most common NSAID to cause drug anaphylaxis was acetylsalicylic acid (36.7%), followed by diclofenac (26.7%). Anaphylaxis to ketorolac was found only in 1.3% of the patients who developed anaphylaxis after receiving NSAIDs, suggesting ketorolac to be a rare cause of NSAID-induced anaphylaxis(3). Diagnosis of anaphylaxis is based mainly upon careful history describing exposure, the onset of symptoms, and its progression. Features of anaphylaxis are manifested primarily in the skin (itching, flushing, hives, and angioedema), followed by respiratory symptoms (cough, dyspnea, hoarseness, stridor, wheeze), gastrointestinal (nausea, vomiting, diarrhea, abdominal pain), cardiovascular (dizziness, hypotension, shock, incontinence) and nervous system (headache)(2). In our case, there were predominant skin manifestations (generalized swelling and erythema). Laboratory tests such as plasma histamine levels and serum or plasma total tryptase levels may help further confirm anaphylactic reactions(2). In suspected cases of anaphylaxis, a skin prick test with ketorolac might be performed to determine the presence of IgE response to ketorolac. Our setup lacks such laboratory testing facilities; hence, our diagnosis was entirely based on the history of drug exposure, clinical findings, and the Naranjo probability scale. The casual relationship between the ketorolac and adverse event was assessed in our case using the Naranjo probability scale. This scale has ten questions with scores ranging from -4 to +13 (definite: +9 and above, probable: +5 to +8, possible: +1 to +4, and doubtful:0 and less). A score of 7 was calculated in this case, which indicated a possible relationship to adverse drug reactions (4).

Scala et al. reported a case of a 60-year-old woman with a selective severe anaphylactic reaction to ketorolac, but no adverse reaction was seen following the administration of aspirin and other NSAIDs. This showed

the existence of selective sensitivity to ketorolac(5). Similarly, Goetz et al. reported a 37-year-old man with an anaphylactoid reaction to parenteral ketorolac with no prior allergic history or risk factors associated with NSAID-induced hypersensitivity reactions(6). Our patient also had no personal or family history of atopic disease or drug hypersensitivity and denied a previous history of adverse events following NSAID exposure. There is still a lack of knowledge regarding what component of ketorolac or if ketorolac itself causes anaphylaxis.

The first line for management for anaphylaxis due to any etiology is IV adrenaline and fluids. The role of antihistamines in the treatment of anaphylaxis is limited. Corticosteroid decreases the severity of the acute reaction and prevents the risk of developing an biphasic response following anaphylaxis(7). Novembre et al. reported a biphasic anaphylactic reaction to ketorolac in a 13-year-old girl who developed symptoms twice at an interval of 16 hours. Thus, emphasizing the need for 24 hours of observation after the resolution of symptoms(8). A retrospective review of 34 patients concluded that biphasic reactions are seen in those patients who need a high dose of adrenaline (1.2 mg) during the first attack compared to the patient requiring a low dose (0.6 mg) who had only an early reaction(9). In our case, the requirement of a low dose of adrenaline (0.5 mg) and administration of corticosteroid to manage anaphylactic reaction might be the reason for no delayed reaction during 24-hour observation in ER.

### **Conclusion**

Anaphylactic reaction to ketorolac is rare yet fatal even in their therapeutic dose. Screening patients based on anamnesis for NSAID allergy might help less due to the existence of selective sensitivity to ketorolac. Corticosteroids or 24-hour observation seem to prevent delayed biphasic reactions. Our case report adds further knowledge on the risk-benefit profile while using this common drug.

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### **Ethical Approval**

Our institution does not require ethical approval for reporting individual cases.

### **Consent**

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

### **Guarantor**

Susmin Karki is the guarantor of this case report

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