Case Report

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

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Abstract

A 26-year male came to the emergency department complaining of left flank pain. On examination, the patient was afebrile with stable vitals. With clinical features, lab investigations, and ultrasonographic findings, a diagnosis of left hydroureteronephrosis was made. He was managed with intravenous ketorolac 30mg, after which he developed an anaphylactic reaction, and the patient was contained in the red area of the emergency. Anaphylactic reaction to intravenous ketorolac is rarely reported. Ketorolac is one of the common drugs used in pain management in acute care settings; health professionals should be aware of the possible complication in the form of an 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]. Biphasic reaction and selective sensitivity to ketorolac have been noted, which makes the drug more suspicious[2-4]. 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 patient is a 26-year 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 and non-distended, with normal bowel sounds and tenderness in the left flank. Renal angle tenderness was absent. Other system examinations were within the standard limit.

His routine blood investigations revealed an increased total leukocyte count of 14,600/mm^3, average 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 expected, 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

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involve the trunk and lower limbs. 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.

Because of 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 0.5 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 swelling recovery 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, 1g 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 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 emergency settings where immediate pain relief is of utmost priority. Although morphine has a faster onset of action, ketorolac is widely used to manage pain in emergency conditions due to cost-effectiveness and fewer side effects while achieving the same level of anesthesia. Ketorolac is commonly 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 hemorrhage, concurrent use with other NSAIDs or lithium, allergy to ketorolac or its ingredients[1].

Anaphylaxis is an acute onset, potentially life-threatening reaction involving Immunoglobulin E (IgE) and less commonly through non-immunological mechanisms[5]. 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[6]. Diagnosis of anaphylaxis is based mainly upon careful history describing exposure, the onset of symptoms, and its progression. Features of anaphylaxis are manifested primarily on 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)[5]. 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[5]. 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 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 probable relationship to adverse drug reactions[7].

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 aspirin and other NSAIDs. This shows the existence of selective hypersensitivity to ketorolac[2]. 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[8]. 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 whether ketorolac itself or what components of IV ketorolac 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 a biphasic response following anaphylaxis[9]. Ikegawa et al. and Brazil et al. reported a biphasic anaphylactic reaction to ketorolac, thus, emphasizing the need for observation after the resolution of symptoms[3,4]. 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[4]. In our case, the requirement of a low dose of adrenaline (0.5 mg) and corticosteroid administration to manage anaphylactic reactions might be the reason for no delayed response during 24-hour observation in an emergency.

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 selective sensitivity to ketorolac. Corticosteroids and observation seem to help in delayed biphasic reactions. Our case report adds further knowledge on the risk-benefit profile while using this common drug.

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Author contributions

SK, SKY, SA, and AP drafted the manuscript, reviewed the literature, and edited the manuscript. GSS and RS supervised, revised, and edited the manuscript.

Consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

Guarantor

Susmin Karki is the guarantor of this case report

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