Anaphylactoid reaction after injection of ketorolac in a loading dose for patient-controlled analgesia
-A case report-

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Anaphylaxis is a severe and life-threatening systemic hypersensitivity reaction. Ketorolac is a popular drug used for patient-controlled analgesia. Although anaphylactic reaction to ketorolac has not been frequently reported, it can develop by way of several mechanisms. A 41-year-old male patient was scheduled for laparoscopic correction of a perforated gastric ulcer. Emergency surgery was performed under general anesthesia with no complications. Near the end of anesthesia administration, ketorolac in a loading dose was administered intravenously in order to launch patient-controlled analgesia. Following injection, urticaria-like skin lesions, including rashes and wheels appeared systemically; tachycardia and breathing difficulty with oxygen desaturation also developed. Through additional inquiry into the patient’s drug history, past experience with ibuprofen allergy was identified. Antihistamine, steroid, and aminophylline were administered, and continuous positive airway pressure by full facial mask was applied to relieve bronchospastic symptoms. The patient recovered without further complications. (Korean J Anesthesiol 2010; 58: 565-568)

Key Words: Anaphylaxis, Ketorolac, Patient-controlled analgesia.

Nowadays, most anesthesiologists not only administer anesthesia for surgery, but have also extended their role to the area of postoperative pain relief. After surgery, drugs and pain relief methods are used in a variety of ways; the most common drugs are narcotic analgesics and nonsteroidal antiinflammatory drug (NSAIDs), which are commonly mixed with a patient-controlled analgesia (PCA) device via intravenous line. Reduction of the side effects of narcotic analgesics while at the same time maintaining optimal conditions for the purpose of a pain relief drug as a secondary is an advantage of using PCA with NSAIDs [1,2]. Ketorolac is the most commonly used drug for intravenous injection, and ketorolac can cause anaphylaxis associated with anesthetic complications. NSAID-induced anaphylaxis can be triggered by both the immune system and the non-immune system. Therefore, if the reaction is anaphylactoid via a non-immune mechanism, anaphylaxis can occur regardless of the structure of the NSAIDs. Therefore, patients who have shown hypersensitivity to NSAIDs require
special care in with regard to use of NSAIDs [3].

In this case, we report on a case of anaphylactoid reaction that developed after ketorolac injection in a loading dose for PCA, along with a review of the literature.

Case Report

A 41-year-old patient visited the emergency center with a complaint of acute abdominal pain. The height of the patient was 175 cm, and his weight was 71 kg. He was diagnosed with acute gastric ulcer perforation, and underwent emergency surgery for laparoscopic repair. Other than drinking one bottle of distilled liquor daily, the patient’s past medical history revealed no unusual findings. Premedication was not administered. Meperidine and nalbupine were injected in an intravenous loading dose, followed by intravenous administration of Meperidine 200 mg mixed with a normal saline drip for the purpose of pain control during the patient’s entry into the operation room. After preoxygenation, the original anesthetic consisted of thiopental and succinylcholine administered intravenously for induction. This was followed by administration of sevoflurane and vecuronium for maintenance of anesthesia. Before administration of anesthesia, the patient’s vital signs included a blood pressure of 119/82 mmHg, regular sinus rhythm of pulse rate 91 beats/min, and peripheral oxygen saturation of 100%. Surgery was performed without unusual findings. For control of postoperative pain, fentanyl 1,000 μg and ketorolac 180 mg in the saline solution were made by mixing 100 ml total, of which the loading dose of 10 ml and the remaining 90 ml prepared as a PCA device (Accufuser plus 1008M, Wooyoung medical, Korea) and were mounted inside. Following surgery of 1 hour 40 minutes duration, the loading dose of 9 ml of 10 ml (fentanyl 90 μg, ketorolac 16.2 mg) for PCA was administered intravenously for control of postoperative pain. PCA was then connected to the intravenous line by 1 ml/hr basal continuous infusion. Neuromuscular blocker was then reversed by pyridostigmine and glycopyrrolate. Exubtation was performed without complications, and the patient was transported to the postanaesthetic care unit (PACU). At that time, his vital signs included blood pressure of 122/83 mmHg, regular sinus rhythm of pulse rate 80 beats/min, and normal peripheral oxygen saturation. Skin examination showed no unusual finding.

After 30 minutes in PACU, erythematous rashes developed on the neck. Therefore, chlorpheniramine 4 mg and dexamethasone 5 mg were administrated intravenously. After 10 minutes, wheals with erythematous rashes developed on the neck and upper limbs. Therefore, chlorpheniramine 4 mg and hydrocortisone 100 mg were administrated intravenously. After 5 minutes, angioedema of the face was newly observed, with no relief from any symptoms; both erythematous rashes and wheals spread over the entire body, including both extremities. At that time, body temperature indicated mild hyperthermia at 37.4°C. His vital signs showed low normal borderline blood pressure; however, his pulse rate increased gradually, up to 120 beats per minute. Oxygen saturation decreased 92% by peripheral oxygen saturation. Findings from arterial blood gas analysis were pH 7.38, Pco2 41.6 mmHg, Po2 55.9 mmHg, and oxygen saturation 89.1%. Findings from examination with auscultation included wheezing, stridor on both lung fields, and a decreased breathing sound on both lower lung fields. Further inquiry into the patient’s past medical history revealed hypersensitivity to ibuprofen, one of the NSAIDs. Therefore, anaphylaxis was suspected. Consequently, the PCA device was removed from the patient’s intravenous line. In addition, aminophylline 250 mg and hydrocortisone 200 mg mixed in 100 ml normal saline respectively were administrated intravenously during intravenous fluid challenge. A full face mask (Mirage Quattro, ResMed, Australia) was applied with FiO2 1.0 and continuous positive airway pressure (CPAP) for improvement of oxygen saturation. After 5 minutes, his oxygen saturation improved. After 15 minutes, his oxygen saturation was maintained at 100% by FiO2 0.6. Therefore, the full face mask was replaced with a re-breathing oxygen mask (Medium concentration oxygen mask, Telflex Medical, USA) as 5 L/minute oxygen. His symptoms showed no further worsening. After an hour, his general condition showed significant improvement with reduced erythematous rashes and wheals; however, he was transferred to the surgical intensive care unit due to the need for continuous monitoring. The next day, he was transferred to the general ward, and was discharged without further complications.

Discussion

The European academy of allergy and clinical immunology (EAACI) nomenclature committee proposed a broad definition of anaphylaxis as a severe, life-threatening, generalized or systemic hypersensitivity reaction [4]. Therefore minor, localized or non-systemic reactions, such as erythematous rashes or wheals are not included in the definition of anaphylaxis. Clinical features of anaphylaxis may be identical; however, anaphylaxis may be divided into allergic anaphylaxis and non-allergic anaphylaxis. Allergic anaphylaxis is further subdivided into an immunoglobulin E mediated reaction and an immunological mechanism (such as IgG, complement activation) mediated reaction, with the exception of IgE [3]. A general example of an IgE mediated allergic anaphylaxis is an allergic reaction to peanut ingestion, and blood transfusion reactions are an example of an non-IgE mediated allergic
In this case, when the patient received preoperative intra-
venous administration of meperidine for control of pain, he
did not develop symptoms or signs associated with meperi-
dine. Therefore, opioids can be excluded as a cause of ana-
phylaxis. Also, drugs administered between the period
following surgery and PACU before anaphylaxis were drugs
for PCA and pyridostigmine and glycopyrrolate for reversal
of neuromuscular blocker. Through further inquiry into his
past medical history, hypersensitivity to ibuprofen and a
hypersensitivity reaction were found to have occurred after
injection of an intravenous loading dose for PCA. Hence,
comprehensively, ketorolac was more suspicious than fentanyl
as the PCA’s that caused anaphylaxis. Also, anaphylaxis
occurred 30 minutes after injection of ketorolac, and the
patient had experienced hypersensitivity reactions to other
NSAIDs. Therefore, in this case, anaphylaxis can be presumed
anaphylactoid reaction as non-allergic anaphylaxis less than
IgE-mediated allergic anaphylaxis reaction definitely.

When anaphylaxis is diagnosed, rapid management is critical.
Immediate treatment of allergic anaphylaxis and non-allergic
anaphylaxis are identical. The major immediate treatments
consist of epinephrine, oxygen 100%, intravenous fluid
challenge, and intubation for airway maintenance [3,12,13].
Epinephrine should be administered as early as possible. An
initial dose of 50 μg (0.5 ml, 1 : 10,000 solution) intravenously
or 300–500 μg (0.3–0.5 ml, 1 : 1000 solution) intramuscularly
is recommended [6]. Epinephrine has alpha-agonist activity,
which reverses vasodilation. In addition to having a beta-
agonist, which is inotropic, and also a bronchodilator, it
reduces further release of mediators, such as histamine and
leukotrienes [14]. Epinephrine is metabolized in liver and its
half-life is 15 minutes. Therefore, epinephrine should be given
repeatedly or infused continuously if necessary. Intravenous
injection of chlorpheniramine 10 mg as an anti-histamine
agent and hydrocortisone 200 mg (0.25–1.0 g) as a steroid are
recommended. In case of severe bronchospasm, aminophylline,
salbutamol, and magnesium sulphate can be given, and a beta-
2 agonist may be inhaled using a metered-dose inhaler [3,6].
Hypotension leads to systemic vasodilation. Therefore, 0.9%
normal saline or lactated Ringer’s solution are given rapidly,
and the patient should be placed in the supine position.
Hypotensive patients must avoid a sitting or elevated upper
body position. Symptoms of dizziness and loss of consciousness
can be induced by hypotension. At that time, the patient should
be placed in the supine position, and venous return can be
increased by elevation of both legs if necessary [3,15].

In this case, the patient showed a mild hypersensitivity
reaction. Therefore, only anti-histamine and steroid were
administered intravenously. When the hypersensitivity reaction
became systemic, tachycardia and de-saturation developed.
However, hypotension requiring adrenaline did not occur. To
relieve bronchospasms, administration of aminophylline and establishment of CPAP with full face mask were attempted. At that time, the patient was mentally alert and had no severe bronchospasm. Hence, improvement of arterial oxygenation by use of a non-invasive full face mask, without intubation was attempted. Application of a full face mask was effective for improvement of arterial oxygenation, even though he had a naso-gastric Levin tube.

Even if anesthesia-related anaphylaxis is uncommon, anaphylaxis is fatal. A number of drugs are administrated simultaneously during the peri-operative period, and the patient can come in contact with causal agents directly through the site of the operation. Therefore, in the event of anesthesia-related anaphylaxis, identification of the causes of anaphylaxis is difficult. Hence, standardized methods for selection of high risk patients must be established through reported cases of anaphylaxis and close examination of the patient. In addition, we must be fully aware of differential diagnosis and appropriate treatment for anaphylaxis. In so doing, diagnosis and management of anaphylaxis must be rapid and exact.

References