

Midazolam hypersensitivity during the transportation to theater

-A case report-

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This report describes a rare case of perioperative midazolam hypersensitivity in a patient without any history of allergy. A 39-year-old man was admitted for endoscopic pansinus surgery. During transportation to the operating room after injecting antibiotic and midazolam intravenously, the patient complained of shortness of breath. At 3 months after the event, an intradermal sensitivity test for midazolam proved positive indicating the incident was caused by midazolam hypersensitivity. (Korean J Anesthesiol 2010; 59: S1-S2)

Key Words: Anesthesia, Hypersensitivity, Midazolam.

Drug hypersensitivity refers to any noxious, unintended, or undesirable reactions to drugs mediated by a specific immune system [1,2], and is one of the most serious complications during the perioperative period. The incidence of perioperative drug hypersensitivity is difficult to estimate, but a report published in England claimed an incidence of 1 in 3,500 between 1988 and 1990 [3].

Perioperative hypersensitivity may be caused by a variety of agents including local anesthetics, muscle relaxants, opioids, induction drugs, antibiotics, or latex [4,5]. However, hypersensitivity to benzodiazepines, particularly midazolam, is extremely rare [4,6]. Here, we report a case of perioperative midazolam hypersensitivity in a patient without an allergy history.

Case Report

A 39-year-old man (weight 65 kg; height 168 cm) was scheduled to undergo endoscopic pansinus surgery for the treatment of chronic sinusitis. With the exception of well-controlled hypertension, he was in good health, and the routine preoperative laboratory tests, chest radiography and electrocardiography were normal.

In the preanesthetic room, after confirming negativity by the skin testing, ceftizoxime 1 g was injected intravenously. Intravenous midazolam 2 mg was then injected as a premedication, and he was transferred to the operating room. However, while being moved to an operating bed, he complained of dyspnea. Without delay, oxygen was supplied

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via a facial mask at 5 L/min. Arterial pulse oxygen saturation, electrocardiography and noninvasive blood pressure were monitored. Blood pressure was 203/105 mmHg and heart rate was 110 beats/min, but despite this oxygen supply, his oxygen saturation decreased gradually to 90%. To secure an airway without resorting to muscle relaxant, propofol 60 mg was administered, and manual ventilation with oxygen initiated. After confirming loss of consciousness, a laryngeal mask airway was inserted. One hour later, the patient recovered and was fully awake. The laryngeal mask airway was then removed and he was transported from the operating room to a postanesthetic room for further care. IgE immunoassays for penicilloyl G and penicilloyl V returned normal results. Total IgE was slightly elevated at 102 IU/ml (normal range: 0–100 IU/ml). The operation was postponed, and he was discharged two days later without any sequelae.

Skin prick and intradermal tests for midazolam and ceftizoxime were conducted three months after the event. The intradermal test revealed a positive reaction to midazolam. The patient was diagnosed as having midazolam hypersensitivity. Four months later, the operation was performed uneventfully without the use of midazolam.

Discussion

This is a rare case report of midazolam hypersensitivity during the perioperative period. Although anaphylactoid reactions to midazolam have been reported, no serologic or skin tests were performed [7]. Furthermore, midazolam has been used safely as an anesthetic agents in patients with drug allergy [6,8].

Almost all drugs used during the perioperative period can lead to drug hypersensitivity, though times of onset and manifestations can vary. Clinical findings may reveal isolated symptoms ranging from minimal changes in blood pressure to life-threatening cardiopulmonary collapse. However, if drug hypersensitivity occurs as an anaphylaxis, the onset is rapid and the results can be potentially life threatening [9]. One report on the anaphylactic reactions during anesthesia documented that cutaneous symptoms are more frequent in non-allergic anaphylaxis, whereas cardiovascular collapse and bronchospasm are more frequent in cases of anaphylaxis [5]. In the present case, the typical symptoms and signs of anaphylactic reactions were not shown; the main symptom was respiratory difficulty without cardiovascular collapse or cutaneous symptoms. Furthermore, the reaction occurred

shortly after the injection of antibiotic and midazolam, and thus we suspected the drug hypersensitivity.

Whereas the initial diagnosis of perioperative anaphylaxis relies on history taking and a physical examination, the retrospective diagnosis is based on serologic and skin tests [6]. Serum tryptase and histamine are helpful indicators of anaphylactic reactions. However, in our case, blood sampling was delayed and these serologic tests could not be evaluated. In vitro skin testing is a method used for the retrospective diagnosis of anaphylactic reactions. Generally, skin testing should be performed 4–6 weeks after the anaphylactic episode due to subsequent depletion of mast cell and basophil-mediator [6]. In the present case, skin prick and intradermal sensitivity tests for ceftizoxime and midazolam were performed three months after the event, and the intradermal test to 1 : 10 midazolam was positive, proving that the episode was caused by midazolam hypersensitivity.

This case demonstrates that midazolam, which is considered safe even in allergic patients, can induce hypersensitivity reactions. Accordingly, we advise that this possibility should be borne in mind when midazolam is administered.

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