

An experience with midazolam anaphylactoid reaction

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To the Editor:

Perioperative hypersensitivity is not a common occurrence in day-to-day practice. It may be caused by a variety of agents including muscle relaxants, latex, antibiotics, local anesthetics, induction drugs, or opioids [1, 2]. Among these, muscle relaxants and latex are the most common causative agents [1]. Although midazolam is considered a safe drug, hypersensitivity reactions have been reported rarely [2–4]. Here, I report a case of midazolam hypersensitivity.

A 37-year-old man, 68 kg and 170 cm, was scheduled to undergo surgery for tennis elbow. He had no significant medical, surgical, family, or allergic history. All routine investigations were normal. Intradermal sensitivity test for bupivacaine was found to be negative. Supraclavicular block was planned. The patient was moved into the operation theater with running Ringer's lactate, and all monitors (ECG, SpO₂, blood pressure) were placed. Then, 2 mg midazolam was given intravenously to allay anxiety. Within 2 min of drug injection, patient complained of pruritus, tightness of chest, and dyspnea, and became restless. Urticarial rashes were noticed over left upper limb and trunk. We found a fall in blood pressure (from 130/70 to 60/30 mmHg), heart rate (from 84 to 48 beats per minute, bpm), and SpO₂ (from 99 % to 85 %). The patient was immediately given 100 % oxygen using Bain's circuit; later, assisted mechanical bag mask ventilation was initiated to support his respiration. Tracheal

intubation was not needed, and the patient had not lost consciousness. Simultaneously, 0.1 mg adrenaline was given intravenously, as an anaphylactoid reaction to midazolam was suspected. Crystalloids were given rapidly. Chlorpheniramine 45 mg, hydrocortisone 200 mg, and ranitidine 150 mg intravenously were also given. After injecting adrenaline, initially heart rate increased to 140 bpm. Blood pressure increased to 120/70 mmHg and SpO₂ became 99 %; heart rate decreased to 110 bpm within 15 min after the onset of the anaphylactoid reaction. Surgery was postponed; the patient was admitted to the post-anesthetic care unit and discharged 2 days later without any sequelae. Anaphylactoid reaction in this patient was probably caused by midazolam as he developed signs immediately after receiving it. Plasma beta-tryptase level at the time of anaphylactoid reaction was 3 ng/ml (normal plasma level, <1 ng/ml). The patient underwent an intradermal drug sensitivity test after 3 months, which revealed a positive reaction to midazolam.

Anaphylactic reaction refers to a type I hypersensitivity reaction with mast cell/basophil degranulation mediated by antigen binding of specific immunoglobulin E [1]. Anaphylactoid reactions occur through a direct nonimmune-mediated release of mediators from mast cells/basophils or result from direct complement activation, but they present with clinical symptoms similar to those of anaphylaxis [1]. Histamine, proteases, proteoglycans, platelet-activating factor, leukotrienes, and prostaglandins are the mediators involved in these reactions [1].

Immediate discontinuation of the drug, airway support with 100 % oxygen, and early administration of epinephrine are the cornerstones of treatment [5].

Although a serum tryptase confirms the diagnosis, the offending drug can be identified by skin prick, intradermal testing, or serological testing [1].

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Midazolam may provoke a hypersensitivity reaction, although rarely, and should be used cautiously.

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