Anaphylaxis with midazolam – Our experience

Sir,

The overall incidence of anaphylaxis considering all agents used (local, general, regional) has been reported as 1 in 13,000 anesthetic procedures.[1] Midazolam hydrochloride is a short-acting imidazobenzodiazepine central nervous system (CNS) depressant commonly used for conscious sedation for a variety of procedures. Severe adverse reactions, including respiratory depression, laryngospasm,[2] respiratory arrest, tonic clonic seizures,[3] pruritis,[4] cardiac arrhythmias,[5] anaphylactic and anaphylactoid reactions have been described by manufacturers.

We present a 26 year old, 53 kg, 165 cm tall male coming for cervical lymph node biopsy on an out patient basis. He had no previous drug or food allergies or atopy. He had undergone cervical lymph node biopsy under local anaesthesia supplemented with sedation (details unavailable) uneventfully. After institution of electrocardiogram (ECG), Oxygen saturation (SpO_2), non-invasive blood pressure (NIBP) monitoring, an intravenous cannula was secured in the right forearm and lactated Ringer's solution infusion was started. Midazolam 1 mg was given intravenously to allay anxiety.

Within 2 minutes of administration of intravenous Midazolam, the patient complained of pruritis over the right forearm and trunk, and urticarial wheals were noticed over these sites. The blood pressure decreased to 60/30 mm Hg and the heart rate decreased from 80 to 50/minute along with decrease in SpO_2 to 85%. Patient was given 100% oxygen via face mask and injection Adrenaline 50 mcg was administered promptly. The intravenous fluids were rushed and the patient also received Chlorpheniramine 45 mg, Hydrocortisone 100 mg and Ranitidine 150 mg intravenously. Absent stridor or wheezing on auscultation ruled out airway

involvement due to the drug reaction. Although the heart rate increased to 135/minute after injection of Adrenaline, no dysrrhythmias were observed. The blood pressure increased to 130/80 mm Hg, SpO_2 increased to 100% and heart rate decreased to 116/minute within 15 minutes. The urticarial wheals disappeared and pruritis resolved 20 minutes after the injection of adrenaline. The surgical procedure was abandoned and the patient was monitored in the post-anaesthesia care unit (PACU) for any delayed response to the allergen. Blood samples were drawn for estimation of serum tryptase and sent to Ranbaxy laboratories. The patient underwent skin prick test 6 weeks later. The allergic reaction was documented in the patient's file. He was notified about the adverse reaction. The pathophysiology of anaphylaxis begins with binding of an allergen to Immunoglobulin E (IgE) on the surface of mast cells and basophils, with cross linking of receptors and subsequent cell activation. The resultant massive release of mediators such as histamine, leukotrienes, kinins, and eosinophil chemotactic factor leads to bronchoconstriction, vasodilatation, and increased capillary permeability. This process can continue, with progressive inflammation leading to a delayed "second wave" of symptoms six to eight hours later.[6]

The anaphylactic reaction in our patient was due to Midazolam as he developed signs of anaphylaxis 2 minutes after receiving it. Ringer's lactate solution could not be implicated as the allergen as it had been checked for any precipitates prior to infusion and 300 ml of the solution had already been administered without any allergic signs and symptoms. He was not given any other medication prior to Midazolam. Beta-tryptase level tested by the mature tryptase immunoassay was 2 nanogram/milliliter and total-to-beta-tryptase ratio was 9, both suggesting severe anaphylaxis. Skin prick test was positive for Midazolam and negative for latex and other common drugs.

Treatment of perioperative anaphylaxis includes removing the likely trigger, hydration and abandoning the procedure. One hundred percent oxygen should be applied. Epinephrine, the treatment of choice for anaphylaxis causes increased vasoconstriction, decreased mucosal edema, increased inotropy/chronotropy, and bronchodilation. Additionally, the β-agonist effect of epinephrine inhibits further mediator release from mast cells and basophils. H_1 and H_2 antagonists and corticosteroids blunt the recurrence of the reaction. Tryptase, a protease released from activated mast cells, can be used as a marker of immune activation. Serum beta –tryptase levels are raised in patients with systemic anaphylaxis. Total-to-beta tryptase ratio of 10 or less suggests systemic anaphylaxis.[7]

This case describes an otherwise healthy man who experienced preoperative anaphylaxis most likely due to a widely used drug, Midazolam. Clinicians should remain cognizant of the risk of anaphylaxis as well as its treatment.

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REFERENCES

1. Laxenaire MC. Epidemiology of anesthetic anaphylactic reactions. Fourth multicenter survey (July 1994-December 1996). Ann FrAnesthReanim 1999;18:796-809.
2. Davis DP, Hamilton RS, Webster TH. Reversal of midazolam-induced laryngospasm with flumazenil. Ann Emerg Med 1998;32:263-5.
3. Robb ND. Epileptic fits under intravenous midazolam sedation. Br Dent J 1996;181:178-9.
4. Yates A, Russell D. A reaction to midazolam: A topical solution. Anaesthesia 1989;44:449.
5. Rodrigo CR, Rosenquist JB, Cheng CH. Cardiac dysrhythmias with midazolam sedation. Anesth Prog 1990;37:20-3.
6. Roizen MF, Fleisher LA. Anesthetic implications of concurrent diseases. In: Miller RD (Editor). Anesthesia, 6th ed. Philadelphia: Elsevier; 2005. p. 1092-3.
7. Schwartz LB. Bradford TR. Rouse C, Irani AM, Rasp G, Van der Zwan JK, *et al*. Development of a new, more sensitive immuno-assay for human tryptase: Use in systemic anaphylaxis. J Clin Immunol 1994;14:190-204.

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Quick response code	Website: www.ijaweb.org
	DOI: 10.4103/0019-5049.90633