

Anaphylaxis following intravenous ranitidine: A rare adverse reaction of a common drug

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» Abstract

Ranitidine hydrochloride is a widely used drug that is generally well-tolerated. Anaphylaxis is rarely observed with ranitidine. We report a case who developed severe anaphylaxis following single dose of intravenous ranitidine. The article highlights the importance of recognition of this serious adverse event and re-emphasizes the need for cautious use of drugs, especially in those with known history of allergy.

Keywords: Allergy, anaphylaxis, hypersensitivity, ranitidine

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» Introduction



Ranitidine is a competitive reversible H₂ receptor antagonist, commonly used to treat peptic ulcer, gastroesophageal reflux disease, Zollinger-Ellison syndrome and related disorders. It is a well-tolerated drug usually with mild side-effects such as gastrointestinal adverse effects, headache or somnolence; has a very low incidence of anaphylactic reaction. However, both oral and intravenous infusion of ranitidine have been rarely associated with severe allergic reactions such as bronchospastic reaction, toxic epidermal necrolysis, ultraviolet B, photosensitivity and exanthematous pustulosis.^[1] The incidence of anaphylactic reaction to H₂ receptor blockers (cimetidine and ranitidine) and proton pump inhibitors (lansoprazole, omeprazole and pantoprazole) together has been reported to be 0.2-0.7%.^[2] Its prompt recognition and recording is essential to institute appropriate and timely therapy.

We report a case of severe anaphylaxis to ranitidine. This case report re-emphasizes a potentially serious, rare, adverse effect of ranitidine.

» Case Report



This is case report of a 60-year-old male patient who was brought to the emergency department in drowsy state with skin eruptions over the chest and abdomen. Prior to the present episode the patient had severe epigastric discomfort for which the doctor gave him injection ranitidine 50 mg (Peptac 50 mg/2 ml, containing phenol 0.5% as preservative). Within minutes of the injection, the patient developed above symptoms. There was no history of intake of any other medication. He had no other medical illness. The patient gave positive history of allergy to amoxicillin.

On examination, he was found to be drowsy and had edema of the face. Pulse rate was 100 beats/min, blood pressure - 80/40 mmHg, temperature - 36.8°C, respiratory rate - 26/min and oxygen saturation of 83% by pulse oximetry. Wheals were present all over the chest and abdomen suggestive of urticaria. Cardiac and respiratory system examination was unremarkable.

Investigations: Hemoglobin: 16.7 g %, total leukocyte count: 11,500, neutrophils - 80%, lymphocytes 14%, monocytes 2%, eosinophil's 4%, random blood sugar: 102 mg/dl, urea: 30 mg/dl, creatinine: 1.5 mg/dl, serum sodium: 141 mEq/l, serum potassium: 3.9 mEq/l, serum chloride: 102 mmol/l, electrocardiogram was suggestive of right bundle branch block with left axis deviation.

Based on history and findings, the patient was diagnosed as a case of anaphylaxis subsequent to injection ranitidine. He was administered intravenous adrenaline 0.5 mg, hydrocortisone 100 mg and pheniramine 25 mg. He did not require ventilatory support and responded to the treatment. His vitals improved gradually and he was discharged after 3 days. Subsequent test revealed a raised

immunoglobulin E (IgE) levels (1658 IU/ml).

Intradermal test with ranitidine in dilution of 1:1000 was found to be negative. However, patient did not give consent for further testing due to obvious reasons.

A lucid temporal relationship was observed between the administration of the drug (ranitidine) and the commencement of symptoms. Using Naranjo probability scale the relationship between the drug and the event was categorized as probable. [\[3\]](#)

» Discussion



Anaphylaxis is a clinical syndrome that affects multiple organ systems and is characterized by rapid onset of life-threatening respiratory and cardiovascular symptoms as the first recognized signs in most severe cases. Anaphylaxis is generally an unanticipated severe allergic reaction involving mast cells and basophils which mostly occurs on reexposure to a specific antigen and requires the release of proinflammatory mediators, but it can also occur on first exposure. Anaphylactoid reactions differ from true anaphylaxis as they occur through a direct non-immune-mediated release of mediators from mast cells and/or basophils or as a result from direct complement activation. [\[4\]](#)

Anaphylaxis at first exposure has been documented for ranitidine. Antonicelli *et al.* in their study have reported a case of an 18-year old male patient who developed intra-operative anaphylaxis with raised specific IgE to ranitidine. The patient had never received ranitidine before, which confirms the possibility of anaphylaxis at first exposure. [\[5\]](#) One other case of severe anaphylaxis to ranitidine in which specific IgE antibody was demonstrated has been reported in literature. [\[6\]](#)

Another case of intra-operative anaphylaxis has been reported in a 25-year-old female patient who underwent caesarean section. In addition to this anaphylactoid reactions have also been reported with ranitidine in obstetric patients. [\[7\]](#)

A rare case of fatal anaphylaxis has also been reported in a 51-year-old male patient who was prescribed 50 mg ranitidine intravenously as a routine post-surgical prophylaxis. [\[8\]](#)

Recently, a case of post-operative anaphylaxis has been reported where the patient had a prior history of allergy to ranitidine which was not disclosed to the treating doctor. Inquiry to staff nurse helped to conclude the serious condition as a result of injection ranitidine which was given in the recovery room. The skin and intra-dermal tests confirmed the diagnosis. Patient's relative revealed that similar episode was observed 15 years back after open cholecystectomy surgery. Furthermore, his old reports revealed reaction to ranitidine. [\[9\]](#) This case emphasized that recording in anesthesia notes and preserving records for further reference is necessary.

From the literature available it is evident that both immunological and non-immunological mechanisms are involved in immediate type of reactions to ranitidine.

Anaphylaxis subsequent to oral ranitidine has also been reported and it was observed that all cases of anaphylaxis induced by oral ranitidine were of moderate severity and did not require ventilatory support. On the contrary whenever ranitidine was given intravenously, anaphylaxis was severe and required resuscitation. [\[10\]](#)

Only one case of fatal anaphylaxis has been reported until date. Specific IgE antibodies to ranitidine

were detected in two cases. In majority of the cases the skin prick test was performed and was found to be positive. ^[10] In some of the reported cases intradermal test was found to be positive in others the oral challenge test with ranitidine, done subsequently revealed positive symptoms. ^{[2],[6],[9]} History of allergy to ranitidine or any other drug, asthma, allergic rhinitis was observed in some cases including the present case ^{[5],[9]} [Table 1](#). In few of the cases cross-reactivity to other H2 or H1 blocker was tested either by skin prick test or intradermal test. In one case the patient had a positive intradermal test to ranitidine, hydroxyzine and dexchlorpheniramine. ^[10]

Table 1: Summary of reported cases of anaphylaxis with ranitidine

Patient	Route	Reaction	Onset	Management	History of allergy	Test done	Reference
49-year-old woman	50 mg intravenous	Numbness all over the body, dyspnea, dysphonia and edema of the face, lips, throat and tongue	Within a minute	Nasal oxygen therapy, pheniramine, prednisolone	None	Oral challenge test was positive	Demirkan <i>et al.</i> 2006
55-year-old man	One tablet of ranitidine	Skin rash, pruritus, dyspnea, irritability and syncope	30 min	Epinephrine, antihistamine, dopamine, steroid, bronchodilator	None	Oral challenge test, skin prick tests and specific serum IgE were positive	Koh <i>et al.</i> 2006
51-year-old man	50 mg, intravenous, in normal saline solution	Wheezing, dyspnea and hypotension followed by loss of consciousness	Within minutes	Despite intensive resuscitation attempts, the patient died 30 min later	None	Patient died	Oliva <i>et al.</i> 2008
65-year-old man	Intravenous	Drowsy, unresponsive, reduced pulse rate	Post-operatively after 90 min	Inotropic and ventilator support given	Allergic to ranitidine	Skin and intra-dermal tests were positive	Vyas <i>et al.</i> 2011
36-year-old man	50 mg, slow intravenous bolus	Cold sweat, trembling, dyspnea and deterioration of consciousness	Within the first minute	Ventilatory and inotropic support	None	Skin prick tests positive	Aouam <i>et al.</i> 2012
18-year-old boy	50 mg, slow intravenous infusion	Tachycardia, hypotension, diminished vesicular breathing	Intra-operative	Hydrocortisone and norepinephrine	Grass pollen-induced seasonal allergic rhinitis	Skin prick test and serum-specific IgE against ranitidine was positive	Antonicelli <i>et al.</i> 2012
25-year-old female	50 mg, intravenous	Restless, itching in upper limbs, face and chest, coughing	Intra-operative	100% oxygen, ventilatory support, pheniramine, hydrocortisone, adrenaline, deriphylline	None	None	Sripriya <i>et al.</i> 2013
60-year-old man	50 mg, intravenous	Tachycardia, edema of face, urticaria, drowsy, left axis deviation, right bundle branch block	Within minutes	Adrenaline, hydrocortisone, pheniramine	Allergic to amoxicillin	Serum IgE raised, intradermal test (1:1000) was negative	Our case

Anaphylaxis is by and large an unanticipated severe allergic reaction. One way to prevent such adverse reaction is by evading the administration of drugs to which the patient is allergic. Avoiding administration of the same medication to the patient in the future necessitates knowing and documenting that the patient had a history of sensitivity to the particular drug. However, most of the time when a patient develops an allergy or sensitivity, this information is not recorded, resulting in patients receiving drugs to which they have known allergies or sensitivities. Documenting hypersensitivity to specific drugs by use of electronic medical records can prevent such hypersensitivity to the same drug and simultaneously educating the patients and their relatives about anaphylaxis to a drug is also very important.

Awareness of this rare but fatal adverse reaction to ranitidine, a commonly used drug, could help in early recognition of the event if faced suddenly.

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