

## CASE REPORT

# Ranitidine-Induced Anaphylaxis in a Patient with Acute COPD Exacerbation

İnsu Yılmaz, Murat Türk

Department of Chest Diseases, Division of Allergy and Clinical Immunology, Erciyes University School of Medicine, Kayseri, Turkey

**Cite this article as:** Yılmaz İ, Türk M. Ranitidine-Induced Anaphylaxis in a Patient with Acute COPD Exacerbation. Turk Thorac J 2017;18:94-5.

## Abstract

Ranitidine is a well-tolerated H<sub>2</sub>-receptor antagonist commonly used in peptic ulcer treatment and stress ulcer prophylaxis. Anaphylaxis is rarely observed with ranitidine. We report the case of a patient who developed anaphylaxis after intravenous injection of ranitidine for acute COPD exacerbation. This article underlines the importance of awareness that in COPD acute exacerbation treatment, ranitidine, which is usually administered with methylprednisolone, also has anaphylaxis potential.

**KEYWORDS:** Drug allergy, ranitidine, anaphylaxis

**Received:** 16.01.2017

**Accepted:** 21.04.2017

## INTRODUCTION

Ranitidine is a H<sub>2</sub>-receptor antagonist widely used worldwide for the treatment of gastroesophageal reflux, peptic ulcers, and stress ulcers prophylaxis. It has an excellent safety profile and allergic reactions to ranitidine are very rare [1]. We herein report the case of a patient with ranitidine anaphylaxis treated for acute chronic obstructive pulmonary disease (COPD) exacerbation. Diagnosis was confirmed with a typical history of anaphylaxis developing within minutes after drug injection and positive skin prick test.

## CASE PRESENTATION

A 57-year-old male patient was referred to our outpatient clinic with a history of anaphylaxis. He experienced three episodes of anaphylaxis in the last 6 months and the last one was 3 months ago. He had no other disease other than COPD. Every episode occurred a short time after treatment at the emergency room for acute exacerbation of COPD. At his last admission, after co-administration of inhaler salbutamol, intravenous (iv) methylprednisolone and iv ranitidine, he developed facial swelling and hives throughout his body, red eye, worsening difficulty in breathing, and syncope. The same medicine was given and the same clinical presentation had occurred at the other two episodes as well. There was no concurrent use of antibiotics or analgesics or any suspicious food intake. His symptoms, including cough, sputum, and dyspnea, had worsened in the last 3 months; nevertheless, because of his anxiety and fear that treatment may worsen his condition, he had increased his intake of short acting beta-agonist therapy to 7-8 times a day in addition to his stage-D COPD therapy (salmeterol/fluticasone 50/500 2 × 1, tiotropium bromide 18 mg/day, theophylline 300 mg/day) and refused admission to any hospital. He had no history of atopia or drug allergy, neither did his family. Since the allergic reaction started within minutes of co-administration of acute exacerbation treatment drugs, and this event had occurred three times, the reaction was considered to be secondary to ranitidine or methylprednisolone. Skin tests with ranitidine (Ulcuran®; 25 mg/mL) and methylprednisolone (Prednol®; 20 mg/mL) were performed. Direct prick tests and intradermal (1:10 diluted and direct) tests with methylprednisolone were negative. Direct prick test with ranitidine revealed a 10 × 9 mm weal surrounded by erythema, and the test was considered positive (Figure 1). Oral provocation (OP) tests with methylprednisolone and esomeprazole were also performed with ranitidine positivity taken into consideration. Alternative safe drugs were identified and COPD treatment regimen was rearranged (methylprednisolone for 5 days, azithromycin for 3 days, and esomeprazole for 5 days were added to his routine COPD treatment). During his follow-up, the patient was reported to be able to get his exacerbation treatment without any problem since the safe drugs were initiated.

## DISCUSSION

Ranitidine is a well-tolerated H<sub>2</sub>-receptor antagonist commonly used in peptic ulcer and gastroesophageal reflux treatment. Its availability in both oral and intravenous forms, low toxicity, obtainability with ease, and lower price than proton

**Address for Correspondence:** Murat Türk, Erciyes Üniversitesi Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı, Allerji ve Klinik İmmünoloji Bilim Dalı, Kayseri, Türkiye  
E-mail: mrttrk@gmail.com

©Copyright 2017 by Turkish Thoracic Society - Available online at [www.turkthoracj.org](http://www.turkthoracj.org)





**Figure 1.** Direct prick test with ranitidine revealed a 10 × 9 mm wheal surrounded by erythema

H: histamine; N: negative control; DP: direct prick with ranitidine

pump inhibitors has made it the drug of choice for peptic ulcer treatment and stress ulcer prophylaxis in most emergency rooms.

The patient was diagnosed with ranitidine-related anaphylaxis based on his typical history of anaphylaxis developing within minutes of drug injection, his positive skin prick test with ranitidine, and his negative skin and oral provocation tests with methylprednisolone. As ranitidine is generally well-tolerated, cases with anaphylaxis are rarely reported [1-6]. Our patient had rapidly developed reaction immediately after iv administration of the drug and showed positive reaction with prick test. These features suggest that the hypersensitivity reaction was mediated by IgE. Koh et al. [7] detected ranitidine-specific IgE in serum in a patient with anaphylaxis secondary to ranitidine. Anaphylaxis at presence of stage-D COPD and respiratory failure makes our case stand out amongst others. The anaphylaxis was so severe that the patient avoided emergency room at his following COPD exacerbations due to his anxiety about drugs in his treatment regimen.

In the literature, cross reaction between ranitidine and other H<sub>2</sub>-receptor antagonists remains contradictory. Two cases were reported in which skin prick tests were positive for famotidine, ranitidine, and nizatidine and negative for cimetidine

after anaphylaxis [8,9]. It was stated that this condition may be related to the similarity of side chains among the first three drugs. Nevertheless, cases that demonstrate no cross reaction among H<sub>2</sub>-receptor blockers in skin tests and OP test are also present [3,7,10]. Our patient was not tested with other H<sub>2</sub>-receptor blockers due to possible cross reactions. OP test with esomeprazole, one of proton pump inhibitors with whom a cross reaction was not expected, revealed no reactions.

We report a case of anaphylaxis due to a H<sub>2</sub>-receptor antagonist, which is safe and commonly used in clinical practice as a part of anaphylaxis therapy. Our case underlines the importance of awareness that in COPD acute exacerbation treatment, ranitidine, which is usually administered with methylprednisolone, also has anaphylaxis potential. Thus, anaphylactic reactions that may cause mortality in severe COPD patients, such as our patient, can be prevented.

**Informed Consent:** Written informed consent was obtained from the patient participated in this case.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - İ.Y., M.T.; Design - İ.Y., M.T.; Supervision - İ.Y., M.T.; Data Collection and/or Processing - İ.Y., M.T.; - İ.Y., M.T.; Literature Search - İ.Y., M.T.; Writing Manuscript - İ.Y., M.T.; Critical Review - İ.Y., M.T.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has received no financial support.

## REFERENCES

1. Mills JG, Koch KM, Webster C, et al. The safety of ranitidine in over a decade of use. *Aliment Pharmacol Ther* 1997;11:129-37. [\[CrossRef\]](#)
2. Demirkan K, Bozkurt B, Karakaya G, Kalyoncu AE. Anaphylactic Reaction to Drugs Commonly Used for Gastrointestinal System Diseases: 3 Case Reports and Review of the Literature. *J Investig Allergol Clin Immunol* 2006;16:203-9.
3. Aouam K, Boudia W, Ben Fredj N, et al. Severe ranitidine-induced anaphylaxis: a case report and literature review. *J Clin Pharm Ther* 2012;37:494-6. [\[CrossRef\]](#)
4. Han TY, Jang WS, Yu M, et al. Anaphylactic reaction to ranitidine (Zantac®). *Int J Dermatol* 2011;50:1397-9. [\[CrossRef\]](#)
5. Park KH, Pai J, Song DG, et al. Ranitidine-induced anaphylaxis: clinical features, cross-reactivity, and skin testing. *Clin Exp Allergy* 2016;46:631-9. [\[CrossRef\]](#)
6. Neema S, Sen S, Chatterjee M. Ranitidine-induced perioperative anaphylaxis: A rare occurrence and successful management. *Indian J Pharmacol* 2016;48:221-2. [\[CrossRef\]](#)
7. Koh YI, Park HS, Choi IS. Ranitidine-induced anaphylaxis: detection of serum specific IgE antibody. *Allergy* 2006;61:269-70. [\[CrossRef\]](#)
8. Bossi A, Romeo G, Pezzoli A. Side-effects, structure, and H<sub>2</sub>-receptor antagonists. *Lancet* 1992;339:1366. [\[CrossRef\]](#)
9. Kim YI, Park CK, Park DJ, et al. A Case of famotidine-induced anaphylaxis. *J Investig Allergol Clin Immunol* 2010;20:166-9.
10. Morisset M, Moneret-Vautrin DA, Loppinet V, Grandidier S. Cross-allergy to ranitidine and nizatidine. *Allergy* 2000;55:682-3. [\[CrossRef\]](#)