Case Report

Rhinitis and asthma due to ranitidine

J.C. Martínez Alonso, A. Callejo Melgosa, MªJ. Fuentes Gonzalo[1], C. Martín García

[1] Family Medicine Department. Z.B.S-Zamora, Spain. Allergy Unit. Hospital Virgen de la Concha. Zamora, Spain

Summary. Few reports exist on allergic reactions to ranitidine. We present a case of bronchospastic reaction to ranitidine occurred during a drug challenge test. After administration of a therapeutic dose of ranitidine, the patient showed dyspnea, cough and bronchospasm in all the lung fields. Personal respiratory background was negative for respiratory disease and asthma. On reviewing the literature we found no reports of bronchospastic reaction to ranitidine. Quickness and the clinical characteristics of the adverse reaction suggest a pathogenic mechanism of immediate-type hypersensitivity.

Key words: Asthma, famotidine, gastroesophageal reflux, oral challenge test, rhinitis, ranitidine.

Resumen. Existen pocos informes de reacciones alérgicas a la ranitidina. Aquí se presenta un caso de reacción broncoespástica a la ranitidina durante una prueba de provocación farmacológica. Tras la administración de la dosis terapéutica de ranitidina, el paciente experimentó disnea, tos y broncoespasmo en todos los campos pulmonares. El paciente no presentaba antecedentes personales de enfermedades respiratorias ni asma. Tras revisar la literatura, no se ha hallado ningún informe de reacciones broncoespásticas a la ranitidina. La rapidez y las características clínicas de la reacción adversa indican un mecanismo patogénico de hipersensibilidad de tipo inmediato.

Palabras clave: asma, famotidina, reflujo gastroesofágico, prueba de provocación oral, rinitis, ranitidina.

Case report

Ranitidine is an H_2-receptor antagonist used in peptic ulcer disease therapy, acute stress ulcers, gastroesophageal reflux, Zollinger-Ellison syndrome, and related disorders. This drug has an excellent safety record and fewer than 1% of patients receiving ranitidine develop gastrointestinal adverse effects, headache or somnolence [1].

Hypersensitivity reactions caused by ranitidine are not frequent in everyday clinical practice. This drug has been associated with urticaria [2], anaphylactic reaction [3], cutaneous delayed reaction [3], toxic epidermal necrolysis [4], allergic contact dermatitis [5] lichenoid eruptions [6], UVB photosensitivity [7] and exanthematous pustulosis [8]. Cross-reactivity with other H_2- receptor antagonists is exceptional, and there is only one case published with nizatidine [9].

Although respiratory reactions have been noted with several drugs, there are no existing reports associated with ranitidine. We report a patient who experienced upper and lower airway reactions due to ranitidine without cutaneous symptoms.

A 60-year-old man, diagnosed of gastroesophageal reflux, presented sneezes, rhinorrhea, nasal itching, cough, chest tightness and dyspnea after receiving the fourth dose of ranitidine (Zantac®, GlaxoSmithKline, Madrid, Spain) 150mg 2 x daily. This treatment was interrupted and the symptoms responded promptly to parenteral steroids. No urticaria or angioedema was observed. He had previously taken ranitidine two years ago without any reaction**.** He had no other drug allergy and did not have respiratory antecedents or previous episodes of asthma**.**

Skin prick tests were performed with common airborne, latex, *Anisakis simplex* (1 mg/ml), and a common food battery (IPI, Madrid, Spain and Leti, Barcelona, Spain). They were all negative with a normal response to the histamine control. Skin prick-test with ranitidine (10 mg/ml) was performed and proved negative. The intradermal tests with ranitidine were negative with dilutions 1:100 and 1:10, as well as famotidine (1%). Pulmonary function testing with spirometry and

provocative challenge with inhaled methacholine were normal.

A double-blind oral challenge test with commercial ranitidine 150 mg was performed showing nasal itching, sneezing, dyspnea, cough, wheezing and sensation of chest tightness within ten minutes from start of the test. Physical examination of the patient showed tachypnea, prolongation of expiration and wheezes heard by auscultation**.** The reaction was resolved using parenteral corticosteroids, oxygen and inhaled ß$_2$-adrenergic agonist. A double-blind placebo controlled oral challenge test was performed without any adverse reaction.

In order to find an alternative treatment, we performed an oral challenge test with famotidine 40 mg and nizatidine 300 mg, and they were both well tolerated with no symptoms or respiratory reactions 3 hours after the test. There were no further episodes of rhinitis or asthma in the patient after withdrawal of the involved drug.

In our case, the immediate response in the oral challenge test suggests that ranitidine was the drug responsible for the clinical reaction, that could have been produced by a pathogenic mechanism of immediate-type hypersensitivity. To our knowledge, we report the first case of a bronchospastic reaction to ranitidine, presumably type I hypersensitivity.

References

1. Penston J, Wormsley KG. Adverse reactions and interactions with H2-receptor antagonist. Medical Toxicology 1986;1: 192-216.
2. Picardo M, Santucci B. Urticaria from ranitidine. Contact Dermatitis 1983; 9: 327.
3. Lazaro M, Compaired JA, de la Hoz B, Igea JM, Marcos C, Davila I, Losada E. Anaphylactic reaction to ranitidine. Allergy 1993; 48: 385-7.
4. Gonzalo-Garijo MA, Revenga-Arranz F, Rovira-Farre I. Cutaneous delayed reaction to ranitidine. Allergy 1996; 51: 659-60.
5. Juste S, Blanco J, Garces M, Rodríguez G. Allergic Dermatitis due to oral ranitidine. Contact Dermatitis 1992; 27: 339-340.
6. Ryan PJ, Rycroft RJ, Aston IR. Allergic contact dermatitis from occupational exposure to ranitidine hydrochlorid. Contact Dermatitis 2003; 48: 67-8.
7. Kondo S, Kapeya M, Yamada Y, Matsusaka H, Jimbow K. UVB photosensitivity due to ranitidine. Dermatology 2000; 201: 71-73.
8. Martinez MB, Salvador JF, Aguilera GU, Mas IB, Ramírez JC. Acute generalized exanthematous pustulosis induced by ranitidine hydrochloride. Contact Dermatitis 2003; 49: 47.
9. Morissset M, Moneret-Vantrin DA, Loppiret V, Grndidier S. Cross-allergy to ranitidine and nizatidine. Allergy 2000, 55: 682-683.

Allergy Unit. Hospital Virgen de la Concha
Avda. Requejo, 31-33
49022. Zamora, Spain
Tel.: +34 980 54 82 00
Fax: +34 980 51 28 38
E-mail: med023218@nacom.es