

Anaphylaxis to Intravenous Ranitidine in a Child

Francesca Mori^a Simona Barni^a Lisa Pecorari^b Lucrezia Sarti^a Neri Pucci^a
Elio Novembre^a

^aAllergy Unit, Department of Pediatrics, University of Florence, Anna Meyer Children's University Hospital, Florence,

^bS. Anna Hospital, Department of Pediatrics, Ferrara, Italy

Key Words

Anaphylaxis · Child · Ranitidine

Abstract

Although reversible H₂ receptor antagonists are usually well tolerated, there are few reports on anaphylactic reactions triggered by ranitidine. Here we report the first case of anaphylaxis to ranitidine in a child. This was an IgE-mediated event occurring in a patient who had never used ranitidine before.

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Introduction

Ranitidine is a competitive reversible H₂ receptor antagonist. It is widely used and typically well tolerated by patients.

Anyway, anaphylactic reactions to ranitidine may occur. Recently, a review collecting all reported cases of anaphylaxis to ranitidine has been published [1].

No pediatric cases have been described so far. We report a case of severe anaphylaxis to ranitidine in a child.

This case re-underlines a potentially severe adverse effect of ranitidine and highlights the importance of a well-performed allergy work-up.

Case Report

This is a case report of a 7-year-old Pakistani male admitted to hospital because of acute cholecystitis. He was promptly treated with intravenous antibiotic (Ampicillin-Sulbactam) therapy and intravenous ranitidine in order to prevent stress-induced ulcers.

After two hours from the first antibiotic intake and 10 minutes after the ranitidine administration, the child showed edema of the lips, hypotension, tachycardia and loss of consciousness.

Intramuscular epinephrine, hydrocortisone, and fluids were provided. Symptoms rapidly improved with therapy.

A month later, the child was referred to the Anna Meyer Allergy Unit and he was tested with both the used drugs. He had no history of atopy and he had never used ranitidine before. Skin prick tests with common inhalants and food allergens (i.e. pollens, mites, molds, cat and dog epithelia, milk, albumen, soy, wheat, cod fish, peanut, latex; commercial extracts, at 0.1 mg/ml concentration Alk Abellò, Milan, Italy) were performed and resulted positive to mold (*Alternaria alternata*). In vivo tests with Ampicillin-Sulbactam and ranitidine were performed according to the European Network on drug allergy (ENDA) recommendations (table 1) [2, 3].

Table 1. Allergy work-up

Drug	Total IgE	ImmunoCAP RAST (kUA/l)	SPT concentration (mg/ml); wheal/erythema (mm/mm)	IDT concentration (mg/ml); wheal/erythema (mm/mm)	PT
Ranitidine	279 kU/l	–	10, 3/5	1:1,000, 0/0 1:100, 11/30 immediate reading	–
Ampicillin-Sulbactam		Ampicillin negative	5, 0/0	–	1,000 mg negative

SPT = Skin prick test; IDT = intradermal test; PT = provocation test.

Parents signed a written informed consent before performing the intravenous provocation test (PT) with Ampicillin-Sulbactam. Moreover, PT was conducted in a two-steps grading challenge (i.e. 100 and 900 mg after 30 min). The child was observed for two hours from the last dose administration without reactions.

Discussion

Anaphylaxis to ranitidine may occur even after oral intake, but the most severe cases commonly followed the intravenous administration of the drug [4]. Both immunological and non-immunological mechanisms are involved in immediate types of reactions to ranitidine; consequently, a careful allergy work up is of paramount importance to detect specific IgE to ranitidine.

Thinking to an IgE-mediated mechanism the drug most probably implicated should be the one administrated closer to the reaction. In fact, the longer the interval between the onset of reaction and time of drug intake, the less probable the reaction is IgE-induced [5]. In particular, immediate reactions typically occur within 1 hour from antibiotic intake and in that case, Ampicillin-Sulbactam was administered two hours before the onset of symptoms [6]. Anyway, since the incidence of anaphylaxis to beta-lactams (i.e. penicillin 0.7–10% of all cases of anaphylaxis) [7, 8] is higher than that to ranitidine (0.2–0.7%) [9], initially it was easier to think that anaphylaxis was probably due to Ampicillin-Sulbactam rather than to ranitidine.

This case showed the presence of an IgE-mediated reaction to ranitidine occurring suddenly after the intravenous drug administration. In fact, the time delay from the drug administration was less with ranitidine compared with Ampicillin-Sulbactam. This is in agreement with the fact that the peak blood ranitidine concentration is reached in 15 minutes after intravenous administration.

Anaphylaxis at first exposure has been previously documented for ranitidine [10, 11] and neuromuscular

blocking agents [12]. Antonicelli et al. reported a case of an 18-year-old male patient who developed intra-operative IgE-mediated anaphylaxis to ranitidine. The patient had never received ranitidine before, which confirms the possibility of anaphylaxis at first exposure. The production of specific IgE involved in such reaction is unknown; environmental agents have been speculated as having a sensitizing role in case of neuromuscular blocking agents' reactions [12].

This is the first case of anaphylaxis to ranitidine in pediatric age; anyway, both treatment and timing of presentation are the same as those reported in the literature [1].

Awareness of this rare adverse event to ranitidine, a commonly used drug, could help in the prompt treatment of the reaction. Moreover, this case report was prepared to highlight that such a rare and unusual adverse reaction to such a widely used drug, can occur also in children. Consequently, caution is necessary when administering intravenously this drug even in children beside a negative history for possible previous sensitization.

Disclosure Statement

All authors disclose any conflicts of interest.

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