ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Anaphylactic reaction to ondansetron in a pediatric patient: a rare case report

Anafilaxia a ondasetron em idade pediátrica: um caso clínico raro

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ABSTRACT

Although ondansetron is a widely used antiemetic medication, hypersensitivity to ondansetron is rare. We report a clinical case of a child who had an anaphylactic reaction after a single oral dose of ondansetron. An immunoglobulin E-mediated mechanism was determined by positive intradermal tests.

Keywords: Anaphylaxis, case reports, antiemetics, pediatrics.

RESUMO

Ondansetron é um medicamento antiemético amplamente utilizado, mas a hipersensibilidade ao mesmo é rara. Apresentamos um caso clínico de uma criança com anafilaxia após tomar dose única de ondansetron, via oral, onde se demonstra um mecanismo mediado por IgE através de testes intradérmicos positivos.

Descritores: Anafilaxia, relatos de casos, antieméticos, pediatria.

Introduction

Ondansetron, an antiemetic drug that acts as a 5-hydroxytryptamine (5-HT3) receptor antagonist, is commonly used to treat or prevent chemotherapy-induced nausea and vomiting and as a prophylactic treatment for nausea and vomiting in perioperative settings. The most commonly reported adverse effects include headache, feeling hot, and constipation. Hypersensitivity reactions to ondansetron appear to be rare. Only a few cases have been reported in the literature, including systemic reactions[1-7] and isolated cutaneous reactions.[8]

Only 7 cases of anaphylaxis have been documented[1,2 9-13], with an IgE-mediated mechanism confirmed by skin tests in 3 cases[1,9,10], 2 of which were pediatric.[10,11]

The authors describe a rare case of immediate hypersensitivity to ondansetron in a 9-year-old boy who presented with anaphylaxis. A suspected IgE-mediated mechanism was validated by positive intradermal tests.

Case report

A 9-year-old boy presented to the emergency department with a 2-day history of nausea and vomiting. He had no fever or other gastrointestinal symptoms and denied other associated symptoms or complaints. He was given ondansetron 4mg per os, but 20 minutes after administration a generalized urticarial rash appeared with associated pruritus but no angioedema or associated respiratory or cardiovascular symptoms. He was administered an antihistamine (hydroxyzine 25mg per os), which resulted in clinical improvement, and he was discharged after 2 hours.

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However, he returned 2 hours after discharge due to renewed vomiting and progression of the skin rash. In addition to the previous cutaneous symptoms, he had angioedema of the lower and upper lips and wheezing. Vital signs were within normal limits. He was treated with adrenaline (0.3mg/0.3mL, IM), methylprednisolone 20mg IV, clemastine 2g IV, and 400µg of nebulized salbutamol, which resulted in clinical improvement. Four hours later the skin lesions worsened and wheezing recurred, so adrenaline, methylprednisolone, clemastine, and salbutamol were administered again. Treatment with methylprednisolone 20mg IV and clemastine 2g IV was repeated four hours later due to the recurrence of cutaneous symptoms. The patient remained under surveillance and was discharged 12 hours later with a prescription of oral prednisolone 20mg and levocetirizine 5mg for 3 days. He was referred to the allergy department for diagnostic investigation. No information on tryptase levels was provided. The patient had no other medical history apart from a previous diagnosis of asthma and allergic rhinitis (controlled with daily fluticasone furoate 27.5µg and levocetirizine 5mg, with salbutamol 100µg/dose as needed) and had never been exposed to ondansetron.

Despite the nonexistence of validated concentrations, given the severity of the reaction, a basophil activation test was performed (Basotest®, ORPEGEN Pharma, Heidelberg, Germany) with an ondansetron solution (2mg/mL), the result of which was negative.

The patient also underwent skin testing with ondansetron (Figure 1). The recommended concentrations found in literature for both prick and intradermal tests were used.[1] In addition, 4 control tests (2 exposed patients, 2 non-exposed volunteers) were also performed to exclude possible false positive results.

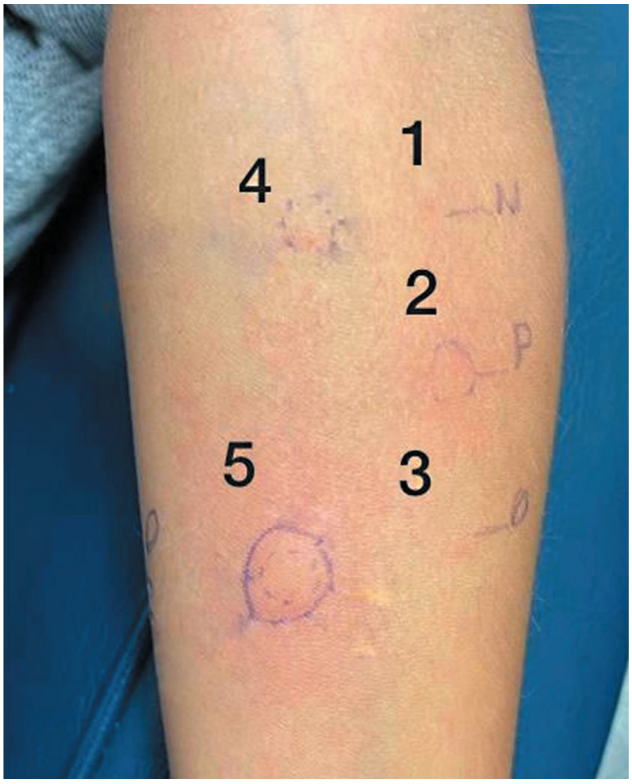

Figure 1
Skin tests with ondansetron: 1) skin prick test with saline solution; 2) skin prick test with histamine; 3) skin prick test with ondansetron at a concentration of 2mg/mL; 4) intradermal test with ondansetron at a concentration of 0.002mg/mL; 5) intradermal test with ondansetron at a concentration of 0.02mg/mL

The skin prick test results for ondansetron at a concentration of 2mg/mL were negative; the intradermal test results for ondansetron at a concentration of 0.002mg/mL was negative, but the patient tested positive in an intradermal test at a concentration of 0.02mg/mL: the initial wheal diameter increased 8 mm and erythema increased 6mm. None of the 4 controls had a positive wheal reaction at this concentration.

Due to the severity of the initial reaction, no oral provocation test with ondansetron was performed. The patient was told to avoid ondansetron and has not had similar episodes to date.

Discussion

Although ondansetron is commonly used, hypersensitivity reactions seem to be rare. Still, life threatening reactions can occur.[2] Chen et al. analyzed U.S. Food and Drug Administration records, identifying 24 reports of adverse anaphylactoid-anaphylactic reactions associated with ondansetron.[5] Sapkota et al. described the case of an anaphylactic reaction to ondansetron with a rapid and severe onset, which unfortunately was fatal despite prompt medical treatment.[2]

We found 7 cases reports of allergic reactions to ondansetron in the literature,[1,2,9-13], of which 3 involved an IgE-mediated mechanism confirmed by skin prick and/or intradermal tests.[1,9,10] Two of these 3 occurred in pediatric patients. Tan et al. described a case of anaphylaxis after initial sublingual administration of ondansetron in a 12-year-old child, and an IgE-associated mechanism was confirmed through intradermal tests.[10] Demir et al. reported a case of anaphylaxis after the fourth dose of ondansetron in a 1-year-old child undergoing chemotherapy for neuroblastoma.[11]

Our case involved a similar clinical presentation, with cutaneous symptoms appearing in the first few minutes after exposure and progression to anaphylaxis. As in the case reported by Tan et al., the patient had no previous exposure to the drug.

This is a rare case of immediate hypersensitivity to ondansetron in a pediatric patient, in which an IgE-mediated mechanism was confirmed by a positive intradermal skin test, as also described by Tan et al.[10].

Skin prick/intradermal tests for other 5-HT3 antagonists were not performed, since the patient did not require recurrent treatment with antiemetics. Since the basophil activation test results were negative, it was not useful for diagnosis in this case. The mechanism by which the patient became sensitized to ondansetron remains unknown, given that this was most likely his first contact with the drug.

Some authors suggest that a class effect, possibly involving cross-reactivity, may be involved in ondansetron anaphylaxis.[14] However, other authors reported successful ondansetron use in a patient allergic to granisetron.[15] This would suggest a drug-specific effect rather than a class effect. The authors do not recommend using ondansetron or other 5-HT3 receptor antagonists in patients who have had a severe hypersensitivity reaction to another 5-HT3 receptor antagonist.

For ondansetron-allergic patients indicated for long-term antiemetic treatment, allergological study with a skin prick/intradermal test and, if necessary, a drug provocation test for alternative drugs under medical supervision seems advisable.

We highlight the importance of using ondansetron with caution, especially in children. Healthcare professionals must be prepared to identify and manage uncommon, but severe, adverse effects, including anaphylactic reactions.

References

1. Fernando SL, Broadfoot AJ. Ondansetron anaphylaxis: a case report and protocol for skin testing. Br J Anaesth. 2009 Feb;102(2):285-6. doi: 10.1093/bja/aen376.
2. Sapkota K, Bhagat R. Fatal anaphylaxis to intravenous ondansetron: A case report. Clin Case Rep. 2021 May 5;9(5):e04110. doi: 10.1002/ccr3.4110.
3. Ouni B. Fatal anaphylactic reaction to intravenous infusion of Ondansetron: a report of two cases. Int J Pharmacovigil 2(2):1-3. doi: http://dx.doi.org/10.15226/2476-2431/2/2/00119.
4. Ross AK, Ferrero-Conover D. Anaphylactoid reaction due to the administration of ondansetron in a pediatric neurosurgical patient. Anesth Analg. 1998 Oct;87(4):779-80. doi: 10.1097/00000539-199810000-00007.
5. Chen M, Tanner A, Gallo-Torres H. Anaphylactoid-anaphylactic reactions associated with ondansetron. Ann Intern Med. 1993 Oct 15;119(8):862. doi: 10.7326/0003-4819-119-8-199310150-00026.
6. Kossey JL, Kwok KK. Anaphylactoid reactions associated with ondansetron. Ann Pharmacother. 1994 Sep;28(9):1029-30. doi: 10.1177/106002809402800906.
7. Firew E, Huang H, Anand A, Asfaw YA, Parikh C, Khan HR. Ondansetron-induced pseudoallergy with non-ischemic myocardial injury: A rare case report of Kounis syndrome. Clin Case Rep. 2022 Dec 22;10(12):e6781. doi: 10.1002/ccr3.6781.
8. Bousquet PJ, Co-Minh HB, Demoly P. Isolated urticaria to ondansetron and successful treatment with granisetron. Allergy. 2005 Apr;60(4):543-4. doi: 10.1111/j.1398-9995.2005.00754.x

9. Goyal P, Paramesh K, Puranik S, Proctor M, Sanghvi M. Delayed diagnosis of anaphylaxis secondary to ondansetron: A case report. Eur J Anaesthesiol. 2016 Feb;33(2):146-7. doi: 10.1097/EJA.0000000000000372.
10. Tan J, Mehr S. Anaphylaxis to an ondansetron wafer. J Paediatr Child Health. 2012 Jun;48(6):543-4. doi: 10.1111/j.1440-1754.2011.02124.x.
11. Demir HA, Batu ED, Yalçın B, Civelek E, Saçkesen C, Büyükpamukçu M. Anaphylactic reaction owing to ondansetron administration in a child with neuroblastoma and safe use of granisetron: a case report. J Pediatr Hematol Oncol. 2010 Nov;32(8):e341-2. doi: 10.1097/MPH.0b013e3181ea214a.
12. Weiss KS. Anaphylactic reaction to ondansetron. Arch Intern Med. 2001 Oct 8;161(18):2263. doi: 10.1001/archinte.161.18.2263.
13. Mehra KK, Gogtay NJ, Ainchwar R, Bichile LS. Hypersensitivity to intravenous ondansetron: a case report. J Med Case Rep. 2008 Aug 14;2:274. doi: 10.1186/1752-1947-2-274.
14. Kataja V, de Bruijn KM. Hypersensitivity reactions associated with 5- hydroxytryptamine(3)-receptor antagonists: a class effect? Lancet. 1996 Mar 2;347(9001):584-5. doi: 10.1016/s0140-6736(96)91275-1.
15. Kanny G, Beaudouin E, Moneret-Vautrin DA. IgE-mediated allergy to granisetron and safe use of ondansetron. J Allergy Clin Immunol. 2001 Dec;108(6):1059-60. doi: 10.1067/mai.2001.119744.

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