

Anaphylactic Reaction Owing to Ondansetron Administration in a Child With Neuroblastoma and Safe Use of Granisetron: A Case Report

Hacı Ahmet Demir, MD, MSc,* Ezgi Deniz Batu, MD,† Bilgehan Yalçın, MD,*
Ersoy Civelek, MD,‡ Cansın Saçkesen, MD,‡ and Münevver Büyükpamukçu, MD*

Summary: A 1-year-old girl with stage-IV neuroblastoma developed ondansetron hydrochloride anaphylaxis. Safe use of granisetron as an antiemetic after skin prick, oral, and intravenous challenge tests is presented. We present this case to emphasize that ondansetron hydrochloride may cause a serious anaphylactic reaction. In such a case, granisetron may be given to patients as an antiemetic after some provocative tests performed.

Key Words: anaphylactic reaction, anaphylaxis, children, ondansetron, chemotherapy, antiemetics

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Ondansetron hydrochloride is a selective 5-hydroxytryptamine₃ (5-HT₃) receptor antagonist used as an effective antiemetic especially for the prevention of chemotherapy-induced nausea and vomiting.^{1,2} Headache (17%), diarrhea (16%), and fever (8%) are relatively common side effects of ondansetron.³ There have also been reports of electrocardiographic changes and coronary vasospasm in some patients.³ But anaphylactic reaction in association with ondansetron administration is a rare condition.

We describe here a case of anaphylactic reaction owing to ondansetron used in a patient with neuroblastoma for the prevention of the chemotherapy-induced nausea/vomiting and safe use of granisetron in the same patient.

CASE REPORT

A 1-year-old girl with stage-IV neuroblastoma was scheduled to undergo chemotherapy on December 2008. Since then she had received 4 cycles of carboplatin and etoposide, and later 1 cycle of vincristine, ifosfamide, dacarbazine, and adriamycin and another cycle of cisplatin, cyclophosphamide, and etoposide. For each chemotherapy course, she was hospitalized and 5, 6, 4, 10, 27 doses of ondansetron (5 mg/m²/dose) were applied in each cycle, respectively. For the last cycle of chemotherapy, she had received 5 doses of granisetron (0.04 mg/kg/dose). She was then hospitalized to take the seventh chemotherapy cycle including vincristine, ifosfamide, dacarbazine, and adriamycin. When she was receiving ifosfamide and mesna on the first day of chemotherapy, ondansetron was also administered.

During the intravenous administration of the fourth dose of ondansetron in this chemotherapy course, she immediately experienced flushing of her face, edema of the lips, and shortness of breath. In 10 seconds, cardiac arrest and apnea followed, which lasted for 15 seconds and after positive pressure ventilation and 100% oxygen were applied, heart beats and respiration returned to normal. At this time also chlorpheniramine maleate (1 mg/kg, intravenous) and methylprednisolone (2 mg/kg, intravenous) were administered. After that she was monitored for 6 hours, but she did not experience another episode.

We considered that this was a reaction to ondansetron, as anaphylaxis occurred right after the injection of ondansetron. Also during ifosfamide and mesna administration again on the second day of chemotherapy, there was no evidence of hemodynamic instability.

After 2 weeks, we conducted granisetron prick, intradermal, and oral provocation tests to be sure that we can use granisetron safely. Prick tests to granisetron (pure concentration: 1 mg/mL) at concentrations of 1/100, 1/10, 1/1, and intradermal tests at concentrations of 1/1000, 1/100, 1/10, 1/1 were all negative. Oral provocation test was done by dividing 1 dose of granisetron (0.04 mg/kg) into 3 and giving at 30 minutes intervals. The patient also expressed no reaction. After those tests, we gave granisetron intravenously in divided doses at 30 minutes intervals. The patient did not experience any reaction and completed her next chemotherapy without any allergic reaction.

DISCUSSION

The 5-HT₃ receptor antagonists (ondansetron, tropisetron, granisetron, dolasetron, and palonosetron) are well tolerated, potent antiemetic drugs that are used in prevention of chemotherapy-induced nausea and vomiting and considered to be relatively safe.^{2,3} However, besides the mild side effects such as diarrhea, fever, and headache, these drugs also have been reported to cause coronary vasospasm,³ generalized tonic-clonic seizures,² and allergic reactions that may be fatal.^{4,5}

This case represents the anaphylactic reaction to one of the recurrent doses of ondansetron. She did not experience a positive reaction to granisetron prick, intradermal, and oral provocation tests and granisetron was safely used for antiemesis. In the literature, cases of anaphylaxis to the 5-HT₃ receptor antagonists have been described and some investigators think that there is a class effect.^{6,7} But there is no shown crossreactivity between ondansetron and granisetron. This may be because of the different chemical structure of these drugs. Ondansetron and tropisetron share a common indol ring, whereas granisetron does not.^{2,6}

Anaphylaxis is an acute-onset, potentially fatal systemic allergic reaction and prior exposure to an antigen is required for IgE dependent anaphylactic reaction.^{1,8} In our case this was the 56th dose of ondansetron that caused anaphylaxis and the patient received the earlier doses with

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From the *Department of Pediatric Oncology, Institute of Oncology; Departments of †Pediatrics; and ‡Pediatric Allergy and Asthma, Faculty of Medicine, Hacettepe University, Ankara, Turkey.
Reprints: Hacı Ahmet Demir, MD, MSc, Department of Pediatric Oncology, Institute of Oncology, Hacettepe University, 06100, Ankara, Turkey (e-mail: hdemir@hacettepe.edu.tr).
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no adverse reaction. Earlier doses have probably led to her sensitization.

Management of the anaphylactic signs and symptoms requires both supportive and preventive approaches.^{1,8} In our case the apnea and cardiac arrest lasted only for 15 seconds so we could not apply epinephrin, but supported the patient with positive ventilation and 100% oxygen. And for the prevention, we administered diphenhydramine and methylprednisolone for 5 days.

In conclusion, ondansetron is a valuable antiemetic drug for chemotherapy-induced nausea and vomiting. Rarely, anaphylactic reaction may occur like in our case. In such conditions, granisetron can be a safe choice for antiemesis, because of the absence of crossreactivity between those 2 drugs that have different chemical structures.

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