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IgE-mediated allergy to granisetron and safe use of ondansetron

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To the editor:

5-hydroxytryptamine₃ (5-HT₃) receptor antagonists (granisetron, ondansetron, tropisetron, and dolasetron) are new, well-tolerated antiemetic drugs. Very few hypersensitivity reactions have been reported.¹⁻⁵ We document for the first time an IgE-mediated hypersensitivity proved by positive immediate intradermal test (IDT) and leukocyte histamine release test (LHRT) results.

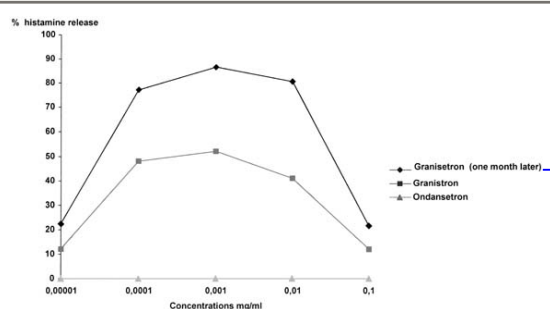
A 38-year-old housewife was undergoing chemotherapy for breast cancer. Within a few minutes after the first intravenous infusion of granisetron (3 mg) and methylprednisolone (60 mg) in saline solution, the patient presented palmar itching, abdominal pain, and malaise, followed by a generalized erythematous rash and conjunctivitis. Her pulse, blood pressure, and temperature were normal. The symptoms disappeared within 90 minutes.

Skin prick tests (SPTs) were carried out with methylprednisolone, granisetron, and ondansetron, each at 1 mg/mL; IDTs with initial papule of 3 mm in diameter were carried out with these drugs at concentrations ranging from 0.001 to 0.1 mg/mL. The result of SPT with granisetron was doubtful, with erythema of 1 mm in diameter and no wheal. At 15 minutes, the result of IDT with granisetron was positive at 0.001 mg/mL, with a wheal 8 mm in

diameter and erythema of 30 mm. Results of SPT and IDT with methylprednisolone and ondansetron were negative. Controls performed in 2 patients suspected of being intolerant to 5-HT₃ receptor antagonists were negative. The small number of controls cannot completely exclude the possibility that IDT with granisetron was irritating, but for ethical reasons, we did not perform IDT with 5-HT₃ receptor antagonists in healthy patients.

The result of LHRT carried out according to our previously published procedure⁶ was positive with granisetron but negative with ondansetron. Four weeks later, the LHRT result was even more strongly positive with granisetron (Fig 1).

Fig. 1. Leukocyte histamine release test to granisetron and ondansetron.



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IgE-dependent reaction to granisetron was proved. The absence of positive skin test results with ondansetron and the negative LHRT result were taken as evidence against cross-reactivity with granisetron, and we decided to give ondansetron. The patient subsequently received ondansetron without incident.

The absence of cross-reactivity between granisetron and ondansetron might be explained by the difference in the chemical structures of the 2 drugs. Kataja and de Bruijn³ reported 2 cases of anaphylactic reactions to tropisetron with clinical evidence of cross reaction with ondansetron and suggested that there is a class effect rather than drug-specific hypersensitivity for 5-HT₃ receptor antagonists. No cases of cross-reactivity of granisetron with other 5-HT₃ receptor antagonists have been described.³ Tropisetron and ondansetron share an indole heterocycle, which could be the drug epitope. In contrast, granisetron does not have this indole heterocycle. The use of ondansetron was proposed in our case, and it turned out to be quite well tolerated. This observation documents the importance of screening for cross-reactivity with a molecule in the same pharmaceutical class when a type I hypersensitivity mechanism has been demonstrated for one molecule of this class in order to use a molecule that has similar pharmacologic properties but does not share its immunological cross-reactivity. Only when results of tests (skin tests, LHRT) with the drug that caused the reaction are positive do negative tests with the related drugs have a strong negative value and indicate that they can be used safely, as has been previously

demonstrated for muscle relaxants.⁷

The mechanism by which this patient became sensitized to granisetron, given that she had never received it, remains unknown. This was certainly the first time that the patient had received this drug, which leaves us in the dark about the origin of sensitization. The absence of prior contact with the drug, usually required for sensitization, occurs more frequently than is realized. It is well known for muscle relaxants: 30% of patients who have an anaphylactic reaction to muscle relaxants are undergoing general anesthesia for the first time in their life.⁷

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