Repeated Anaphylactic Responses Induced by Oral Challenge with Ranitidine

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Sir,

Drug hypersensitivity reactions are very common in clinical practice; they comprise approximately 15% of adverse drug reactions (1). If history, skin testing and *in vitro* laboratory tests do not yield conclusive results, drug challenge tests are the only reliable way to establish or exclude hypersensitivity to a drug (1–4). Careful risk-benefit assessment for each individual patient is a prerequisite of drug challenges. For assessment of immediate type hypersensitivity reactions, dosing intervals of at least 30 min are recommended (3).

CASE REPORT

We report here the case of a 31-year-old man who presented with a history of a severe anaphylactic reaction after taking 600 mg ranitidine orally for treatment of a duodenal ulcer. Within 10 min he had developed generalized itching and urticaria, angioedema of the face, bronchial obstruction, abdominal cramps and, eventually, loss of consciousness. He was found lying on the floor of his apartment. He recovered without sequelae after treatment in an emergency room. Prior medical history revealed that he had developed an episode of severe hypotension after administration of 300 mg ranitidine 6 months previously.

A skin prick test with ranitidine (suspended in physiological saline), performed on the volar surface of the patient's forearm, gave a 6-mm wheal and a 10-mm flare, whereas the other constituents of the ranitidine tablet (tested in the same way) induced no skin prick test reaction. However, corresponding tests with ranitidine in five control persons also yielded whealing of 2 mm. To prove that ranitidine was the eliciting compound we performed challenge tests, following installation of an intravenous line and with close monitoring in the intensive care unit. Increasing doses of ranitidine (3, 30, 150 mg) in gelatine capsules were administered orally at intervals of 30 min, which is in accordance with current guidelines for drug provocation tests (4).

Five minutes after administration of 150 mg ranitidine, the patient developed facial flushing, conjunctivitis, dyspnoea, gastrointestinal cramps and hypotension. After treatment with epinephrine, prednisolone and dimethindene maleate he had fully recovered within minutes. However, 30 and 60 min after this reaction two more episodes with less severe symptoms occurred, each of which had to be treated intravenously with epinephrine. In addition, minor symptoms recurred after 6 h, which resolved with antihistamine and corticosteroid treatment.

DISCUSSION

Ranitidine is an H_2-receptor antagonist generally used in the therapy of gastroduodenal ulcer and gastroesophageal reflux diseases. It is also used for premedication in anaesthesia and chemotherapy (5). Ranitidine is usually associated with a low incidence of adverse reactions. There have been only a few cases of immediate type hypersensitivity reactions to ranitidine (5–7). An IgE-dependent mechanism was suggested for anaphylactic reactions to ranitidine, but also non-immunological mechanisms may be involved in immediate type reactions to ranitidine (8). In one case specific IgE antibodies to ranitidine could be detected (7). Furthermore, in several cases oral challenge tests with ranitidine revealed positive objective symptoms (7, 9, 10).

This case report illustrates that the currently favoured interval of 30 min between administrations of challenge doses might be too short in certain situations. As it cannot be foreseen when this might be the case, we recommend that, at least in patients with severe reactions, intervals between oral administration of test doses should be prolonged to 90 min in order to avoid unnecessary and potentially harmful reactions and treatment. In our patient it is possible that the recurrence of symptoms after several hours might have been avoided by such a modified test procedure.

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