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**Can $H_2$-histamine receptor upregulation and raised histamine explain an anaphylactoid reaction on cessation of ranitidine?**

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**Introduction:** Drug-induced anaphylaxis has increased in frequency with the advent and administration of a widening array of therapeutic agents. Ranitidine, an $H_2$ receptor antagonist, is one such medication which has been reported, albeit rarely, to cause anaphylaxis upon initiation [1]. Although hyperacidity following cessation of ranitidine has been well-documented, to the best of our knowledge wider histaminergic symptoms have not been reported in patients.

**Case:** Anaphylactoid symptoms, culminating in administration of adrenaline, following cessation of high dose ranitidine, is reported here in a white, British female, aged 19, with co-morbidities of hypermobile Ehlers-Danlos syndrome, mast cell activation syndrome, and postural tachycardia syndrome. The hospital recorded observations included in this abstract were made available to the authors following written authorisation by the patient.

**Details:** The patient had been advised to stop gastric acid-altering medication in preparation for a gastroscopy, and had gradually reduced the dose of omeprazole over a one week period; dosing had stopped 10 days prior to the anaphylactoid event. In the three days preceding the event, ranitidine was reduced as follows: day 1 - morning dose was omitted and 300mg was taken in the evening; day 2 – morning dose was taken and further dosing stopped. The patient became symptomatic from the evening of day 3 onwards, with symptoms worsening from the morning of day 4. The patient had not experienced anaphylaxis before. She was following a low-FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) diet and low histamine diet and had not eaten anything different to normal in the days leading up to the event.

**Discussion:** A mechanism for the reaction is proposed in the context of ranitidine, as an inverse agonist, causing upregulation of $H_2$ histamine receptors and raised histamine levels due to enzyme induction. This effect, following extended and/or high antihistamine dosing may have implications for other individuals with a disorder of mast cell activation, such as mastocytosis or mast cell activation syndrome. There are potential policy and patient guidance implications for primary and secondary care with respect to cessation of $H_2$ antagonists.

**References:**

1. Aouam K et al. *J Clin Pharm Ther*. 2012;**37**(4):494-496