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RANITIDINE INDUCED HYPERSENSITIVITY – A RARE CASE REPORT

Miss Ruby Sharma[1], Miss. Aparna Joshi[2], Dr. Darpanarayan Hazra[*3] & Dr. Shahid Mahdi[4]

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Abstract

Ranitidine is a very commonly used drug in clinical practice for acid peptic disease and has an excellent safety record. Studies from Uppsala Monitoring Center database cited that the frequency of hypersensitivity reactions for proton pump inhibitor and H2- histamine receptor antagonist is between 0.2% and 0.7%. Only a few cases of hypersensitivity to ranitidine have been reported. We report a case of 3 years old boy who developed hypersensitivity reaction after administration of Inj. Ranitidine, which subsided on removal of offending drug.

Introduction

Ranitidine is H2-receptor antagonist, which is usually used for the treatment of peptic ulcer, gastro esophageal reflux disease, Zollinger-Ellison syndrome and other gastric acid related disorders. It is considered to have excellent safety profiles. Use of Ranitidine is rarely associated with anaphylaxis and hypersensitivity reactions.

Here, we report a case of H_2-receptor antagonist-induced hypersensitivity reaction that presented with sudden dyspnea, redness and rashes over the right hand and neck associated with itching sensation (urticaria).

Case Report

A 3 years old boy presented to emergency room with complains of severe colicky abdominal pain and diarrhea for 3 days associated with nausea and vomiting. He had no complaints of fever, dysphagia, jaundice and bloody or tarry stools.

General examination of the patient revealed a conscious, oriented, dehydrated and afebrile patient, with heart rate 102/min, B.P-90/70 mmHg and respiratory rate of 20/min. Cardiac examination showed regular sinus rhythm with S1, S2 heard in all areas, no murmurs were heard. Abdominal examination revealed soft abdomen, no rebound tenderness, no guarding, no masses were palpable, and bowel sounds were heard normally. Rest of the systemic examination was normal. Routine blood investigations were normal.

Diagnosis of acute gastroenteritis was made and patient was started on Inj. Ranitidine 25 mg. Three minutes into infusion of Ranitidine, patient suddenly developed dyspnea, flushing of face, eyes, and urticarial rashes over the right hand and neck. General examination revealed a dyspnoeic patient with heart rate 112/min, B.P-104/70mmHg and R.R 25/min and on local examination, purpuric, non-blanchable, and palpable lesions associated with itching were noticed in the right hand and neck.

Inj. Ranitidine was promptly stopped and patient was started on Inj. Pheniramine and Inj. Hydrocortisone to control the hypersensitivity reaction, which he responded well. After stabilization of the patient, Inj. Pantoprazole was initiated. He had no similar complications and was discharged in a stable condition.

Discussion

The introduction of specific H_2-receptor antagonists in the 1970s revolutionized the management of gastric acid-related disorders. Ranitidine was introduced in 1981, and it was designed by replacing the imidazole ring of cimetidine with a furan ring. Ranitidine has only 10% of the affinity to CYP450 than that of cimetidine. (1-3)

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Ranitidine is a competitive and reversible inhibitor of histamine at the histamine H2-receptors, which includes the receptors on the gastric cells. The empirical formula is C13H22N4O3S -HCl, representing a molecular weight of 350.87(Fig: 1). It is 50% absorbed after oral administration, compared to an intravenous (IV) injection. Absorption is usually not impaired by the administration of food or antacids. The volume of distribution is about 1.4 L/kg. The principal route of excretion is the urine, with approximately 30% of the orally administered dose collected in the urine as unchanged drug in 24 hours. H_2-receptor antagonists inhibit histamine action on gastric parietal cells, thus decreasing acid production and hence commonly used for peptic ulcer disease, gastro esophageal reflux disease, Zollinger-Ellison syndrome and other gastric acid related disorders.

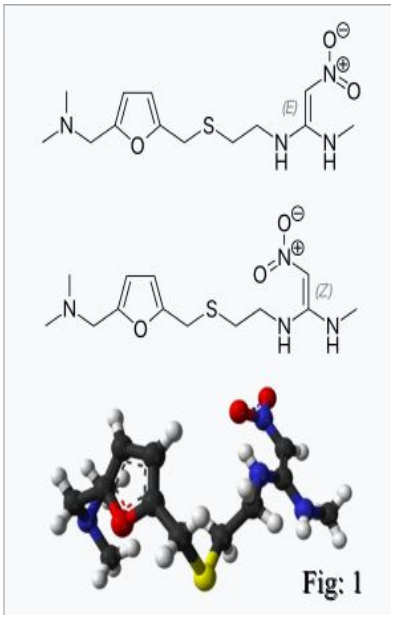

Fig: 1 - Structure of H2-Receptor antagonist - Ranitidine

Amongst the other H_2-Receptor antagonist, Cimetidine was known to have some drug interactions. Other H_2-receptor antagonists like Ranitidine and Famotidine, have very less affinity to CYP450. That is why it is not being associated with significant drug interactions and therefore is generally well tolerated (4,5).

Direct challenge test is considered the gold standard for diagnosis of any drug allergies. In some scenarios direct challenge test to a patient may be difficult, due to potential fatalities or unknown underlying diseases, in these cases a skin or *in vitro* test can be helpful (6). However in our case, a challenge test was not performed with Ranitidine.
In accordance to "Naranjo" adverse drug reaction analysis (7) this case would fall under probable ADR (5 scoring), as it was immediate in onset, with mild severity, uncommon in nature, that is not predictable.

Some of the adverse effects of Ranitidine that are reported in clinical trials or routine management are listed as follows:

1. Central Nervous System: Malaise, dizziness, somnolence, insomnia, and vertigo. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported.
2. Cardiovascular System: Rare reports of arrhythmias such as tachycardia, bradycardia, atrioventricular block, and premature ventricular beats have been reported.
3. Gastrointestinal System: Constipation, diarrhea, nausea/vomiting, abdominal discomfort/pain, and rare reports of pancreatitis.
4. Hepato-Biliary System: There have been occasional reports of hepatocellular, cholestatic, or mixed hepatitis, with or without jaundice.
5. Musculoskeletal System: Rare reports of arthralgia and myalgia were reported.

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6. Hematological System: Blood count changes (leukopenia, granulocytopenia, and thrombocytopenia) have occurred in a few patients, which were usually reversible. Rare cases of agranulocytosis, pancytopenia, sometimes with marrow hypoplasia, and aplastic anemia and exceedingly rare cases of acquired immune hemolytic anemia have also been reported.
7. Endocrine System: Occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving ranitidine.
8. Integumentary System: Urticaria, including rare cases of erythema multiforme, alopecia and vasculitis.
9. Respiratory System: A large epidemiological study suggested an increased risk of developing pneumonia in current users of histamine-2-receptor antagonists (H2RAs) compared to patients who had stopped H2RA treatment.

Others include rare cases of hypersensitivity reactions (e.g., bronchospasm, fever, rash, eosinophilia), anaphylaxis, angioneurotic edema and acute interstitial nephritis.

Conclusion

Ranitidine is a histamine-2-receptor antagonist widely used with an excellent safety record. Here we have reported a rare case of Ranitidine induced Hypersensitivity reaction. This case has been reported to remind clinicians that even commonly used and generally well-tolerated drugs can cause serious side effects which if neglected can pose a threat to a patient's life.

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Conflicts of interest: *There are no conflicts of interest.*

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