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Case Study

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RANITIDINE CAUSING ANAPHYLAXIS IN AN ACUTE FEBRILE ILLNESS PATIENT: A CASE REPORT

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ABSTRACT

Ranitidine is a H2 receptor blocker/antagonist used widely for variety of gastrointestinal problems as well as urticaria. Overall, ranitidine is usually well tolerated in humans but the incidence of few general side effects not more than 2% is almost similar to the placebo. Tiredness, headaches, mild gastrointestinal disturbance such as nausea, constipation and diarrhoea are among mostly reported complaints, resulted in stopping treatment effects. Anaphylaxis to ranitidine is a rare case but is a serious condition to be monitored. Here we present a case of anaphylaxis to ranitidine in which the dechallenge and rechallenge was also done.

KEYWORDS: Ranitidine, Anaphylaxis, SOB, Rashes, Case report, Pheniramine maleate, dexamethasone, hydrocortisone.

INTRODUCTION

Ranitidine belongs to the drugs class Histamine-2 blockers used for the decreasing the production of the acid produced in the stomach.[1] It can be taken 75mg-300mg orally daily before food and 1mg/ml-15mg/ml IV, it is a well-tolerated drug with mild side effects such as GI adverse effects, headache, somnolence and very rarely anaphylaxis. The incidence of anaphylactic reaction to H2 receptor blockers (cimetidine and ranitidine) and proton pump inhibitors (lansoprazole, omeprazole and pantoprazole) together has been reported to be 0.2-0.7%.[2,4]

Ranitidine was first marketed in the year 1981 since then many ofthe patients were treated and much experience had accumulated depending on the safety of the histamine H_2-receptor antagonist in treating gastroduodenal disease.[1] Basically, a wide array of the side effects that are associated with ranitidine has been described as so much information is available, the aim of this case report is to assess the evidence for the causal link between ranitidine (H2- receptor agonist) and the reported sideeffect.[3] The cardiovascular side effects associated with ranitidine are extremely rare and are usually unpredictable with the normal dose of oral ranitidine (1 in 1 million patients).[5] They usually will comprise atrioventricular blockade and sinusal bradycardia, mostly after the rapid intravenous administration, receding after the cessation of drug.[7] The clinical studies have not shown the significant pharmacological effect of ranitidine on the cardiovascular system through H_2-receptors, but the individual sensitivities still cannot be ruled out in few of the isolated reports.[9] Direct hepatotoxic effects of ranitidine have not been reported but a transient change in the liver function tests had been noted in 1 in 100 to 1 in 1000 patients and also few cases of mixed hepatitis were also reported, but only few reports were fully documented.[10,12] Hence, the incidence of ranitidine associated acute hepatitis was estimated to be less than 1 in 100 000 patients.Neuropsychiatric complications associated with ranitidine may be less common and are clinically similar to those complications which have been reported with cimetidine, that is, disorientation, confusion, delirium or hallucinations. These side effects have been reported especially in the critically ill patients and the patients withmultiple-therapy or patients with chronic hepatic failure or renal failure, because of that the direct link with the treatment of ranitidine was difficult to ascertain. Though the H_2-receptor-mediated effect is known as an attractive hypothesis the similar complications were noted with other H_2-receptor antagonists. "White cell injury" also known as agranulocytosis is known to be most frequent haematological complication but only few case reports are documented.[11] Basically, the mechanism is still unknown but ranitidine is unlikely to behaematotoxic. Few of the anecdotal reports of thrombocytopenia and anaemia have been published. In the disagreement with some of the poorly documented case reports and also in contrast to 'cimetidine', the clinical studies have suggested that ranitidine has no side effects on the endocrine functions, in any of the particular androgenic function or the prolactin secretion.Among the other side

effects that are associated with the treatment of ranitidine, cutaneous effects including the nonspecific skin reactions associated with urticaria, vasculitis and contact dermatitis.[13] When compared with cimetidine, ranitidine had failed to enhance immune responsiveness both in animals andhumans.[13,14] Drug interactions with ranitidine had been controversial, Although it may be sometimes loosely bound to cytochrome P450 components but there is no clinical evidence that these interactions may occur with many drugs i.e.β-blocking drugs, anticonvulsants, benzodiazepines, oral anticoagulants, lidocaine (lignocaine), calcium antagonists, tricyclic antidepressants or oral hypoglycaemic drugs and only few clinical case reports suggest that ranitidine may also interfere with theophylline, but all the human pharmacokinetic studies have been negative.[14,15]

Ranitidine has been used to treat and prevent ulcers in the stomach and intestines. It is also used to treat conditions in which the stomach produces too much acid, such as Zollinger-Ellison syndrome.[8]

Ranitidine is also used to treat gastroesophageal reflux disease (GERD) and other conditions in which acid backs up from the stomach into the oesophagus, causing heartburn.

Ranitidine has been withdrawn from the US market in April 2020 due because of concerns over levels of the contaminant N-nitroso dimethylamine, which can increase with time and temperature, posing a risk of cancer.[6]

CASE STUDY

A 23yrs old female patient was admitted to hospital in ER department during day time around 11am with complaint of SOB, rashes, swelling of the face, itching, loss of consciousness. She was treated with IV Corticosteroids (Hydrocortisone, dexamethasone), IV Anti-allergic (pheniramine maleate). As soon as the treatment was initiated the patient's symptoms started reducing and the patient was also feeling better, by the time the treatment was completed the symptoms completely got reduced and patient was feeling better.

On interview with the patient it was noted that the patient has taken TabRantac150mg(ranitidine) with Tab Dolo 650 (paracetamol650mg) in the morning after her breakfast as she was suffering from gastric acidity, burning sensation in stomach, body pains and mild temperature. After she took the drugs within half an hour of the ingestion, she started experiencing the symptoms of uneasiness, difficulty in breathing, itching all over the body, her parents noticed the swelling and puffiness of her face and rushed to the nearby hospital. After the treatment the patient was discharged.

After 1monthrechallenge was done (unintentionally) the patient again suffered from gastric burning sensation and again took tab Rantac 150mg on empty stomach and again started experiencing the same symptoms, but this time the drug was taken alone and on empty stomach without paracetamol, and same symptoms were seen but not that much severe as last time, this time the patient within half an hour after taking the drug was started experiencing the symptoms such as uneasiness, difficulty in breathing, puffiness of face with rashes and itching all over the body, as the patient has experienced these symptoms prior also, without was wasting her time she rushed to the nearby hospital and was successfully managed with IV corticosteroids (dexamethasone) IV anti-allergic (pheniraminemaleate).

DISCUSSION

Ranitidine is used a H2 receptor blocker since long time, it is used to reduce the gastric acid production also in patients with zolinger-edison syndrome and also for the patients who are on multiple drug therapies with co-morbidities. As seen in the case discussed above the ADR was more severe when ranitidine was taken after food with paracetamol and less severe when taken alone on empty stomach. A previous study "Anaphylactic reaction associated with ranitidine in a patient with acute pancreatitis, UlfinRethnam and Rajam Sheeja Yesupalan"[8] suggestsabout a patient with acute pancreatitis was givenIV ranitidine developed anaphylactic reaction and the symptoms seen were a grossly swollen face and neck, swollen tongue, congested conjuctivae.

CONCLUSION

Ranitidine is a H2 receptor blocker used to reduce the gastric acidity in patients with zolinger-edison syndrome and also for the patients who are on multiple drug therapies with co-morbidities. Anaphylaxis to ranitidine is a rare reaction and as discussed in the above case the symptoms were more severe when ranitidine was taken after food along with paracetamol compared to when taken alone on empty stomach. In the above case patient developed SOB, rashes and pluffiness of face which was managed by IV corticosteroids, anti-allergics, and for rashes calamine lotion was prescribed for local application. The ADR was not long prolonged and started reducing as soon as the treatment was initiated. As this patient was allergic to ranitidine and developed anaphylactic reaction to the drug it should be noticed that the patient must also be careful before using any other H2 receptor blockers other than ranitidine and also should be cautious before using any proton-pump inhibtors or any other antacids.

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