

Fatal anaphylaxis of ranitidine injection : have we not learnt the lesson yet?

Y.Y. Chuah¹, Y.Y. Lee², L.F. Lin¹, C.J. Kuo¹

(1) Division of Gastroenterology and Hepatology, Department of Internal Medicine, Ping Tung Christian Hospital, Taiwan ; (2) Department of Medicine, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia.

To the Editor,

A 75-year-old man was admitted with complaints of fever and right upper quadrant pain for one day. He underwent a cholecystectomy three months ago. His conscious level was clear (Glasgow Coma Scale or GCS of E4V5M6) with temperature of 38.1 degree Celsius. His blood pressure was 107/53mmHg and pulse rate was 78 bpm. Physical examination showed tenderness without a rebounding pain over his right upper abdomen. His laboratory studies revealed leukocytosis with neutrophils predominant (WBC:11.79 $10^3/uL$, Neutrophil: 86.3%) and impaired liver function (AST:476 IU/L; ALT: 332 IU/L) with hyperbilirubinemia mainly of direct type (D-bilirubin:1.7 mg/dL; T-Bilirubin: 3.0 mg/dL). Neither elevation of cardiac enzymes (CPK:81IU/L, CKMB:1.73ng/mL, Troponin I<0.16ng/mL) nor ST changes in electrocardiogram was found. Under a provisional diagnosis of acute cholangitis, he was started on cefoxitin eight hours earlier before admission to ward which was uneventful. Intravenous ranitidine was given at ward for prophylaxis of stress ulcer, although the risk for gastrointestinal bleeding in this patient was not high. Just within minutes after the injection of one ampule of ranitidine (Zantac (Getway), 50mg/2ml/amp) in slow push mode (within 10 seconds), patient complained about itchiness all over his body with facial redness. He started to have shortness of breath and cold sweating. Shortly after his conscious levels deteriorated (GCS: E1V2M1) followed by cardio-respiratory collapse. In addition to endotracheal intubation and cardiopulmonary cerebral resuscitation (CPCR) for his cardiorespiratory collapse, adequate doses of hydrocortisone and anti-histamine were given. However, patient did not survive the CPCR and expired 30 mins later. His blood culture yielded *E. Coli* which was compatible with the initial diagnosis of acute cholangitis. Based on his previous medical record, he did not have any atopic predisposition or drug allergy history. He was ever given with intravenous proton pump inhibitor during cholecystectomy one and a half year ago without a record of allergy.

Discussion

Fatal deaths from ranitidine-associated anaphylaxis was rare with two deaths reported by Ritesh Mahajan et al. and Antonia Oliva et al. thus far (1,2). Similar to

our case, both cases died after being given ranitidine intravenously for prophylaxis of stress ulcer. Similarly, both cases developed immediate anaphylactic symptoms followed by CPCR. Autopsy was performed in the former case report by Ritesh Mahajan et al. with findings of pulmonary congestion and upper airway edema where abundant mast cells were seen microscopically at the hypo-laryngeal and pharyngeal mucosa. One study proposed that a fast infusion of ranitidine might have a blockade effect on the cardiac H₂ receptors leading to bradycardia and hypotension (3). However, fatal allergy seems to occur regardless of the route of injection. For example, Gupta Sunanda et al. reported a patient that developed cardiac collapse and death despite ranitidine being given intramuscularly rather than intravenously (4).

A routine use of acid-suppressive agents has not been shown to benefit patients in a non-intensive care setting (5). The American Society of Health System Pharmacists guidelines does not recommend stress ulcer prophylaxis in patients admitted to general care wards. One study showed it only decreases the gastrointestinal bleeding rate from 0.33% to 0.22% (6). Based on the same guideline, only patients in intensive care unit (ICU) with coagulopathy, mechanical ventilation use for more than 48 hours, history of GI bleeding or ulcer within the past year, sepsis, more than one week stays at ICU, occult bleeding for more than 6 days and glucocorticoid therapy with more than 250mg of hydrocortisone daily, are recommended for prophylaxis of stress ulcer (6). By reporting this case, we do not recommend inappropriate use of ranitidine for prophylaxis of stress ulcer without a clear indication and such a practice might lead to unfortunate event such as ours.

Author contributions

YY Chuah and CJ Kuo performed the chart and literature review and wrote the manuscript. LF Lin and CJ

Correspondence to : Yoen Young Chuah M.D., Chih Jung Kuo M.D. Division of Gastroenterology and Hepatology, Department of Internal Medicine, Ping Tung Christian Hospital , 60, Dalian road, Ping Tung City, Ping Tung, Taiwan.
E-mail : yoenyongchuah@gmail.com, cjkuo@gmail.com

Submission date : 11/01/2019
Acceptance date : 24/02/2019

Acta Gastro-Enterologica Belgica, Vol. LXXXII, July-September 2019

Kuo took care of patients. YY Lee helped in proofreading the manuscript and giving precious advices.

Supportive foundations

Nil

Institutional review board statement

This study was reviewed and approved by the Institutional Review Board at Ping Tung Christian Hospital.

Conflict of interest statement

The authors have no conflict of interest to disclose.

References

1. RITESH M., NAGARAJ T.M., PRAVEEN K., SHIWANAGOUDA P., ROSHINA M. A rare case report : Single intravenous dose of ranitidine leading to cardiac arrest. *International Journal of Pharma and Bio Sciences*, 2014 Jan, **5(1)** : (B) 1043-1045.
2. ANTONIA O., SARA P., VINCENZO A., FABIO D.G., CATIA C., NADIA F., *et al.* Fatal injection of ranitidine: a case report. *Journal of Medical Case Reports*, 2008, **2** : 232.
3. KAMLESH J.U., SARITA J.P., ROHAN P.P., PRASHANT K.G. Intravenous ranitidine : Rapid bolus can lead to cardiac arrest. *J. Pharmacol Pharmacother*, 2015 Apr-Jun, **6(2)** : 100-102.
4. GUPTA S., RATHORE P., RAIGER L.K. Severe cardiovascular collapse with fatal outcome following intramuscular ranitidine hydrochloride. *J. Obstet Gynecol. Indian.*, 2007 January-February, **57(1)**.
5. JOEL J.H., JOHN M.I. Magnitude and Economic Impact of Inappropriate Use of Stress Ulcer Prophylaxis in Non-ICU Hospitalized Patients. *Am. J. Gastroenterology*, 2006, **101** : 2200-2205.
6. BARKUN A.N., BARDOU M., PHAM C.Q., MARTEL M. Proton pump inhibitors vs histamine 2 receptor antagonists for stress-related mucosal bleeding prophylaxis in critically ill patients : a meta-analysis, *Am. J. Gastroenterol.*, 2012, **107** : 507-520.