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Intraoperative anaphylaxis to ranitidine during cesarean section

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Abstract

Ranitidine, a widely used drug, is known to be well tolerated. This case report illustrates a severe anaphylactic reaction after a single intravenous dose of 50 mg ranitidine during the emergency cesarean section under spinal anesthesia. Anaphylaxis was successfully managed with Inj. adrenaline, Inj. hydrocortisone, ventilatory, and inotropic support following which she had a full recovery. Awareness of this rare but fatal adverse reaction to this commonly used drug could help in early recognition of the event if faced suddenly.

Keywords: *Anaphylaxis, cesarean section, ranitidine*

INTRODUCTION

Anaphylactic reactions during anesthesia are rare, but can be fatal if not promptly recognized and treated. Reactions can vary in severity and presentation. Drugs used for premedication, anesthetic agents, plasma expanders, and antibiotics used in the perioperative period can all cause anaphylaxis.[1] Anaphylaxis is a serious event, diagnosed clinically and the treatment has to be instituted immediately. All anesthesiologists should be familiar with an algorithm for treatment of anaphylaxis.[2] Herewith we present a case of intraoperative anaphylaxis during the cesarean section. The sequence of occurrence of events after Inj. ranitidine administration suggested that anaphylaxis was probably due to it.

CASE REPORT

A 25-year-old, 55-kg ASA-1 primigravida with no past history of drug allergy was posted for the emergency cesarean section for oligohydramnios. The patient was connected to monitors and co-loaded with 500 ml of lactated ringer solution, while 1.8 ml of hyperbaric bupivacaine was administered using a 25G spinal needle to achieve a sensory block level of T6. After baby delivery, 10U oxytocin was added to the IV fluids and the patient was sedated with Inj. midazolam 1 mg and Inj. pethidine 25 mg. As the uterus was atonic, Inj. methylergometrine 0.2 U was given intravenously slowly. After 5 min, 50 mg ranitidine hydrochloride was given intravenously. Immediately, the patient became restless, complaining of itching in upper limbs, face, and chest. She appeared flushed and was coughing. 100% oxygen was administered with face mask, with closed circuit, and the tidal volume was found to be adequate. Auscultation showed the presence of mild bilateral wheeze. We suspected an allergic reaction and as the patient was hemodynamically stable, Inj. pheneramine maleate 50 mg, Inj. hydrocortisone 100 mg, and Inj. deriphylline 220 mg (etofylline and theophylline hydrate) were given intravenously immediately. Within minutes, peripheral pulses became feeble, the heart rate increased from 68 to 130/min, consciousness deteriorated, and respiration was inadequate and non-invasive blood pressure was showing cuff error.

A probable diagnosis of anaphylactic shock was made and Inj. adrenaline 1 ml of 1:10,000 was given

intravenously and 500 ml lactated ringer solution was rushed. Simultaneously, intubation was accomplished with 7.0 mm ID cuffed oral ETT, after administering Inj. midazolam 2 mg, Inj. fentanyl 40 mcg. and Inj. succinylcholine 75 mg. With a second bolus of Inj. adrenaline, peripheral pulses began to improve and blood pressure recorded as 80/61 mmHg. Second intravenous access was secured and Inj. adrenaline infusion 0.1 mcg/kg/min was started and continued postoperatively to prevent effects of residual histamine release. The patient was shifted to the intensive care unit for ventilatory support. Bedside echocardiography showed empty cardiac chambers. Ultrasound-guided right internal jugular vein cannulation was performed, and the central venous pressure was 3 cm H₂O. Then, 500 ml lactated ringer solution and 500 ml 6% hydroxyethyl starch were administered in 30 min resulting in the reduction of the pulse rate from 154 to 122/min and an increase of the blood pressure from 80/55 to 102/69 mmHg. Adrenaline infusion was continued and slowly tapered over the next 8 h. The patient was weaned from the ventilatory support and was extubated the next morning. Further course was uneventful, and the patient was discharged on the 10th postoperative day with an advice to come back after 4 weeks for an intradermal skin testing in the intensive care unit to confirm that ranitidine produced anaphylaxis. The patient and her relatives were alerted and educated that ranitidine was the probable cause for the event.

DISCUSSION

Perioperative anaphylaxis is an unanticipated acute event which needs early recognition. As most of the patients are sedated and covered with drapes, early cutaneous signs of anaphylaxis are often missed, making bronchospasm, and cardiovascular collapse as the first recognized signs of anaphylaxis. Recognition of anaphylaxis during the cesarean section is further delayed because key features such as hypotension, tachycardia, and bronchospasm are also seen in amniotic fluid embolism, peri-partum cardiomyopathy, and aspiration. Drugs commonly involved in perioperative anaphylaxis as described by Laxenaire *et al.*[1] are described in [Table 1](#).

Allergic reactions can be mild, presenting with bronchospasm, flushing and mild hypotension requiring only intravenous fluids and Inj. ephedrine or may be severe, presenting with life-threatening cardiovascular collapse that requires aggressive treatment with intensive care and organ support.[3] Adkinson *et al.* described various clinical manifestations of anaphylaxis under anesthesia[4] which are described in [Table 2](#). Anaphylactic reaction can be recognized early under regional anesthesia when compared to general anesthesia.

Ranitidine is a H₂ receptor antagonist with an excellent safety profile.[5] It is widely used in obstetric cases for aspiration prophylaxis. Anaphylactoid reactions due to ranitidine had been reported in obstetric patients.[6–8] Demirkan *et al.* have reported three cases of anaphylactic reaction due to ranitidine of 8304 first referral patients over a 13-year-period whose incidence is around 0.3–0.7%.[9]

The appearance of flushing and pruritus and the rapidity of development of events sequentially after administration of ranitidine were in favor of anaphylaxis to it. The response to Inj. adrenaline was dramatic, which further confirmed our diagnosis. Had it been general anesthesia, it would have been more difficult to pin-point which drug was the cause as most of the anesthetic agents are implicated in anaphylaxis.

The blood tests to confirm anaphylaxis such as serum tryptase level and radio-allergo-sorbent tests (RAST) could not be done due to unavailability of these tests in our institute. An intradermal skin testing was planned in the intensive care setting after 4 weeks, but the patient was not willing for the test due to her dreadful experience and so testing could not be done to confirm that ranitidine was the definite cause.

CONCLUSION

Anaphylactic and anaphylactoid reactions during anesthesia occur rarely making individual anesthesiologists encounter only a few cases in their working lifetimes. The possibility of anaphylaxis must be specifically considered whenever flushing or urticaria, or sudden hypotension or bronchospasm occurs. Following an algorithmic approach in the management of anaphylaxis should prevent mortality

and morbidity resulting from the reaction. Awareness of this rare but fatal adverse reaction to ranitidine, a commonly used drug, could help in early recognition of the event if faced suddenly.

Footnotes

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Conflict of Interest: None declared

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Figures and Tables

Table 1

Substance Incidence (%)	Most commonly associated
Muscle relaxants 69.2	Succinylcholine, Rocuronium, Atracurium,
Natural rubber latex 12.1	Latex gloves. Torniquets, Foleys catheters
Antibiotics 8	Pencillin and other b-lactams
Hypnotics 3.7	Propofol thiopentone
Colloids 2.7	Dextran, Gelatin
Opioids 1.4	Morphine, Pethidine
Others 2.9	Aprotinin, Protamine, Bupivacaine

Drugs involved in perioperative prophylaxis

Table 2

Organ system	Signs under anesthesia
Cutaneous	Flushing, Urticaria, angioedema
GIT	Nausea, vomiting, abdominal cramps
Respiratory	Increased peak inspiratory pressure, ETCO ₂ , Decreased oxygen saturation, wheeze, bronchospasm
Cardiovascular	Tachycardia, hypotension, arrhythmias, cardiac arrest
Renal	Decreased urine output
Hematological	Increased oozing or bleeding

Clinical manifestations under anesthesia

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