J Anesth (2003) 17:199–200
DOI 10.1007/s00540-003-0178-4

Journal of
Anesthesia

Severe anaphylactoid reaction to ranitidine in a parturient with subsequent fetal distress

Kazuhiro Kaneko and Hideo Maruta

Department of Anesthesia, Odawara City Hospital, Kuno 46, Odawara 250-8558, Japan

Key words: Allergy · Anaphylaxis · Ranitidine · Anesthesia · Obstetrics

Introduction

H_2 receptor antagonists have been widely used for prophylaxis of acid aspiration [1] and are also used in the treatment of anaphylaxis [2]. We report a nullipara who was scheduled for a cesarean section and had an anaphylactoid shock caused by intravenous premedication with ranitidine. To our knowledge, there have been only three reports regarding anaphylaxis or anaphylactoid reactions to ranitidine in obstetric patients [3–5]. This is the first report in which ranitidine administered to a parturient resulted in an emergency cesarean section because of the decreased fetal heart rate.

Case report

A 30 year-old nullipara at 40 weeks of gestation, 154 cm in height and 65 kg in weight, was undergoing cesarean section because of failure to progress. Her medical history was not remarkable, and she was not allergic to any food or medicine. In her room on the labor ward, an infusion of ranitidine 50 mg diluted in saline 100 ml was initiated because she had had a light meal 5 h previously. A few minutes after the initiation of ranitidine (approximately 5 mg injected), she complained of numbness in both hands and then dyspnea and nausea. Ranitidine infusion was immediately discontinued, and oxygen 8 l·min^{-1} was given via a face mask. Cutaneous flushing and swelling occurred, and her radial pulse was not palpable. She was dizzy but conscious. Chest auscultation revealed no wheezing. Despite intravenous injection of ephedrine 20 mg, epinephrine 2 mg, and hydrocortisone sodium succinate 300 mg in divided doses with left displacement of the uterus, the systolic arterial pressure remained at 60 mmHg and the fetal heart rate decreased from 145 to 70 bpm. She was transferred to the operating room for an emergency cesarean section. The arterial pressure returned to 104/44 mmHg with a heart rate of 102 bpm on arrival in the operating room. General anesthesia was induced with ketamine 75 mg, thiopental 75 mg, and suxamethonium chloride 120 mg. Her trachea was intubated with application of cricoid pressure. Four minutes after the induction of anesthesia, a baby was delivered with Apgar scores of 1 at 1 min and 4 at 5 min. The baby was transferred to the neonatal intensive care unit (NICU) after the trachea was intubated. Maternal anesthesia was maintained with nitrous oxide, propofol, fentanyl, and vecuronium. Even after infusion of 1700 ml of acetated Ringer's solution, the blood cell count revealed that the hematocrit had increased to 45.8% from 37.4% measured 1 week previously. During the surgery, intravenous methylergometrine 0.4 mg and intramyometrial oxytocin 5 units were administered. The estimated intraoperative blood loss was 1000 ml. The trachea was extubated 80 min after the induction. The postpartum uterine tone was insufficient despite continuous infusion of dinoprost (total 2 mg) over 2 h. Blood gas analysis revealed a Pa_{O_2} of 108 mmHg, a Pa_{CO_2} of 28 mmHg, and a base excess of -4.3 mmol·l^{-1} at an FI_{O_2} of 0.5 via a face mask 2 h after the extubation. Acetated Ringer's solution 3500 ml, lactated Ringer's solution 500 ml, and 5% human serum albumin 750 ml (total 4750 ml) given over 4 h after the infusion of ranitidine did not ameliorate tachycardia (120–130 bpm) or hypotension (80–95 mmHg). The hemoglobin concentration was 9.6 g·dl^{-1}. Transfusion of red blood cells 840 ml and fresh frozen plasma 480 ml and diuresis with dopamine were started 4 h after the

Address correspondence to: K. Kaneko
Received: March 19, 2003 / Accepted: May 2, 2003

delivery. In the next 30 min, however, she became more hypoxic ($S_{p_{O_2}}$ 93% on oxygen 8 l·min^{-1} by a face mask) without apparent upper airway obstruction. Frothy sputum was suctioned after her trachea was intubated again. A central venous line placed via the right internal jugular vein revealed a central venous pressure (CVP) of 9 mmHg while the patient was spontaneously breathing without positive end-expiratory pressure (PEEP). Diuresis and overnight ventilatory support with PEEP resolved pulmonary edema, and the trachea was extubated the next day. She was discharged without any sequelae on the 8th postoperative day.

A blood sample taken 70 min after ranitidine infusion revealed a slight decrease in C_3 and C_4. Mast cell tryptase was not elevated 8 h after ranitidine infusion. An in vitro study performed 2 months later revealed that both the histamine release test [6] and the cell antigen stimulation test [7] with ranitidine were negative.

The neonate required phenobarbital and midazolam for seizure-like movement in the NICU, but she was discharged home on day 19. Eight months later, the baby was still taking phenobarbital but did not show any physical or developmental abnormalities and did not have seizures.

Discussion

Routine use of H_2 antagonists for premedication is not recommended in elective surgery [1]. Premedication with H_2 antagonists for the prevention of aspiration pneumonia, however, may yield benefits to patients with risk factors for gastric regurgitation, such as full stomach, obesity, and pregnancy. Although spinal anesthesia was scheduled in the present patient, administration of ranitidine was thought prudent because her stomach might be full as a result of a light meal taken after her labor pains started [8].

Anaphylactoid reactions in parturients can be catastrophic. Ephedrine is generally considered the vasopressor of choice for parturients, but ephedrine was not effective in the present patient. The systolic arterial pressure remained at 60 mmHg even after intravenous administration of epinephrine 2 mg, resulting in an emergency cesarean section. Furthermore, during the postpartum period, maternal cardiovascular management was complicated; postpartum uterine contraction increased the central blood volume; the anaphylactoid reaction might have retained a vasodilatory effect or, on the contrary, its vasodilatory effect might have already been attenuated; mild postpartum bleeding seemed to continue; continuous administration of dinoprost might have had vasoconstrictive effects on pulmonary vasculature [9]. In the present patient, transfusion of red blood cells and fresh frozen plasma was followed by pulmonary edema, although the treatment was considered appropriate for ameliorating tachycardia and hypotension. CVP or pulmonary artery catheterization could assist in the management of maternal blood volume during a postpartum period complicated by anaphylactoid reactions.

In both anaphylaxis and anaphylactoid reactions, nausea, flushing, edema, and refractory hypotension may occur. The patient denied having prior contact with ranitidine or other H_2 antagonists. The radioallergosorbent test (RAST) for ranitidine was not available in our country, and a specific IgE test was not performed. We did not perform skin tests, considering the severity of the consequences. Histamine and sulfidoleukotriene released by ranitidine added to the patient's blood in vitro were measured by the histamine release test [6] and the cell antigen stimulation test [7], respectively. These two tests were negative, suggesting an anaphylactoid reaction in the patient.

Although ranitidine has been widely prescribed for premedication, careful vigilance is required during intravenous infusion. Anaphylactoid reactions in parturients can be catastrophic, resulting in an emergency cesarean section because of the decreased fetal heart rate. Furthermore, blood volume management can be complicated during the postpartum period in anaphylaxis or anaphylactoid reaction, a CVP or pulmonary artery catheter, therefore, should be applied to monitor the circulating blood volume.

References

1. Engelhardt T, Webster NR (1999) Pulmonary aspiration of gastric contents in anaesthesia. Br J Anaesth 83:453–460
2. Lin RY, Curry A, Pesola GR, Knight RJ, Lee H-S, Bakalchuk L, Tenenbaum C, Westfal RE (2000) Improved outcomes in patients with acute allergic syndromes who are treated with combined H_1 and H_2 antagonists. Ann Emerg Med 36:462–468
3. Greer IA, Fellows K (1990) Anaphylactoid reaction to ranitidine in labour. Br J Clin Pract 44:78
4. Barry JES, Madan R, Hewitt PB (1992) Anaphylactoid reaction to ranitidine in an obstetric patient. Anaesthesia 47:360–361
5. Powell JA, Maycock EJ (1993) Anaphylactoid reaction to ranitidine in an obstetric patient. Anaesth Intens Care 21:702–703
6. Østergaard PA, Ebbesen F, Nolte H, Stahl Skov P (1990) Basophil histamine release in the diagnosis of house dust mite and dander allergy of asthmatic children. Allergy 45:231–235
7. Kubota Y, Imayama S, Toshitani A, Miyahara H, Tanahashi T, Uemura Y, Koga T, Sugawara N, Kurimoto F, Hata K (1997) Sulfidoleukotriene release test (CAST) in hypersensitivity to nonsteroidal anti-inflammatory drugs. Int Arch Allergy Immunol 114:361–366
8. McKenzie AG (2000) Pulmonary aspiration of gastric contents in obstetrics. Br J Anaesth 84:420–421
9. Hankins GDV, Berryman GK, Scott RT Jr, Hood D (1988) Maternal arterial desaturation with 15-methyl prostaglandin F_2 alpha for uterine atony. Obstet Gynecol 72:367–370