Case Report/*Olgu Sunumu*

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Methylergonovine Use as a First Line Choice During Cesarean Delivery in a Parturient with a Previous Anaphylaxis History to Oxytocin

Oksitosine Karşı Anafilaksi Öyküsü Olan Bir Gebenin Sezaryenle Doğumunda İlk Seçenek Olarak Metilergonovin Kullanımı

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ABSTRACT

We aimed to present the management of a multiparous pregnant woman with a history of oxytocin anaphylaxis scheduled to undergo emergency cesarean delivery under spinal anesthesia by addressing preoperative planning, monitoring and using appropriate medications. Hereby we presented our successful and uneventful management by using methylergonovine as a 1st line uterotonic for the 1st time in such a particular case to maintain uterine tone and prevent a potential atony associated bleeding.

Keywords: Oxytocin, methylergonovine, cesarean delivery, spinal anesthesia, anaphylaxis

ÖZ

Spinal anestezi altında acil sezaryen operasyonu planlanan ve oksitosin anafilaksisi öyküsü olan multipar gebenin yönetiminde preoperatif planlama, takip ve uygun ilaç kullanımını ele alarak sunmayı amaçladık. Burada uterus tonusunu korumak ve olası atoniye bağlı kanamayı önlemek için uterotoniklerden metilergonovini 1. tercih olarak böyle bir olguda ilk kez kullanarak başarılı ve sorunsuz yönetimimizi sunduk.

Anahtar sözcükler: Oksitosin, metilergonovin, sezaryen spinal anestezi anafilaksi

INTRODUCTION

Oxytocin or its synthetic analog, carbetocin, is administered after delivery during cesarean section (CS) to maintain uterine tone and decrease likelihood of peri- or postpartum hemorrhage (PPH) (1,2). A few cases with severe non-immune-mediated anaphylaxis to synthetic oxytocin and/or latex allergy during labor have been documented (3-6). Hereby, we aimed to present the management of a multiparous pregnant woman with a known history of oxytocin anaphylaxis scheduled to undergo emergency CS under spinal anesthesia.

CASE PRESENTATION

A 31-year-old American Society of Anesthesiology (ASA) II parturient in labor with a known oxytocin anaphylaxis history underwent emergency CS under spinal anesthesia after approval for publishing and obtaining written informed consent including information about potential complications related to avoid oxytocin use. In her previous cesarean delivery history, respiratory distress and laryngeal edema immediately after oxytocin administration followed by discontinuation of oxytocin infusion which further resulted in uterine atony and subsequent bleeding that ended up in intensive care unit was documented.

Preoperative laboratory results showed a hemoglobin level of 12.6 g dL^{-1}, a platelet count of 151.000 μL^{-1}, plasma fibrinogen level of 501.4 mg dL^{-1}, aPTT of 28.7 sec and normal INR values. Due to a positive COVID-19 PCR test, CS operation was performed in negative pressure operating room. After standard monitoring (blood pressure: 165/95 mmHg, electrocardiogram and heart rate: 118 bpm, and SpO_2: 98%), two large-bore intravenous (IV) catheters were inserted. Spinal anesthesia was performed at the sitting position using a 25G

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spinal needle between L3-L4 intervertebral space to administer 10 mg of hyperbaric 0.5% bupivacaine with 100 µg of morphine and 10 µg of fentanyl into the subarachnoid space. Spinal anesthesia induced hypotension was treated with a total of 50 mg of IV ephedrine and nausea was treated with 3 mg of IV granisetron. Eleven minutes after the skin incision, a male baby was born with APGAR score of 8 out of 10 at 1 min. To maintain uterine tone, 0.3 mg of methylergonovine was administered slowly via IV infusion over 20 minutes with effective uterine massage over 10 minutes. After delivery of the newborn, 40 mg of IV prednisolone and 22.5 mg of IV phenyramine maleate was administered prophylactically for a possible allergic reaction because of the anaphylaxis history of the patient. Fortunately, no allergic reaction or anaphylaxis occurred. Estimated blood loss was approximately 1600 mL. The hemoglobin level decreased to 10.6 g dL^{-1}. Concomitantly, 1 g of tranexamic acid infusion was administered according to severe perioperative bleeding guidelines due to high-risk of bleeding (2). Peroperative hypotension was treated with 150 µg of noradrenalin. After completion of the surgery, patient was first admitted to postanethesia care unit and then discharged uneventfully to the ward after 8 hours.

DISCUSSION

We have addressed preoperative planning, monitoring and using medications to prevent a potential atony and further bleeding in the present case having non-immune-mediated anaphylaxis history. Uterotonic agents are the mainstay drugs to maintain uterine tone and minimize blood loss in such cases (1, 2, 7). Most commonly used 1st line uterotonic agent for prophylaxis and treatment of PPH due to uterine atony has been still oxytocin which acts via oxytocin receptors in myometrial cells. Oxytocin's synthetic analog, carbetocin is indicated for prevention of uterine atony by binding oxytocin receptors. While methylergonovine, carboprost, and misoprostol are listed as 2nd line rescue therapeutic uterotonic drugs (1, 7). In routine clinical practice, oxytocin is the first choice after umbilical cord clamping during CS and methylergonovine is the 2nd line uterotonic agent of choice in non-hypertensive parturients refractory to oxytocin to maintain uterine tone to prevent PPH during CS when needed (1). Meanwhile, in case of patients with either low or high risk for PPH, carbetocin is associated with reduced need for additional uterotonics for cesarean or vaginal delivery (7). Herein, since we did not consider using either oxytocin or carbetocin, we administered 0.3 mg of methylergonovine via IV infusion at the first place for this particular case. It is typically prescribed to administer at a dose of 0.2-0.4 mg via intramuscular injection. However, in case of bleeding due to refractory atony, 0.2-0.4 mg can be considered to administer via slow IV injection or infusion (1, 2). Concurrently, tranexamic acid was administered because it has been one of the early steps in the management of PPH as described in patient blood management guideline for maternity and obstetrics by the Turkish Ministry of Health (8).

A rare case of non-IgE immune-mediated anaphylaxis to synthetic oxytocin during labor in a healthy 26-year-old was reported. Since further immunological testing including serial tryptase IgE, Complement 3 and 4 and latex Ab-IgE were within normal reference limits, it was diagnosed as a true non-immune-mediated anaphylactic reaction (3). However, in another case report, anaphylactic reaction after oxytocin infusion was observed in a patient underwent CS under spinal anesthesia due to a latex sensitization which was confirmed postoperatively by high level of specific anti-latex IgE, 10.8 kUA L^{-1} (normally <0.35 kUA L^{-1}) (6). Parturients with allergic history whether immune or non-immune mechanism may also be sensitized to antibiotics, latex and/or anesthetic drugs (3-6). In case of an anticipated anaphylaxis suspicion most likely to oxytocin as in our present case, due to the possible cross reaction between oxytocin and latex, potential allergic monitoring equipment are best avoided. As indicated in the literature, putative cross-reaction between latex antigen and oxytocin has been reported in parturients suffered from anaphylactic reaction after oxytocin administration during CS (4,6). Herein, we primarily did not use of oxytocin and/or its analog carbetocin after delivery and any prophylactic antibiotic as well. Due to reported cross reactivity between oxytocin and latex, allergic sensitization to latex might predispose anaphylactic reaction to oxytocin (4,6).

According to the recent systematic review, anaphylactic reactions which are unpredictable during pregnancy varying from subjective cutaneous symptoms to anaphylaxis/lethal anaphylactic shock mostly occurred during CS (74.47%). Identified allergens were antibiotics (penicillines and cephalosporins), anesthetics (suxamethonium, mepivacaine), latex, oxytocin, sodium and sucrose iron, laminaria, misoprostol, rubber from Foley catheter, oral phytomenadione, ranitidine, chamomile, and ant sting. Two cases of maternal death related to latex and IV iron sucrose, and six infants with neurological disease were mostly related to antibiotics (9). However, favorably successful maternal and neonatal outcome was provided with careful preanesthetic evaluation followed by emergency management that includes planning spinal anesthesia and choosing appropriate medications.

Although some may argue that baseline plasma fibrinogen concentration should have been checked preoperatively in a parturient at high risk for PPH because of the concrete evidence that peroperative fibrinogen level less than 2 g L^{-1} has known to have a 100% predictability of 100% severe postpartum haemorrhage, unfortunately this hypothesis could not be shown in 2015 (10). In this study, fibrinogen concen-

tration was determined at admission to the labour ward in 1951 healthy women and in a subgroup of women (n=80) also after the placenta was delivered. Additionally, postpartum bleeding volume was estimated by weighing surgical sponges and pads and by measuring collected blood. Mean fibrinogen concentration was 5.3 ± 0.8 g L^{-1}. Median estimated blood loss was 450 mL and 12.8% of women bleeding>1000 mL. It was found out that fibrinogen concentration was not correlated with postpartum haemorrhage in the entire cohort (r_s=0.003, P=0.90) or in any subgroup. Fibrinogen concentration was not associated with bleeding >1000 mL (P=0.93) and did not differ significantly before and after delivery (10). Despite a decade old published data, it has been recently stated in 2025 that there are still no data for prophylactic or preemptive fibrinogen supplementation. Since patients without hypofibrinogenemia at baseline did not benefit from fibrinogen supplementation, suggesting that fibrinogen concentrate is only effective in patients in cases of deficiency (11). We had the preoperative fibrinogen level in our case though it is not a mandatory laboratory test as also mentioned even for this particular patient population in the latest severe bleeding guidelines launched by ESAIC as well (2).

In conclusion use of a 2nd line uterotonic methylergonovine via slow IV infusion with close monitoring to replace 1st line uterotonic oxytocin can be considered to prevent a life-threatening anaphylaxis without development of uterine atony and further bleeding.

AUTHOR CONTRIBUTIONS

Conception or design of the work: SE, GE
Data collection: OA, GE
Data analysis and interpretation: SE, BG, NCE
Drafting the article: SE, BG, OA
Critical revision of the article: BG, NCE
The author (SE, GE, OA, NCE, BG) reviewed the results and approved the final version of the manuscript.

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