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Original contribution

Carbetocin for prevention of postcesarean hemorrhage in women with severe preeclampsia: a before-after cohort comparison with oxytocin☆,☆☆,★

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Abstract

Study objective: The aim of the study was to compare the incidence of the use of additional uterotonics before and after the change of carbetocin to oxytocin for the prevention of postpartum hemorrhage after cesarean delivery in women with severe preeclampsia.

Design: This was an observational retrospective before-and-after study.

Setting: Operating room, postoperative recovery area.

Patients: Sixty women with severe preeclampsia undergoing cesarean delivery under spinal anesthesia; American Society of Anesthesiologists 3.

Interventions: Observational study.

Measurements: Blood pressure, heart rate, and biological data (hemoglobin, platelets, haptoglobin, prothrombin time index, activated partial thromboplastin time ratio, blood uric acid, aspartate aminotransferase, alanine aminotransferase, serum urea, serum creatinine, and albumin).

Main results: The incidence of additional uterotonic administration in the carbetocin and oxytocin groups was 15% and 10%, respectively (P = .70).

Conclusions: As carbetocin appears to be as effective and safe as oxytocin in preeclamptic women, its advantages make it a good uterotonic option in this particular setting.

1. Introduction

Postpartum hemorrhage (PPH) accounts for 20% to 25% of maternal deaths worldwide. Cesarean section is a recognized risk factor for PPH, and its incidence is increasing in developed countries. Uterine atony is the main mechanism of PPH, as it is involved in 59% of cases. Its prevention implies the use of uterotonics after childbirth. Although oxytocin is the first-line pharmacological agent given for this purpose, carbetocin was proposed more recently, its advantage being its

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longer duration of action [1,2]. Although some authors reported a lesser need for additional uterotonic with carbetocin [3,4], most studies showed that both agents have a similar efficacy and safety profile [5-9].

The use of carbetocin in women with preeclampsia was reported in only 1 study [10]. In our institution, carbetocin is used daily for prevention of uterine atony during cesarean delivery for several years, including women with severe preeclampsia. In the late 2012, carbetocin was no more available from the pharmaceutical company for 8 months. Therefore, we used oxytocin for PPH prevention during this period. This rapid therapeutic change can be considered as a sentinel event, allowing the study of the efficacy and side effects of the uterotonic prevention during the use of carbetocin and oxytocin. The aim of our study was to compare the incidence of the use of additional uterotonics before and after the change of carbetocin to oxytocin for the prevention of postpartum hemorrhage after cesarean delivery in women with severe preeclampsia.

2. Patients and methods

This observational retrospective before-and-after study was conducted in our university hospital level 3 obstetric unit. We compared the efficacy and safety of 2 preventive protocols for PPH in women with severe preeclampsia based on the use of carbetocin or oxytocin. The study was approved by the institutional review board, and given its retrospective nature, patient written informed consent was waived. All preeclamptic women admitted in our obstetric unit from July 2011 to August 2013 and who had a cesarean delivery were included. They were identified via the birth registry that is updated daily by midwives. Patients in labor; those with chronic hypertension, multiple gestations, diabetes, coagulopathy; or those given tocolytic drugs were not included in the study. Criteria for the diagnosis of severe preeclampsia were those reported in the 2009 guidelines published by the French Society of Anesthesiology and Critical Care Medicine [11]. These criteria included (1) severe hypertension (systolic blood pressure [BP] >160 mm Hg and/or diastolic BP >110 mm Hg) associated with proteinuria or (2) hypertension associated with oliguria (<500 mL/d), severe proteinuria (>5 g/d or +++), HELLP syndrome, neurologic symptoms, eclampsia, oligohydramnios, or intrauterine growth retardation. Pharmacologic treatment of hypertension before cesarean was recommended when mean arterial BP (MAP) was >130 mm Hg, with associated symptoms of end-organ involvement. According to the French guidelines, intravenous (IV) nicardipine was the first-line antihypertensive treatment, and IV MgSO4 (4.5 g initial dose over 20-30 minutes followed by 1 g/h continuous maintenance infusion) was given as seizure prophylaxis in patients with neuromuscular hyperexcitability.

All patients were given an IV infusion (500 mL) of lactated Ringer's solution before the anesthetic. BP and heart rate (HR) were monitored using a Datex-Ohmeda S/5 monitor (Datex-Ohmeda S.A.S., Limonest, France) and stored online in the Opesim database (Opesim Version 3; Evolucare, Carcassone, France). Baseline BP and HR were the mean of the last 3 consecutive measurements taken immediately before spinal anesthesia. Then, hyperbaric 0.5% bupivacaine (10 mg), sufentanil (2.5 μg), and preservative-free morphine hydrochloride (100 μg) were injected intrathecally, and the patient was returned to the supine position with a left lateral tilt of the operating table. The upper sensory level was checked regularly to make sure that a T4 sensory level was achieved within 10 minutes. The study medication (100 μg carbetocin or 5 IU oxytocin) was diluted in 5-mL normal saline and administered slowly (over 30-60 seconds) intravenously by the anesthetist after the birth of the infant. The slow administration has been shown to reduce the potentially harmful hemodynamic effects of oxytocin [12]. A continuous infusion of oxytocin was given after the initial bolus. Maternal BP and HR were recorded at 1-minute intervals from the spinal injection until at least 15 minutes after the uterotonic agent injection. We defined hypotension and tachycardia in both study groups as a decrease in BP to <70% and an increase in HR to >120% of the respective baseline values. Hypotension and tachycardia occurring within 5 minutes of oxytocin or carbetocin injection were considered, at least partly, related to these medications. Hypotension was treated using a mixture of ephedrine (3 mg/mL) and phenylephrine (50 μg/mL). Blood hematology and biochemistry were obtained before delivery, and test values were compared with those obtained at discharge.

All data were retrieved from our computerized medical database. Obstetrical data were collected from ICOS Maternité (ICOS Maternité Version ICOS_FSE 1.01; Icogem, Auriol, France); clinical and anesthetic data, from Opesim (Opesim Version 3; Evolucare); and biological data, from Clinicom (Clinicom Version 6.5; Intersystems, Courbevoie, France). Biologic data were collected before cesarean section and before discharge from the hospital. The primary end point was the need for additional uterotonics (sulprostone or oxytocin) during a 24-hour period a delivery. Categorical data were analyzed using χ^2 or Fisher exact test, and quantitative data were analyzed using the Student *t* test or analysis of variance, when appropriate. Hemodynamic data were analyzed using repeated-measure analysis of variance. $P = .05$ was considered to indicate statistical significance.

3. Results

Data from 60 consecutive women reaching inclusion criteria from July 2011 to August 2013 were studied: 40 were given carbetocin during the first 18 months of the study period, and 20 received oxytocin during the last 8 months. The baseline maternal and neonatal characteristics of both groups were similar (Table 1). Because of a very low umbilical arterial pH (pH 6.98) in 1 neonate in the oxytocin group, mean pH was lower in this group compared with the carbetocin group.