Egyptian Journal of Anaesthesia (2016) 32, 117–121

HOSTED BY

Egyptian Society of Anesthesiologists

Egyptian Journal of Anaesthesia

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Research Article

Comparative study between effect of carbetocin and oxytocin on isoflurane-induced uterine hypotonia in twin pregnancy patients undergoing cesarean section

Neveen Gerges Fahmy *, **Hend Mohamed Yousef, Hany Victor Zaki**

Department of Anesthesiology, Intensive Care, and Pain Management, Faculty of Medicine, Ain-Shams University, Cairo, Egypt

Received 29 March 2015; revised 9 August 2015; accepted 30 September 2015
Available online 7 November 2015

KEYWORDS

Twin pregnancy;
Caesarian section;
Postpartum hemorrhage;
Carbetocin;
Oxytocin

Abstract *Background:* Carbetocin is a long acting structural analog of human oxytocin and is given as single IV bolus following the delivery; it is effective as an oxytocin infusion for several hours because the latter has a very short duration of action which requires a continuous infusion to achieve sustained uterotonic activity.
Multiple pregnancy is one of the most common causes of postpartum hemorrhage. This study was done to compare the effect of carbetocin and oxytocin on uterine contraction and though the use of other uterotonic drugs postoperative in multiple pregnancy patients undergoing elective C.S.
Patients and methods: Sixty patients were enrolled in this study, and they were classified randomly into two groups: group C = received 100 μg carbetocin, group O = received 20 IU oxytocin. We compared between the two groups as regard hemodynamic parameters (heart rate and mean arterial blood pressure), uterine contraction, amount of blood loss and number of patients who needed to reduce isoflurane concentration.
Results: As regards uterine contraction group O needed methylergometrine postoperative significantly more than group C and as regards blood loss; it was significantly decreased more in group C and though less reduction in blood pressure and less effect on heart rate than group O.
Conclusion: Single dose of carbetocin appears to be more effective than oxytocin for several hours on uterine contraction and though preventing postpartum hemorrhage in multiple pregnancy patients undergoing elective caesarian section.

1. Introduction

Primary postpartum hemorrhage (PPH) is the most common form of major obstetric hemorrhage. Definition of PPH is

* Corresponding author. Cellular: +20 1005282785.
E-mail address: nivengerges@hotmail.com (N.G. Fahmy).
Peer review under responsibility of Egyptian Society of Anesthesiologists.

http://dx.doi.org/10.1016/j.egja.2015.09.012

the loss of 500 ml or more of blood from the genital tract within 24 h of the delivery of baby [1].

Minor PPH (blood loss 500–1000 ml) and major PPH (more than 1000 ml). Many patients known to be high risk for developing PPH: twin pregnancy, known placenta previa, placental abruption, obesity with BMI > 35; anemia < 9 g/dl, previous PPH and age > 40 years [2].

Almost 500,000 women die for this preventable cause each year especially hemorrhage that occurred at time of delivery [3].

Other nonfatal complications may occur as Sheehan's syndrome (Pituitary infarction), coagulopathy, and organ damage due to hypotension, shock, and risk of hysterectomy [4].

Uterine atony is the first cause of hemorrhage at time of delivery; therefore, active management is better than expectant management of the third stage of labor [5,6]. Third stage of labor is that period following the delivery of baby till placental delivery (see Fig. 1).

Uterotonic agents as oxytocin (10 IU) intramuscularly usually prevent PPH in low-risk vaginal and caesarian deliveries, or intravenous infusion (20–40 IU in 1000 ml, 150 ml/h) which is another alternative because of its short duration (its half-life is approximately 3.5 min) [7,8].

Misoprostol (600 μg orally) is not effective when compared with oxytocin in prevention of PPH, also carries increased adverse effects which are dose related [9].

A long-acting oxytocin derivative, carbetocin, is licensed in the UK specifically for the indication of prevention of PPH. It is given as an IV bolus 100 μg over one minute.

Carbetocin is a synthetic oxytocin analog 1-deamino-1-monocarbo (2-O-methyltyrosine) – oxytocin that binds to oxytocin receptors with higher affinity. Oxytocin receptors are G-protein coupled [10] and there mechanism of action involves second messengers and the production of inositol phosphate [11]. Each ampule contains 100 μg (0.1 mg) of carbetocin (manufacture: Ferring Gmbh, Kiel, Germany) (marketing authorization holder: Ferring Gmbh, Kiel, Germany) (date of revision: June 2006). It is as effective as oxytocin infusion with respect to blood loss following delivery [12–14]. Its contractile effects of the uterus are apparent within two min. and can be observed for approximately one hour [15]. It has half-life of 40 min (4–10 times longer than oxytocin). So it is given as single IV bolus following the delivery of baby at elective or emergency cesarean section [16] and if further uterine stimulation is needed, treatment with other uterotonic drugs should be used. Carbetocin has also been shown to stimulate milk letdown due to its action on oxytocin receptors on the myoepithelial cells and there was not a significant amount of it in breast milk [17]. Side effects are nausea, vomiting, chest pain, tachycardia, hypotension and respiratory distress. Contraindications do not use before delivery (it should not be used to induce or augment labor since it could cause cardiac or respiratory distress to mother or infant) [18] hypersensitivity to carbetocin or oxytocin.

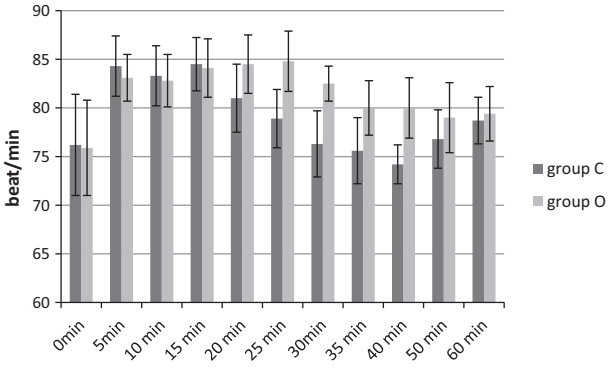

Figure 1 Heart rate values. Group C: Those patients who received carbetocin. Group O: Those patients who received oxytocin.

The aim of the present study was to compare the effect of carbetocin versus oxytocin on the hemodynamics and the effectiveness of uterine contraction and blood loss in twin pregnancy patients undergoing elective C.S. under general anesthesia using isoflurane and though it may contribute carbetocin as substitute to oxytocin for elective C.S. at our institution as well as others.

2. Patients and methods

After getting approval from hospital ethical committee and written informed consent from patients, 60 twin pregnancy patients ASA physical status I, aged 28–36 years, were scheduled for elective cesarean section in Ain Shams University Hospital in the period between November 2012 and June 2013. Exclusion criteria included patients with hypertension, pre-eclampsia, cardiac, respiratory, renal or liver disease, pre-existing bleeding disorder such as hemophilia and women taking therapeutic anticoagulants, hypersensitivity to carbetocin or oxytocin. Patients with preoperative hemoglobin less than 9.5 gm% and those who are pregnant with more than two babies were also excluded from the study.

Pre-operative investigations in the form of ECG, complete blood picture, coagulation profile, liver and kidney functions were performed. A venous cannula 18G size was inserted and basic monitoring (ECG, pulse oximeter, NIBP) was applied. All patients underwent general anesthesia; pre-oxygenation with 100% O_2 for 4 min then induction with intravenous thiopentone sodium 4–7 mg/kg, cisatracurium 0.5 mg/kg to facilitate endotracheal intubation (as all patients underwent elective C.S. and were fasting for at least 8 h) and anesthesia was maintained with oxygen (FiO_2 0.4), isoflurane (MAC 1) and intermittent doses of cisatracurium. Lactated Ringer's solution was infused at a rate of 10–15 ml/kg.

Patients were randomly allocated to lie into two equal groups: group C (no = 30) received 100 μg carbetocin in 10 ml saline, and group O (no = 30) received 20 IU oxytocin in 10 ml of saline solution. Randomization was performed by using computer-generated program. Both drugs were prepared preoperatively and coded so that the working investigator and the obstetrician were blinded of the type of drug injected. The uterotonic drug was injected slowly IV over one minute after delivery of babies.

In all patients, the following parameters were recorded:

- hemodynamic parameters (heart rate and mean arterial blood pressure),
- uterine contraction score; assessed by the obstetrician and scored as very good (4), good (3), sufficient (2), poor (1) or atony (0), and