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Original Research Article

Carbetocin is Better than Oxytocin in the Post Ceasarian Case

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Abstract:

Background and Objectives: Prevention of post-partum haemorrhage (PPH) is a major issue due to its impact on maternal morbidity and mortality. To compare the haemodynamic effects of oxytocin and carbetocin and to assess the efficacy of these two drugs in terms of blood loss in caesarean- section at high risk of primary post-partum haemorrhage

Methods: This is a prospective, case-control study conducted from July 2022 and October 2022 within the department of Obstetrics and Gynaecology. Two hundred three women undergoing elective caesarean section were consecutively enrolled, with risk factors for primary post-partum haemorrhage such as: multiple pregnancy, two or more previous caesarean section, presence of uterine fibroids, previous myomectomy, presence of placenta previa, past history of PPH, fetal macrosomia and fetal malformations associated with polyhydramnios. A written informed consent was asked from eligible women on admission. Ethical clearance was obtained from Institutional ethics committee.

Results: All relevant maternal subject characteristics in both study groups were comparable, except for the significantly increased use of anticoagulant drugs during pregnancy in carbetocin group (19.6% vs 3.9%, $p<0.05$). The main gestational age at caesarean was 38 weeks in the carbetocin group and 37 in the control group. There was significant difference in the amount of estimated blood loss and in the incidence of primary post-partum haemorrhage (>1000 ml) in both groups as seen after 24 hours caesarean section ($p<0.05$). Suggests the loss of maternal blood was less in Carbetocin as compared to oxytocin.

Conclusion: In the third stage and the first 24 hours following delivery, which are both considered to be the "four stage of labor," a single injection of carbetocin appears to be more efficient than a continuous infusion of oxytocin to maintain adequate uterine tone, with a low maternal blood loss and similar safety profile and minor antidiuretic effect.

Keywords: Carbetocin, Oxytocin, Post-Partum Haemorrhage, Caesarean Section, Uterine Tone.

Introduction

Due to its effects on maternal morbidity and mortality, post-partum hemorrhage (PPH) prevention is a significant issue. When there is a blood loss of more than 500 mL following greater than 1000 mL following a caesarean section and vaginal birth that takes place within 24 hours of delivery. [1]

Almost 500.000 women every year pass away from this potentially curable condition year, and up to a fifth of these fatalities are thought to be caused by occur as a result of bleeding at the time of delivery. Non-fatal PPH can result in further interventions, severe anaemia, need of blood transfusion, Sheehan's syndrome (pituitary infarction), coagulopathy and organ damage due to hypotension and shock. [2] PPH diagnosis is based on International Classification of Disease (ICD) codes recorded in Perinatal Database (ICD-9 and ICD-10). Subtypes of PPH identified with ICD-9 and ICD-10 diagnostic codes included: 1) PPH due to retained placenta, 2) PPH due to uterine atony (occurring within 24 hours following delivery), 3) delayed and secondary PPH (occurring after the first 24 hours following delivery) and 4) PPH due to a coagulation defects. [3]

There is universal agreement that active management of the third stage of labor rather than expectant management is preferable because uterine atony is the primary source of hemorrhage at the moment of delivery. It is advised to manage in Labor's third stage is and the time frame starting after delivery and ending with the placing of the placenta. [4] The main focus of active care is the use of uterotonic medications, which effectively

prevent PPH and sharply reduce its incidence. The chosen medicine for the prophylaxis of PPH in low-risk vaginal and caesarean deliveries is oxytocin (10 IU), delivered intramuscularly. After the anterior shoulder has been delivered, healthcare professionals should start giving this medicine. As an alternative for the active management, intravenous oxytocin infusion (20 to 40 IU in 1000 mL, 150 mL/hour) is suitable. [5] To prevent PPH and lessen the need for therapeutic uterotonics after an elective caesarean section, carbetocin can be given as a 100-g IV bolus over a minute in place of a continuous oxytocin infusion. [6]

Although oxytocin is the most well-known uterotonic agent, other medications are also available; nonetheless, it is still unclear which medicine is best for prophylactic use. [5] Carbetocin, also known as 1-deamino-1-monocarbo-(2-O-Methyltyrosine)-oxytocin, is a synthetic, long-acting oxytocin analogue. [6] After intravenous injection of the recommended dosage of 100 g, it has a half-life of 40 minutes (about 4–10 times longer than oxytocin), and uterine contractions start to happen in less than two minutes. Regarding the rise in uterine tone and the decrease in the risk of PPH during elective caesarean delivery, a single dosage of carbetocin has been hypothesized to act as a 16-hour intravenous oxytocin infusion.

Materials and Methods-

This is a prospective, case-control study conducted from July 2022 and October 2022 within the department of Obstetrics and Gynaecology. Two hundred three women undergoing elective caesarean section were consecutively enrolled, with risk factors for primary post-partum haemorrhage such as: multiple pregnancy, two or more previous caesarean section, presence of uterine fibroids, previous myomectomy, presence of placenta previa, past history of PPH, fetal macrosomia and fetal malformations associated with polyhydramnios. A written informed consent was asked from eligible women on admission. Ethical clearance was obtained from Institutional ethics committee.

The exclusion criteria included the presence of hypertension, preeclampsia, cardiac, renal or liver diseases, epilepsy and general anaesthesia, as well as women with history of hypersensitivity to carbetocin. Firstly we recruited One hundred two women who received carbetocin (case group A), then we enrolled one hundred one women who received oxytocin (control group B). Women in the carbetocin group (group A) received a bolus of 100 µg IV at delivery of the anterior shoulder; women in the control group (group B) received 20 IU of oxytocin in 1000 ml of 0,9% NaCl solution IV (150 mL/ hour) at delivery of the anterior shoulder.

Methodology

Following the administration of this anesthesia, patients were placed in a supine position and a limb cuff was inserted for continuous blood pressure monitoring. We compared the drop in blood pressure after combined spinal-epidural (CSE) procedure, 1 minute, 3 minutes, and 5 minutes after drug administration, at the time of uterine repair and at the term of caesarean procedure, on left recumbent position, to evaluate the haemodynamic effects of carbetocin and oxytocin.

We kept track of any instances of diarrhoea, nausea, vomiting, flushes, headaches, and tachycardia. The requirement for further uterotonic drugs and the assessment of the decline in hemoglobin level by comparing the haemoglobin concentration on admission with the measure at 2 hours and 24 hours following delivery were the study's last significant findings. Additionally, the amount of blood lost is measured very away after a caesarean section, with a blood loss of 1000 ml or more being considered a hemorrhage. [5] The surgeon determined the amount of blood loss using the standard methods (visual estimates, number of used swabs, and amount of aspirated blood). [7] Blood pressure (in mmHg), uterine tone, uterine position (with respect to the umbilical point, UP) were monitored 2 hours, 12 hours and 24 hours after delivery by the same midwife. All patients had the Foley catheter and urobag in situ for 24 hours after caesarean section and the amount of urine was monitored 2 hours and 12 hours after delivery by the midwife.

Statistical Analysis-

The statistical analysis was performed using SPSS for windows version 22.0 software (Mac, and Linux). The findings were present in number and percentage analyzed by frequency, percent. Chi-square test was used to find the association among variables. The critical value of P indicating the probability of significant difference was taken as <0.05 for comparison.

Results

Table 1: Demographic details of study population

	Carbetocin (A) (n=102)	Oxytocin (B) (n=101)	P value
Maternal Age (mean, SD)	37.3±5.5	36.3±4.2	0.31
Gestational age at delivery (median-range)	38(37-39)	37(36-38)	0.01
Weight increase in pregnancy (mean, SD)	12.4±4.5	13.4± 4.1	0.11
Previous Abdominal surgery (n, %)	32 (31.8%)	22 (21.7%)	0.07
Use of anticoagulant in pregnancy (n, %)	20 (19.6%)	4 (3.9%)	0.01

As per table 1All relevant maternal subject characteristics in both study groups were comparable, except for the significantly increased use of anticoagulant drugs during pregnancy in carbetocin group (19.6% vs 3.9%, p<0.05). The main gestational age at caesarean was 38 weeks in the carbetocin group and 37 in the control group.

Table 2: Indications of Caeserean Section

	Carbetocin (A) n=102	Oxytocin (B)n=101
Two or more CS	26.4% (27)	23.7% (24)
Fetal Macrosomia	11.8% (12)	2% (2)
Placenta praevia	11.8% (12)	11.8% (12)
Uterine fibroids	3.9% (4)	0
History of PPH	0	0
Twin pregnancy	21.6% (22)	41.6% (42)
Fetal polyhydramnios	0	5.9% (6)
Previous myomectomy	17.6% (18)	15.7% (16)

As per table 2 Population profile and indication to elective caesarean section were similar for each group, however in the group B the main indication has been the twin pregnancy (21.6% vs 41.6% but it was not significant.

Table 3: Maternal Blood Loss

	Carbetocin (A)	Oxytocin (B)	P value
During caesarean section	**n**	**n**	
< 500 ml	69	70	0.11
500- 1000 ml	32	29	
> 1000 ml	1	2	
2h after caesarean section < 500 ml	50	60	0.31
500- 1000 ml	50	40	
1000 ml	2	1	
12h after caesarean section			
< 500 ml	51	61	
500-1000 ml	51	40	0.11
>1000 ml	0	0	
24h after caesarean section			
<500 ml	41	31	
500-1000 ml	61	70	0.01*
>1000 ml	0	0	

As per table 3 there was significant difference in the amount of estimated blood loss and in the incidence of primary post-partum haemorrhage (>1000 ml) in both groups as seen after 24 hours caesarean section (p<0.05). Suggests the loss of maternal blood was less in Carbetocin as compared to oxytocin.

Table 4: Complete Hemogram before and after Caesarean Section

	Carbetocin (A)			Oxytocin (B)		P value
Pre-Operative Hb (median interquartile ranges)						
Hb (g/dl)	11.4	(10.7 - 12.1)	11.8		(10.9 - 12.3)	0.31
Ht (%)	34.6	(32 - 36.2)	34		(30.9 - 36.8)	0.82
PLT	222	(180 - 266)	206		(162 - 236)	0.06
Post-Operative Hb Drop (median interquartile ranges)						
Hb 2 h after CS (g/dl)	-0.6	(-1.1 ; -0.1)	-0.7		(-1.3 ; -0.3)	0.43
Hb 12 h after CS (g/dl)	-0.7	(-1.3 ; 0.0)	-1.1		(-1.9 ; -0.2)	0.07
Ht 2 h after CS (%)	-1.4	(-2.8 ; -0.1)	-1.8		(-4.0 ; 0.4)	0.29
Ht 12 h after CS (%)	-1.4	(-3.2 ; 0.2)	-1.9		(-5.3 ; 0.2)	0.24
PLT 2 h after CS	-20	(-52 ; 0)	-7		(-28 ; 1)	0.11
PLT 12h after CS	-18	(-46 ; 0)	-12		(-29 ; 8)	0.14

As per table 4 in both study groups haemoglobin levels before and after 2 hours and 24 hours apart from delivery were similar, confirming no significant difference in the level of blood loss although we found a tangentially lower Hb decrease at 12 hours from delivery in the carbetocin group (- 0.7 g/dl vs - 1.1 g/dl, p 0.074).

Discussion

The examination of the immediate haemodynamic effects of carbetocin delivery is the study's main finding. We are aware that an oxytocin bolus has significant haemodynamic effects, including systemic vasodilation, substantial hypotension, tachycardia, and an increase in cardiac output, which cause dose-dependent hypotension and tachycardia [8,9].

Myocardial ischemia may result from these hemodynamic adverse effects, particularly in patients with hypovolemia or cardiac conditions [10]. According to a recent study by Moertl et al., patients treated with carbetocin have similar effects on the cardiovascular system but experience more significant hypotension and hemodynamic rebound when treated with oxytocin [11].

In agreement, we report a good hemodynamic profile in the carbetocin group with substantially unaltered systolic and diastolic blood pressure levels with respect to the start of the surgical procedure. In addition, we describe lower BP levels in the control group (group B) in nearly all study times after drug administration, even though this situation appears to be tangential and not always statistically significant. According to this finding, carbetocin appears to have a favourable haemodynamic safety profile. Pre-eclampsia, eclampsia, and general anesthesia are currently indicators that carbetocin administration should be avoided, but these data propose a new threshold in the effort to broaden the indications for therapy.

In the Cochrane reviews from 2007 and 2012, Su et al. concluded that the use of carbetocin is more effective than oxytocin for preventing PPH in women undergoing caesarean sections, but the data and the evidences were still insufficient [4,13]. Regarding the carbetocin literature, Danzereau et al. [14] initially noted that women who received carbetocin immediately after giving birth required less further uterotonic treatment for uterine atony.

We reach the same conclusions as many other studies [7,8] and Borruto et al. [12] also described a lower rate of additional oxytocic need in women receiving carbetocin administration during CS, but it is challenging to compare our study with the ones mentioned due to the strict risk factor selection of our study population. For instance, in their intriguing paper, Attilakos et al. eliminated pregnant women who were less than 37 weeks gestation from the study as well as placenta previa and multiple pregnancies [15].

None of the women in our carbetocin subgroup experienced the maternal tachycardia and facial flushes that have been reported in earlier trials [13,14]. The detection of carbetocin's effects on diuresis dates back to the early 1960s, when clinical findings revealed that systemic administration of high doses of oxytocin to pregnant patients caused antidiuresis, indicating effects akin to those of vasopressin [8,15]. In actuality, these two hormones are produced in the human hypothalamus and transported via the neurohypophysial tract to the posterior pituitary gland for storage or secretion.

Conclusion

Therefore, despite the fact that carbetocin is a synthetic oxytocin analog, the slight molecular structure difference could determine not only the stronger uterotonic action but also the difference in the biologic function, such as the absence of antidiuretic effect. This is an important finding in the quest to define a more thorough carbetocin profile.

Therefore, we draw the conclusion that, in the third stage and the first 24 hours following delivery, which are both considered to be the "four stage of labor," a single injection of carbetocin appears to be more efficient than a continuous infusion of oxytocin to maintain adequate uterine tone, with a low maternal blood loss and similar safety profile and minor antidiuretic effect.

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