ORIGINAL ARTICLE

Carbetocin Versus Oxytocin for the Prevention of Atonic Postpartum Hemorrhage after Elective Caesarean Section in High Risk Women

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Abstract

Background: ***One leading cause of maternal illness and death is postpartum hemorrhage. Ten percent or more of all births include it, and it's the leading cause of maternal mortality (at 25%).***

Aim and objectives: ***When it came to preventing atonic postpartum hemorrhage (PPH), we compared carbetocin with oxytocin in high-risk women who had elective cesarean sections to find out which one was safer and more successful.***

Subjects and methods: ***There were two equal groups of 200 women who underwent elective cesarean sections under regional anesthesia and were at high risk for primary atonic postpartum hemorrhage (defined as a gestational age of more than 37 weeks): In the first group, 100 women were given 100 micrograms of carbetocin intravenously. 100 women made up Group II; each of them got 10 IU of oxytocin intravenously. We examined the effects of the two medications on uterine atony, blood loss, and pre- and post-operative vital sign changes.***

Results: ***The two drugs' expected blood loss was substantially different (p=0.002). In addition, the two drugs differed significantly (p=0.048) in their effects on postpartum blood loss. The two drugs were not statistically comparable when it came to supplemental needs, such as the need for more uterotonic therapy or blood transfusions.***

Conclusion: ***Preventing atonic postpartum hemorrhage and reducing intrapartum hemorrhage are both improved by carbetocin. When it came to the administration of extra oxytocic drugs and blood transfusions, though, carbetocin and oxytocin were identical.***

Keywords: Carbetocin; Oxytocin; Caesarean section; Atonic postpartum hemorrhage

1. Introduction

The most prevalent and potentially life-threatening consequence of giving birth is obstetric hemorrhage. If the expected blood loss following a cesarean section is more than 1000 mL or more than 500 mL, then the patient is considered to have postpartum hemorrhage (PPH), according to traditional criteria.[1]

The most effective uterotonics for preventing postpartum hemorrhage include intravenous boluses of carbetocin and oxytocin and intramuscular ergometrine and oxytocin.[2]

Postpartum hemorrhage ranks first among maternal illnesses and deaths globally. About seventy to eighty percent of these cases involve uterine atony, the most common kind of this hemorrhage. To this day, pharmacotherapy is still the gold standard for postpartum hemorrhage prevention. Both monotherapy (using drugs like oxytocin or carbetocin) and combination therapies (using drugs like ergometrine or prostaglandin analogs or tranexamic acid) are possible.[3]

Patients at risk for PPH can be identified so that they can be diagnosed and treated quickly. Several steps can be taken to reduce the risk of postpartum hemorrhage. These include checking for and treating iron deficiency anemia, keeping a PPH cart or medication kit on hand, and using prophylactic uterotonic-carbetocin either alone or in combination with antifibrinolytics like oxytocin and methylergometrine or oxytocin and tranexamic acid.[4]

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The gold standard first-line pharmacologic drug for avoiding PPH is oxytocin, a cyclic nonapeptide that causes uterine contractions by binding to myometrial receptors. It takes 1 to 6 minutes for intravascular administration and 3 to 5 minutes for intramuscular administration to start working, and 30 to 60 minutes for it to reach its maximum plasma concentration.[5]

A more recent long-acting analogue of oxytocin, carbetocin, shares many of the same pharmacologic features as the original drug but has superior thermal stability and a half-life that is four to ten times longer. In comparison to oxytocin, carbetocin has no dose-response variability, no oxytocin receptor desensitization, and may be more effective than oxytocin with fewer side effects after a single dose.[6]

In order to better understand how carbetocin and oxytocin handle atonic postpartum hemorrhage (PPH), this study compared the two drugs in a group of high-risk women who underwent elective cesarean sections.

2. Patients and methods

The 200 pregnant women who presented to the antenatal clinic and had caesarean sections between 2023 and 2024 at Aga Central Hospital were part of this observational, comparative, prospective study. All of the women had at least one risk factor for postpartum hemorrhage.

Ethical Consideration:

This project has already received approval from the obstetrics and gynecology department at Cairo's Al-Azhar University Hospitals. Verbal informed consent was obtained from all participants in this study.

Sample size calculation:

The World Health Organization's method for determining sample sizes in health studies was used to compute the sample size. Lemeshow et al.,[7] for hypothesis testing for two population means. 95% confidence interval, a margin of error (d) of 5% and a power of the study 80%. The formula n [(Zα/2+Zβ) 2×2(ó) 2¦] was used to determine that 100 would be an appropriate sample size for each group.The expression /(μ1-μ2)2

Inclusion Criteria:

Term pregnant women undergoing elective cesarean section; those with multiple pregnancies, grand multiparity, or advanced maternal age; women with scarred uteruses (resulting from myomectomy or prior cesarean section); women with uterine fibroids; those with a history of atonic pelvic pain; pregnant women with fetal macrosomia or malformations linked to polyhydramnios; and intrauterine foetal development (IUFD).

Exclusion Criteria:

Women who are pregnant should not have the following conditions: a gestational age of less than 18 years, placenta praevia, placental abruption, suspected placenta accreta, systemic disease (such as hypertension, hemorrhagic blood disease, endocrine disease, or liver dysfunction that needs treatment), abnormal coagulation, severe anemia that required a transfusion, or a known hypersensitivity to carbetocin or oxytocin.

Every single one of the subjects had to endure:

Comprehensive patient history taking, with an emphasis on long-term health conditions; physical examination (both internal and external); and, if necessary, an ultrasound of the abdomen to establish inclusion and exclusion criteria. The following tests should be run prior to surgery: a full blood count (CBC), prothrombin time, activity, and INR, bleeding time, clotting time, liver function tests (ALT, AST), and kidney function tests (urea, creatinine).

Blood preparation for the possibility of PPH:

There were two categories for all women who were eligible and met the inclusion criteria:

Include 100 eligible women in Group I, the carbetocin group. Following the C-shaped uterine incision for PPH prophylaxis, the women in this group were administered a single slow intravenous (IV) injection comprising 1 milliliter of a carbetocin solution (Pabal, 1 milliliter ampoule 100μg/ml, Ferring Pharmaceuticals, Kiel, Germany) containing 100μg of carbetocin.

To avoid postpartum hemorrhage (PPH), 100 women who were eligible for the study were included in Group II, which is called the oxytocin group. Following the C-shaped uterine incision in CS, these women were intravenously infused with 20 IU of oxytocin (Syntocinon, Novartis Pharma AG, Basel, Switzerland).

Blood loss estimation:

Blood loss estimation was done by using pictorial charts or weighing swabs and blood HB was also assessed 24 hours after delivery.

Outcome measures:

Examining the intraoperative effects of oxytocin and carbetocin in relation to the following factors: uterine tonicity as measured by uterine consistency (hard or lax), uterine shape (flabby or globular), retractability and contractility of the lower uterine segment (satisfactory or not), and uterine corrugation (lost or present), particularly following closed uterine incision.

The amount of blood loss per vagina was estimated in the first 24 hours postpartum by weighing the packs and sponges used to absorb blood per 24 hours postoperatively (1ml of blood weighs approximately 1gm). Changes in vital signs, fundal level, and uterine tonicity were also taken into account when comparing oxytocin and carbetocin postoperatively.[8]

Statistical methods:

Statistical Package for the Social Science

(SPSS) version 23.0 for Windows was used to tabulate and analyze the acquired data statistically. Median, standard deviation (SD), and range were used to describe parametric numerical data, whereas frequency (number of cases) and percentages were used to describe non-numerical data. Non-parametric numerical data was characterized by the median.

An independent t-test was employed to compare numerical variables among the research groups. The Chi-square (x2) test was used to compare categorical data. Instead of using the expected frequency, an exact test was utilized. The reported level of significance is as follows:

Unsignificant (P>0.05). Significant results are indicated by a P-value less than 0.05. Very significant (P < 0.01).

3. Results

Table 1. Information about the participants' characteristics and demographics.

SOCIO-DEMOGRAPHIC CHARACTERISTICS	CARBETOCIN	OXYTOCIN	SIGNIF. TEST	
	N (100)	N (100)	t-Test	P
AGE IN YEARS			4.457	0.118
MEAN ± SD	27.81±3.001	28.24±3.470		
RANGE	(23-35)	(22-35)		
BMI(KG/M^2)			0.594	0.442
MEAN ± SD	28.66±3.137	29.36±2.844		
RANGE	(22-35)	(23-35)		
GESTATIONAL AGE (W)			0.082	0.775
MEAN ± SD	38.37±0.630	38.42±0.606		
RANGE	(37-39)	(37-39)		
PARITY			0.306	0.581
MEAN±SD	1.96±0.8155	2.04±0.8867		
RANGE	(1-4)	(1-4)		

Note: t:T-test, w: weeks, BMI: body mass index, * Significant (p < 0.05); **Highly significant (P < 0.001).

Age, BMI, GA, and parity did not significantly differ between the two study groups (p-values of 0.118, 0.442, 0.775, and 0.581, respectively), (table 1).

Table 2. Comparing the Carbetocin group's vital signs, hemoglobin levels, hematocrit, and percentage of change before and after labor.

VARIABLE	GROUP (I) CARBETOCIN		SIGNIF. TEST	
	Pre labour	Post labour	Test	P
PULSE				
MEAN ± SD	82.32±5.035	83.30±3.983	2.738	0.007*
SYSTOLIC BLOOD PRESSURE			4.511	0.004*
MEAN ± SD	111.2±9.458	107.6±5.881		
DIASTOLIC BLOOD PRESSURE			2.854	0.002*
MEAN ± SD	69.11±5.327	69.12±3.879		
HB% CONCENTRATION			25.971	<0.001
MEAN ± SD	10.8±0.586	10.125±0.612		**
HCT				
MEAN ± SD	32.30±2.139	30.37±1.838	16.206	<0.001 **

Note: t: T-test, *Significant (p<0.05), **Highly significant (P<0.001).

Pre- and post-labor administration of therapeutic medications showed a statistically significant difference in hemodynamic data, such as HR, SBP, and DBP, compared to the carbetocin group (p<0.05). However, there was a significantly significant difference in hematocrit % and hemoglobin concentration (P<0.001), (table 2).

Table 3. Comparing the vital signs, hemoglobin levels, hematocrit, and percentage of change before and after labor in the oxytocin group.

VARIABLE	GROUP (II) OXYTOCIN		SIGNIF. TEST	
	Pre labour	Post labour	Test	P
PULSE				
MEAN ± SD	83.74±4.482	84.08±3.738	0.884	0.379
SYSTOLIC BLOOD PRESSURE			0.954	0.401
MEAN ± SD	109.3±9.568	108.4±8.425		
DIASTOLIC BLOOD PRESSURE			0.847	0.399
MEAN ± SD	67.70±5.659	67.10±4.561		
HB% CONCENTRATION			28.58	<0.001 **
MEAN ± SD	10.835±0.532	10.205±0.542		
HCT				
MEAN ± SD	32.505±1.596	30.615±1.625	28.582	<0.001 **

Note: t: T-test, *Significant (p<0.05), **Highly significant (P<0.001).

There was no statistically significant distinction in hemodynamic data (HR, SBP, and DBP) between the oxytocin group before and after therapeutic drug delivery (p-values of 0.379, 0.401, and 0.399, respectively). There were highly substantial variations between pre- and post-labor in hemoglobin concentration and hematocrit percent with the oxytocin group (P<0.001), (table 3).

Table 4. Comparing how the two medications affect blood loss.

VARIABLE	CARBETOCIN	OXYTOCIN	SIGNIF. TEST	
	N (100)	N (100)	Test	P
INTRAPARTUM BLOOD LOSS (ML)			t=2.64	0.002*
MEAN ± SD	286.88±153.97	362.35±263.49		
POSTPARTUM BLOOD LOSS > 500 ML			χ2=3.835	0.048*
N (%)	2 (2)	8 (8)		

Note: t: T test, x2 Chi square; * Significant (p < 0.05); ** Highly significant (P < 0.001).

A statistically significant difference was observed in the predicted blood loss from the two drugs (p=0.002). In addition, the two drugs differed significantly (p=0.048) in their effects on postpartum blood loss, (table 4).

Table 5. Extra needs for patients in the oxytocin and carbetocin groups.

VARIABLE	CARBETOCIN	OXYTOCIN	SIGNIF. TEST	
	N (%)	N (%)	χ2	P
REQUIREMENT OF ADDITIONAL UTEROTONIC MEDICATION	12 (12)	15 (15)	0.385	0.340
NEEDS FOR BLOOD TRANSFUSION	2 (2)	4 (4)	0.687	0.407

The two medications did not differ statistically significantly in terms of extra requirements, (table 5).

4. Discussion

In both developed and developing countries, primary pulmonary hemorrhage (PPH) ranks high among the causes of maternal mortality. According to their findings, the main determinant for severe PPH is an abnormal third stage of labor.[9]

Atony and dysfunctional uterine musculature are the leading causes of pelvic inflammatory disorder (PPH). Reasons for this widespread assumption include the absence of placental tissue retention or rips, the persistence of bleeding until uterine contractions are triggered, in both developed and developing countries (PPH), and the fact that these features are present in the majority of mild hemorrhage cases.[10]

Although the carbetocin group needed fewer extra uterotonic medicines and blood transfusions than the oxytocin group, the difference was not statistically significant (P>0.05).

Holleboom et al.,[11] developed in collaboration with five collaborating Dutch hospitals, administered 100 μg of intravenous Carbetocin to 50-100 pregnant patients at term. Following the hospital's protocol for uterine atony prevention, each center extracted an additional 250 patients who had received oxytocin (5 IU, 10 IU, or 5 IU followed by 10 IU in 2 hours). Based on the data from the five hospitals, 462 participants were included in the carbetocin group and 1,122 in the oxytocin group. After carbetocin, 3.1% of individuals required extra uterotonic treatment (95% CI 1.7-5.1%), and after oxytocin, 7.2% required additional treatment (5.8%-8.9%); Comparative risk was 0.41(0.19-0.85); p{0.0110. When comparing carbetocin with oxytocin, the former was more successful and required fewer blood transfusions and further uterotonic medicine (3.2 vs. 9.3%, p=0.0067 and 2.2 vs. 3.6%, p=0.0357). The authors discovered that the need for further uterotonics was decreased by more than 50% when carbetocin was used as a preventative treatment for uterine atony after an elective CS.

Both intrapartum (p=0.002) and postpartum (p=0.048) blood loss was dramatically reduced by carbetocin, according to the current study. This finding makes sense because carbetocin has a longer half-life than oxytocin, which means it causes more uterine response—that is, more contractions, both in frequency and amplitude. However, there was no significant difference between the two groups in terms of the need for additional uterotonics and blood transfusions following elective caesarean section (p>0.05).

On this item, Su et al.,[12] The use of carbetocin is more effective than oxytocin for preventing postpartum hemorrhage (PPH) in women undergoing caesarean section, according to the Cochrane 2007 study on "oxytocin agonists for preventing postpartum hemorrhage" and the Cochrane 2012 study on "carbetocin for preventing postpartum hemorrhage," although the data and evidence were still lacking.

As a result of our research, Kang et al.,[13] the research revealed that neither group differed significantly from the other in terms of postpartum blood loss, blood transfusions, or extra surgical operations. Differences in the population studied and the methodology used to calculate blood loss after caesarean sections can explain why our results differ from those of other studies. Volume in the suction bottle and absorption in the surgical drapes, gauzes, and pads were used to calculate blood loss in their investigation. Due to the incorporation of amniotic fluid in the measurement, its accuracy was compromised.

Larciprete et al.,[14] conducted studies to determine whether carbetocin and oxytocin effectively reduced postpartum hemorrhage risk and the requirement for additional uterotonic fluids in women undergoing cesarean sections. Extra uterotonic medicines were needed by more women in the oxytocin group (23.5% vs. 0%, p<0.01), although neither the estimated blood loss nor the lowered hemoglobin level varied significantly (p>0.05). We disagreed with the findings of this study.

Sotillo et al.,[15] proved that the levels of hemoglobin fell more sharply in the group given oxytocin (1.7 vs. 1.2, P=.02). Also, the need for blood transfusions was significantly higher in the control group (9.3% vs.1.3%, P=0.03). Carbetocin has the added advantage of reducing the need for additional pharmaceutical administration during the postpartum period, which is an advantage over oxytocin.

Displeased with our results, Delorme et al.,[16] evaluated the rates of caesarean deliveries between two time periods using a retrospective cohort analysis.

It would appear that oxytocin was more cost-effective than carbetocin when comparing the two uterotonic medicines. However, due to the high-risk nature of the patients, who are more likely to experience complications and morbidities such as uterine atony and postpartum hemorrhage, carbetocin is preferred for these patients. This is because it is more effective and requires fewer interventions, which ultimately reduces the risk of surgical interventions, which can be costly.

Recommendations: Further research with higher volume samples and randomization will be required to assess whether prophylactic carbetocin is superior to conventional uterotonic agents and whether carbetocin reduces the

incidence of PPH following caesarean section in low and high-risk women.

If carbetocin is shown to have a similar hemodynamic profile to oxytocin, it may become the medication of choice for women with hypertensive disorders or cardiac problems.

Carbetocin should be limited to women with a high risk for PPH due to the high cost.

4. Conclusion

Compared to other methods, carbetocin reduces intrapartum bleeding and prevents atonic postpartum hemorrhage more effectively. Nevertheless, in terms of blood transfusions and extra oxytocic medications, carbetocin and oxytocin were identical.

Disclosure

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