

Comparison of the efficiency of oxytocin and carbetosin for prevention of postpartum bleeding in low risk pregnancies

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Abstract

Objective: To compare the effectiveness of carbetocin and oxytocin in the prophylaxis of postpartum hemorrhage (PPH).

Methods: Data from 136 cases who gave birth at Selçuk University Faculty of Medicine Hospital between January 1, 2023, and September 30, 2023, were retrospectively analyzed. Cases with risk factors for PPH were not included in the study. Data on mothers who received carbetocin and oxytocin during the active management of birth were obtained from the hospital electronic system and patient files. The amount of PPH was compared between the two groups.

Results: Carbetocin was administered to 67 cases in the study group and oxytocin to the remaining 69 cases. No statistically significant difference was found between the two groups in terms of changes in hemoglobin (Hgb) (0.6 ± 0.9 - 0.7 ± 0.8), hematocrit (Htc) (2.0 ± 3.0 - 2.1 ± 2.3), and platelet (Plt) (10.6 ± 56.8 - 14.2 ± 32.8) (p: 0.790, p: 0.733, p: 0.645). The estimated blood loss was 306 ± 113 milliliters (mL) in the carbetocin group, while it was 333.05 ± 165 mL in the oxytocin group (p=0.715). The estimated blood loss in vaginal births was 319.1 ± 157 mL in the oxytocin group and 294 ± 109 mL in the carbetocin group (p=0.576). In the Cesarean section (CS) group, the estimated blood loss was 354.0 ± 172 mL in the oxytocin group and 323 ± 128 mL in the carbetocin group (p=0.691).

Conclusion: Oxytocin and carbetocin demonstrate similar efficacy in the prophylaxis of PPH. Carbetocin can be safely used as an alternative to oxytocin in cases with low risk.

Keywords: Carbetocin, oxytocin, postpartum hemorrhage, estimated average blood loss

Introduction

Postpartum hemorrhage (PPH) is generally defined as a blood loss exceeding 500 mL following vaginal delivery or 1000 mL after a cesarean section.^[1] The American College of Obstetrics and Gynecology has suggested the use of varied criteria for the diagnosis of PPH.^[2] These include a hematocrit drop of more than 10%, the need for blood transfusion, and hemodynamic instability.^[3] PPH is a potentially life-threatening complication in both vaginal and cesarean deliveries. Particularly in developing countries, PPH constitutes one of the most significant factors in maternal morbidity and mortality.^[4] It accounts for one-quarter of all maternal deaths worldwide.^[5]

Active management of the third stage of labor is ad-

vocated over passive observation to reduce the risk of PPH. This approach is particularly emphasized due to the high incidence of PPH in this stage of labor.^[6] Active management includes several actions, the main one being the planned administration of uterotonic drugs after the baby is born, along with the gentle, controlled pulling on the umbilical cord until the placenta separates. Pharmacotherapy, in this context, is a well-established and effective strategy. Hence, the standard practice of administering uterotonics routinely to all women during the third stage of labor is recommended.^[7,8] In situations where atony-induced bleeding remains unresponsive to medical intervention, alternative strategies such as surgical interventions and intrauterine balloon tamponade are employed. Additionally, mechanical techniques like vaginal packing are considered viable options for mana-

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ging atonies in the lower uterine segment.^[9]

Oxytocin is a preferred and proven effective agent for the prevention of PPH following both cesarean and vaginal deliveries.^[10,11] Carbetocin is a synthetic analogue of oxytocin with a prolonged effect. It is administered as a single dose either intravenously (IV) or intramuscularly (IM). Because carbetocin causes a sustained uterine contractility response that lasts for up to an hour after a single intravenous (IV) dose, there is no need for an ongoing infusion.^[12]

In the literature, studies investigating the efficacy of carbetocin or oxytocin for the prophylaxis of PPH have yielded varied results. While some researchers report superior effectiveness of carbetocin^[13-15], others have demonstrated comparable efficacy between these two uterotonic agents.^[16,17] The objective of this study is to conduct a retrospective analysis of cases at our institution in which carbetocin or oxytocin was utilized for the prophylaxis of PPH.

Methods

This study was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine, Selcuk University, between January 1, 2023, and September 30, 2023. Patient data were retrospectively obtained from file archives and electronic medical records. A total of 136 cases, all of whom had their entire pregnancy follow-up and delivery at our hospital, were included in the study. Patients were categorized into two groups based on the uterotonic agent used for PPH prophylaxis: first group received oxytocin, and the second group received carbetocin. In this study, pre-delivery hospital admission and complete blood parameters (hemoglobin, hematocrit, platelets) up to 6 hours postpartum were compared between two groups. The estimated blood loss of the cases was calculated by reviewing labor monitoring records and employing the method previously defined by Stafford et al. This method estimates blood loss by multiplying the estimated pregnancy blood volume with the percentage of estimated blood loss, calculated as $\{(\text{preoperative hematocrit} - \text{postoperative hematocrit}) / \text{preoperative hematocrit}\}$.^[18] The estimated blood loss obtained was then compared between the two groups.

All cases included in the study group were selected from those with singleton pregnancies who delivered at term. Cases with risk factors for postpartum hemorrhage (such as bleeding diathesis, polyhydramnios, placental invasion anomalies, gestational hypertensive disorders, maternal comorbidities, etc.) were excluded from the study. Structural/chromosomal fetal anomalies, preterm births, and multiple pregnancies were also excluded from the

study.

In all cases, the third stage of labor was actively managed. Uterotonic medication was administered immediately after the birth of the baby, without waiting for the separation of the placenta. This was followed by cord traction and uterine massage to facilitate controlled removal of the placenta. The dose of oxytocin was administered as per the guidelines of the Ministry of Health, with 10 units given intravenously (IV) over 3-5 minutes. For cesarean births, in addition to rapid oxytocin infusion, a continuous infusion of 20 units of oxytocin was added to either 1000 cc of 0.9% sodium chloride (NaCl) or 1000 cc of Ringer's lactate solution, administered at a rate of 125 cc/hour. Carbetocin was administered to all patients as a slow IV infusion of a single 100 microgram dose over 90-120 seconds immediately after clamping the cord.^[19]

The study was designed in accordance with the principles of the Helsinki Declaration. The Local Ethics Committee of the Faculty of Medicine at Selcuk University (Ethics Committee number: 2023/440) granted it ethical approval before its start.

Statistical analysis. Analyses were conducted using SPSS (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL) version 22. In this study, continuous variables were presented as means $\pm$ standard deviation (Mean $\pm$ SD) and categorical variables were presented as counts and percentages (n, %). The normal distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. Comparisons between two groups were performed using either the Student's t-test or the Mann-Whitney U test. A p-value of less than 0.05 was considered statistically significant in the analyses.

Results

In our study, carbetocin was administered to 67 patients (49.3%), while oxytocin was given to a total of 69 patients (50.7%). There was no need for additional uterotonic drugs in either group. When examining the mode of delivery, the rate of vaginal births was found to be 53.7% (n=73), whereas cesarean deliveries constituted 46.3% (n=63) of the cases.

The comparison of maternal demographic characteristics, obstetric, and fetal data is presented in Table 1. Both groups were similar in terms of age, obstetric history, body mass index (BMI), gestational week at birth, birth weight, and gender ($p>0.05$ for each comparisons).

The data on the change in prepartum and postpartum blood parameters (Hgb, Hct, PLT) and estimated blood loss for both groups are shown in Table 2. The decrease in hemoglobin (Hb), hematocrit (Hct), and platelets (PLT)

was similar between the two groups ($p=0.790$, $p=0.733$, $p=0.645$, respectively). The average estimated blood loss was 306 ± 113 mL in the carbetocin group, while it was 333.05 ± 165 mL in the oxytocin group ($p=0.715$).

Table 1. Comparison of general characteristics of the groups

	Oxytocin (n=69) Mean $\pm$ SD	Carbetocin (n=67) Mean $\pm$ SD	p-value
Age	29.4 $\pm$ 5.3	28.5 $\pm$ 5.6	0.062
Gravida	2.6 $\pm$ 1.3	2.2 $\pm$ 1.6	0.098
Parity	1.2 $\pm$ 1.0	1.0 $\pm$ 1.3	0.354
Weight	77.4 $\pm$ 13.4	76.6 $\pm$ 10.5	0.696
Height	160.0 $\pm$ 6.0	161.4 $\pm$ 5.8	0.158
BMI	30.2 $\pm$ 4.3	29.3 $\pm$ 3.3	0.212
Birth weight	3318.7 $\pm$ 366.5	3347.1 $\pm$ 361.7	0.650
GW at birth	38.7 $\pm$ 1.2	38.8 $\pm$ 1.2	0.505
Gender (female/male)	36/33	33/34	0.733

BMI: Body mass index, SD: Standard deviation; GW: Gestational week

Table 2. Comparison of blood parameters changes and estimated bleeding amount according to uterotonic agent

	Oxytocin (n=69)	Carbetocin (n=67)	p-value*
Hgb change	0.7 $\pm$ 0.8	0.6 $\pm$ 0.9	0.790
Hct change	2.1 $\pm$ 2.3	2.0 $\pm$ 3.0	0.733
Plt change	14.2 $\pm$ 32.8	10.6 $\pm$ 56.8	0.645
Estimated amount of bleeding (mL)	333.05 $\pm$ 165	306 $\pm$ 113	0.715

*Student t-test. All variables expressed as mean $\pm$ standard deviation.
Hgb: Hemoglobin Hct: Hemotocrit Plt: Platelet.

The impact of the mode of delivery on the changes in hemogram parameters and the estimated amount of blood loss for both groups is presented in Table 3. In cases where oxytocin was used, the estimated blood loss for vaginal and cesarean deliveries was found to be 319.1 ± 157 mL and 354.0 ± 172 mL, respectively ($p=0.612$). For those who received carbetocin, the estimated blood loss in vaginal and cesarean deliveries was 294 ± 109 mL and 323 ± 128 mL, respectively ($p=0.624$). It was observed in both groups that the estimated blood loss was higher in cesarean deliveries compared to normal vaginal births, but this difference was not statistically significant. The effect of the mode of delivery on the estimated amount of postpartum blood loss is shown in Table 4. It was observed that the decreases in hemoglobin (Hb), hematocrit (Hct), and platelets (Plt) were similar in both the normal delivery and C/S groups. In vaginal deliveries, the estimated blood loss in those who received oxytocin was 319.1 ± 157 mL, while it was 294 ± 109 mL in those who received carbetocin ($p=0.576$). In the CS group, the estimated blood loss was 354.0 ± 172 mL for those who received oxytocin and 323 ± 128 mL for those who received carbetocin ($p=0.691$).

Table 3. Effect of uterotonic drugs on changes in blood parameters and estimated amount of bleeding according to the type of birth

	Oxytocin			Carbetocin		
	Vaginal delivery (n=37)	C/S (n=32)	p-value*	Vaginal delivery (n=36)	C/S (n=31)	p-value*
Hgb change	0.7 $\pm$ 1.0	0.8 $\pm$ 0.9	0.555	0.6 $\pm$ 0.7	0.6 $\pm$ 0.9	0.325
Hct change	2.3 $\pm$ 3.2	2.4 $\pm$ 2.7	0.377	1.9 $\pm$ 1.9	1.6 $\pm$ 2.9	0.365
Plt change	16.6 $\pm$ 50.7	19.1 $\pm$ 62.4	0.156	13.5 $\pm$ 24.2	15.1 $\pm$ 41.1	0.856
Estimated amount of bleeding (mL)	319.1 $\pm$ 157	354.0 $\pm$ 172	0.612	294 $\pm$ 109	323 $\pm$ 128	0.624

*Student t-test. All variables expressed as mean $\pm$ standard deviation.
Hgb: Hemoglobin Hct: Hemotocrit Plt: Platelet.

Table 4. Comparison of uterotonic agent effectiveness according to mode of delivery

	Oxytocin Vaginal delivery (n=37)	Carbetocin Vaginal delivery (n=36)	p-value*	Oxytocin C/S (n=32)	Carbetocin C/S (n=31)	p-value*
Hgb change	0.7±1.0	0.6±0.7	0.578	0.8±0.9	0.6±0.9	0.336
Hct change	2.3±3.2	1.9±1.9	0.538	2.4±2.7	1.6±2.9	0.266
Plt change	16.6±50.7	13.5±24.2	0.516	19.1±62.4	15.1±41.1	0.266
Estimated amount of bleeding (mL)	319.1±157	294±109	0.576	354.0±172	323±128	0.691

*Student t-test. All variables expressed as mean±standard deviation.
Hgb: Hemoglobin Hct: Hemotocrit Plt: Platelet.

Discussion

In our country, the Ministry of Health has published guidelines recommending the administration of uterotonics for postpartum hemorrhage prophylaxis in all pregnant women.^[19] Oxytocin has been used for this purpose for many years, and more recently, the use of carbetocin has also become feasible.^[20]

Carbetocin's major advantages include its lack of a cold chain, ease of administration, long half-life, absence of the need for repeated dosing, and limited fluid replacement. The efficacy of carbetocin in the prophylaxis of postpartum hemorrhage (PPH) has been demonstrated in previous studies. Some clinicians have suggested that the use of carbetocin should be individualized in place of continuous oxytocin infusion for elective cesarean deliveries.^[21,22] A recent meta-analysis found that carbetocin is as effective and safe as oxytocin in preventing postpartum hemorrhage in women who have vaginal deliveries. It has even been argued that choosing carbetocin for prophylaxis might be a more rational option.^[20]

In a study conducted in India, the prophylactic use of carbetocin in elective cesarean sections was compared with both oxytocin and misoprostol. It was found that the use of carbetocin for PPH prophylaxis was associated with less blood loss. From a cost-effectiveness standpoint, prophylactic administration of carbetocin has been shown to be an effective practice.^[23] In a similar study, the cost-effectiveness of administering carbetocin and oxytocin for the prevention of PPH after vaginal delivery was investigated. The results indicated that the total cost of carbetocin was less compared to oxytocin.^[24] Another study in Canada considered the cost-effectiveness and advocated for the transition to using carbetocin as the primary prophylactic drug in PPH.^[25]

In Turkey, limited studies are comparing the effectiveness of carbetocin and oxytocin in the prevention of postpartum hemorrhage (PPH). Studies reported from Turkey have yielded varied results. While some researchers have indicated the effectiveness of carbetocin, others have expressed the view that carbetocin is not as effective as oxytocin.^[26-28]

The World Health Organization (WHO) has noted in its recommendations that the use of carbetocin for the

prevention of PPH can halve the need for additional uterotonics. In terms of efficacy, there are reports suggesting that carbetocin is comparable to, and even more effective than, oxytocin. It has been argued that carbetocin can be used as the primary agent in the long term when its cost is comparable to other effective uterotonics.^[16]

In our study, the findings indicate that, although not statistically significant, the use of carbetocin in both vaginal section and elective cesarean sections is associated with less blood loss.

Our study has some limitations. These include the single-center nature of the study, the limited number of patients, and the fact that the patient group consisted only of those considered to be at low risk for bleeding diathesis.

Conclusion

The findings from our study suggest that the use of oxytocin and carbetocin demonstrates similar efficacy in patients with low bleeding risk. In cases of low risk for postpartum hemorrhage, the use of carbetocin as an alternative to oxytocin is considered to be safe and effective for postpartum hemorrhage prophylaxis.

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