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Carbetocin- A Promising Alternative to Oxytocin for Prevention of Postpartum Hemorrhage in Elective Cesarean Section in High-Risk Women

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Abstract

Introduction: Postpartum hemorrhage (PPH) is a leading cause of maternal mortality, responsible for approximately 140,000 deaths annually, with significant morbidity associated with blood transfusions and extended hospital stays. Effective management strategies are critical, particularly during cesarean sections, which are recognized as significant risk factors for PPH.

Objective: This study aims to evaluate the efficacy and safety of carbetocin compared to oxytocin in preventing PPH among high-risk women undergoing elective cesarean sections.

Methods: A prospective comparative analysis was conducted at SMS Medical College, Jaipur, from November 2022. Pregnant women at term with high-risk factors for PPH were included, while those with specific medical conditions were excluded. A total of 100 patients were randomly assigned in two groups. Group 1 receives 100 µg carbetocin intravenously while group 2 receives 10 IU oxytocin intramuscularly after delivery. Pre-operative and post-operative parameters, including blood pressure, pulse rate, and hemoglobin levels, were monitored and statistically analyzed.

Results: The study population predominantly comprised women aged 26-30 years, with no significant differences in baseline characteristics between the carbetocin and oxytocin groups. Both groups exhibited similar trends in blood pressure and pulse rate post-administration. Notably, carbetocin demonstrated a lower incidence of PPH and reduced overall blood loss compared to oxytocin.

Conclusion: Carbetocin, with a quicker onset, longer action, and better stability, proved more effective, leading to less blood loss, fewer PPH cases, and reduced need for additional uterotonics. Its safety profile is comparable to oxytocin, making it a promising alternative for PPH prevention and improved maternal outcomes.

Keywords: Postpartum hemorrhage, carbetocin, oxytocin, cesarean section, maternal mortality, uterotonics, blood loss, high-risk pregnancy.

Introduction

Postpartum hemorrhage (PPH) is a major contributor to maternal mortality, responsible for approximately one-quarter of all maternal deaths globally, with an estimated 140,000 fatalities each year.[1] PPH complicates 2–4% of vaginal deliveries and 6% of cesarean sections, making it the leading cause of maternal death worldwide, accounting for 35% of fatalities, with India reporting 38% of maternal deaths linked to PPH.[2] Beyond mortality, PPH increases maternal and neonatal morbidity due to blood transfusions, prolonged hospital stays, and reduced newborn care capacity, straining healthcare resources.

PPH is categorized into primary and secondary types. Primary PPH involves blood loss of ≥500 ml after vaginal delivery or ≥1000 ml after cesarean section within 24 hours, while secondary PPH occurs with excessive bleeding at least 24 hours after delivery.[3] It can also be defined by hypovolemia, a 10% decrease in hematocrit, or an increased need for blood transfusion. Common subtypes include retained placenta, uterine atony, trauma, and coagulation defects, with uterine atony accounting for up to 80% of cases. Immediate use of uterotonics is essential in preventing PPH, favoring active management of the third stage of labor, which can reduce PPH incidence by nearly 50%[8] and blood loss by 3-16.5%.[4]

Uterotonics like oxytocin and carbetocin play a pivotal role in managing the third stage of labor. Oxytocin, commonly administered at a dose of 10 IU im, effectively reduces PPH by 40%, but its short half-life necessitates continuous administration and may cause adverse effects.[5] Carbetocin, a long-acting analogue of oxytocin, shows rapid onset and prolonged duration of action, making it effective in preventing uterine atony following cesarean sections. With a half-life 4-10 times longer than oxytocin, carbetocin has been shown to reduce the need for additional uterotonics and lower PPH risk in cesarean sections.[6]

As cesarean sections are recognized risk factors for PPH, especially with their rising rates since 1990,[7] strategies for minimizing PPH risk include thorough preoperative assessments and vigilant postoperative monitoring. Effective collaboration among healthcare professionals is crucial in addressing the challenges of PPH.

This study aims to assess the efficacy and safety of carbetocin compared to oxytocin for preventing postpartum hemorrhage in high-risk women undergoing elective cesarean sections.

Materials and Methods

This hospital-based interventional study was designed as a prospective comparative analysis conducted in the Department of Obstetrics and Gynecology at SMS Medical College, Jaipur, starting from November 2022. The study population consisted of all pregnant women at term (≥37 weeks) admitted to the labor room for elective cesarean sections with a high risk of postpartum hemorrhage (PPH).

Selection Criteria

- **Inclusion Criteria:** Women scheduled for cesarean sections with high-risk factors for PPH, including placenta previa, multiple pregnancies, uterine fibroids, fetal macrosomia, a past history of PPH, previous uterine scars, and fetal polyhydramnios. Participants were required to be willing to provide written informed consent and not involved in any other study.
- **Exclusion Criteria:** Women with cardiac, liver, or renal diseases, asthmatic patients, and those with a

history of hypersensitivity to carbetocin or oxytocin were excluded from the study.

The sample size was calculated to include 50 patients in each group, based on previous studies indicating a minimum detectable difference of mean blood loss (>1000 ml postpartum) of 7 with a standard deviation of 5.2, achieving an 80% power and a 0.05 alpha error.

Methodology

Pregnant women at term (≥37 weeks) scheduled for elective cesarean sections with a high risk of postpartum hemorrhage (PPH) were recruited after obtaining informed consent. A comprehensive medical history and physical examination were performed, along with routine blood tests (CBC, ABO-Rh, RFT, LFT, serology, and urine analysis). Ultrasound was conducted to assess placenta previa and placental invasion. Participants were randomly assigned to two groups: Group 1 received 100 µg carbetocin intravenously, and Group 2 received 10 IU oxytocin intramuscularly, administered after delivery and before placenta removal. Blood pressure and pulse were monitored at specified intervals. Blood loss was quantified using suction jars and pre-weighted sponges. In cases of excessive bleeding, carboprost (250 µg IM) was administered, and a postpartum CBC was performed. Blood transfusions were given as needed, and surgical interventions were conducted for patients unresponsive to medical management.

Statistical Analysis

Data were recorded in an Excel spreadsheet. Quantitative data were expressed as mean and standard deviation, while qualitative data were represented as percentages and proportions. Appropriate statistical tests were applied, with a significance level set at $P < 0.05$.

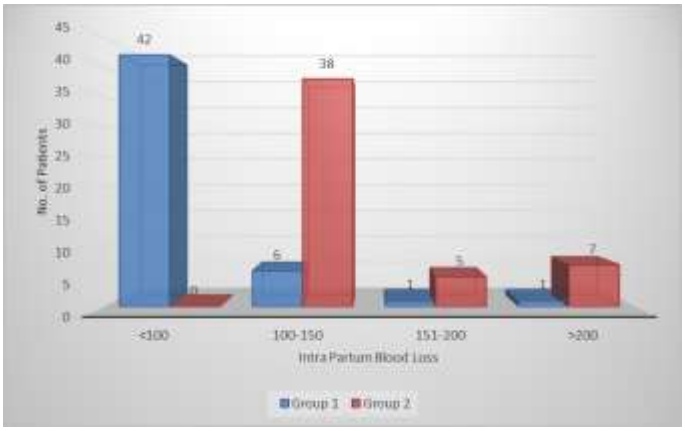
Result and Observation

Here we summarize the age, religion, locality, education, socioeconomic status, and parity distribution between the Group 1 and 2. In the Group 1, most patients were aged 26-30 years (n=30), with fewer in the 20-25 (n=14), 31-35 (n=5), and 36-40 (n=1) age ranges. The Group 2 similarly had most patients aged 26-30 (n=39), with fewer in other age groups. The majority of patients in both groups were Hindu (Group 1: n=36, Group 2: n=34), while the rest were Muslim. Urban-rural distribution was similar, with slightly more rural patients in both groups. Educational levels ranged from illiterate to graduates, with most having secondary education. Both groups mainly consisted of lower and lower-middle socioeconomic classes. In terms of parity, the Group 1 had 9 primigravida and 41 multigravidas, while the Group 2 had 5 primigravida and 45 multigravida.

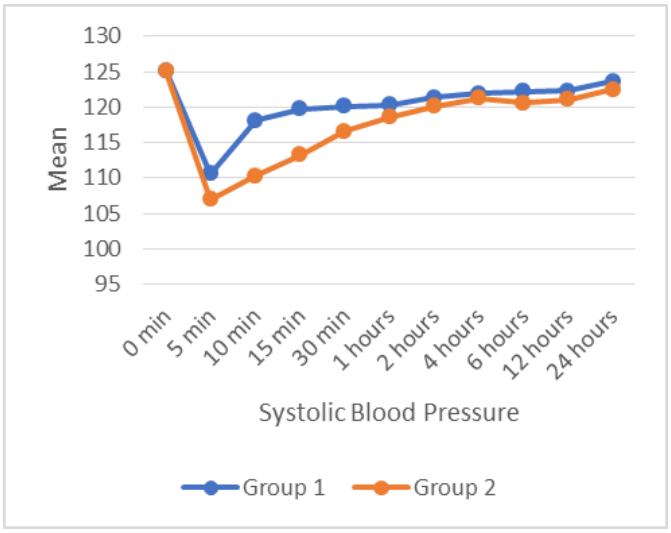
Table 1: Distribution of cases according to intra partum blood loss

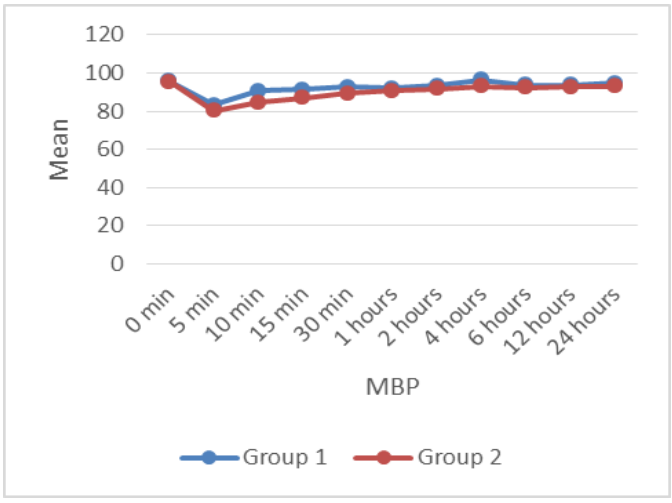
Intra Partum Blood Loss	**Group 1**		**Group 2**	
	No. of Patients	Percentage	No. of Patients	Percentage
<100	42	84	0	0
100-150	6	12	38	76
151-200	1	2	5	10
>200	1	2	7	14
Total	50	100	50	100
Mean±SD	91.8±35.16		167.8±83.86	
P-Value	0.0001			

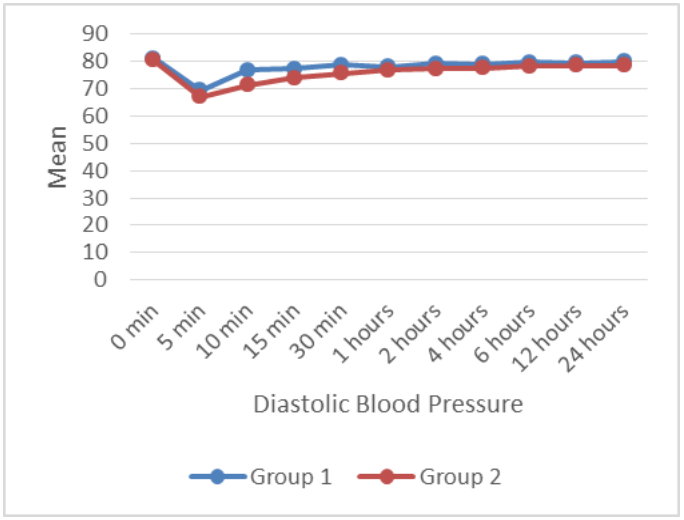
The table compares the distribution of intra-partum blood loss (in milliliters) between the both Groups. In the Group 1, mean blood loss was 91.8±35.16,while in the Group 2, mean blood loss was 167.8±83.86. (p<0.0001)

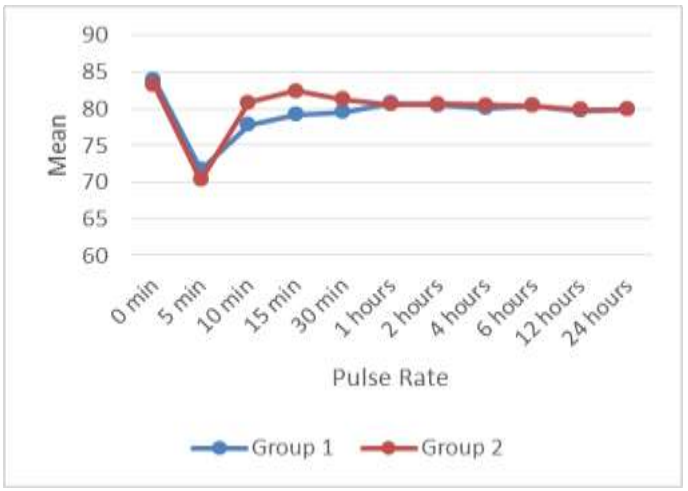


Graph 1: Distribution of cases according to SBP, DBP, MBP and Pulse rate









The table compares systolic, diastolic, mean arterial blood pressure (MBP), and pulse rate between both Group at various time points post-administration. Initially, systolic BP was similar (Group 1; 125.14 mmHg, Group 2; 125.04 mmHg), with both dropping at 5 minutes (Group 1; 110.58, Group 2 107), then gradually rising. Diastolic BP followed a similar trend, starting around 81 mmHg for both groups, decreasing at 5 minutes, and stabilizing over time. MBP initially dropped at 5 minutes (Group 1; 83.24, Group 2; 80.33) but stabilized afterward. Pulse rate dropped in both groups at 5 minutes and fluctuated slightly before stabilizing around 79 bpm by 24 hours.

Our data compares pre-operative parameters between the both groups. In the Group 1, hemoglobin was 11.46 g/dL,

systolic blood pressure 126.4 mmHg, diastolic blood pressure 81.98 mmHg, mean blood pressure 96.78 mmHg, and pulse rate 84.16 beats per minute. In the Group 2, hemoglobin was 11.51 g/dL, systolic blood pressure 125.64 mmHg, diastolic blood pressure 81.72 mmHg, mean blood pressure 96.36 mmHg, and pulse rate 83.3 beats per minute.

Table 2: Distribution of cases according to hemoglobin difference in both group

Hemoglobin Difference (Pre & post cesarean)	Group 1		Group 2	
	No. of Patients	Percentage	No. of Patients	Percentage
≤0.5	4	8	2	4
0.6-1	43	86	24	48
1.1-1.5	1	2	17	34
1.6-2	1	2	2	4
2.1-2.5	1	2	2	4
2.6-3.0	0	0	2	4
>3.0	0	0	1	2
Total	50	100	50	100
Mean±SD	0.71±0.28		1.15±0.59	
P-Value	<0.001			

The table compares hemoglobin differences (preoperative and postoperative value) between the both groups. The mean hemoglobin difference was 0.71 ± 0.28 for Group 1 and 1.15 ± 0.59 for Group 2 ($p < 0.001$).

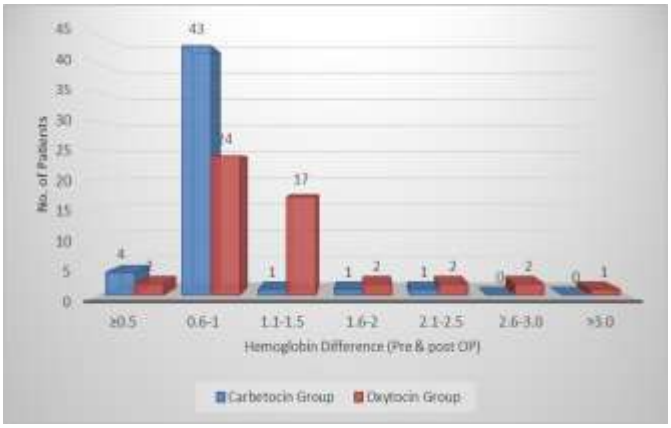
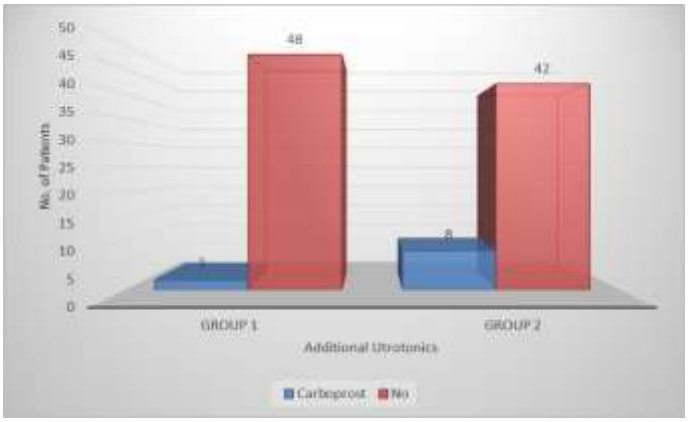


Table 3: Distribution of cases according to use of additional Uterotonics

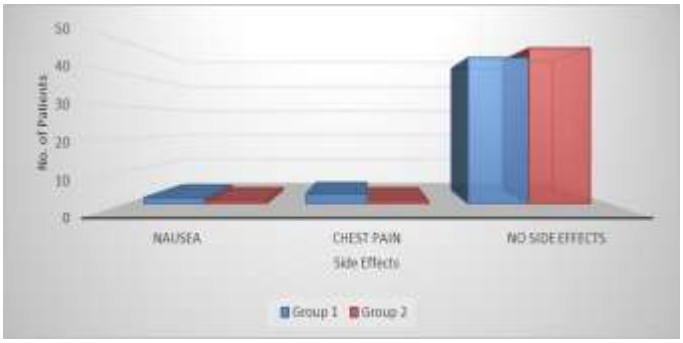
Additional Uterotonics	Group 1		Group 2		P-Value
	No. of Patients	Percentage	No. of Patients	Percentage	
Carboprost	2	4	8	16	0.04
No	48	96	42	84	
Total	50	100	50	100	

In above table, In the Group 1, 2 patients received Carboprost, while 48 did not. Conversely, in the Group 2, 8 patients received Carboprost, and 42 did not, which is statistically significant.



Graph 2: Distribution of cases according to Side Effects

In the Group 1, 2 patients experienced nausea, 3 reported chest pain, and 45 had no side effects. In the Group 2, 1 patient experienced nausea, 1 reported chest pain, and 48 had no side effects.



Discussion

Postpartum hemorrhage (PPH) is a leading cause of maternal deaths, with uterine atony responsible for up to 80% of cases. Oxytocin, commonly used to prevent PPH, has a short half-life, requiring frequent dosing. Carbetocin, a longer-lasting oxytocin analogue, offers more stability. This study compared the efficacy of carbetocin and oxytocin in preventing PPH during elective cesarean sections in high-risk women, finding that blood loss was significantly lower in the Group 1.

In Group 1, average intrapartum blood loss was less than 100 mL (91.8 ± 35.16 mL), while Group 2 had an average blood loss of over 100 mL (167.8 ± 83.86 mL), a statistically significant difference (p = 0.0001). Kang et al.[8] reported no significant difference between Carbetocin and Oxytocin groups in blood loss (Carbetocin: 370.3 ± 177.4 mL, Oxytocin: 386.6 ± 191.6 mL). Seow et al.[9] found higher blood loss in the control group (922.8 ± 430 cc) compared to the study group (871 ± 305 cc).

In our study, Group 2 exhibited a greater initial drop in systolic blood pressure (SBP) compared to Group 1 during the first hour, stabilizing towards pre-operative values by 24 hours with no statistically significant difference in changes observed. Ahmed M E et al.[10] reported similar findings; at 0 minutes, SBP averaged 127.80 ± 10.78 mmHg for Carbetocin and 126.81 ± 11.28 mmHg for Oxytocin (p=0.648). This trend continued at 15 and 30 minutes, with no significant differences across subsequent intervals. In contrast, Esseissah S A et al.[11] found significantly higher SBP in the Oxytocin + ergometrine group (116.46 ± 9.39 mmHg) compared to Carbetocin (111.65 ± 5.3 mmHg, p=0.01). Similar patterns were observed for diastolic blood pressure (DBP), which dropped more in Group 2 initially but stabilized by 24 hours, with no significant differences noted. Ahmed M E et al.[10] reported DBP averages of 68.97 ± 7.70 mmHg for Carbetocin and 69.18 ± 9.34 mmHg for Oxytocin at 0 minutes (p=0.481), showing consistent non-significant differences throughout. Esseissah S A et al.[11] also noted higher DBP in the Oxytocin + ergometrine group (81.37 ± 11.43 mmHg) compared to Carbetocin (76.56 ± 3.7 mmHg, p=0.03). For mean blood pressure (MBP), our study found similar drops in Group 2, stabilizing without significant differences, corroborated by Ahmed M E et al.[10] Additionally, both groups showed a drop-in pulse rate during the first 15 minutes due to sympathetic block from spinal anesthesia, normalizing thereafter with no significant differences. Ahmed M E et al.[10] reported initial pulse rates of 90.49 ± 4.91 bpm for Carbetocin and 90.76 ± 5.46 bpm for Oxytocin (p=0.484), with

fluctuations but no significant differences noted at subsequent intervals. Overall, our findings align with existing literature, suggesting comparable hemodynamic responses between Carbetocin and Oxytocin post-anesthesia.

In our study, there was a greater decrease in postpartum hemoglobin levels in Group 2 compared to Group 1. The mean hemoglobin difference was 0.71 ± 0.28 for Group 1 and 1.15 ± 0.59 for Group 2, with a statistically significant p-value of <0.001. Similarly, Himaja A et al.[12] found a difference in the incidence of severe anemia between the groups, reporting that in the Carbetocin group, 45 women (90%) did not experience severe anemia, while 5 women (10%) did. In contrast, in the Oxytocin group, 40 women (80%) did not have severe anemia, and 10 women (20%) did. However, Elgarhy E et al.[13] reported no statistically significant difference in post-labor anemia between the two groups, with a p-value of 0.08, suggesting variability in findings across different studies.

In our study, the incidence of side effects such as nausea and chest pain was higher in Group 1 compared to Group 2, likely due to the stronger uterotonic action of carbetocin. However, this difference was not statistically significant (p=0.09). Jha A et al.[14] reported similar findings, noting that in Group 2, 3 patients experienced abdominal pain, 1 reported nausea and vomiting, 2 had chest pain, and 2 experienced flushing. In Group 1, only 1 patient had abdominal pain and 1 had flushing, with no instances of nausea, vomiting, or chest pain. Mohamed Maged et al.[3] (2015) found that adverse effects, including nausea, vomiting, flushing, dizziness, headache, shivering, metallic taste, dyspnea, palpitation, and itching, were comparable between the both groups.

Conclusion

In conclusion, this study evaluated the efficacy of carbetocin versus oxytocin in preventing postpartum hemorrhage (PPH) in elective high-risk cesarean sections. The findings indicate that carbetocin, with its rapid onset, longer duration of action, better stability at room temperature, and similar safety profile, is a more potent uterotonic than oxytocin. Carbetocin significantly reduced blood loss, lowered the incidence of PPH, and decreased the need for additional uterotonics, highlighting its potential to improve maternal outcomes and reduce PPH-related complications.

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