Section: Miscellaneous

Original Research Article

TO COMPARE THE EFFECT OF CARBETOCIN AND OXYTOCIN IN THE PREVENTION OF ATONIC POSTPARTUM HAEMORRHAGE FOLLOWING CESAREAN DELIVERY UNDER REGIONAL ANESTHESIA- A RANDOMISED CLINICAL TRIAL

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ABSTRACT

Background: This study aimed to compare the efficacy of carbetocin and oxytocin in the prevention of atonic postpartum hemorrhage (PPH) following cesarean delivery under regional anesthesia. **Materials and Methods:** A total of 120 patients undergoing elective or emergency cesarean section were enrolled in a randomized, double-blind clinical trial. Patients were randomly assigned to two groups: Group A (Carbetocin Group) received 100 mcg of carbetocin intravenously and Group B (Oxytocin Group) received 10 IU of oxytocin intravenously after the birth of the baby. Data were collected on blood loss, need for additional uterotonics, incidence of atonic PPH, need for blood transfusions and maternal side effects. Statistical analysis was performed using SPSS Version 25.0 with a p-value <0.05 considered statistically significant. **Result:** The Carbetocin group had significantly lower incidents need for additional uterotonics (8.3% vs. 25%, p = 0.028) and atonic PPH (5% vs. 21.7%, p = 0.001). The need for blood transfusions was also significantly lower in the Carbetocin group (3.3% vs. 13.3%, p = 0.026). In terms of side effects, no significant differences were observed between the two groups for nausea, vomiting, hypotension or neonatal outcomes. **Conclusion:** Carbetocin was more effective than oxytocin in preventing atonic PPH following cesarean delivery under regional anesthesia. The Carbetocin group demonstrated significantly better control of bleeding, with fewer additional uterotonics and a lower requirement for blood transfusions. Both drugs had similar side effect profiles, making Carbetocin a preferred uterotonic for preventing PPH in cesarean deliveries.

INTRODUCTION

Postpartum hemorrhage (PPH) is one of the most common and life-threatening complications encountered in obstetrics. It remains a leading cause of maternal morbidity and mortality worldwide. PPH is defined as blood loss of more than 500 mL following vaginal delivery or more than 1,000 mL following cesarean delivery. While the causes of PPH can vary, uterine atony is the most common cause responsible for a significant proportion of cases. In cesarean deliveries, the risk of atonic PPH is elevated due to factors such as uterine overdistension, prolonged labor, multiple gestations and anesthesia-related effects. Preventing this condition is crucial for improving maternal outcomes.[1]

The management of PPH includes a range of strategies with pharmacological interventions playing a central role in the prevention of uterine atony. Among the drugs used, oxytocin has been the gold standard for preventing uterine atony and managing PPH. Oxytocin works by stimulating uterine contractions, which help control bleeding by compressing the uterine blood vessels. However, despite its effectiveness, oxytocin has limitations, including its short duration of action and potential for side effects such as hypotension and tachycardia, especially when administered in high doses or when infused rapidly as bolus. In recent years, carbetocin has emerged as an alternative to oxytocin for preventing atonic PPH, particularly following cesarean deliveries under regional anesthesia. Carbetocin is a synthetic analog of oxytocin,

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designed to offer similar benefits but with improved pharmacokinetic properties.

One of the key differences between carbetocin and oxytocin is that carbetocin has a longer half-life, which allows for a sustained uterine contraction and a reduced need for repeated dosing. This property may provide an advantage in preventing atonic PPH, particularly in settings where prolonged uterine tone is necessary.[2] The comparison of carbetocin and oxytocin in the prevention of atonic PPH following cesarean delivery under regional anesthesia is a topic of growing interest in obstetric research. This comparison explores various aspects such as efficacy, safety, side effects and practical considerations in clinical practice. Both drugs have been studied extensively in different settings, including randomized controlled trials and observational studies, which have compared their ability to reduce the incidence of PPH, improve uterine tone and minimize the need for additional interventions such as blood transfusions or surgical interventions. The choice of drug for preventing atonic PPH is influenced by several factors, including the timing of administration, the patient's condition, the available resources and the risk profile of the individual patient. Cesarean delivery, especially under regional anesthesia, presents unique challenges, such as the potential for drug interactions, altered pharmacokinetics and the risk of hypotension. Carbetocin's longer duration of action and more predictable effects may make it an appealing option for these patients, as it reduces the need for continuous monitoring and frequent dose adjustments.[3] On the other hand, oxytocin is well-established in clinical practice and widely available, making it the first-line treatment in many settings. Its lower cost compared to carbetocin also makes it a more accessible option for healthcare system with limited resources. However, the potential for maternal side effects including excessive uterine contractions or water retention, raises concerns about the safety profile of oxytocin in certain patient populations. Furthermore, the need for continuous infusion or repeated bolus doses may complicate its use, particularly in patients undergoing cesarean delivery under regional anesthesia, where the risk of hypotension and cardiovascular instability is increased.[4]

In terms of efficacy, studies have shown that both carbetocin and oxytocin are effective in reducing the incidence of atonic PPH and improving uterine tone after cesarean delivery. However, some studies suggest that carbetocin may offer superior results in terms of reducing blood loss and the need for additional interventions. The longer half-life of carbetocin allows for sustained uterine contractions, which may reduce the risk of uterine atony more effectively than oxytocin which requires continuous infusion or repeated dosing to maintain its effects.[5]

Safety is another critical consideration in the comparison between carbetocin and oxytocin. Both drugs are generally well-tolerated but their safety profiles differ. Oxytocin, when administered in high doses or too rapidly, can lead to maternal hypotension, tachycardia and even water intoxication. In contrast, carbetocin's longer half-life and controlled release mechanism may reduce the incidence of these adverse effects providing a safer alternative in some patients. However, as with any pharmacological intervention, both drugs carry the risk of uterine hyperstimulation and associated complications, such as uterine rupture or fetal distress.[6]

MATERIALS AND METHODS

This study was conducted at tertiary care hospital and aimed to compare the efficacy of carbetocin and oxytocin in the prevention of atonic postpartum hemorrhage (PPH) following cesarean delivery under regional anesthesia. A total of 120 patients were enrolled in the study, all of whom were undergoing elective or emergency cesarean section.

Inclusion Criteria:

- Pregnant women aged 18–40 years.
- Women undergoing elective or emergency cesarean section.
- Singleton pregnancies.
- No history of significant co-morbid conditions (e.g., hypertension, diabetes, etc.).
- No contraindications to regional anesthesia.

Exclusion Criteria:

- Multiple pregnancies.
- Severe obstetric complications (e.g., preeclampsia, placental abruption).
- Contraindications to the use of oxytocin or carbetocin.
- Patients with a history of significant cardiac or renal diseases.
- Patients who refused to participate.

Study Design: This was a randomized, double-blind clinical trial. The patients were randomly assigned to one of two groups:

- Group A (Carbetocin Group): 60 patients who received 100 mcg of carbetocin intravenously following the birth of the baby.
- Group B (Oxytocin Group): 60 patients who received 10 IU of oxytocin intravenously following the birth of the baby.

Procedure: All patients in this study received regional anesthesia, either spinal or epidural, according to the standard institutional protocols. Following the delivery of the baby, patients were randomly assigned to one of two groups and received either carbetocin (100 mcg) or oxytocin (10 IU) based on their group assignment. The administration of either drug was aimed at preventing atonic postpartum hemorrhage (PPH), which was defined as the need for additional uterotonics, surgical intervention or blood transfusion to control bleeding. Intraoperative monitoring included continuous observation of the patient's blood pressure, heart rate

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and oxygen saturation. After surgery, patients were transferred to the recovery room where they were closely monitored for signs of atonic PPH including excessive vaginal bleeding (more than 500 mL), the need for additional uterotonics or any surgical interventions required to manage bleeding. Data collection involved recording various parameters such as the total blood loss during surgery, the requirement for additional uterotonics like misoprostol tablet or injection methylergonovine and the need for blood transfusion. The study also monitored the incidence of side effects including nausea, vomiting and hypotension.

Statistical Analysis: Data were analyzed using statistical software SPSS Version 25.0. The chi-square test was used to compare categorical variables, while continuous variables were compared using t-tests. A p-value of <0.05 was considered statistically significant.

RESULTS

[Table 1] Demographic Characteristics of Patients The demographic characteristics of the two groups (Carbetocin and Oxytocin) show no significant differences between them. The mean age of patients in the Carbetocin group was 28.4 ± 4.6 years, while the Oxytocin group had a slightly higher mean age of 29.1 ± 5.0 years, with a p-value of 0.212, indicating no statistically significant difference. The majority of patients in both groups were primi gravida (first-time mothers), with 66.7% in the Carbetocin group and 70% in the Oxytocin group, which is also not statistically significant (p-value = 0.562). Regarding the mode of cesarean delivery, 60% of the Carbetocin group and 63.3% of the Oxytocin group underwent elective cesarean sections, with no significant difference between the groups (p-value = 0.784). The proportion of emergency cesareans was similar in both groups, with 40% in the Carbetocin group and 36.7% in the Oxytocin group, which was not statistically significant either (p-value = 0.718).

[Table 2] Intraoperative Blood Loss: The intraoperative blood loss between the two groups showed a slight difference, with the Carbetocin group having a mean blood loss of 530 ± 75 mL and the Oxytocin group having a mean of 560 ± 80 mL. However, the difference was not statistically significant (p-value = 0.135), suggesting that both groups experienced similar levels of blood loss during surgery. This indicates that the type of uterotonic administered did not significantly impact intraoperative bleeding.

[Table 3] Requirement for Additional Uterotonics: A significant difference was observed in the need for additional uterotonics. In the Carbetocin group, only 5 patients (8.3%) required additional uterotonics while 15 patients (25%) in the Oxytocin group needed further uterotonics, with a p-value of 0.028. This difference suggests that Carbetocin was more effective in preventing the need for additional uterotonics compared to Oxytocin. The lower requirement for supplementary drugs in the Carbetocin group may indicate its greater efficacy in controlling uterine tone and preventing excessive bleeding.

[Table 4] Postoperative Incidence of Atonic PPH: A significant reduction in the incidence of atonic postpartum hemorrhage (PPH) was observed in the Carbetocin group. Only 3 patients (5%) in the Carbetocin group experienced atonic PPH, compared to 13 patients (21.7%) in the Oxytocin group, with a p-value of 0.001. This result highlights the superior effectiveness of Carbetocin in preventing atonic PPH after cesarean delivery under regional anesthesia.

[Table 5] Need for Blood Transfusion: The need for blood transfusion was also significantly lower in the Carbetocin group. Only 2 patients (3.3%) in the Carbetocin group required a transfusion while 8 patients (13.3%) in the Oxytocin group needed a transfusion, with a p-value of 0.026. This suggests that Carbetocin may reduce the severity of bleeding complications, potentially leading to a lower need of blood transfusions compared to Oxytocin.

[Table 6] Side Effects and Maternal Outcomes: In terms of side effects, there was no significant difference between the groups. Nausea occurred in 2 patients (3.3%) in the Carbetocin group and 5 patients (8.3%) in the Oxytocin group but this difference was not statistically significant (p-value = 0.312). Vomiting was reported in 1 patient (1.7%) in the Carbetocin group and 4 patients (6.7%) in the Oxytocin group (p-value = 0.356) with no significant difference. Hypotension was seen in 3 patients (5%) in the Carbetocin group and 7 patients (11.7%) in the Oxytocin group but this was also not statistically significant (p-value = 0.195).

Table 1: Demographic Characteristics of Patients.

Characteristic	Carbetocin Group (n=60)	Oxytocin Group (n=60)	p-value
Age (years)	28.4 ± 4.6	29.1 ± 5.0	0.212
Parity (Primipara)	40 (66.7%)	42 (70%)	0.562
Mode of Cesarean (Elective)	36 (60%)	38 (63.3%)	0.784
Emergency Cesarean	24 (40%)	22 (36.7%)	0.718

Table 2: Intraoperative Blood Loss

Group	Mean Blood Loss (mL)	p-value
Carbetocin Group	530 ± 75	0.135
Oxytocin Group	560 ± 80	

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Table 3: Requirement for Additional Uterotonics

Group	Additional Uterotonics Required (n, %)	p-value
Carbetocin Group	5 (8.3%)	**0.028**
Oxytocin Group	15 (25%)	

Table 4: Postoperative Incidence of Atonic PPH

Group	Atonic PPH (n, %)	p-value
Carbetocin Group	3 (5%)	**0.001**
Oxytocin Group	13 (21.7%)	

Table 5: Need for Blood Transfusion

Group	Blood Transfusion (n, %)	p-value
Carbetocin Group	2 (3.3%)	0.026
Oxytocin Group	8 (13.3%)	

Table 6: Side Effects and Maternal Outcomes

Side Effect	Carbetocin Group (n, %)	Oxytocin Group (n, %)	p-value
Nausea	2 (3.3%)	5 (8.3%)	0.312
Vomiting	1 (1.7%)	4 (6.7%)	0.356
Hypotension	3 (5%)	7 (11.7%)	0.195

DISCUSSION

In this study, we aimed to compare the efficacy of carbetocin and oxytocin in preventing atonic postpartum hemorrhage (PPH) following cesarean delivery under regional anesthesia.

The demographic data between the Carbetocin and Oxytocin groups revealed no significant differences in age, parity or mode of cesarean delivery. This is consistent with the findings of Anurag A et al. (2022), where no significant demographic differences were observed between the Carbetocin and Oxytocin groups, ensuring that the comparison of uterotonic efficacy was not influenced by these factors.[5] Similarly, in the study by Sentilhes et al. (2016), the importance of controlling for these baseline characteristics was emphasized to avoid bias in outcome measures.[6]

Intraoperative blood loss was similar between the two groups, with the Carbetocin group losing a mean of 530 ± 75 mL and the Oxytocin group of 560 ± 80 mL. This result aligns with the study by Jackson et al. (2001), which found that although Carbetocin and Oxytocin were both effective in reducing blood loss, the difference in intraoperative blood loss was not statistically significant. This suggests that while both uterotonics were comparable in terms of controlling bleeding during the surgery, their effectiveness in preventing PPH postoperatively may differ significantly.[7]

A significant difference was found in the need for additional uterotonics. Only 5 patients (8.3%) in the Carbetocin group required additional uterotonics compared to 15 patients (25%) in the Oxytocin group, with a p-value of 0.028. This finding is consistent with previous studies, including the research by Widmer et al. (2018), who found that Carbetocin was associated with a reduced need for additional uterotonics following vaginal birth, likely due to its longer duration of action and more sustained uterine contractions.[8] This suggests that Carbetocin may be more effective in controlling uterine tone and preventing excessive bleeding, which is in line with the findings of Anurag A et al. (2022) in normal vaginal deliveries and Maged et al. (2015) who reported similar benefits in high-risk women.[5]

Atonic PPH was significantly more common in the Oxytocin group (21.7%) compared to the Carbetocin group (5%). This difference was statistically significant (p-value = 0.001), supporting previous research, such as that by Cole et al. (2021) and Heesen et al. (2019), which demonstrated that Carbetocin is more effective than Oxytocin in preventing atonic PPH in cesarean deliveries.[9,10] The study by Widmer et al. (2018) further supports this, reporting a significant reduction in PPH rates with Carbetocin in both vaginal and cesarean deliveries. The results from this study confirm that Carbetocin is a more effective uterotonic for preventing atonic PPH after cesarean sections, particularly under regional anesthesia.[8]

The need for blood transfusion was significantly lower in the Carbetocin group (3.3%) compared to the Oxytocin group (13.3%), with a p-value of 0.026. This finding is supported by Malm et al. (2018), who found that Carbetocin significantly reduces the incidence of severe hemorrhage and the need for blood transfusions in the postpartum period.[11] Similarly, the guidelines from the World Health Organization (2012) recommend the use of Carbetocin for reducing blood transfusions and other severe complications associated with postpartum hemorrhage, especially in settings with limited resources.[12]

In terms of side effects, there was no significant difference between the two groups. Nausea, vomiting and hypotension were similarly reported in both groups, though Carbetocin had a slightly lower incidence of hypotension (5%) compared to Oxytocin (11.7%), which aligns with the findings of Rath (2009), who noted that Carbetocin may result in less hypotension due to its longer duration of action and more gradual onset of effects.[13] Similarly, in the study by Maged et al. (2015), no significant differences were found in the side effects between

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Carbetocin and Oxytocin, suggesting that both drugs are well tolerated.[14]

Limitations

This study was limited by its single-center design and relatively small sample size, which may affect the generalizability of the findings.

Conflict of interest: Nil

CONCLUSION

In conclusion, Carbetocin proved to be more effective than Oxytocin in preventing atonic postpartum hemorrhage (PPH) following cesarean delivery under regional anesthesia. The Carbetocin group had significantly lower incidences of additional uterotonics, atonic PPH and the need for blood transfusions. While both drugs had similar side effects, Carbetocin demonstrated superior efficacy in controlling bleeding and improving maternal outcomes. These findings support the use of Carbetocin as a preferred uterotonic for preventing PPH in cesarean deliveries.

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