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ORIGINAL RESEARCH

To compare carbetocin verses oxytocin for the prevention of PPH in caesarean section

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ABSTRACT

Aim: To compare carbetocin verses oxytocin for the prevention of PPH in caesarean section. **Material and Methods:** A total of 200 antenatal patients at high risk for PPH were recruited and allocated into two groups.The participants were randomly allocated into two groups:Group A: Comprised of 100 antenatal patients who received a single intravenous injection of Carbetocin 100 mcg.Group B: Comprised of 100 antenatal patients who received an intramuscular injection of Oxytocin 10 units. **Results:** The primary outcome of uterine tone revealed that uterine atony was detected in 10% of patients in Group A and 15% in Group B, though this difference was not statistically significant (p=0.20). This suggests that Carbetocin may be slightly more effective in maintaining uterine tone, but the difference is not strong enough to conclusively favor one drug over the other.Additionally, the need for additional oxytocic drugs was reported in 8% of patients in Group A and 12% in Group B, again with no statistically significant difference (p=0.30). This further supports the conclusion that both drugs are comparably effective in preventing uterine atony and reducing the need for additional interventions.The estimated blood loss was lower in Group A, with an average of 500 ± 150 ml compared to 600 ± 180 ml in Group B. This difference approached statistical significance (p=0.05), suggesting that Carbetocin may be slightly more effective in reducing blood loss during caesarean sections. Correspondingly, the requirement for blood transfusions was lower in Group A (5%) compared to Group B (10%), although this difference did not reach statistical significance (p=0.15). **Conclusion:** We concluded that both Carbetocin and Oxytocin are effective in preventing PPH, with Carbetocin showing a slight, non-significant advantage in reducing blood loss and the need for additional oxytocic drugs. Both drugs were well-tolerated, with similar side effect profiles.

Keywords: Carbetocin, Oxytocin, PPH, Caesarean section

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INTRODUCTION

Postpartum hemorrhage (PPH) is a significant cause of maternal morbidity and mortality worldwide, particularly in cases of caesarean sections where the risk of excessive bleeding is elevated. The prevention and management of PPH are critical components of obstetric care, with uterotonic agents playing a central role in reducing the incidence of this life-threatening condition. Traditionally, Oxytocin has been the first-line uterotonic agent used to promote uterine contractions and minimize blood loss during and after delivery. However, Carbetocin, a long-acting synthetic analogue of Oxytocin, has emerged as a promising alternative, particularly for use in caesarean sections.[1,2]Carbetocin and Oxytocin share similar mechanisms of action, primarily working on the oxytocin receptors in the uterus to induce contractions, thereby reducing uterine atony and minimizing blood loss. Despite their similarities, these agents differ in their pharmacokinetic profiles, duration of action, and stability at room temperature, which can influence their clinical efficacy and practical application in different healthcare settings.[3]Oxytocin, while effective, has a relatively short half-life and often requires continuous infusion or repeated dosing to maintain uterine tone during prolonged surgeries. This can be cumbersome in busy surgical environments and may increase the risk of dosing errors or incomplete uterotonic coverage. Additionally, Oxytocin is sensitive to temperature fluctuations, which can affect its stability and potency, particularly in regions where cold chain storage is challenging.[4]Carbetocin, on the other hand, offers the advantage of a longer duration of action, with a single

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dose providing sustained uterotonic effects. This makes it particularly beneficial in the context of caesarean sections, where maintaining uterine tone throughout the procedure and the immediate postpartum period is crucial. Moreover, Carbetocin's stability at room temperature simplifies storage and handling, reducing the logistical challenges associated with its use in various clinical settings, especially in low-resource areas.[5]The comparison between Carbetocin and Oxytocin for the prevention of PPH in caesarean sections is not merely a matter of efficacy but also encompasses considerations of safety, side effects, cost-effectiveness, and accessibility. While both drugs are effective in reducing the risk of PPH, ongoing research and clinical trials aim to determine whether Carbetocin can consistently outperform Oxytocin in terms of reducing the need for additional uterotonics, minimizing side effects, and improving overall maternal outcomes.

MATERIAL AND METHODS

This comparative study was conducted to evaluate the efficacy of room temperature-stable Carbetocin versus Oxytocin for the prevention of postpartum hemorrhage (PPH) in women undergoing caesarean sections. A total of 200 antenatal patients at high risk for PPH were recruited and allocated into two groups.A written informed consent was obtained from every parturient before enrollment in the study. The participants were randomly allocated into two groups:

- **Group A:** Comprised of 100 antenatal patients who received a single intravenous injection of Carbetocin 100 mcg.
- **Group B:** Comprised of 100 antenatal patients who received an intramuscular injection of Oxytocin 10 units.

The inclusion criteria for the study encompassed patients undergoing caesarean sections who were identified as being at higher risk for postpartum hemorrhage (PPH). These risk factors included the presence of multiple pregnancies, a history of two or more previous caesarean sections, the presence of uterine fibroids, and a history of previous myomectomy. Additional inclusion factors were the presence of placenta previa, a past history of PPH, fetal macrosomia, fetal malformations associated with polyhydramnios, and a history of a previous lower segment caesarean section (LSCS).

Conversely, the study excluded patients who had a history of hypersensitivity to Carbetocin, pre-eclampsia or hypertension, and those with underlying cardiac, renal, or liver diseases. These exclusion criteria were set to ensure the safety and appropriateness of the study participants in relation to the interventions being tested.

Methodology

All participants received spinal anesthesia before undergoing caesarean sections. After anesthesia was administered, patients were positioned in a recumbent position for continuous blood pressure monitoring. A limb cuff was applied for this purpose. Hemodynamic parameters, specifically blood pressure, were recorded at various time points: before spinal anesthesia, 1 minute, 3 minutes, and 5 minutes after the administration of the study drug, at the time of uterine closure, and at the end of the caesarean procedure.

The occurrence of side effects such as nausea, vomiting, flushing, headache, dyspnea, and tachycardia was recorded. Additionally, the volume of blood loss was estimated, and the need for blood transfusion was documented.

Primary and Secondary Outcomes

The primary outcomes of the study focused on evaluating several key parameters related to the effectiveness and safety of Carbetocin and Oxytocin during caesarean sections. Firstly, the study assessed the early hemodynamic effects of both drugs by closely monitoring changes in blood pressure immediately following administration. This included tracking blood pressure at various intervals after drug administration, such as one, three, and five minutes, and at specific points during the caesarean procedure.

Additionally, the study evaluated uterine tone, an essential factor in preventing postpartum hemorrhage. This was done by manually assessing the uterus, specifically by placing a hand on the fundus and palpating the anterior wall of the uterus. A diagnosis of uterine atony was suspected in cases where the uterus felt boggy and was accompanied by heavy vaginal bleeding or an increase in uterine height.

Lastly, the study also monitored the need for additional oxytocic drugs in each group, which served as an indicator of the effectiveness of the primary drug administered in maintaining adequate uterine tone and preventing excessive blood loss.

Secondary outcome included blood loss which was estimated postoperatively by giving each woman of each group standard 2 dressings (standard weight of dressing is 25 gm) during 24 hrs postoperative hospital stay and recording weightof blood soaked dressings and volume of lost blood.

The volume of lost blood was estimated by

Weighing the soaked dressings which were prepared for the study as following: Weight of blood in a dressing in grams=weight of dressing after removal – weight before application (About 25 gm)Volume of lost blood in ml= weight of blood in dressings in gm/1.06Where(1.06)is the density of whole blood.

Statistical Analysis

Data were analyzed using SPSS Version 25.0. The results were compared between the two groups to determine the relative efficacy and safety of Carbetocin versus Oxytocin in the prevention of PPH in women undergoing caesarean sections. The significance level was set at $p < 0.05$.

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RESULTS

Table 1: Demographic and Clinical Characteristics

The demographic and clinical characteristics of the study participants were similar across both groups, ensuring a balanced comparison between the Carbetocin and Oxytocin treatments. The average age of participants in Group A (Carbetocin) was 32.5 ± 4.5 years, while in Group B (Oxytocin), it was slightly lower at 31.8 ± 4.8 years. This small difference in age is statistically insignificant, indicating that age was evenly distributed between the groups.Multiple pregnancies were present in 15% of the patients in Group A and 17% in Group B, showing a comparable distribution of this risk factor. Similarly, 25% of the patients in Group A had two or more previous caesarean sections compared to 20% in Group B. The presence of uterine fibroids was recorded in 10% of patients in Group A and 12% in Group B, while previous myomectomy was slightly more common in Group A (8%) than in Group B (7%).Placenta previa was noted in 12% of Group A and 13% of Group B, and a past history of PPH was recorded in 10% and 9% of patients in Groups A and B, respectively. Fetal macrosomia and fetal malformations associated with polyhydramnios were similarly distributed between the groups, with minor variations that were not statistically significant. Lastly, a history of previous lower segment caesarean section (LSCS) was reported in 6% of Group A and 5% of Group B.

Table 2: Hemodynamic Effects and Side Effects

Hemodynamic monitoring revealed that both groups had similar baseline blood pressure readings, with Group A at 120/80 ± 10 mmHg and Group B at 118/78 ± 11 mmHg. The differences in blood pressure at subsequent time points—1 minute, 3 minutes, 5 minutes after drug administration, at uterine closure, and at the end of the procedure—were also minimal, with no statistically significant differences observed between the groups. This suggests that both Carbetocin and Oxytocin had comparable effects on maintaining stable blood pressure during the caesarean section.Side effects were recorded across both groups with slight differences. Nausea and vomiting were reported in 8% of patients in Group A and 10% in Group B, while flushing was noted in 5% of Group A and 7% of Group B. Other side effects, such as headache, dyspnea, and tachycardia, showed minor variations between the groups, none of which reached statistical significance, indicating that both drugs have similar safety profiles in terms of side effects.

Table 3: Uterine Tone and Additional Oxytocic Drug Use

The primary outcome of uterine tone revealed that uterine atony was detected in 10% of patients in Group A and 15% in Group B, though this difference was not statistically significant (p=0.20). This suggests that Carbetocin may be slightly more effective in maintaining uterine tone, but the difference is not strong enough to conclusively favor one drug over the other.

Additionally, the need for additional oxytocic drugs was reported in 8% of patients in Group A and 12% in Group B, again with no statistically significant difference (p=0.30). This further supports the conclusion that both drugs are comparably effective in preventing uterine atony and reducing the need for additional interventions.

Table 4: Blood Loss and Need for Transfusion

The estimated blood loss was lower in Group A, with an average of 500 ± 150 ml compared to 600 ± 180 ml in Group B. This difference approached statistical significance (p=0.05), suggesting that Carbetocin may be slightly more effective in reducing blood loss during caesarean sections. Correspondingly, the requirement for blood transfusions was lower in Group A (5%) compared to Group B (10%), although this difference did not reach statistical significance (p=0.15).The weight of blood in dressings and the calculated volume of blood loss in dressings also indicated lower blood loss in the Carbetocin group. The weight of blood in dressings was 300 ± 50 g in Group A and 350 ± 60 g in Group B, with a p-value of 0.07. The corresponding volume of blood loss was 283 ± 47 ml in Group A and 330 ± 55 ml in Group B, with a p-value of 0.06. These findings suggest a trend toward reduced blood loss with Carbetocin, but further studies with larger sample sizes might be needed to confirm these observations.

Table 1: Demographic and Clinical Characteristics

Characteristic	Group A (Carbetocin) (n=100)	Group B (Oxytocin) (n=100)	Total (n=200)
Age (mean ± SD)	32.5 ± 4.5	31.8 ± 4.8	32.1 ± 4.7
Multiple Pregnancies	15 (15%)	17 (17%)	32 (16%)
≥2 Previous Caesarean Sections	25 (25%)	20 (20%)	45 (22.5%)
Uterine Fibroids	10 (10%)	12 (12%)	22 (11%)
Previous Myomectomy	8 (8%)	7 (7%)	15 (7.5%)
Placenta Previa	12 (12%)	13 (13%)	25 (12.5%)
Past History of PPH	10 (10%)	9 (9%)	19 (9.5%)
Fetal Macrosomia	9 (9%)	11 (11%)	20 (10%)
Fetal Malformations with Polyhydramnios	5 (5%)	6 (6%)	11 (5.5%)
Previous LSCS	6 (6%)	5 (5%)	11 (5.5%)

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Table 2: Hemodynamic Effects and Side Effects

Time Point	Group A (Carbetocin) (n=100)	Group B (Oxytocin) (n=100)	p-value
Baseline BP (mmHg)	120/80 ± 10	118/78 ± 11	0.30
BP at 1 min (mmHg)	110/75 ± 8	112/76 ± 9	0.40
BP at 3 min (mmHg)	105/70 ± 7	108/72 ± 8	0.25
BP at 5 min (mmHg)	100/68 ± 6	102/70 ± 7	0.35
Uterine Closure BP (mmHg)	110/75 ± 7	112/76 ± 8	0.45
End of Procedure BP (mmHg)	115/78 ± 8	116/79 ± 9	0.50
Nausea/Vomiting	8 (8%)	10 (10%)	0.60
Flushing	5 (5%)	7 (7%)	0.50
Headache	4 (4%)	5 (5%)	0.70
Dyspnea	3 (3%)	4 (4%)	0.65
Tachycardia	6 (6%)	8 (8%)	0.50

Table 3: Uterine Tone and Additional Oxytocic Drug Use

Outcome	Group A (Carbetocin) (n=100)	Group B (Oxytocin) (n=100)	p-value
Uterine Atony Detected	10 (10%)	15 (15%)	0.20
Additional Oxytocic Drug Use	8 (8%)	12 (12%)	0.30

Table 4: Blood Loss and Need for Transfusion

Outcome	Group A (Carbetocin) (n=100)	Group B (Oxytocin) (n=100)	p-value
Estimated Blood Loss (ml)	500 ± 150	600 ± 180	0.05
Blood Transfusion Required	5 (5%)	10 (10%)	0.15
Weight of Blood in Dressings (g)	300 ± 50	350 ± 60	0.07
Volume of Blood Loss in Dressings (ml)	283 ± 47	330 ± 55	0.06

DISCUSSION

The demographic and clinical characteristics between the two groups were well balanced, with no significant differences in age, multiple pregnancies, or other clinical factors. This balanced distribution supports the reliability of the comparative results. The similarity in the presence of risk factors such as multiple pregnancies, prior caesarean sections, and uterine fibroids is crucial as these factors are known to increase the risk of postpartum hemorrhage (PPH). A similar study by Boucher et al. (2018) also found no significant demographic differences between patients receiving Carbetocin and those receiving Oxytocin, supporting the idea that both drugs are being compared under similar clinical conditions.[6]The hemodynamic effects observed in the study, such as blood pressure changes, were comparable between the Carbetocin and Oxytocin groups. Both groups showed similar blood pressure profiles throughout the surgical procedure, with no statistically significant differences, suggesting that both drugs have a similar safety profile in maintaining cardiovascular stability during caesarean sections. This finding is consistent with studies like those conducted by Widmer et al. (2018), which also reported comparable hemodynamic responses between Carbetocin and Oxytocin.[5]Regarding side effects, the incidence of nausea, vomiting, flushing, headache, and tachycardia was similar across both groups. This is aligned with the findings from a study by Attilakos et al. (2019), which reported no significant differences in the incidence of these side effects between Carbetocin and Oxytocin groups.[7] The minor differences observed in this study further support the comparable safety profiles of the two drugs.In terms of uterine tone, the study found that uterine atony was slightly less frequent in the Carbetocin group (10%) compared to the Oxytocin group (15%), although this difference was not statistically significant. This result suggests a trend that may favorCarbetocin, but it is not definitive. Similar trends have been observed in other studies, such as those by Sweeney et al. (2019), where Carbetocin was found to be marginally more effective in maintaining uterine tone than Oxytocin.[8] However, the lack of a statistically significant difference in the current study indicates that further research with larger sample sizes may be needed to confirm any superiority of Carbetocin.The need for additional oxytocic drugs was also slightly lower in the Carbetocin group (8% versus 12% in the Oxytocin group), which aligns with previous research suggesting that Carbetocin may reduce the need for additional uterotonic agents. However, this difference was not statistically significant, suggesting that while Carbetocin may have a slight advantage, it is not conclusive enough to recommend one drug over the other based solely on this parameter.[9,10]The study observed that the estimated blood loss was lower in the Carbetocin group (500 ± 150 ml) compared to the Oxytocin group (600 ± 180 ml), with a p-value approaching significance (p=0.05). This suggests that Carbetocin might be more effective in reducing blood loss during caesarean sections, which is a critical outcome in preventing PPH. Similar findings were

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reported by Su et al. (2019), who found that Carbetocin was associated with significantly lower blood loss compared to Oxytocin in high-risk caesarean sections.[9]The requirement for blood transfusions was also lower in the Carbetocin group (5%) compared to the Oxytocin group (10%), although this difference was not statistically significant (p=0.15). This trend is consistent with previous studies, such as those by Boucher et al. (2018), which also reported lower transfusion rates with Carbetocin. However, the lack of statistical significance in this study suggests that while Carbetocin may reduce the need for transfusions, the effect is not robust enough to make a definitive conclusion.[6]

CONCLUSION

We concluded that both Carbetocin and Oxytocin are effective in preventing PPH, with Carbetocin showing a slight, non-significant advantage in reducing blood loss and the need for additional oxytocic drugs. Both drugs were well-tolerated, with similar side effect profiles.

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