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Assessing Efficacy and Safety: Oxytocin Monotherapy vs. Oxytocin + Carbetocin Combination Therapy

Mohammad Kaif A. Mansuri[1], Vishwa J. Mehta[2,*]

Abstract

Objective: Comparing the Effectiveness between Oxytocin monotherapy and Oxytocin + Carbetocin. Methods: A prospective, non-randomized, observational study focusing on 221 women with CS was conducted. The patients eligible based on inclusion and exclusion criteria were screened and final sample size was 139. Individual patient data including patient demographics, medical history, OT notes, pre and post CBC reports, and safety data were obtained from the patient records. The study compared between Oxytocin monotherapy which included 67 patients and Oxytocin + carbetocin combination which has 72 pateints. The desired outcome was to compare blood loss, Hb, HCT and the administration of the treatment in preexisting conditions. Results: The incidence of blood loss was higher in Oxytocin monotherapy compared to oxytocin + carbetocin (421.94 ± 120.48 vs 356.25 ± 116.89; P=0.0003) suggesting that addition of carbetocin reduces blood loss and reduces the risk of PPH. The decline in Hb (P=0.16) and HCT (P=0.27) levels between the treatment groups did not show any discernible differences. The Administration of Oxytocin + carbetocin was slightly higher in PIH patients (53.48%) compared to Oxytocin monotherapy (34.88%), however there was no significant difference determined (P=). Also there was no difference in the usage of this treatment groups in Anaemic patients. Conclusion: There was a significant reduction in blood loss when carbetocin was added in the treatment regimen. However it has no effect on the Hb and HCT levels and its increase in utilization in pre-exsiting conditions suggesting no significant difference.

Keywords: Blood loss, PPH, HB, CS, oxytocin, carbetocin

INTRODUCTION

Post-Partum Hemorrhage (PPH) is a condition characterized by excessive bleeding after childbirth, posing serious health risks and potential fatality. Well-defined as an increasing blood loss of 500 ml or more within 24 hours, severe PPH involves a blood loss of 1000 ml or more go with by signs of hypovolemia. This condition is a leading cause of maternal morbidity and mortality, particularly prevalent in low-income countries, affecting approximately 1% to 6% of all deliveries. The World Health Organization (WHO) attributes about a quarter of global maternal deaths to PPH [1, 2].

***Author for Correspondence**
Vishwa J. Mehta
E-mail: Vishwa,mehta@lmcp.ac.in

[1]Pharm D Intern, Department of Pharmacy Practice, L. M. College of Pharmacy, Navrangpura, Ahmedabad 380009, Gujarat, India
[2]Assistant Professor, Department of Pharmacy Practice, L. M. College of Pharmacy, Navrangpura, Ahmedabad 380009, Gujarat, India

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The causes of PPH are diverse, with uterine atony, inadequate uterine contraction, being the primary contributor in 70-80% of cases [3]. Factors like uterine overdistension and postoperative uterine contractility deficiency contribute to uterine atony [4]. Trauma-related bleeding from uterine rupture, genital tract lacerations, or episiotomies is another common cause [5]. Retained fetal tissue and amniotic membranes, coagulation issues, and invasive placenta also play significant roles [6, 7]. Various risk factors increase the likelihood of PPH, including antepartum hemorrhage, augmented

labor, chorioamnionitis, fetal macrosomia, anemia, maternal obesity, multifetal gestation, preeclampsia, primiparity, prolonged labor, and episiotomy [8].

For PPH treatment, guidelines recommend a multifaceted approach involving identification, ascertainment of etiology, and implementation of relevant therapies. Medicinal, surgical, and procedural interventions, along with adjuvant therapies like blood and fluid replacement, are employed [9]. Dynamic treatment all through the third stage of labor, including the administration of anticipatory uterotonic medication, cutting and clamping of the umbilical cord, and controlled cord traction of the placenta, has been shown to be effective in dropping PPH incidence [10-12]. Uterotonic agents are medications that are used to cause the uterus to contract or become more tonic. They are used both to start labour and to lessen postpartum haemorrhage [8]. The agents including oxytocin and carbetocin, play a crucial role in PPH prevention and management. Oxytocin is the drug of choice, administered intramuscularly or intravenously. The optional dose is 10 IU. It has a half-life of 1-6mins [13]. Oxytocin works by stimulating the formation of prostaglandins and raises the intracellular calcium ion levels in myometrial cells, causing an increase in uterine contractions [14]. Carbetocin, a synthetic compound mimicking oxytocin, is used in high-risk patients. Carbetocin binds to the same receptors as Oxytocin in the myometrium, which is the muscle layers of the uterus, and stimulate contractions. The half-life of carbetocin is 40mins and the optimal dosage is 100mcg administered as IV or IM rout [15]. If uterine atony persists, second-line uterotonics such as misoprostol, carboprost, and methergine may be recommended. Combinations of uterotonic agents have been found effective in reducing PPH incidence, as per WHO guidelines [16].

In the past decade, significant advancements have emerged in the prevention and treatment of PPH. These developments encompass technological innovations, such as the utilization of inhalational oxytocin and non-pneumatic antishock garments. Additionally, novel treatment strategies have been implemented, including the proactive distribution of prophylactic misoprostol for self-administration after childbirth, the administration of oxytocin via Uniject, and the implementation of care bundles for the management of PPH. Furthermore, large-scale multicountry trials have been conducted to evaluate the efficacy of tranexamic acid for PPH treatment and the development of a heat-stable formulation of carbetocin for PPH prevention [17-19]. According to multiple literature sources [8-10], there is a growing body of evidence proposing that the preemptive use of carbetocin could serve as a viable substitute for oxytocin in averting post-partum hemorrhage. Nevertheless, the debate persists regarding the optimal uterotonic agent for prophylactic purposes. Despite this discourse, it is emphasized that the initial prevention of post-partum hemorrhage hinges on the evaluation of discernible risk factors [20, 21]. The present study also compares the effectiveness of oxytocin alone versus the combination of oxytocin and carbetocin to see the beneficial activity of carbetocin in preventing PPH.

Postpartum hemorrhage poses a risk of hypovolemic shock due to blood loss, leading to various physiological changes when around 20% of blood volume is depleted. Symptoms include tachycardia, tachypnea, narrowed pulse pressure, and delayed capillary refill, potentially resulting in ischemic damage to vital organs such as the liver, brain, heart, and kidneys. Excessive blood loss can also give rise to complications in the form of Sheehan syndrome or postpartum hypopituitarism. In terms of management-related complications, there is a potential for Transfusion-Related Acute Lung Injury (TRALI), Infections and hemolytic transfusion reactions [22].

Caesarean section (C-section), a surgical delivery method, has seen a significant increase globally, accounting for about one-third of births in the United States. The WHO reports a rising trend, with C-sections expected to constitute nearly 29% of all deliveries by 2030 [23]. Various factors, including prior C-section, maternal request, breech presentation, fetal macrosomia, labor dystocia, twin pregnancy, placental previa, and eclampsia/pre-eclampsia, contribute to the decision for a C-section [24].

In summary, PPH is a critical postpartum complication with multifactorial causes, necessitating a comprehensive approach for prevention and management. Uterotonic agents, particularly oxytocin and

carbetocin, play key roles in preventing excessive bleeding. The increasing prevalence of C-sections globally requires attention to associated implications and potential strategies for reducing the rate. A holistic understanding of these aspects is crucial for maternal health and the well-being of newborns.

METHODOLOGY

This research was a single-centre, randomized, prospective and observational associating the Oxytocin monotherapy and Oxytocin + Carbetocin combination in anticipation of PPH after elective caesarean section. A total of 221 pregnant women were involved in this research from October 2022 to march 2023 (Figure 1). The patients that did not fit into the eligibility criteria were excluded. 82 patients were excluded from the study during screening due to their failure to meet the predetermined inclusion and exclusion criteria. This research was directed in unity with Declaration of Helsinki and Good Clinical Practice Guidelines. The protocol had been approved by ethics committee institutional review board of participating centre GCS Medical College Hospital and research centre and L. M. college of Pharmacy (LMIEC).

Pregnant women aged 18 years and above, undergoing C-section, who provide signed informed consent and participants who has received either oxytocin monotherapy or oxytocin in combination with carbetocin were enrolled in this study. The exclusion criteria included Pregnant women with a history of cardiovascular-affecting diseases or therapies, including heart disease, cardiac arrhythmia, liver/renal/endocrine disorders, as well as those with a history of dengue, Typhoid, deep vein thrombosis (DVT), or undergoing coagulant therapy, are excluded. Patients who had recieved medications other than oxytocin monotherapy or oxytocin combined with carbetocin.

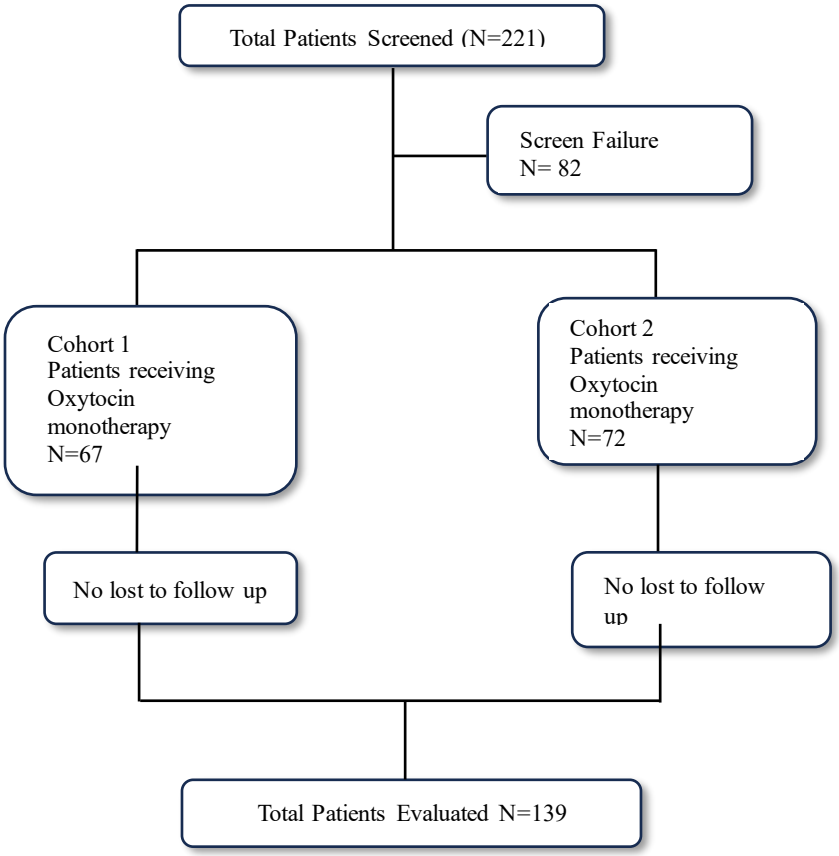

Figure 1. A total of 221 patients were screened and taken consent for this study. There were 82 patients which has screening failure i.e they did not met our inclusion and exclusion criteria. The Cohort 1 has Oxytocin monotherapy which included 67 patients and Cohort 2 has Oxytocin + Carbetocin combination which included 72 patients. There was no missing follow up in individual groups and final enrolled patients were 139.

INTERVENTIONS

The final enrolled patients were grouped into two different cohorts. One cohort patients who received Oxytocin monotherapy at a dose of 10 IU and second cohort patients who received Oxytocin 10 IU and carbetocin 100 ug combination.

Outcomes Measurement

The outcomes encompassed the assessment of blood loss, stratified into two categories: blood loss equal to or less than 500 ml, and blood loss exceeding 500 ml. The latter category denotes a heightened susceptibility to postpartum hemorrhage (PPH). Additionally, alterations in hemoglobin (Hb) and hematocrit (HCT) levels subsequent to cesarean section were examined. Furthermore, the adverse effect profiles of both cohort groups were meticulously evaluated

Statistical Analysis Plan

z test

The statistical analysis of the obtained data was performed by using z test. The z-test is a statistical analysis method employed to assess whether two large data samples exhibit significant differences in their means. This hypothesis test is suitable when the standard deviation and variance are already known, and it is specifically applicable to populations that adhere to a normal distribution. Typically, the z-test is employed when the size of the data samples exceeds 30. This test collectively provided a comprehensive approach to analyzing and interpreting the data.

Chi square test

The Chi-Square test, a non-parametric statistical test, was used to evaluate disparities between observed and expected data, aiding in understanding the connection between categorical variables and determining whether differences are due to chance or indicate a relationship

RESULTS

Patient Demographics and Administration of Uterotonic Agents

The Comparison of **Blood Loss**

The Table 2 **compares** the effectiveness of two regimens, Oxytocin Monotherapy and Oxytocin + Carbetocin, in terms of blood loss following childbirth, with data presented as mean ± standard deviation (SD) and associated P values. The oxytocin monotherapy group had 23 patients experiencing blood loss ≤ 500 ml and 44 patients experiencing blood loss ≥ 500 ml, with a mean blood loss of 421.94 ml ± 120.48. The P value associated with this group is 0.0003, indicating a statistically significant difference compared to the oxytocin plus carbetocin group (Figure 2).

In contrast, the oxytocin plus carbetocin group had 15 patients experiencing blood loss ≤ 500 ml and 57 patients experiencing blood loss ≥ 500 ml, with a lower mean blood loss of 356.25 ml ± 116.89. The incidence of patients experiencing blood loss of 500 ml or greater was notably higher in the group where carbetocin was not administered alongside oxytocin. This observation recommends a potential connection between the nonattendance of carbetocin and increased blood loss. The statistically significant P value (0.0003) suggests that the combination regimen of oxytocin and carbetocin is associated with significantly lower blood loss during the procedure compared to oxytocin monotherapy

Comparison of Fall in Hb Levels After C-Section Delivery

This Table 3 compares the effects of oxytocin monotherapy and oxytocin combined with carbetocin on hemoglobin levels. The mean difference in Oxytocin monotherapy is 1.14 ± 0.70 while in Oxytocin + Carbetocin is 1.31 ± 0.78. Both groups showed a decrease in hemoglobin post-treatment, with the oxytocin plus carbetocin group experiencing a slightly larger decrease compared to the oxytocin monotherapy group. However, the difference in hemoglobin levels post-treatment between the two groups was not statistically significant (p=0.16).

Table 1 presents a snapshot of demographic and clinical features for 139 patients, segregated into two treatment cohorts: Oxytocin monotherapy (n=67) and Oxytocin + Carbetocin (n=72). Both groups display comparable mean ages, with Oxytocin Monotherapy at 27.67 ± 4.28 years and Oxytocin + Carbetocin at 27.63 ± 4.23 years, indicating a balanced age distribution. The distribution across gravida status reveals nearly equal proportions in Gravida 1-2, with 48.54% for Oxytocin Monotherapy and 51.45% for Oxytocin + Carbetocin. In Gravida 3-4, Oxytocin Monotherapy comprises 47.05%, while Oxytocin + Carbetocin constitutes 52.94%. Noteworthy variations emerge in the history of abortion, with Oxytocin Monotherapy favored in cases of one abortion (35.71%), whereas Oxytocin + Carbetocin is predominant (64.28%) in the same category. Conversely, in cases of two abortions, Oxytocin Monotherapy dominates (85.71%) compared to Oxytocin + Carbetocin (14.28%). The requirement for blood transfusions is evenly distributed, with Oxytocin Monotherapy at 47.36% and Oxytocin + Carbetocin at 52.63%. Overall, the table underscores nuances in patient characteristics and treatment preferences, offering valuable insights into the interplay between clinical factors and therapeutic decisions.

Comparison of Blood Loss

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Table 1. Patients Demographics.

Total number of patients (n=139)	**Oxytocin monotherapy (n=67)**	**Oxytocin + Carbetocin (n=72)**
Mean Age(years)	27.67± 4.28	27.63±4.23
Gravida status		
1 – 2(n=103)	50 (48.54%)	53 (51.45)
3 – 4(n=34)	16 (47.05%)	18 (52.94%)
≥4(n=2)	1 (50%)	1 (50%)
History of Abortion		
1(n-28)	10 (35.71%)	18 (64.28%)
2(n=7)	6 (85.71%)	1 (14.28%)

Blood transfusion(n=19)	9 (47.36%)	10 (52.63%)

Table 2. Comparison of blood loss between two treatment regimens.

Regimen	Blood loss ≤ 500 ml	Blood loss≥ 500 ml	Blood loss(ml) Mean ± SD	P value
Oxytocin Monotherapy (n=67)	23	44	421.94 ± 120.48	0.0003
Oxytocin + Carbetocin (n=72)	15	57	356.25 ± 116.89	

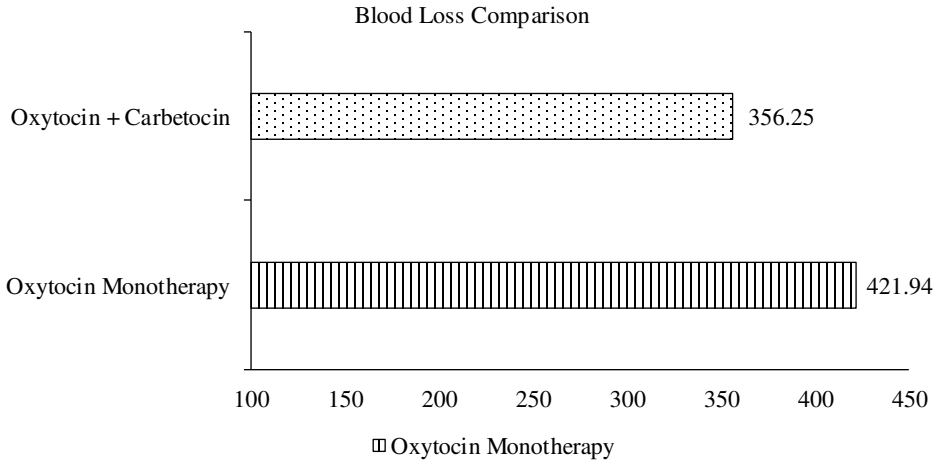

Figure 2. The following graph represents the comparison of blood loss between Oxytocin monotherapy and Oxytocin + Carbetocin and it suggests that the combination therapy has lower blood loss.

Comparison of Reduction in HCT Levels Following C-Section Delivery

The Table 4 presents a comparison between two drug regimens, Oxytocin Monotherapy and Oxytocin + Carbetocin, in terms of their impact on hematocrit (HCT) levels post-administration. In the Oxytocin Monotherapy group, the mean difference in HCT post-Oxytocin treatment is reported as 2.97 ± 1.98, while the Oxytocin + Carbetocin group reported a mean difference of 3.36 ± 2.29. The p value determined by z test is 0.27. It give the impression that there is no significant difference between the both the groups.

Comparing utilization pattern of Oxytocin monotherapy and Oxytocin + carbetocin on Co-existing conditions (PIH)

The Table 5 summarizes treatment regimens for patients with coexisting conditions such as PIH, along with complications like Eclampsia/Pre-eclampsia, history of LSCS, Fetal distress, and Induction failure. The data reveals that Oxytocin monotherapy was administered to 34.88% of patients with PIH, whereas Oxytocin + Carbetocin was utilized in 53.48% of patients with PIH and additional complications. This suggests that the combined regimen of Oxytocin + Carbetocin may be favoured in patients with multiple complications to mitigate further risks and potentially reduce the incidence of PPH.

Comparing of utilization pattern of Oxytocin monotherapy and Oxytocin + carbetocin on Co-existing conditions (Anemia)

The (Table 6) shows data about the patients HB before and after the delivery. The ratio of Oxytocin Monotherapy was found to be 1.48 while that of Oxytocin + carbetocin was 1.51. This suggest that there was no impact of this agents on reduction of Anemia.

Table 3. Hb Level Changes Post-Operative C-Section: A Comparative Analysis of Oxytocin Monotherapy and Oxytocin + Carbetocin.

Drug Groups	Hemoglobin (Hb)			
	Pre Hb (mean)	*Post Hb (mean)*	*Mean Difference in HB post OT*	*P value*

Oxytocin monotherapy (n=67)	11.76	10.62	1.14 ± 0.70	0.16
Oxytocin + Carbetocin (n=72)	11.75	10.43	1.31 ± 0.78	

Table 4. HCT Changes After C-Section: A Comparative Analysis Between Oxytocin Monotherapy and Oxytocin + Carbetocin.

Drug Groups	Pre HCT (mean)	Post HCT (mean)	Hematocrit (HCT)	
			The mean difference in HCT post-OT	*P value*
Oxytocin monotherapy (N=67)	37.48	34.38	2.97 ± 1.98	0.27
Oxytocin + Carbetocin (N=72)	37.14	33.77	3.36 ± 2.29	

Table 5. Administration of Oxytocin monotherapy and Oxytocin + Carbetocin groups in co-existing conditions (PIH).

Coexisting condition (n=139)	Oxytocin monotherapy n=67)	Oxytocin + Carbetocin (n=72)	P value
PIH(n=43)	15(34.88%)	23(53.48%)	0.206
Non PIH(n=96)	52(54.16%)	49(51.04%)	

Table 6. Administration of Oxytocin monotherapy and Oxytocin + Carbetocin in co-existing conditions (Anemia).

Coexisting condition (n=139)	Pre Hb < 12	Post Hb < 12	Ratio
Oxytocin monotherapy (n=67)	39	58	1.48
Oxytocin + Carbetocin (n=72)	41	62	1.51

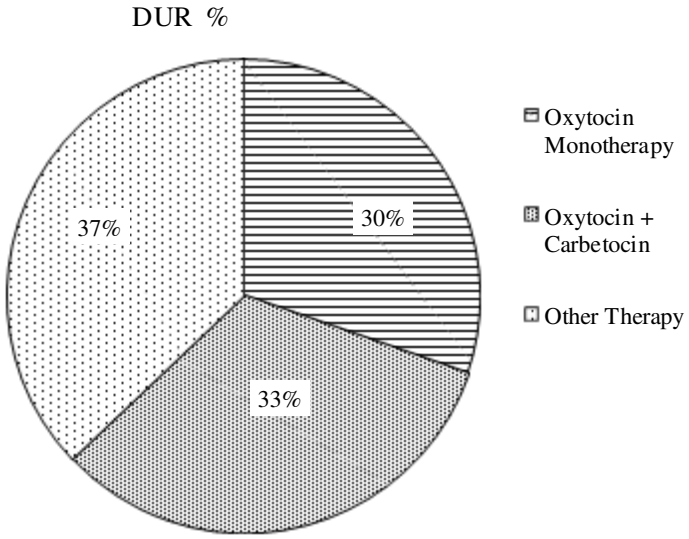

Figure 3. The pie chart shows DUR of the uterotonic drugs that are used for the prevention of PPH in C-section.

Table 7. Adverse effect profile observed in patient.

Adverse effect	Oxytocin Monotherapy (n=67)	Oxytocin + Carbetocin (n=72)
Vomiting	2 (2.98%)	3 (4.16%)
Nausea	1 (1.49%)	3 (4.16%)
Headache	1 (1.49%)	0 (0%)
Abdominal pain	0 (0%)	2 (2.77%)

Hypertension	2 (2.98%)	1 (1.38%)
Fever	0 (0%)	0 (0%)
Diarrhea	0 (0%)	0 (0%)
Shivering	0 (0%)	1 (0%)

DRUG UTILIZATION REVIEW OF UTEROTONIC AGENTS IN C-SECTION

A total of 221 patients were screened in this study. The following Pie chart Figure 3 shows that Oxytocin monotherapy was administered in 30% of patients, Oxytocin + Carbetocin was administered in 33% of patients while other therapies were administered in 37% of patients which included different uterotonic agents in combinations.

SAFETY PROFILE OUTCOMES

The outcomes associated with the therapy are listed in Table 7 . No major ADRs were observed in both the groups. The occurrences of anticipated adverse effects were meticulously documented, revealing incidences of nausea, vomiting, Abdominal pain etc. in the observed patient population. Nonetheless, statistical analysis indicated a lack of significant differentiation in the outcomes between the two study groups.

DISCUSSION

Postpartum hemorrhage, a perilous circumstance arising after childbirth, manifests as an alarming discharge exceeding 500 ml of blood within the initial 24 hours post-delivery [22]. This phenomenon stands as a prominent contributor to maternal health challenges and fatalities on a global scale. In our research, we assessed the efficacy of two treatment regimens by evaluating parameters such as blood loss, levels of hemoglobin (Hb) and hematocrit (HCT), and safety through monitoring potential side effects. The primary method for PPH is the administration of uterotonic agents during C-section. While oxytocin is traditionally used as the standard intervention due to its cost-effectiveness and well-established safety profile, there is emerging interest in the use of carbetocin, a faster-acting alternative, in conjunction with oxytocin to mitigate the risk of PPH..Also clinical studies propose that carbetocin matches oxytocin's efficacy in PPH prevention and may offer certain advantages related to ease of administration.

Regarding the demographic inforation, there were (n=139) patients in the study, divided into Oxytocin monotherapy (N=67) and Oxytocin + Carbetocin (N=72). The research participant's ages between 20 to 41 years old, with a mean age of 27.6 ± 4.2. The patient's typical ages were the equivalent. The gravida status of the patients presented with CS ranges from 1 to 5. There were 103 patients with a gravida status of 1 to 2, and of them, 48.54% of them received oxytocin monotherapy and 51.45% received oxytocin + carbetocin. Also a total of 34 patients were present in gravida status 3 - 4. Among them oxytocin + carbetocin (52.94%) was again given slightly higher than the oxytocin monotherapy (47.05%). The patients with the first abortion received more of the oxytocin + carbetocin regimen, but the patients with the second abortion received more oxytocin monotherapy. A total of 19 patients had blood transfusions, and there was no difference in the requirement of blood transfusion in both the treatment groups.

C-section significantly increases the risk of PPH, a serious complication associated with childbirth [25]. Utilizing uterotonic medications prophylactically can effectively decrease the average amount of blood loss during delivery, consequently diminishing the incidence of maternal morbidity and mortality [26]. In this present study the mean blood loss of both the treatment groups was determined and revealed that there was significant difference. The mean blood loss in patients with Oxytocin monotherapy was 421.94 ± 120.48 and that of oxytocin + carbetocin was 356.25±116.89. The P value (p=0.003) was determined by using z test. Thus, the patients has lower blood loss when they were administered oxytocin + carbetocin combination. A study titled "Efficacy of carbetocin vs oxytocin and methergine

in prevention of PPH after CS" conducted by Esseissah et al found out that mean blood loss was very less in carbetocin group and it was statistically significant [27]. In another study led by Voon et al, it was determined that the administration of Carbetocin during cesarean deliveries effectively reduces the need for additional uterotonics, as well as decreases the incidence of postpartum hemorrhage and the requirement for transfusions [28]. Moreover, various prior research has indicated that carbetocin effectively decreases blood loss and lowers the incidence of postpartum hemorrhage during cesarean section when compared to oxytocin [29] [21].

The fall in Hb level following CS between two regimens was found to be (1.14 ± 0.70 vs 1.31 ± 0.78) and it was observed that there was no significant difference and that infers both the groups has no effect on Hb level ($p>0.05$). The mean difference in HCT ((2.97 ± 1.98 vs 3.36 ± 2.29) was calculated to determine the fall in HCT levels. It was experiential that there was no significant difference concerning the fall of HCT levels ($p>0.05$). A study conducted by larciprete et al determined the same results as that there was no significant difference in HB and HCT in both the oxytocin and carbetocin groups (15). Another research conducted by Maged et al among expectant mothers with two or more risk factors for postpartum hemorrhage found that carbetocin outperformed oxytocin in terms of reducing postpartum blood loss, impacting haemoglobin levels, and decreasing the necessity for uterine massage following vaginal delivery. However our study did find some significant difference in blood but there were no similar results regarding HB and HCT.

This research also laminated the participants constructed on the presence or absence of Pregnancy-Induced Hypertension (PIH). Our study also considered pre-existing conditions in both study cohorts. Among the total subjects (n=139), a subset of participants had PIH (n=43). Specifically, within this PIH subgroup, 34.88% (n=15) received Oxytocin monotherapy, while 53.48% (n=23) received a combination of Oxytocin + Carbetocin. However, the difference in the distribution of these two treatment groups among individuals with PIH was not found to be statistically significant (P value = 0.206). This indicates that there was no significant variation in treatment allocation based on the presence of PIH in our study population. But on the basis of the findings the combination therapy can be given to complicated patients to reduce the chances of PPH.

Similarly in (Table 6), it shows the effect of the oxytocin monotherapy and combination of Oxytocin + Carbetocin on Anemia. There was no significant effect highlighted in both the groups as they had no impact on reduction on Anemia.

The Table 4 compares adverse effects between Oxytocin Monotherapy (n=67) and Oxytocin + Carbetocin (n=72). Both groups exhibit generally low incidence of adverse events. Oxytocin Monotherapy reports slightly lower rates of nausea and vomiting, with one case each of headache and hypertension. In contrast, Oxytocin + Carbetocin has a higher incidence of abdominal pain but shows no cases of headache. Both groups have no reported cases of fever, diarrhoea, or shivering. Overall, the differences in adverse effects between the two treatments are relatively modest, emphasizing their safety profiles. A study by Jin et al's suggested that carbetocin is equally effective and safe compared to oxytocin in preventing postpartum hemorrhage among women undergoing vaginal delivery [30].

In summary, this comprehensive investigation into the comparative effectiveness of oxytocin monotherapy and oxytocin + carbetocin in preventing PPH reveals nuanced demographic and clinical considerations. The study provides valuable insights into the nuanced distribution of treatments based on gravida status, abortions, and pre-existing conditions. The observed reduction in mean blood loss with oxytocin + carbetocin reinforces the potential benefits of this combination. However, the study emphasizes the need for further research to elucidate optimal treatment strategies in specific clinical contexts, contributing to the evolving landscape of PPH prevention

CONCLUSION

Based on the data presented in the study, the main goal is to compare the effectiveness of both the treatment groups in CS for the prevention of PPH. The study analyzed various parameters such as demographic information, mean blood loss, fall in Hb level, fall in HCT level and administration of these agents in co-existing conditions. The data suggested that Oxytocin + carbetocin was given slightly higher irrespective of gravida and abortion status. There was a significant difference in the amount blood loss as the oxytocin + carbetocin resulted in reduced blood loss. However both the groups had no impact on the Hb and HCT levels before and after the surgery. Also the use of combination agents was more in pre-existing conditions like PIH and Anemia. Thus it was observed that adding carbetocin resulted in reduction of blood loss and hence prevent PPH but it has no effect on Hb and HCT.

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Contributions

MAM - Manuscript first draft preparation and subsequent editing, Literature and data survey, Figures and diagram designing, Manuscript draft review and editing, Referencing. Table construction. VJM - Topic conception, Design of content and skeleton, Reviewed Manuscript first and subsequent draft; Figures and Tables conception.

Ethical declarations

- Competing interests:
- The Authors declare no competing interest.
- Ethical approval and consent to participate:
- This study was approved by institutional ethics committee (IEC) GCS medical college hospital and research centre and IEC L.M college of Pharmacy.

REFERENCES

1. Khan KS, Wojdyla D, Say L, Gülmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. Lancet (London, England). 2006;367(9516):1066-74.
2. Bazirete O, Nzayirambaho M, Umubyeyi A, Karangwa I, Evans M. Risk factors for postpartum haemorrhage in the Northern Province of Rwanda: A case control study. PloS one. 2022;17(2):e0263731.
3. Rogers J, Wood J, McCandlish R, Ayers S, Truesdale A, Elbourne D. Active versus expectant management of third stage of labour: the Hinchingbrooke randomised controlled trial. Lancet (London, England). 1998;351(9104):693-9.
4. Oyelese Y, Ananth CV. Postpartum hemorrhage: epidemiology, risk factors, and causes. Clinical obstetrics and gynecology. 2010;53(1):147-56.
5. Stones RW, Paterson CM, Saunders NJ. Risk factors for major obstetric haemorrhage. European journal of obstetrics, gynecology, and reproductive biology. 1993;48(1):15-8.
6. Weeks AD, Mirembe FM. The retained placenta-new insights into an old problem. European journal of obstetrics, gynecology, and reproductive biology. 2002;102(2):109-10.
7. Silver RM, Major H. Maternal coagulation disorders and postpartum hemorrhage. Clinical obstetrics and gynecology. 2010;53(1):252-64.
8. Mousa HA, Blum J, Abou El Senoun G, Shakur H, Alfirevic Z. Treatment for primary postpartum haemorrhage. The Cochrane database of systematic reviews. 2014;2014(2):Cd003249.

9. Miller S, Fathalla MMF, Youssif MM, Turan J, Camlin C, Al-Hussaini TK, et al. A comparative study of the non-pneumatic anti-shock garment for the treatment of obstetric hemorrhage in Egypt. 2010;109(1):20-4.
10. Maughan KL, Heim SW, Galazka SS. Preventing postpartum hemorrhage: managing the third stage of labor. American family physician. 2006;73(6):1025-8.
11. Salati JA, Leathersich SJ, Williams MJ, Cuthbert A, Tolosa JE. Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage. The Cochrane database of systematic reviews. 2019;4(4):Cd001808.
12. Hofmeyr GJ, Mshweshwe NT, Gülmezoglu AM. Controlled cord traction for the third stage of labour. The Cochrane database of systematic reviews. 2015;1(1):Cd008020.
13. Vogel JP, Williams M, Gallos I, Althabe F, Oladapo OT. WHO recommendations on uterotonics for postpartum haemorrhage prevention: what works, and which one? BMJ global health. 2019;4(2):e001466.
14. Kota SK, Gayatri K, Jammula S, Kota SK, Krishna SV, Meher LK, et al. Endocrinology of parturition. Indian journal of endocrinology and metabolism. 2013;17(1):50-9.
15. Larciprete G, Montagnoli C, Frigo M, Panetta V, Todde C, Zuppani B, et al. Carbetocin versus oxytocin in caesarean section with high risk of post-partum haemorrhage. Journal of prenatal medicine. 2013;7(1):12-8.
16. Jones AJ, Federspiel JJ, Eke AC. Preventing postpartum hemorrhage with combined therapy rather than oxytocin alone. American journal of obstetrics & gynecology MFM. 2023;5(2s):100731.
17. Fernando D, Siederer S, Singh S, Schneider I, Gupta A, Powell M, et al. Safety, Tolerability and Pharmacokinetics of Single Doses of Oxytocin Administered via an Inhaled Route in Healthy Females: Randomized, Single-blind, Phase 1 Study. EBioMedicine. 2017;22:249-55.
18. Diop A, Daff B, Sow M, Blum J, Diagne M, Sloan NL, et al. Oxytocin via Uniject (a prefilled single-use injection) versus oral misoprostol for prevention of postpartum haemorrhage at the community level: a cluster-randomised controlled trial. The Lancet Global health. 2016;4(1):e37-44.
19. Pileggi-Castro C, Nogueira-Pileggi V, Tunçalp Ö, Oladapo OT, Vogel JP, Souza JP. Non-pneumatic anti-shock garment for improving maternal survival following severe postpartum haemorrhage: a systematic review. Reproductive health. 2015;12:28.
20. Attilakos G, Psaroudakis D, Ash J, Buchanan R, Winter C, Donald F, et al. Carbetocin versus oxytocin for the prevention of postpartum haemorrhage following caesarean section: the results of a double-blind randomised trial. BJOG : an international journal of obstetrics and gynaecology. 2010;117(8):929-36.
21. Borruto F, Treisser A, Comparetto C. Utilization of carbetocin for prevention of postpartum hemorrhage after cesarean section: a randomized clinical trial. Archives of gynecology and obstetrics. 2009;280(5):707-12.
22. Wormer KC, Jamil RT, Bryant SB. Acute Postpartum Hemorrhage. StatPearls. Treasure Island (FL) ineligible companies. Disclosure: Radia Jamil declares no relevant financial relationships with ineligible companies. Disclosure: Suzanne Bryant declares no relevant financial relationships with ineligible companies.: StatPearls Publishing Copyright © 2024, StatPearls Publishing LLC.; 2024.
23. Angolile CM, Max BL, Mushemba J, Mashauri HL. Global increased cesarean section rates and public health implications: A call to action. Health science reports. 2023;6(5):e1274.
24. Cegolon L, Mastrangelo G, Maso G, Dal Pozzo G, Ronfani L, Cegolon A, et al. Understanding Factors Leading to Primary Cesarean Section and Vaginal Birth After Cesarean Delivery in the Friuli-Venezia Giulia Region (North-Eastern Italy), 2005-2015. Scientific reports. 2020;10(1):380.
25. Alkema L, Chou D, Hogan D, Zhang S, Moller AB, Gemmill A, et al. Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group. Lancet (London, England). 2016;387(10017):462-74.

26. Mannaerts D, Van der Veeken L, Coppejans H, Jacquemyn Y. Adverse Effects of Carbetocin versus Oxytocin in the Prevention of Postpartum Haemorrhage after Caesarean Section: A Randomized Controlled Trial. Journal of pregnancy. 2018;2018:1374150.
27. Esseissah SA, Mohamed HI, Elnoury MA, Ali AN. Efficacy of Carbetocin versus Oxytocin and Ergometrin in Prevention of Postpartum Hemorrhage after Cesarean Section %J Benha Journal of Applied Sciences. 2022;7(1):109-15.
28. Voon HY, Suharjono HN, Shafie AA, Bujang MA. Carbetocin versus oxytocin for the prevention of postpartum hemorrhage: A meta-analysis of randomized controlled trials in cesarean deliveries. Taiwanese Journal of Obstetrics and Gynecology. 2018;57(3):332-9.
29. El Behery MM, El Sayed GA, El Hameed AA, Soliman BS, Abdelsalam WA, Bahaa A. Carbetocin versus oxytocin for prevention of postpartum hemorrhage in obese nulliparous women undergoing emergency cesarean delivery. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet. 2016;29(8):1257-60.
30. Jin XH, Li D, Li X. Carbetocin vs oxytocin for prevention of postpartum hemorrhage after vaginal delivery: A meta-analysis. Medicine. 2019;98(47):e17911.

