ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Comparative Study Of Room Temperature Stable Carbetocin Versus Oxytocin For The Prevention Of PPH In Caesarean Section.

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ABSTRACT

PPH is one of the leading causes of maternal mortality and morbidity globally, particularly among low and middle-income countries. FIGO and WHO encourage the use of heat-stable Carbetocin in resource-challenged and warm climate settings. All other injectable uterotonics require cold transport and storage at 2-8 °C. Heat-stable Carbetocin overcomes the challenges of fragile cold chain infrastructure in struggling health systems by minor modifications of the Oxytocin peptide structure. Comparative study between Carbetocin and Oxytocin. 100 antenatal patients who are at high risk of developing Postpartum Hemorrhage. Heat-stable Carbetocin is found to be superior to Oxytocin for the prevention of Postpartum Haemorrhage, with the advantage of single intravenous administration. Carbetocin was more hemodynamically stable than oxytocin. The volume of blood loss was significantly more in the Oxytocin group than in the Carbetocin group. The mean decrease in hemoglobin levels was also similar between carbetocin and oxytocin. The proportion of contracted uterus was higher in the Carbetocin group than in the Oxytocin group. Carbetocin was either comparable to or advantageous over Oxytocin concerning all the parameters studied.

Keywords: Heat-stable carbetocin, oxytocin, postpartum haemorrhage

https://doi.org/10.33887/rjpbcs/2025.16.3.15

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INTRODUCTION

Postpartum Hemorrhage is defined as the cumulative blood loss of greater than or equal to 1000 ml or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours after the birth process, regardless of route of delivery [1]. PPH, one of the leading causes of maternal deaths in low-income countries, is the main cause of almost one-fourth of deaths worldwide. Uterine atony is its principal cause, responsible for nearly 70% of the cases. In active management of the third stage of labor, routine uterotonics are administered following the separation of the placenta [2]. The first choice as a uterotonic is intravenous Oxytocin. Oxytocin has a half-life of 3 minutes and requires a maintenance dose. Metabolized by renal and hepatic routes. The main indication for which Carbetocin has been proposed is Cesarean delivery, because this mode of delivery is associated with a higher prevalence of severe PPH and requires invasive second line therapies three times more often than vaginal delivery [3]. Quantification of blood loss in cases of Cesarean deliveries is always difficult, due to the incomplete collection of losses, the mixing of amniotic fluid with maternal blood, etc. To identify women who had PPH after a Cesarean delivery, the last hemoglobin concentration measured before the delivery, and the hemoglobin concentration on postoperative day one and three. PPH is defined as a decline in hemoglobin concentration of more than 2 g/dl and severe PPH by a reduction in hemoglobin of more than 4 g/dl [4]. Carbetocin, a synthetic Oxytocin analogue with a half-life of 40 minutes, provides better efficacy and a greater ease of use. After administration of Carbetocin, uterine contractions start rapidly, and a full contraction is achieved within 2 minutes [5]. The study aims to compare the hemodynamic effects of Oxytocin and Carbetocin, also to evaluate in terms of changes in hemoglobin level, hematocrit level, blood transfusion requirement, hospital stay, and need for Peripartum Hysterectomy.

MATERIALS AND METHODS

This study was conducted in the Department of Obstetrics and Gynaecology, Government Medical College and Hospital, Cuddalore District, Annamalai Nagar, Chidambaram, Tamil Nadu, India, in the year January 2023 to Jan 2024. A written informed consent was obtained from every parturient. Subjects were allocated in two groups:

Group A: Comprising 50 antenatal patients who received Carbetocin 100 mcg single intravenous injection.

Group B: comprising 50 antenatal patients who received an Oxytocin 10 units Intramuscular injection.

Inclusion Criteria: Patients undergoing caesarean section who are at higher risk for postpartum hemorrhage, such as: multiple pregnancy, two or more previous Caesarean sections, presence of uterine fibroids, previous myomectomy, presence of placenta Previa, history of PPH, fetal macrosomia, and fetal malformations associated with polyhydramnios, and previous LSCS.

Exclusion Criteria: Women with a history of hypersensitivity to Carbetocin, history of pre-eclampsia, hypertension, cardiac, renal, and liver diseases.

The primary outcome of this study was the evaluation of the early hemodynamic effects of Carbetocin and Oxytocin, in terms of impact on the blood pressure (BP) immediately after the injection. All the patients had spinal anaesthesia. After anaesthesia, subjects were positioned in the recumbent position, and for continuous blood pressure measurement, a limb cuff was applied. To evaluate the haemodynamic effects between Carbetocin and Oxytocin, we considered the drop in blood pressure comparing the BP after Spinal Anaesthesia, 1 minute, 3 minutes, and 5 minutes after drug administration, at the time of uterine closure, and the end of Caesarean procedure, in left recumbent position. The occurrence of nausea, vomiting, flushing, headache, dyspnea, tachycardia, volume of blood loss, and need for blood transfusion were recorded. Primary outcome, including uterine tone, was assessed by using a hand resting on the fundus and palpating the anterior wall of the uterus. The presence of a boggy uterus with either heavy vaginal bleeding or increasing uterine height can suspect the diagnosis of uterine atony. Also, the need for additional oxytocic drugs in each group population was reported and tabulated as a primary outcome. The 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 the 24-hour postoperative hospital stay and recording the weight of blood-soaked dressings and volume of lost blood.

ISSN: 0975-8585

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 / 1.06 Where (1.06) is the density of whole blood.

RESULTS

Table 1: Change in mean diastolic blood pressure between the groups over time.

Time line	Group A (n=50)		Group B (n=50)		T value	P value
	Mean	SD	Mean	SD		
1 min	76	5.34	72.60	5.64	3.09	0.003
3 mins	71.40	4.95	69	5.05	2.39	0.018
5 mins	70.40	4.93	68.40	5.48	1.91	0.058

*Between-subject effects P value 0.005.

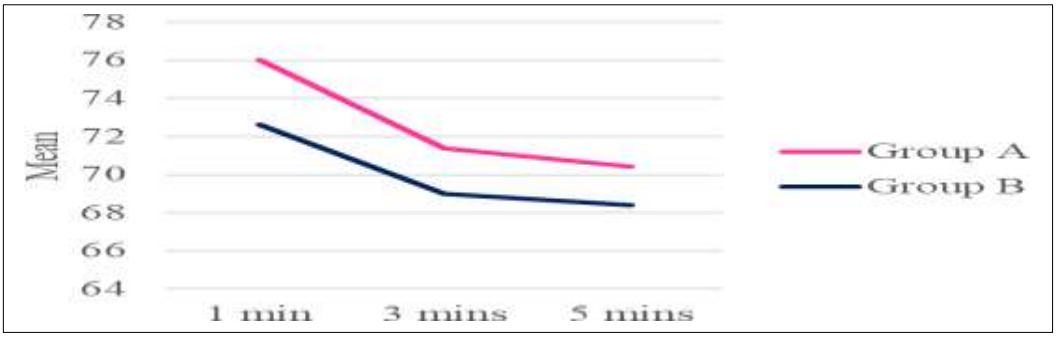


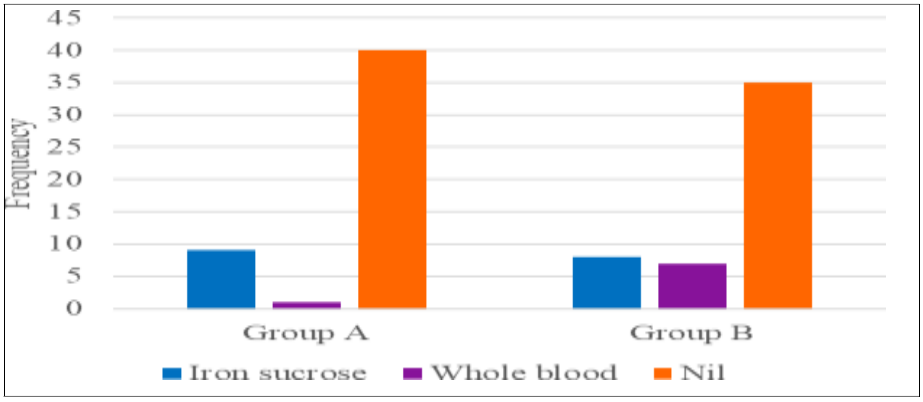
Figure 1: Line diagram showing change in mean diastolic BP between the groups.

The mean diastolic blood pressure among the participants in group A at 1 minute was 76±5.34 mmHg, and for group B it was 72.60±5.64 mmHg. The mean diastolic BP decreased in both groups. At 1 minute and 3 minutes, the diastolic BP was higher in group A than in group B (P value < 0.05), and both groups had similar BP at 5 minutes (P value > 0.05).

Table 2: Distribution according to blood transfusion between the groups.

Blood transfusion	Group A (n=50)		Group B (n=50)		χ^2	P value
	N	%	N	%		
Iron sucrose	9	18	8	16	4.89	0.087
Whole blood	1	2	7	14		
Nil	40	80	35	70		

Figure 2: Bar chart showing the distribution of receipt of blood transfusion between the groups



Among the participants in group A, 18% had received iron sucrose and 2% had received whole blood, while for those in group B, 16% had received iron sucrose and 14% had received whole blood. The proportion was similar in both groups, with a P value of more than 0.05.

Table 3: Distribution according to volume of blood loss between the groups.

Volume of blood loss	Group A (n=50)		Group B (n=50)		χ^2	P value
	N	%	N	%		
Normal limits	50	100	38	76	13.63	0.001
Little excess	0	0	7	14		
Excess	0	0	5	10		

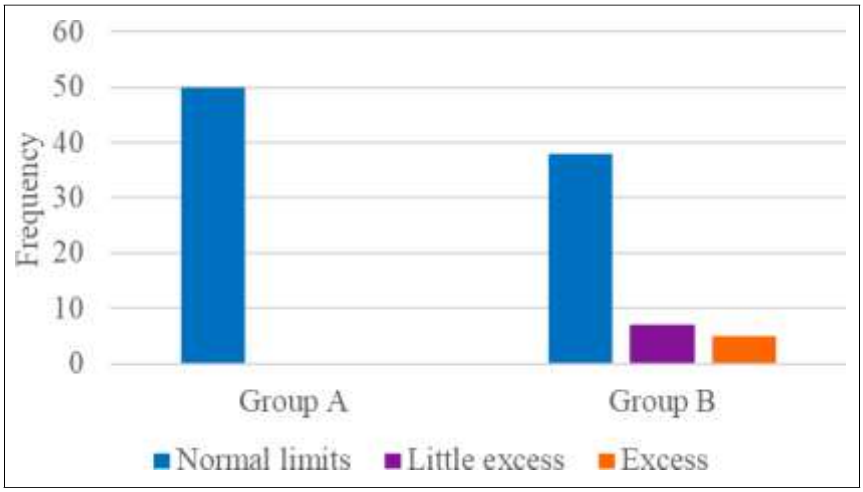


Figure 3: Bar chart showing distribution according to volume of blood loss between the groups.

Among the participants in group A, everyone had a normal limit of blood loss. Among those in group B, 76% had a normal limit, 14% had a little excess, and 10% had an excess limit of blood loss. The volume of blood loss was significantly more in group B than in group A, with a P value of less than 0.05.

Table 4: Change in mean hemoglobin between the groups over time.

Time line	Group A (n=50)		Group B (n=50)		T value	P value
	Mean	SD	Mean	SD		
Preoperative	11.07	0.81	11.43	0.97	1.96	0.051
Postoperative	10.22	0.88	10.46	1.18	1.14	0.255

*Between-subject effects P value 0.112.

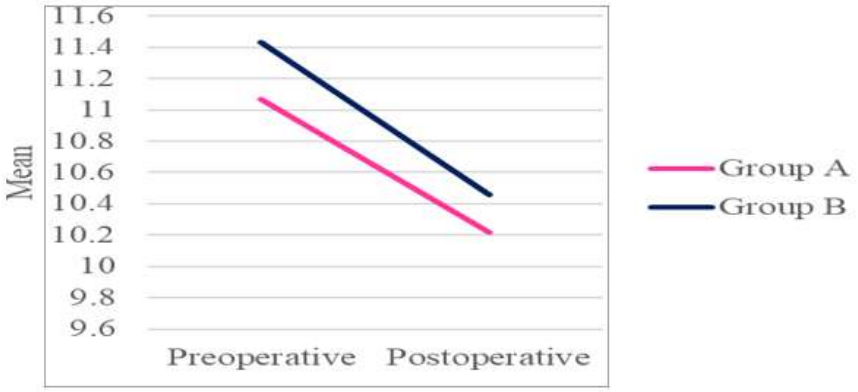


Figure 4: Line diagram showing change in mean haemoglobin levels between the groups.

The mean preoperative hemoglobin levels among the participants in group A and group B were 11.07±0.81 g/dL % and11.43±0.97 g/dL %, respectively. The mean postoperative haemoglobin levels for group A were 10.22±0.88 g/dL % and for group B, it was 10.46±1.18 g/dL. The mean haemoglobin decreased in both groups, but the decrease was not statistically significant, with a P value of more than 0.05.

DISCUSSIONS

Obstetric Hemorrhage is the most common and dangerous complication of childbirth. Traditionally, Postpartum Haemorrhage (PPH) has been defined as greater than 500 mL estimated blood loss in a vaginal delivery as or greater than 1000 mL estimated blood loss at the time of Caesarean delivery. This was redefined in 2017 by the American College of Obstetrics and Gynecology as a cumulative blood loss greater than 1000 mL with signs and symptoms of hypovolemia within 24 hours of the birth process, regardless of the route of delivery. If the blood loss is more than 1000 ml, then it indicates severe postpartum haemorrhage [1]. Globally, PPH is responsible for 25% of all the maternal deaths [2]. It was estimated that each year, 14 million PPH cases occur globally, and 127 thousand die due to the same. About 50% of the deaths occur in Africa and Asia alone [3]. The standard practice of preventing PPH involves administering uterotonics. The most commonly used uterotonic agent is Oxytocin. The problem with Oxytocin is that it requires cold storage and transport to preserve its quality. Cold chains are not very common in a resource-limited setting. In order to overcome the disadvantages of Oxytocin, the alternative option will be the heat-stable Carbetocin. Since it is heat stable, there is no need for cold storage or transport [4]. The present study was a comparative study carried out among pregnant women who were at higher risk of Postpartum Haemorrhage attending the inpatient department of Government Medical College, CuddaloreTamil Nadu. Ethical clearance for the study was obtained from the institutional ethical committee, and informed consent was obtained from all the participants included in the study. A total of 100 patients were included in the study. 50 patients had received room temperature stable Carbetocin, and 50 patients had received Oxytocin. In the present study, mean systolic blood pressure remained statistically higher in the Carbetocin group in comparison to the Oxytocin group at 3 and 5 minutes, respectively. The same pattern was observed with the diastolic blood pressure, too. Shakar RA *et al*. reported a similar pattern with regard to blood pressure changes following the administration of Carbetocin and Oxytocin. The study found that the magnitude of decrease in blood pressure (both systolic and diastolic) was more following the administration of Oxytocin when compared to that of Carbetocin. Zubaidi SA and Alhaidari T, in their study, documented the change in blood pressure to be minimal in the Carbetocin group than in the Oxytocin group. The finding was similar to the present study [6]. Vinayaka J *et al*. (2023) reported Carbetocin to be a more haemodynamically stable drug than that of the Liu H *et al*. in contrast to the present study reported lower blood pressure in the Carbetocin group than in the Oxytocin group 30 minutes into the postpartum period but the study was conducted in a different population than the present study [8]. The number of blood transfusions between the Carbetocin and Oxytocin groups was statistically similar in the present study. Al Zubaidi S and Alhaidari T found Carbetocin to be non-inferior to Oxytocin concerning the proportion of participants receiving blood transfusion [7]. Huang X *et al*. (2022) reported in their meta-analysis that there is no difference in the proportion of women receiving blood transfusion between the Carbetocin group and the Oxytocin group [12]. The number of participants requiring blood transfusion was comparable between those who had received Carbetocin or Oxytocin. In the present study, all the participants who had received Carbetocin as intervention had blood loss within normal limits, while among those who had received oxytocin, 76% had blood loss within normal limits, 14% had little excess blood loss, and 10% had excess blood loss. Sun *et al*. (2022) in a systematic review reported that the volume of blood loss was significantly lowered when Carbetocin was used in place of Oxytocin. The observation made was similar to the observation in the present study [10]. Gursoy A *et al*. (2021) also reported similar results of diminished blood loss volume in the Carbetocin group than the Oxytocin one [12]. Similar results were also reported by Asraf *et al*. (2021) [13]. The blood loss was greater among t h e Oxytocin group than in the Carbetocin group. The changes in the mean haemoglobin level were similar between the Oxytocin and the Carbetocin groups in the present study. Onwochei DN *et al*. had reported that the need for additional uterotonics was greatly reduced with the utilisation of Carbetocin rather than Oxytocin [14]. Jacob D recommended that the utilisation of Carbetocin will bring in a reduction of PPH incidence alongside reducing the requirement of additional uterotonics [15]. Matthijsse S *et al*. (2021) reported that Carbetocin not only reduces the PPH incidence but also brings down the prophylactic treatment costs relative to oxytocin [16].

Limitations

The present study was a single-centre study. A multi-center study will provide a more valid result. Blood loss was measured as a qualitative variable in the present study. Measuring it quantitatively would have resulted in a better comparison. The generalization of the results has to be done with caution. The study failed to address the occurrence of severe PPH. Focusing on severe PPH would have been more informative.

CONCLUSION

Carbetocin was more hemodynamically stable than oxytocin. The volume of blood loss was significantly more in the Oxytocin group than in the Carbetocin group. The side effects profile was comparable between carbetocin and oxytocin, and so was the proportion of blood transfusions required. The mean decrease in haemoglobin levels was also similar between carbetocin and oxytocin. The proportion of contracted uterus was higher in the carbetocin group than in the oxytocin group. Carbetocin was either comparable to or advantageous over oxytocin concerning all the parameters studied.

REFERENCES

[1] Gulmezoglu AM, editor. WHO guidelines for the management of postpartum haemorrhage and retained placenta. World Health Organization; c2009.

[2] Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, *et al.* Global causes of maternal death: A WHO systematic analysis. The Lancet Global Health. 2014 Jun 1;2(6):e323-e333.

[3] Hogan MC, Foreman KJ, Naghavi M, Ahn SY, Wang M, Makela SM, *et al.* The Lancet. 2010 May 8;375(9726):1609-1623.

[4] Gallos ID, Coomarasamy A. Carbetocin: worth the extra expense?. Best Practice & Research Clinical Obstetrics & Gynaecology. 2019 Nov 1;61:55-65.

[5] Arunshankar R, Nevathitha DV, Maheswari P. Comparison of Effects of Carbetocin and Oxytocin In Caesarean Section. International Journal of Academic Medicine and Pharmacy. 2023;5(4):1628-33.

[6] Al Zubaidi S, Alhaidari T. Heat stable carbetocin vs. oxytocin for the prevention of post-partum haemorrhage in emergency caesarean delivery: A randomized controlled trial. Journal of Perinatal Medicine. 2022 Feb 23;50(2):150- 6.

[7] Jannu V, Hanagandi MP, Kalal R, Sabari CG. Comparison of haemodynamic effects of intravenous carbetocin and oxytocin during caesarean section under subarachnoid block. Journal of Obstetric Anaesthesia and Critical Care. 2023 Jul 1;13(2):193-197.

[8] Liu H, Xu XY, Gu N, Ye XD, Wang ZQ, Hu YL, *et al.* Intravenous administration of carbetocin versus oxytocin for preventing postpartum haemorrhage after vaginal delivery in high risk women: a double-blind, randomized controlled trial. Maternal-Fetal Medicine. 2020 Apr 1;2(02):72-79.

[9] McDonagh F, Carvalho JC, Abdulla S, Cordovani D, Downey K, Ye XY, *et al.* Carbetocin vs. oxytocin at elective caesarean delivery: A double-blind, randomised, controlled, non-inferiority trial of low- and high-dose regimens. *Anaesthesia*. 2022 Aug;77(8):892-900.

[10] Sun H, Xu L, Li Y, Zhao S. Effectiveness and safety of carboxytocin versus oxytocin in preventing postpartum haemorrhage: A systematic review and meta-analysis. Journal of Obstetrics and Gynaecology Research. 2022 Apr;48(4):889-901.

[11] Ai W, Zeng Y, Ma Y, Liu L, Fan D, Wu S, *et al.* Side-effects of carbetocin to prevent postpartum haemorrhage: A systematic review and meta-analysis of randomized controlled trials. Pharmacology Research & Perspectives. 2021 Apr;9(2):e00745.

[12] Gursoy A, Ilter E, Celik A, Peker Bh, Serifsoy Te, Atasayan K, *et al.* Carbetocin Versus Oxytocin for Prevention of Postpartum Haemorrhage in Caesarean Section. Journal of Clinical Obstetrics & Gynaecology. 2021 Jan 1;31(1):20-27.

[13] Ashraf F, Akther P, Yasmin N, Islam JA, Akther M, Rahman R, *et al.* Carbetocin versus Oxytocin in Active Management of 3rd stage of Labour following Vaginal Delivery. Bioresearch Communications. 2021;7(1):927-931.

[14] Onwochei DN, Owolabi A, Singh PM, Monks DT. Carbetocin compared with oxytocin in nonelective caesarean delivery: A systematic review, meta-analysis, and trial sequential analysis of randomized-controlled trials. Obstetric Anaesthesia Digest. 2021 Sep 25;41(3):111-112.

[15] Jacob D. Carbetocin vs oxytocin in third stage labour: A quantitative review of low-and middle-income countries. British Journal of Midwifery. 2023 Nov 2;31(11):634-639.

[16] Matthijsse S, Andersson FL, Gargano M, Yip Sonderegger YL. Journal of Medical Economics. 2022 Dec 31;25(1):129-37.