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Original Research Article

A COMPARATIVE STUDY OF CARBETOCIN WITH OXYTOCIN IN THE PREVENTION OF POSTPARTUM HEMORRHAGE IN CAESAREAN SECTION

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Abstract

Background: Postpartum Hemorrhage (PPH) remains the leading cause of maternal mortality worldwide, particularly in India, where it accounts for 38% of maternal deaths. Effective management of PPH, especially during cesarean sections, is crucial in reducing maternal mortality. This study aimed to compare the efficacy of Injection Carbetocin against Injection Oxytocin in preventing PPH during elective cesarean sections at Government General Hospital Mahabubnagar, a tertiary care hospital in Telangana state of South India. **Materials and Methods:** Study designed as compative study between two groups of 100 pregnant women who are undergoing elective cesarean sections at tertiary care hospital over a 6 months of period. Pregnant women are divided equally into two groups: one receiving Carbetocin and the other group receiving Oxytocin. We have observed the parameters of Blood loss, Blood pressure , SpO2 levels, and adverse effects were monitored and analyzed using SPSS version 16, and results are statistical significant with p value less than 0.05. **Result:** Blood loss was significantly lower in the Carbetocin group, as indicated by the weight of surgical mops (p = 0.03). Carbetocin was found to maintain systolic and diastolic blood pressure more effectively compared to Oxytocin, with statistically significant differences noted at multiple time points post-operative period. Adverse effects were minimal and comparable between the two groups. **Conclusion:** Carbetocin demonstrated greater efficacy in preventing PPH in high-risk women undergoing cesarean sections, primarily by maintaining hemodynamic stability, reducing blood loss, and requiring only a single dose administration. These findings support the use of Carbetocin as a superior alternative to Oxytocin for the prevention of PPH in this setting.

INTRODUCTION

Postpartum Hemorrhage (PPH) - is the leading cause of maternal mortality world-wide. Each year, about 14 million women experience PPH resulting in about 70,000 maternal deaths globally. This accounts for 20% of the global maternal deaths annually.[1] The SDG goal 3 Target 3.1 calls for the reduction in the Maternal Mortality Rate to less than 70 per 100 000 live births.[2] In India PPH is the most common cause of Maternal Mortality and accounts for 38% of all deaths. The current MMR for India is 97 per 1 lakh live birth which declined from 103 in 2016-2018. But only 8 states are able to achieve the SDG -3 target for MMR.[3] Thus controlling PPH will definitely help in reducing maternal mortality to achieve global standards pan India.

Uterine Atony is the most common cause of hemorrhagic blood loss during delivery. It is recommended to systematically use uterotonic drugs immediately after delivering the newborn for prevention of PPH.[4] In many of the Cochrane studies Oxytocin has shown to reduce blood loss , but the need for additional uterotonic drug along with oxytocin remains inevitable for management of PPH. Oxytocin binds the myometrial oxytocin receptors to stimulate uterine smooth muscle contraction. It has a fast onset but is of short duration and a maintenance

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infusion in the immediate perioperative period is recommended.[5]

Recently some of the studies have shown that administration of carbetocin is a good alternative to oxytocin for preventing post-partum hemorrhage [6]. Some of the advantages carbetocin over Oxytocin namely are

1. Half life for cabetocin (40min) is 10 folds higher than oxytocin (4-10min).
2. Duration of action of carbetocin is longer than intravenous and intramuscular use of oxytocin (it was found that a single intravenous bolus injection of carbetocin was at least as effective as 16 hrs of continuous oxytocin infusion.
3. There is no need of repeated administration of drug in the case of Carbetocin.
4. No dose variation /single dose of carbetocin is found to be effective in controlling PPH, unlike oxytocin.
5. Carbetocin is heat stable when compared with the Oxytocin.

However in some of the studies carbetocin and oxytocin showed similar outcomes. Thus we are having mixed opinion regarding the effectiveness of carbetocin over Oxytocin.

So to explore the effectiveness of carbetocin against Oxytocin in preventing Post Partum hemorrhage we have carried out this intervention study in our tertiary care hospital.

MATERIALS AND METHODS

The present study is a comparative study conducted from October 2023 to March 2024 within the Department of Obstetrics and Gynecology at Government Medical College in Mahabubnagar. The local ethical committee of the Government Medical College given approval for this study protocol. Informed consent was obtained from all the study participants before commencing the study. The study was conducted among 100 pregnant women who are undergoing elective cesarean section.

Study Design: Prospective comparative study (1:1 ratio).[8]

Inclusion Factor: Patients who undergoing elective caesarean section and given consent for this study.

Exclusion criteria: Pregnancy Induced Hypertension, Emergency caesarean section, Patient who are on tablet Aspirin/Anti Coagulants in antenatal period, All High-risk pregnancies -Twins, Polyhydramnios, Diabettis Mellitus and Placenta Previa. Cardiac diseases, Renal diseases, Liver diseases, Epilepsy, Any history of hypersensitivity to carbetocin .

Sample Size: Thus we took 50 members in each for the two groups after applying all the exclusion criteria.[9]

Statistical analysis

Data was collected, tabulated, and statistically analyzed by SPSS (version 16; SPSS Inc., Chicago, Illinois, USA). The mean ($\bar{X}$) and SD were used as descriptive statistics. Student's t test was used for comparison between two means of normal distributed data. P value less than 0.05 was set to be significant.

RESULTS

After applying inclusion and exclusion criteria we selected 100 pregnant women to participate in the study. Participants were equally divided into two groups who received Oxytocin and Carbetocin respectively. Mean age of pregnant women were 24.7 ± 3.1 in carbetocin group and 25.2 ±3.9 in oxytocin group.

[Table 1] In our study we found that the Oxytocin group showed lower value of Systolic Blood pressure compared to carbetocin group. We found statistically significant difference in Systolic Blood Pressure at 6, 9 and 12 min after infusion of the uterotonic drugs i.e (p value 0.004, 0.00001 & 0.00001). Also after 6 and 9 hours after caesarean section the systolic blood pressure showed lower value for Oxytocin (p value 0.03, 0.0013).

[Table 2] Diastolic blood pressure was found to be same during surgery. After surgery carbetocin was able to maintain the diastolic pressure compared to Oxytocin at 6 and 9 hrs postoperatively i.e (p value 0.003, 0.003).

[Table 3] Throughout the surgery and postoperatively the subject receiving Oxytocin showed high pulse rate compared to carbetocin. The difference was more significant post-operatively after 12 hrs post surgery as effect of uterotonic drug dipped sharply.

[Table 4] To see the Oxygen carrying capacity of the blood SpO2 was measured throughout the surgery and post-operatively. During surgery SpO2 among study participants receiving Oxytocin was lower compared to carbetocin receiving subjects. The difference of SpO2 showed statistical difference post operatively till 9 hrs past LSCS. Thus carbetocin was able to maintain SpO2 among the subjects more effectively as compared to Oxytocin.

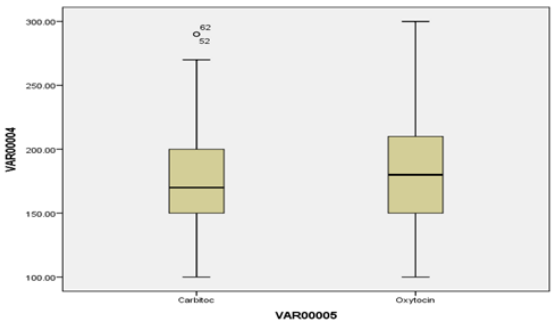

Figure 1: Change in weight of Mop after surgery among two groups

[Table 5] There were no any major adverse effects detected in both groups. The variances were not statistically significant i.e (P>0.05) noted at specific interval.

[Table 6] The weight of the mop which depicts the approximate amount of blood loss during caesarean section was checked. Comparing the weight of the

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mop before and after surgery showed statistically significant, lesser amount of blood lost among subjects receiving carbetocin (p value 0.03). Also [Figure 1] showing the whisker plot graph depicts the mean weight of mop among carbetocin lower than oxytocin group thus showing the efficacy of carbetocin over Oxytocin.

[Table 7] Also we assessed the pre-operative and post-operative hemoglobin level among both the groups. Here among the carbetocin group the post-operative hemoglobin fall was less compared to oxytocin group (10.89±1.16 vs 9.71±1.18), but this difference was not statistically significant (p value > 0.05).

Table 1: Systolic BP during and after cesarean section

Items	Oxytocin (n=50) Mean±SD	Carbetocin (n=50) Mean±SD	Test result (t)	Std error Difference	P value
Systolic BP after uterotonic administration by 3 min	114.1±8.99	112.6±18.4	-0.485	2.845	0.629
Systolic BP after uterotonic administration by 6 min	105.3±13.1	112.7±12.1	2.612	2.934	0.004
Systolic BP after uterotonic administration by 9 min	108.8±8.53	116.6±9.74	4.27	1.831	0.00001
Systolic BP after uterotonic administration by 12 min	105.1±16.77	115.6±8.97	3.906	10.52	0.00001
Systolic BP 3 h after CS	109.2±7.53	114.6±7.79	-1.553	1.53	0.124
Systolic BP 6 h after CS	110.8±8.124	116.6±8.01	0.562	2.994	0.036
Systolic BP 9 h after CS	112.6±8.321	118.4±8.84	3.821	1.954	0.0013
Systolic BP 12 h after CS	114.6±10.08	120.5±10.23	4.35	2.659	0.0865
Independent sample t test applied					

Table 2: Diastolic BP during and after cesarean section

Items	Oxytocin (n=50)	Carbetocin (n=50)	Test result	Std error	P value
	Mean±SD	Mean±SD	(t)	Difference	
Diastolic BP after uterotonic administration by 3 min	70.1±7.4	68.2±7.6	1.2	2.934	0.22
Diastolic BP after uterotonic administration by 6 min	59.4±5.9	64.8±6.1	1.3	3.216	0.018
Diastolic BP after uterotonic administration by 9 min	61.7±7.5	63.9±6.8	1.5	1.864	0.13
Diastolic BP after uterotonic administration by 12 min	61.3±7.9	63.9±6.8	1.6	2.144	0.11
Diastolic BP 3 h after CS	61.9±7.6	64.3±6.7	1.66	1817	0.13
Diastolic BP 6 h after CS	64.4±8.1	68.9±6.7	3.1	2.934	0.003
Diastolic BP 9 h after CS	69.9±6.9	73.8±5.8	3.01	2.831	0.003
Diastolic BP 12 h after CS	70.1±7.14	74.1±7.29	3.27	10.52	0.074
Independent sample t test applied					

Table 3: Pulse pressure (mm Hg) during and after cesarean section

Items	Oxytocin (n=50) Mean±SD	Carbetocin (n=50) Mean±SD	Test result (t)	Std error Difference	P value
Pulse BP after uterotonic administration by 3 min	86.5±12.1	89.4± 12.2	1.18	2.18	0.273
Pulse BP after uterotonic administration by 6 min	87.28±12.66	90.16±14.78	1.04	2.75	0.298
Pulse BP after uterotonic administration by 9 min	93± 13.8	90.04±13.02	0.946	2.69	0.347
Pulse BP after uterotonic administration by 12 min	91.96±9.55	92.8±11.98	-0.397	2.16	0.692
Pulse BP 3 h after CS	83.96±14.87	84.7±13.94	-0.264	2.34	0.387
Pulse BP 6 h after CS	97.52±1.69	87.4±13.61	5.21	1.94	0.0001
Pulse BP 9 h after CS	89.04±11.25	76.46±14.34	-4.88	2.57	0.0001
Pulse BP 12 h after CS	88.68±12.58	79.88±15.52	-6.37	2.82	0.0083
Independent sample t test applied					

Table 4: SpO2 during and after cesarean section

Items	Oxytocin (n=50)	Carbetocin (n=50)	Test result	Std error	P value
	Mean±SD	Mean±SD	(t)	Difference	
SpO2 after uterotonic administration by 3 min	86.5±12.1	89.4± 12.2	1.18	2.18	0.273
SpO2 after uterotonic administration by 6 min	87.28±12.66	90.16±14.78	1.04	2.75	0.298
SpO2 after uterotonic administration by 9 min	93± 13.8	90.04±13.02	0.946	2.69	0.347
SpO2 after uterotonic administration by 12 min	91.96±9.55	92.8±11.98	-0.397	2.16	0.692
SpO2 3 h after CS	83.96±14.87	84.7±13.94	-0.264	2.34	0.387
SpO2 6 h after CS	87.4±13.61	89.52±1.69	1.21	2.27	0.521
SpO2 9 h after CS	84.46±14.34	89.04±11.25	-4.98	2.57	0.316
SpO2 12 h after CS	84.88±15.52	86.68±12.58	-6.37	2.82	0.526
Independent sample t test applied					

Table 5: Adverse effect any noted

Side Effect	Oxytocin (n=50)	Carbetocin (n=50)	p value
Nausea	1	2	0.26
Vomiting	3	0	0.089

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Headache	1	1	0.5
Convulsions	0	0	0.5
Dysnea	0	0	0.5
Arrythmia	0	0	0.5
Fever	0	0	0.5
Abdominal Pain	0	0	0.5
Independent sample t test applied			

Table 6: Change in the weight of the Mop before and after

	Oxytocin (n=50)	**Carbetocin (n=50)**	**P value**
	Mean±SD	**Mean±SD**	
Before (In grams)	52.8±8.58	54.2±8.82	0.423
After (In grams)	194.6±48.9	174.2±39.5	0.036
Independent sample t test applied			

Table 7: Change in Hemoglobin among subject after Uterotonic agent

	Oxytocin(n=50)	**carbetocin (n=50)**	**p value**
	Hb% (mean± SD)	**Hb% (mean± SD)**	
Pre-Operative	11.2 ± 1.72	11.9 ± 1.08	0.573
Post -Operative	9.71± 1.18	10.89±1.16	0.183
Independent sample t test applied			

DISCUSSION

The present study is one of the few studies conducted which have been conducted in the country. And no such study is conducted within the present geographical location. We have tried to compare the efficacy of the oxytocin and carbetocin in maintaining the hemodynamic status of the pregnant women who are at high risk of PPH.

In the present study we found that carbetocin was comparatively more effective in preventing PPH among the study subjects. Among both the groups we did not found any case of PPH. We found agreement of our results with a meta-analysis study in which 24 studies were referred which concluded carbetocin was more effective in preventing PPH as compared to oxytocin of the studies.[10]

The mean age of the study subjects was 24.7 ± 3.1 among the carbetocin group and 25.2 ±3.9 among oxytocin group. Demetz J et al showed that mean age of study subjects in carbetocin group were 26.5 years and 26.7 years among the oxytocin group.[11]

The current study we found that preoperatively and post operatively the carbetocin group was able to maintain the systolic blood pressure effectively as compared to Oxytocin (p value <0.001). Also wrt to diastolic blood pressure hypotension was noted intraoperatively and post-operatively and significant difference was noted when compared to carbetocin group who were able to maintain the DBP more efficiently (p value <0.0010). Thus it was more likely that oxytocin group may land into hypotension. A study from Philippine found that mean preoperative systolic BP of study patients in carbetocin group were 117±6.8 mm of Hg and diastolic BP were 69 ±7.7 mm of Hg and mean preoperative systolic BP were 118±8.3 mm of Hg and diastolic BP were 73±8.5 mm of Hg in Oxytocin group.[12] Another study by N Kabir et al. showed, the mean preoperative systolic BP of patients were 108±8.6 mm of Hg and diastolic BP were 71 ±5.4 mm of Hg in carbetocin group and mean systolic BP were 105±7.2 mm of Hg and diastolic BP were 70±6.2 mm of Hg in oxytocin group which were almost similar with previous study.[13]

The mean pulse rate intra operative and post-operative was high in oxytocin group compared to carbetocin group. Also the pulse rate baseline return was faster in case of carbetocin. This can depict the hemodynamic stability maintainance by carbetocin over oxytocin. A statistically difference was shown post-operatively (p value <0.001). Moertl MG et.al in their study found similar results and carbetocin was more effective in reversal of tachycardia compared to oxytocin.[14] Our results were in agreement to Bhattacharya, et al and El Behery MM et.al who observed that oxytocin was unable to reach the baseline in case of heart rate.[15,16]

Among the two groups SpO2 was assessed throughout the course of delivery. The carbetocin group was able to maintain the SpO2 level intra and post-operatively compared to Oxytocin group. Among Oxytocin group hypoxia was present and post-operatively statistical difference was noted wrt SpO2 with a sudden dip at 6-9 hrs after LSCS. Blood loss during cesarean section may lead to maternal and foetal hypoxia which may lead to irreversible complications. Thus continuous monitoring of SpO2 is necessary. We didn't find any relevant who has monitored SpO2.

During and after surgery the weight of the mop was calculated. This gives the approximate amount of blood loss occurred during the surgery as blood is also mixed with amniotic fluid. The amount of blood loss post-operatively in carbetocin group was less as compared to Oxytocin which was statistically significant (p value 0.05). But when change of Hb% was considered the difference was not found to be statistically significant although post-operative Hb% was stable in carbetocin group. Our results are consistent with the findings of some studies, in which there we found reduced blood loss among study subjects in the general population after receipt of Carbetocin, when compared with Oxytocin.[17-19]

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CONCLUSION

The third stage of the labour is the most importance stage which decides the amount of blood loss. Carbetocin demonstrated greater efficacy in preventing PPH in high-risk women undergoing cesarean sections, primarily by maintaining hemodynamic stability, reducing blood loss, and requiring only a single dose administration. These findings support the use of Carbetocin as a superior alternative to Oxytocin for the prevention of PPH in this setting.

REFERENCES

1. WHO Postpartum Haemorrhage (PPH) Summit. 30 September 2022. https://www.who.int/teams/sexual-and-reproductive-health-and-research-(srh)/overview. Last accessed 07th Jan 2023.
2. United Nation .Department of Economic and Social Affairs Sustainable development. https://sdgs.un.org/goals/goal3. Last accessed 09th Jan 2023.
3. Significant Decline in the Maternal Mortality Ratio (MMR) from 130 in 2014-16 to 97 per lakh live births in 2018-20: Dr. Mansukh Mandaviya. Ministry of Health and Family Welfare. Nov 2022. https://pib.gov.in. Last accessed 12th Jan 2023.
4. Nyfløt LT, Sandven I, Stray-Pedersen B, Pettersen S, Al-Zirqi I, Rosenberg M, et al. Risk factors for severe postpartum hemorrhage:a case-control study. BMC Pregnancy and Childbirth.2017; 17: 17.
5. Heesen M, Carvalho B, Carvalho JC, et al. International consensus statement on the use of uterotonic agents during caesarean section. Anaesthesia 2019; 74: 1305-19.
6. Khan M, Balki M, Ahmed I, et al. Carbetocin at elective cesarean delivery: a sequential allocation trial to determine the minimum effective dose. Can J Anesth 2014; 61: 242-248.
7. Vernekar SS, Goudar SS, Metgud M. et.al. Effect of heat stable carbetocin vs oxytocin for preventing postpartum haemorrhage on post delivery hemoglobin-a randomized controlled trial. J Matern Fetal Neonatal Med. 2022 Dec;35(25):8744-8751.
8. Attilakos G, Psaroudakis D, Ash J, Buchanan R, Winter C, Donald F, Hunt L, Draycott T. Carbetocin versus oxytocin for the prevention of postpartum haemorrhage following caesarean section: the results of a double-blind randomised trial. BJOG 2010;117:929–936.
9. Giovanni Larciprete et.al Carbetocin versus oxytocin in caesarean section with high risk of post-partum haemorrhage. Journal of Prenatal Medicine 12 2013; 7 (1): 12-18.
10. Haiyan Sun, Lei Xu, Yu Li, Shurong Zhao. Effectiveness and safety of carboxytocin versus oxytocin in preventing postpartum hemorrhage: A systematic review and meta-analysis. Journal of Obstetrics and Gynaecology Research 2022; 48(4): 889-901.
11. Demetz J, Clougueur E, D'Haveloose A, Staelen P, Ducloy AS, Subtil D. Systematic use of carbetocin during cesarean delivery of multiple pregnancies: a before-and-after study. Arch Gynecol Obstet 2013;287:875-80.
12. Lynuy D, Atherinep N et al. Carbetocin versus Oxytocin for the Prevention of Postpartum Haemorrhage Following Elective Cesarean Section: Rizal Medical Center Experience; Philippine Journal of Obstetrics & Gynecology. 2013; 37 (2):71-79.
13. N Kabira et.al Efficacy and Safety of Carbetocin in Comparison to Oxytocin for the Prevention of Primary PPH during Caesarean Section: An Open Label Randomized Control Trial. Journal of Bangladesh College of Physicians and Surgeons 2019; 37(1): 19-24.
14. Moertl M, Friedrich S, Kraschl J, Wadsack C, Lang U, Schlembach D. Haemodynamic effects of carbetocin and oxytocin given as intravenous bolus on women undergoing caesarean delivery: a randomised trial. BJOG 2011;118:1349–1356.
15. Bhattacharya S, Ghosh S, Ray D, Mallik S, Laha A.Oxytocin administration during cesarean delivery: Randomized controlled trial to compare intravenous bolus with intravenous infusion regimen. J Anaesthesiol Clin Pharmacol 2013;29:32-5.
16. El Behery MM, El Sayed GA, El Hameed AA, Soliman BS, Abdelsalm WA, Bahaa A. Carbetocin versus oxytocin for prevention of postpartum hemorrhage in obese nulliparous women undergoing emergency cesarean delivery. J Matern Fetal Neonatal Med 2016;29:1257-60.
17. Chen CY, Su YN, Lin TH, et al. Carbetocin in prevention of postpartum hemorrhage: experience in a tertiary medical center of Taiwan. Taiwan J Obstet Gynecol 2016;55:804-9.
18. Mohamed Maged A, Ragab AS, Elnassery N, Ai Mostafa W, Dahab S, Kotb A. Carbetocin versus syntometrine forprevention of postpartum hemorrhage after cesarean section. J Matern Fetal Neonatal Med 2017;30:962-6.
19. Chen YT, Chen SF, Hsieh TT, Lo LM, Hung TH. A comparison of the efficacy of carbetocin and oxytocin on hemorrhage-related changes in women with cesarean deliveries for different indications. Taiwan J Obstet Gynecol 2018;57:677-82.

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