Section: Obstetrics and Gynecology

Original Research Article

COMPARITIVE STUDY OF INJECTION CARBETOCIN AND INJECTION OXYTOCIN IN PREVENTION OF POSTPARTUM HEMORRHAGE

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ABSTRACT

Background: The aim is to study efficacy of heat stable oxytocin analogue injection carbetocin in prevention of PPH in comparision to injection oxytocin by an observational study in 300 patients delivering both vaginally and by caesarean section.

Materials and Methods: The study was conducted at Deccan College of Medical Sciences (Owaisi Hospital and Research Centre and Princess Esra Hospital). The study was conducted from JULY 2023- DEC 2024(18 MONTHS). It is a prospective study comparing injcarbetocin and inj oxytocin in prevention of PPH.300 woman delivering vaginally and by caesarean section were given injcarbetocin and inj oxytocin alternately after delivery of the baby. PPH is preventable and important cause for maternal morbidity and mortality. Patients were divided into two groups 150 each. Group A received injcarbetocin and group B received inj oxytocin after the delivery of the baby.

Results: The dose of injcarbetocin was 1 ml containing 100 microgram carbetocin which was administered by I.M route after the delivery of the baby in vaginal and caesarean deliveries. The dose of inj oxytocin was 10 IU by I.M administration after the delivery of the baby in vaginal and caesarean deliveries. In both the groups the blood loss intrapartum and postpartum was not of much difference. The heat stable carbetocin does not require cold chain for maintenance in contrast to oxytocin which needs cold chain maintainance. Hence its use can be encouraged in developing countries where maintaining cold chain can be challenging.

Conclusion: From this study we come to a conclusion that both injcarbetocin and inj oxytocin are equally efficacious in preventing PPH with equal amount of blood loss intra partum and postpartum.

Keywords: PPH, Carbetocin, Intrapartum, Oxytocin, Ceaserean Section, Postpartum Haemmorhage.

INTRODUCTION

Postpartum hemorrhage is defined as the loss of 500 mL of blood after completion of the third stage of labor. It is a leading cause of maternal mortality and morbidity all over the world but more so in developing countries.

According to the American College of Obstetricians and Gynecologists (20 17 d), postpartum hemorrhage is defined as cumulative blood loss > 1 000 mL in caesarean deliveries and >500ml in vaginal deliveries accompanied by signs and symptoms of hypovolemia.[1]

The most frequent cause of obstetrical hemorrhage is failure of the uterus to contract sufficiently after delivery and to arrest bleeding from vessels at the placental implantation site.

Currently, the World Health Organization (WHO) recommends active management of the third stage of labor for prevention of postpartum hemorrhage.[2] Prophylacticadministration of uterotonic agents is identified as the most important component of active

management of the third stage of labor, which has reduced the incidence of postpartum hemorrhage nearly by 50%.[3]

Oxytocin, which has a short half-life and duration of action, is the current standard therapy for the prevention of postpartum hemorrhage. However, as it is susceptible to heat, its efficacy cannot be assured in many low- and middle- countries where access to cold-chain transport and storage is unavailable, and quality issues such as impurity and insufficient active ingredients also compromise its efficacy.[4] In contrast, carbetocin, which is a long-acting oxytocin analogue, has been widely used in preventing postpartum hemorrhage since 1997, and heat-stable carbentocin, and hasbeen shown to maintain active for more than 36 months at 30 °C and 75% relative humidity.[5]

In this study we have compared efficacy and role of injection carbetocin as an alternative to injection oxytocin in prevention of postpartum hemorrhage.

Aims And Objectives

- To study efficacy of heat stable oxytocin analogue injection carbetocin in prevention of PPH in comparision to injection oxytocin by an observational study in 300 patients delivering both vaginally and by caesarean section.
- To prevent maternal mortality and morbidity.

MATERIALS AND METHODS

The study was conducted at Deccan College of Medical Sciences (Owaisi Hospital and Research Centre and Princess Esra Hospital). The study was conducted from JULY 2023- DEC 2024 (18 Months).

It is a prospective study comparing injcarbetocin and inj oxytocin in prevention of PPH.

300 woman delivering vaginally and by caesarean section were given injcarbetocin and inj oxytocin alternately after delivery of the baby.

- Intrapartum and postpartum blood loss was monitored

Inclusion Criteria

- All woman delivering vaginally and by caesarean section.
- All term and preterm deliveries
- Patients with history of PPH in previous pregnancy.
- Patients with even one risk factor for PPH

Exclusion Criteria

- Patients with cardiovascular, renal and hepatic diseases.

Methodology

- **INJ Carbetocin** – I vial containing 100mcg in 1 ml given I.M immediately after the delivery of the baby.
- **INJ Oxytocin** – 10IU given I.M after the delivery of the baby
- Alternate use of carbetocinn and oxytocin in deliveries by cesarean sections and normal vaginal deliveries.

Statistical Analysis

The data collected during the study was tabulated in Microsoft excel software. Tables and graphs were created using Microsoft word. Chi- square tests were used to determine the differences or associations between findings of different tests. The p value of <0.05 is considered as statistically significant.

RESULTS

Table 1: age group distribution in drug oxytocin vs carbetocin.

			Drug		Total
			Carbetocin	Oxytocin	
Age group	<30	Count	132	135	267
		%	88.0%	90.0%	89.0%
	>30	Count	18	15	33
		%	12.0%	10.0%	11.0%
Total		Count	150	150	300
		%	100.0%	100.0%	100.0%

Chi square = 0.306, P value = 0.580 (Not significant)

There is no signific difference between two age groups

Table 2: Mode of delivery.

			Drug		Total
			Carbetocin	Oxytocin	
Mode of delivery	LSCS	Count	139	134	273
		%	92.7%	89.3%	91.0%
	NVD	Count	11	16	27
		%	7.3%	10.7%	9.0%
Total		Count	150	150	300
		%	100.0%	100.0%	100.0%

Chi square = 1.018, P value = 0.313 (Not significant)

There was no statistical difference between both groups. among patients receiving inj carbetocin 92.70% delivered by cesarean section and 7.30% by NVD among patients receiving inj oxytocin 89.30% delivered by cesarean section and 10.70% by NVD. Hence majority of the patients delivered by cesarean section.

Table 3: Gestational age

			Drug		Total
			Carbetocin	Oxytocin	
Gestation	Pre-term	Count	19	19	38
		%	12.7%	12.7%	12.7%
	Term	Count	131	131	262
		%	87.3%	87.3%	87.3%
Total		Count	150	150	300
		%	100.0%	100.0%	100.0%

Chi square = 0.000, P value = 1.000 (Not significant)

- There was no statistical difference between both groups.
- maximum deliveries were of term gestation

Table 4: Parity

			Drug		Total
			Carbetocin	Oxytocin	
PARITY	MULTI	Count	99	98	197
		%	66.0%	65.3%	65.7%
	PRIMI	Count	51	52	103
		%	34.0%	34.7%	34.3%
Total		Count	150	150	300
		%	100.0%	100.0%	100.0%

Chi square = 0.015, P value = 0.903 (*Not significant)

There was no statistical difference between both groups. Majority of the patients were multigravida.

Table 5: Previous mode of delivery

			Drug		Total
			Carbetocin	Oxytocin	
Previos mode of delivery	LSCS	Count	85	78	163
		%	85.9%	79.6%	82.7%
	NVD	Count	14	20	34
		*%	14.1%	20.4%	17.3%
Total		Count	99	98	197
		%	100.0%	100.0%	100.0%

There was no statistical difference between both groups. Most of the patients were with previous cesarean sections

Table 6: Intrapartum blood loss

	Drug	N	Mean	Std. Deviation	P value
Intrapartum Blood Loss (ML)	Carbetocin	150	331.20	47.627	0.119
	Oxytocin	150	340.20		

There was no statistical difference between both groups. The blood loss intrapartum is almost same with both the drugs.

Table 7: Postpartum blood loss

	DRUG	N	Mean	Std. Deviation	P value
PADS USED POSTPARTUM UPTO 5 DAYS	CARBETOCIN	150	13.36	2.247	
	OXYTOCIN	150	13.67		0.243

There was no statistical difference between both groups. There is no significant difference in blood loss in postpartum period.

DISCUSSION

This study compares the efficacy of heat stable oxytocin analogue injcarbetocin with inj oxytocin in prevention of postpartum hemorrhage. 300 patients delivering vaginally and by caesarean section were included in the study and of which one half -150 were given injcarbetocin and other half were given inj oxytocin after the delivery of the baby.

The amount of blood loss intrapartum and postpartum by counting number of pads used in the post partum period for 5 days was noted. Majority of the deliveries were by caesarean sections with almost equal use of injcarbetocin and inj oxytocin.

Almost all deliveries were of term gestation. Regarding the parity majority of the patients in the study were multigravida who are at more risk for postpartum hemorrhage as risk of PPH is more with high parity. Majority of the caesarean deliveries were with history of previous caesarean section making them more prone for risk of adhesions and intrapartumhemorhage.

The intrapartum blood loss was not of much difference with the use of both injcarbetocin and inj oxytocin. The difference in blood loss post partum is also not significant.

However heat stable carbetocin can be encouraged for use in prevention of PPH and replace oxytocin which requires cold chain for maintainance. Similar to my study another study done in 2019 the meta-analysis of 5 randomized controlled trials (30,314

women) indicated that there was no significant difference between carbetocin and oxytocin in blood loss ≥500 ml in women undergoing vaginal delivery (relative risks (RRs), 0.52; 95% confidence intervals (CIs), 0.24 to 1.15; P =.11; I2 = 69%). Sensitivity analyses showed the same results. No significant differences were found in blood loss ≥1000 ml after caesarean sections.[6]

In high-risk women, carbetocin is superior to oxytocin in preventing 500 ml of blood loss following caesarean section and may represent the most cost-effective uterotonic drug in developing countries with low resources, as suggested by the results of the clinical trial conducted in Mexico. Two recent randomised controlled clinical trials and one retrospective study have indicated that carbetocin may also represent a good alternative to conventional uterotonic agents for prevention of postpartum haemorrhage after vaginal delivery.

When administered as a single 100 mg dose, carbetocin has demonstrated longer duration of action compared with intravenous oxytocin, as indicated by the reduced need for additional uterotonic interventions in high-risk women with carbetocin. Carbetocin is also at least as effective as syntometrine for management of the third stage of labour in low-risk women. Carbetocin has been associated with a low incidence of adverse effects, with a similar tolerability profile to intravenous oxytocin. It has also been associated with a lower incidence of gastrointestinal side effects compared with the combination of oxytocin and ergometrine.

The promising findings from these studies suggest that carbetocin may become the drug of choice for prevention of postpartum haemorrhage after vaginal delivery in high-risk women. More trials in low-risk women who undergo vaginal delivery are needed to assess whether carbetocin is superior to conventional uterotonic drugs forthe majority of pregnant women. Also, further studies could be conducted to determine if single intramuscular administration of carbetocin is advantageous in settings where prophylactic use of intravenous uterotonics is unsafe or impracticable, like in domiciliary practice or in third stage of labour management in developing countries.[7]

There is evidence to suggest that 100 µg of intravenous carbetocin is more effective than oxytocin for preventing PPH in women undergoing caesarean deliveries, but more studies are needed to validate this finding. Carbetocin is associated with less blood loss compared to syntometrine in the prevention of PPH for women who have vaginal deliveries and is associated with significantly fewer adverse effects. Further research is needed to analyse the cost-effectiveness of carbetocin as a uterotonic agent. Current evidence shows that carbetocin significantly reduces the need for therapeutic uterotonics compared to placebo and oxytocin in women undergoing caesarean delivery. Pooled data also showed a lower risk of postpartum haemorrhage (PPH) in women who received carbetocin compared to oxytocin following caesarean deliveries. This is a new finding following our previous review. However, further research is needed to validate this finding, as this result is based on three trials which showed high risk of bias.[8]

In the study of Carbetocin versus oxytocin for prevention of postpartum hemorrhage after vaginal delivery in high risk women, there was nosignificant difference between the two study groups regarding occurrence of major PPH and the need for blood transfusion There was a statistically significant difference between the two study groups regarding amount of bleeding (337.73 ± 118.77 versus 378 ± 143.2), occurrence of PPH (4 versus 16%), need for other uterotonics (23 versus 37%) and hemoglobin difference between before and after delivery (0.55 ± 0.35 versus 0.96 ± 0.62) (all being lower in carbetocin group) and measured hemoglobin 24 h after delivery (being higher in carbetocin group).[9]

In a study of Carbetocin versus oxytocin after caesarean section: similar efficacy but reduced pain perception in women with high risk of postpartum haemorrhage by Maria DeBonis, MichelaTorricelli, Licia Leoni, Paolo Berti, Valentina Ciani, Rosa Puzzutiello shows a single carbetocin injection isefficacious and safe on the maintenance of uterine tone and on the limitation of blood losses, in peri- and in postoperative period. In addition, carbetocin was able to reduce pain perception during postoperative days improving quality life of women.[10]

A total of 29,645 women underwent randomization. The frequency of blood loss of at least 500 ml or the use of additional uterotonic agents was 14. 5% in the carbetocin group and 14.4% in the oxytocin group (relative risk, 1.01; 95% confidence interval [CI], 0.95 to 1.06), a finding that was consistent withnoninferiority. The frequency of blood loss of at least 1000 ml was 1.51% in the carbetocin group and 1.45% in the oxytocin group (relative risk, 1.04; 95% CI, 0.87 to 1.25), with the confidence interval crossing the margin of noninferiority. The use of additional uterotonic agents, interventions to stop bleeding, and adverse effects did not differ significantly between the two groups.[11]

In a study of Carbetocin vs oxytocin for prevention of postpartum hemorrhage after vaginal delivery. This meta-analysis of 5 randomized controlled trials (30,314 women) indicated that there was no significant difference between carbetocin and oxytocin in blood loss ≥500 ml in women undergoing vaginal delivery (relative risks (RRs), 0.52; 95% confidence intervals (CIs), 0.24 to 1.15; P = .11; I2 = 69%). Sensitivity analyses showed the same results. No significant differences were found in blood loss ≥1000 ml.[12]

In contrast to my study another study of Carbetocin versus oxytocin in primigravida for active management of third stage of labor: a prospective study BYAmbikaMounika Puram Vidya A. Thobbi SHOWS Groups A and B, comparable in age, blood pressure, and mild anaemia, exhibited significant gestational age differences (p<0.0001). Group B had higher mean blood loss (377.68 ml) than group A

(345.34 ml) with a significant p=0.0118*. Side effects showed no differences among groups. Postpartum, group B saw a significant 7% incidence of haemorrhage compared to none in group A (p=0.0071). Carbetocin showed superiority over oxytocin in the active management of third stage of labor, exhibiting a statistically significant reduction in PPH incidence and decreased requirement for additional uterotonic drugs.[13]

In a different study of Carbetocin versus Oxytocin with or without Tranexamic. Some previous studies revealed that the carbetocin-only group might be related to lower decrease in hemoglobin and hematocrit concentration from the preoperative to postoperative assessments at the time of vaginal delivery compared to others because they were significantly lower in the carbetocin-only group. Based on this result, the carbetocin-only regimen is not inferior to carbetocin plus TXA, oxytocin alone, or oxytocin plus TXA.[14]

CONCLUSION

From this study we come to a conclusion that both injcarbetocin and inj oxytocin are equally efficacious in preventing PPH with equal amount of blood loss intra partum and postpartum. In both the groups there were equal distribution of caesarean deliveries and vaginal deliveries , equal distribution of term and preterm pregnancies, equal distribution of multigravidas, with equal distribution of previous caesarean sections . hence there is no bias or any confounding factor effecting the study.

REFERENCES

1. Heneghan C, Ward A, Perera R, et al. Self-monitoring of oral anticoagulation: systematic review and meta-analysis of individual patient data. Lancet (London, England) 2012;379:322–34.
2. Westhoff G, Cotter AM, Tolosa JE. Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage. Cochrane Database Syst Rev 2013;Cd001808.
3. Torloni MR, Gomes Freitas C, Kartoglu UH, et al. Quality of oxytocin available in low- and middle-income countries: a systematic review of the literature. BJOG 2016;123:2076–86.
4. Malm M, Madsen I, Kjellstrom J. Development and stability of a heat-stable formulation of carbetocin for the prevention of postpartum haemorrhage for use in low and middle-income countries. J Peptide Sci2018;24:e3082.
5. Oliveira MI, da Costa VS, Mer S, Osório J, Martins AP. Thrombocytopenia in pregnancy, a challenge in the intensive care unit (ICU). Rev EspAnestesiolReanim (Engl Ed). 2019 Aug-Sep;66(7):385-389.
6. Xin-HangJin,MD,a,∗DanLi,BS,b andXiaLi, BSc. Carbetocin vs oxytocin for prevention of postpartum hemorrhage after vaginal delivery. Published online 2019 Nov 22. doi: 10.1097/MD.0000000000017911PMCID: PMC6882650
7. Rath W. Prevention of postpartum haemorrhage with the oxytocin analogue carbetocin. Eur J ObstetGynecolReprod Biol. 2009 Nov;147(1):15-20.
8. Su LL, Chong YS, Samuel M. Carbetocin for preventing postpartum haemorrhage. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD005457. DOI: 10.1002/14651858.CD005457.pub3. Accessed 06 July 2024.
9. Maged, A. M., Hassan, A. M., &Shehata, N. A. (2015). Carbetocin versus oxytocin for prevention of postpartum hemorrhage after vaginal delivery in high risk women. The Journal of Maternal-Fetal & Neonatal Medicine, 29(4), 532–536.
10. De Bonis, M., Torricelli, M., Leoni, L., Berti, P., Ciani, V., Puzzutiello, R., … Petraglia, F. (2011). Carbetocin versus oxytocin after caesarean section: similar efficacy but reduced pain perception in women with high risk of postpartum haemorrhage. The Journal of Maternal-Fetal & Neonatal Medicine, 25(6), 732–735.
11. Widmer M, Piaggio G, Nguyen TMH, Osoti A, Owa OO, Misra S, Coomarasamy A, Abdel-Aleem H, Mallapur AA, Qureshi Z, Lumbiganon P, Patel AB, Carroli G, Fawole B, Goudar SS, Pujar YV, Neilson J, Hofmeyr GJ, Su LL, Ferreira de Carvalho J, Pandey U, Mugerwa K, Shiragur SS, Byamugisha J, Giordano D, Gülmezoglu AM; WHO CHAMPION Trial Group. Heat-Stable Carbetocin versus Oxytocin to Prevent Hemorrhage after Vaginal Birth. N Engl J Med. 2018 Aug 23;379(8):743-752.
12. Jin XH, Li D, Li X. Carbetocin vs oxytocin for prevention of postpartum hemorrhage after vaginal delivery: A meta-analysis. Medicine (Baltimore). 2019 Nov;98(47):e17911.
13. Patil A, Puram M, Thobbi VA. Carbetocin versus oxytocin in primigravida for active management of third stage of labor: a prospective study. Int J Reprod ContraceptObstetGynecol 2024;13:589-93.
14. Caglar Cetin, FatmaBasakTanoglu, ErhanHanligil, Ali Gokce, Ozge Pasin, Pinar Ozcan; Carbetocin versus Oxytocin with or without Tranexamic Acid for Prophylactic Prevention of Postpartum Hemorrhage after a Vaginal Delivery: A Randomized Clinical Trial. GynecolObstet Invest 28 December 2023; 88 (6): 366– 374.