



CASE-CONTROL STUDY OF OXYTOCIN V/S CARBETOCIN IN THE PREVENTION OF POSTPARTUM HEMORRHAGE IN HIGH RISK PATIENTS

Obstetrics & Gynaecology

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ABSTRACT

Introduction: PPH is the leading cause of maternal morbidity in low-income countries and a significant contributor to severe maternal morbidity. As a prophylactic intervention to prevent PPH, active management of third stage of labour was introduced. This has three components out of which one of the components is administration of uterotronics. Out of the many available uterotronics, carbetocin and oxytocin are two most commonly used drugs. Both of them have some advantages and disadvantages. Hence, this study was done to compare the efficacy of both drugs. **Method:** The study was conducted in a tertiary care hospital where the high risk patients were selected and randomly chosen to divide into two groups of 43 patients each. One group was administered carbetocin whereas the other group was administered oxytocin for prevention of PPH, and the efficacy of both drugs was studied in relation to the efficiency to prevent PPH, need of extra uterotronics for management of PPH, need of number of blood and blood products required in case of PPH and the cost of therapy. **Result And Conclusion:** More evidence of PPH was observed in patients of oxytocin group than in carbetocin group. Carbetocin is comparatively more efficient than oxytocin for the prevention of PPH in LSCS. There is no difference in the efficacy of carbetocin and oxytocin for the prevention of PPH in vaginal deliveries. About two fold use of blood and its products was seen in oxytocin group than in carbetocin group. Carbetocin is more cost effective than oxytocin.

KEYWORDS

Post-partum hemorrhage, uterotronics, carbetocin, oxytocin, efficacy

INTRODUCTION

Postpartum hemorrhage (PPH) is the leading cause of maternal mortality in low-income countries⁽¹⁾ and is a significant contributor to severe maternal morbidity, generally associated with substantial blood loss, including severe anemia, cardiac failure and sepsis. Regardless of the method of delivery, PPH was defined by the American Academy of Obstetrics and Gynecology in 2017 as a total blood loss higher than 1000 mL with signs and symptoms of hypovolemia within 24 hours of the birth process. Active Management of the Third Stage of Labour (AMTSL), a prophylactic intervention to prevent PPH, is composed of a package of three components: 1) administration of an uterotonic, immediately after birth of the baby; 2) controlled cord traction (CCT) to deliver the placenta; and 3) massage of the uterine fundus after the placenta is delivered. The administration of an uterotonic to the mother is identified as the most important step⁽²⁾. Two uterotronics, oxytocin and carbetocin are in the Essential Medicines List by the World Health Organization.⁽³⁾ Oxytocin works on receptors of smooth muscle and stimulates the upper uterine segment to contract regularly. Carbetocin is a long-acting synthetic

oxytocin analogue and also works by stimulating the uterus.⁽⁴⁾ A single dose of carbetocin has been hypothesised to act as a 16 hours intravenous oxytocin infusion regarding the increase in uterine tone and the reduction of the risk of PPH in elective caesarean section.⁽⁵⁾ Advantage of carbetocin is its tolerance to heat and does not require cold-chain transport and storage that is needed for oxytocin use and has disadvantage of being costlier than oxytocin. This study aims to evaluate the effect of carbetocin and oxytocin in the prevention of PPH in high risk patients and the purpose of the study is to compare the safety and outcome of both.

MATERIAL AND METHODS

After due permission from the ethical committee, a case-control study was conducted over a period of two years from 2022 to 2024 at labor room and operation theatre of MGM Medical College and Hospital, Aurangabad, a tertiary care centre. All pregnant patients for delivery were graded as high risk or low risk for PPH according to risk score. Patients having risk score of more than 5 were categorized as high risk patients. 86 such patients included in the study.

Risk Score For Postpartum Hemorrhage

Sr. No.	Risk Factor	0	1	2
1.	Parity	-	< 4	≥ 4
2.	Booking status	-	Irregular visits	Not booked
3.	Referred patient	-	-	Referred from primary care centre
4.	History of PPH in previous pregnancy	-	-	Yes
5.	Previous uterine surgery	-	Previous 1 LSCS	- Previous 2 LSCS - Myomectomy
6.	Over-distention	-	-	- Multi-fetal gestation - Polyhydramnios - Good size baby
7.	Placenta Previa	No active bleeding per vaginum	Presented with active bleeding per vaginum	Presented with abruption placenta and placenta previa
8.	Placenta Accreta	Absent	Suspected	Diagnosed
9.	Maternal Body Mass Index	< 25 kg/sq.m	25 – 30 kg/sq.m	>30 kg/sq.m
10.	History of Medical Disease	-	Anemia -1 Preeclampsia -1 DM -1 Heart disease -1 Thyroid disease - 1	Any medical disease with complications

11.	Malpresentation	-	-	+ 2
12.	Intrapartum	-	Induced and delivered	Failure of Induction and Prolonged labor

Low risk = Score ≤ 5 High risk = Score ≥ 6 to ≤ 25

After randomization and consent from the patients, 43 of these high risk patients were given Inj. Carbetocin 100 mcg intravenously and other 43 were given Inj. Oxytocin 10 units intramuscularly, and evidence of postpartum hemorrhage in both groups was then observed. Efficacy of both groups was compared in terms of evidence of PPH, need of extra uterotonics, need of blood and blood products and the cost. The entire data was compiled in MS Excel and analyzed using SPSS software version 22. Qualitative data is presented in the form of frequency and percentages. Quantitative data is presented in the form of mean and standard deviation. Both quantitative and qualitative data is presented in the form of visual representations like bar diagram, pie chart etc. Chi square tests were applied to check significant association between different attributes and p value checked at 5% level of significance.

RESULTS

Table No. 1: Comparison Of Evidence Of PPH Between Cases And Controls (n=86)

PPH	Group	
	Cases (n=43)	Controls (n=43)
Yes	12 (27.9%)	19 (44.2%)
No	31 (72.1%)	24 (55.8%)
p Value = 0.116 (Not Significant)		

More evidence of PPH was observed in patients of oxytocin group than in carbetocin group, thus signifying that carbetocin is efficient than oxytocin.

Table No. 2: Comparison Of Evidence Of PPH Between Cases And Controls According To Mode Of Delivery (n=86)

Mode of Delivery	Group			
	Cases (n=43)	PPH (%)	Controls (n=43)	PPH (%)
Vaginal	8 (18.6%)	1 (12.5%)	7 (16.3%)	1 (14.3%)
p Value	0.919 (Not Significant)			
LSCS	35 (81.4%)	11 (31.4%)	36 (83.7%)	18 (50.0%)
p Value	0.111 (Not Significant)			

In high risk patients, incidence of LSCS is more than vaginal delivery.

Carbetocin is comparatively more efficient than oxytocin for the prevention of PPH in LSCS. There is no difference in the efficacy of carbetocin and oxytocin for the prevention of PPH in vaginal deliveries.

Table No. 3: Comparison Of Management Of PPH Between Cases And Controls With Respect To Additional Uterotonics Needed (n=86)

Management	Group	
	Cases (n=43)	Controls (n=43)
Oxytocin	-	25 (58.1%)
Carbetocin	33 (76.7%)	-
Carbetocin and Others	10 (23.3%)	-
Oxytocin and Others	-	18 (41.9%)
p Value = <0.001 (Significant)		

Need of additional uterotonics for management of PPH was higher in oxytocin group than in carbetocin group.

Table No.4: Comparison Of Need Of Blood And Its Products Between Cases And Controls (n=86)

Need of Blood	Group	
	Cases (n=43)	Controls (n=43)
Yes	7 (16.3%)	13 (30.2%)
No	36 (83.7%)	30 (69.8%)
p Value = 0.126 (Not Significant)		

About two fold use of blood and its products was seen in oxytocin group than in carbetocin group.

As more number of uterotonics and more number of blood and blood products are used in oxytocin group than in carbetocin group, overall cost of therapy is also more in oxytocin group than carbetocin group. Hence, it can be said that carbetocin is more cost effective than oxytocin.

DISCUSSION

In our study, out of 43 patients in cases group, 12 patients (27.9%) had PPH, whereas out of 43 patients in controls group, 19 patients (44.2%) had PPH.

Evidence of PPH was by determined by need of extra uterotonics and need of blood and blood products.

I) Evidence Of PPH In Carbetocin Group As Compared To Oxytocin Group

In our study, from the carbetocin group, 27.9% of the patients had PPH which was significantly lower than in oxytocin group which was 44%. Thus, proving that efficiency of carbetocin is much better than oxytocin in high risk patients.

According to study by **Giovanni Larcipate 2013⁽⁶⁾** named "Carbetocin versus Oxytocin in Cesarean section with high risk of PPH", a case control study including 102 women, where frequency of carbetocin and oxytocin were compared in terms of blood loss and additional uterotonics needed. It concluded that a single carbetocin injection is more effective than continuous infusion of oxytocin to prevent PPH.

According to study by **Diane Korbe et al 2023⁽⁷⁾** named "Effectiveness of prophylactic carbetocin versus oxytocin for preventing severe PPH", with sample size of about 4832 women concluded that, carbetocin is equally efficient to oxytocin in preventing severe PPH.

II) Need Of Extra-uterotonics In Carbetocin Group As Compared To Oxytocin Group

In our study, out of 43 patients in controls group, 18 patients (41.9%) needed extra uterotonics like Methergin, Carboprost, Misoprostol; whereas out of 43 patients in cases group, only 10 patients (23.3%) needed extra uterotonics. P value of the data was < 0.001 which shows that need of extra uterotic was significantly lower in carbetocin group than the oxytocin group.

According to study by **Suya Kang 2022,⁽⁸⁾** a prospective, randomized, open label, controlled trial, with sample size 852, about "Carbetocin versus Oxytocin for prevention of PPH" also stated that carbetocin needed lower rate of additional uterotonics than oxytocin for prevention of PPH in high risk women.

According to other study (Randomized Control Trial) by **Carole Anne Whiaghan et al. December 2016,⁽⁹⁾** with 116 sample size, about "Carbetocin versus Oxytocin to reduce additional uterotic use and non-elective Cesarean sections", it concluded that both have similar need for additional uterotonics and there was no benefit of using carbetocin over oxytocin.

III) Comparison Between Carbetocin And Oxytocin Based On Need Of Blood And Blood Products

In our study, out of 43 patients in control group, 13 patients (30.2%) needed blood and blood products; whereas, only 7 patients (16.3%) in case group needed blood and blood products.

Thus, about two fold increase in blood and blood products was there in oxytocin group than in carbetocin group.

According to study by **Xin-Hang Jin November 2019,⁽¹⁰⁾** "Carbetocin v/s oxytocin for prevention of postpartum hemorrhage after vaginal delivery", a meta-analysis of 5 randomized control trials (30,314 women), there was no difference between both for need of blood and blood products in woman undergoing vaginal delivery.

IV) Comparison Between Carbetocin And Oxytocin Based On Cost Of Therapy

In our study, as more number of additional uterotonics as well as more number of blood and blood products were needed for the control group, thus the cost of therapy has also increased for the control group (oxytocin group).

Out of 43 patients in control group, about 25 patients (58.1%) were managed by oxytocin alone, and about 18 patients (41.3%) needed extra uterotonics.

Whereas in cases group, about 33 patients (76.7%) were managed by carbetocin alone, and about 10 patients (23.2%) needed extra uterotonics.

Alone carbetocin is costlier than oxytocin, but oxytocin increases the need of use of additional uterotonics as well as two fold increased risk of blood and blood products. Thus, using carbetocin is more cost effective than oxytocin.

According to study by **John R Cook et al.** March 2023 ⁽¹¹⁾, “Cost-effectiveness and budget impact of heat stable carbetocin compared to oxytocin and misoprostol for prevention of PPH in women giving birth in India”, carbetocin is known to reduce the number of PPH events and deaths in India. This will lead to reduction of costs to public health care system of India. More use of carbetocin for postpartum hemorrhage prevention could raise India's effort to achieve its maternal health goals and thus increase efficacy of its Public Health spending.

Apart from this additional cost of uterotonics, blood and blood products, few patients may also require ICU for monitoring. This may then add up the total cost of therapy. Such need of ICU admissions is seen more in oxytocin group than in carbetocin group. This again proves the cost – effectiveness of carbetocin over oxytocin.

CONCLUSION

- 1) Carbetocin is more effective than oxytocin for the prevention of PPH in LSCS of high risk patients; whereas, similar efficacy was seen in patients with vaginal delivery.
- 2) Being a tertiary care centre, there were more number of high risk referred patients in whom carbetocin was found more effective than oxytocin.
- 3) More number of additional uterotonics were used along with oxytocin than with carbetocin for the prevention of PPH.
- 4) About two fold increased need of blood and blood products was seen in oxytocin group than in carbetocin group.
- 5) Carbetocin was cost effective than oxytocin.

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Conflicts Of Interest

There are no conflicts of interest.

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