International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Anurag A et al. Int J Reprod Contracept Obstet Gynecol. 2022 Oct;11(10):2665-2668
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20222459

Original Research Article

Comparison of carbetocin and oxytocin in the prevention of atonic post-partum hemorrhage following normal vaginal delivery

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Received: 28 July 2022
Accepted: 08 September 2022

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ABSTRACT

Background: Post-partum hemorrhage is the leading cause of maternal mortality worldwide. Use of uterotonic drugs in active management of third stage of labour has been found to be most effective in prevention of PPH. Aims and objectives were to compare the efficacy and safety of carbitocin and oxytocin for prophylaxis of post-partum hemorrhage after singleton, term vaginal deliveries.
Methods: Prospective randomized interventional study of 250 women with singleton term pregnancies undergoing vaginal delivery at MGM Women and Children's Hospital, Kalamboli from May 2021 to May 2022. Participants randomized into 2 groups, group A and B receiving carbitocin and oxytocin respectively. Post-delivery uterine tone, vaginal bleeding, change in Hb and PCV, occurrence of adverse effects used to assess efficacy and safety of both drugs.
Results: Carbetocin was statistically equal to oxytocin in preventing uterine atony and hence PPH, with similar duration of uterotonic action and lesser requirement of other uterotonic drugs. There was no incidence of adverse effects in either group.
Conclusions: Since carbetocin is an effective, room temperature stable uterotonic drug with minimal side effects, it can be beneficial for use in prevention of PPH in rural settings.

Keywords: Carbetocin, Normal vaginal delivery, Oxytocin, Postpartum hemorrhage

INTRODUCTION

Post-partum hemorrhage is a common complication, seen following 2-4% vaginal deliveries and 6% of caesarean sections. According to the WHO, it is the leading cause of maternal mortality worldwide, accounting for 35% of deaths.[1] 38% of maternal mortality in India can be attributed to postpartum hemorrhage.[2]

Post-partum hemorrhage is defined as blood loss exceeding 500 ml in a vaginal delivery of 1000 ml in a caesarean section. Primary PPH is hemorrhage within the 1st 24 hours of delivery, while secondary PPH occurs after 24 hours but within 6 weeks of puerperium.[3]

Since 2012, the WHO recommends the active management of third stage of labour for the prevention of post-partum hemorrhage. This includes controlled cord traction as well as administration of uterotonic Oxytocin (10 IU i.v./i.m.).[4] Whilst, in addition, the ACOG recommends sustained uterine massage.[5]

The most effective method of prophylaxis of atonic post-partum hemorrhage is the use of uterotonic drugs.[6] Traditionally, oxytocin is the drug of choice. However, carbetocin, a synthetic analogue of oxytocin, has been recently accepted as an alternative uterotonic in the prevention of PPH by the WHO as well as the International Federation of Gynecology and Obstetrics.[7]

Carbetocin has been found to have comparable efficacy to that of oxytocin in prevention of PPH. In addition, it has been found to have a similar onset of action with longer lasting effect on uterine contractility.[8] Carbetocin can be administered as intravenous as well as intramuscular injection, rate of incidence of adverse effects is similarly

low as that of oxytocin with the benefit of reduced need for additional uterotonic agents, making it ideal for use in primary or rural health care centers.

Additionally, injezctable carbetocin is heat stable, as opposed to oxytocin which requires refrigeration between 2-8ºF, making it particularly suited for use in developing nations without efficient cold chain facilities, where post-partum hemorrhage is most rampant.

Use of carbetocin has increased since its development in 1997, however studies on its efficacy are limited.[9] Hence, we wanted to compare the effectiveness of carbetocin and oxytocin in the prophylaxis of PPH in an urban Indian tertiary care setting.

Aims and objectives

To study the efficacy of carbetocin as compared to oxytocin in prevention of postpartum hemorrhage. To study the safety of carbetocin and oxytocin for use in prevention of postpartum hemorrhage.

METHODS

It was a prospective randomized interventional study in department of obstetrics and gynecology, MGM Women and Children's Hospital, Kalamboli over a 1 year period. A total number of 250 women with singleton term pregnancies undergoing vaginal delivery were sampled by simple random method and group allocation was randomized.

Inclusion criteria

Age group 18-35 years, singleton pregnancy, term (37-40 weeks of gestation), vaginal delivery, patients willing to give informed consent

Exclusion criteria

Previous lower segment caesarean section, instrumental vaginal delivery including forceps or vacuum assisted; perineal or cervical tears during labour and delivery; high risk including: antepartum hemorrhage- placenta previa, abruptio placentae, PIH, preeclampsia, eclampsia, GDM, multiple pregnancies, polyhydramnios, macrosomia, patients with gynecological disorders such as myomas**;** medical disorders: anemia (Hb<10 gm%), coagulation disorders, thrombocytopenia (platelets <1.5 lakh), renal disorders, hepatic disorders, heart disease, asthma, epilepsy; patients requiring blood transfusion; known allergy to carbetocin; patients not willing to sign informed consent.

Methodology

Written informed consent was taken of all patients. Complete history and physical and obstetric examination of all participants was carried out. Routine blood investigations and obstetric ultrasound were performed. Patients' demographic data, including age, parity, gestation age was noted. On admission/predelivery values of Hb and hematocrit were noted.

A total of 250 women with term singleton pregnancies undergoing vaginal delivery were randomized into 2 groups.

Group A included 125 women who received 100 µg (room temperature stable) carbetocin diluted in 10 ml normal saline injected intravenously over 1-2 minutes immediately after birth of the baby along with active management of third stage of labour as per WHO criteria.

Group B included 125 women who received 10 IU oxytocin (stored at 2-8ºC) in 500 ml normal saline intravenously at 20-100 drops/minute immediately after birth of the baby along with active management of third stage of labour as per WHO criteria.

Active management of 3rd stage of labour was followed as per WHO criteria (2012): 1) administration of a uterotonic immediately after birth of the baby, 2) controlled cord traction (CCT) to deliver the placenta, 3) massage of the uterine fundus after the placenta is delivered

Outcome measures

Primary outcome

Checked by palpation of tone of uterine fundus as well as active vaginal bleeding. Cases with flabby uterus with poor tone with or without heavy/active vaginal bleeding were considered to be cases of atonic post-partum hemorrhage. Uterine Tone assessed at 0, 1, 2, 3 hours post-delivery and classified at atonic, contracted and well contracted/stony hard. Vaginal bleeding assessed at 0, 1, 2, 3 hours post delivery.

Need for use of additional uterotonic drugs was noted including tablet misoprostol 200 µg sublingual or 600 µg per rectal or injection methergine 0.2 mg intravenously.

Secondary outcome

Assessed by blood loss estimation using change in pre and 48-hour post-delivery values. Post-delivery change in hemoglobin. Post-delivery change in PCV

Drug related adverse effects noted and tabulated such as acute urinary retention, retained placenta, hypotension, pain in abdomen, nausea, vomiting, anaphylaxis.

Data analysis method

Data was entered using secondary data in MS Excel and expressed as a proportion. SPSS statistical package was used for statistical calculation. Data are presented as mean

and standard deviation, p value of <0.05 was considered significant and <0.001 was considered highly significant.

RESULTS

Incidence of uterine atony immediately post-delivery was less in group A (9.6%) and more in group B (12%), however with p value of 0.66, this difference was not found to be statically significant (Table 1).

Uterine atony at 1 hour post-delivery was less in group A (4%) and more in group B (6.4%). Uterine atony at 2 hours post-delivery was equal in both groups (3.2%). At 3 hours post-delivery, no case of uterine atony was seen in group A, with incidence in group B being low (1.6%). There was no significant difference in incidence of hemorrhage between both groups (Table 2).

Overall incidence of post-partum hemorrhage with need for additional uterotonic drugs was lower in group A (16%) than in group B (19.2%). P value was 0.51, hence no statistically significant difference was seen (Table 3).

Blood loss was assessed using fall in post-delivery hemoglobin and hematocrit values. Decrease in post-delivery hemoglobin was slightly lower in group A (1.34 g/dl) compared to group B (1.56 gm/dl), with p value of 0.414. Decrease in post-delivery hematocrit was also marginally lower in group A (1.71%) compared to group B (1.93%) with a p value of 0.1679. Hence, no significant difference in blood loss was found between the 2 groups (Table 4).

No incidence of adverse effects was seen in either group.

Table 1: Uterine tone immediately post delivery.

Uterine tone immediately post delivery								
	Atonic		Contracted		Well contracted		Chi-square test	P value
	N	%	N	%	N	%		
Group A: carbetocin (n=125)	12	9.6	69	55.2	44	35.2	0.8362	0.658301
Group B: oxytocin (n=125)	15	12	72	57.6	38	30.4		

Table 2: Uterine atony with/without vaginal bleeding.

Uterine atony with/without vaginal bleeding								
	1 hour		2 hours		3 hours		Total	
	N	%	N	%	N	%	N	%
Group A: carbetocin (n=125)	5	4	4	3.2	0	-	9	7.2
Group B: oxytocin (n=125)	8	6.4	4	3.2	2	1.6	14	11.2

Table 3: Need for additional oxytocic drugs.

Need for additional oxytocic drugs				
	N	%	Z test	P value
Group A: carbetocin (n=125)	20	16	-0.6643	0.50926
Group B: oxytocin (n=125)	24	19.2		

Table 4: Change in hemoglobin and PCV.

	Group A: carbetocin (n=125)	Group B: oxytocin (n=125)	t-test	P value
Change in hemoglobin				
Pre delivery (mean±SD)	11.60±0.63	11.71±1.01	-0.818	0.414
Post delivery (mean±SD)	10.26±0.63	10.15±1.07		
Change in PCV				
Pre delivery (mean±SD)	38.68±1.41	36.98±1.06	-1.3829	0.1679
Post delivery (mean±SD)	39.01±1.84	37.07±2.04		

DISCUSSION

In this randomized interventional study, we have attempted to compare the efficacy of 100 mcg room temperature stable carbetocin with 10 IU oxytocin for the prevention of postpartum hemorrhage in patients undergoing singleton, term, vaginal deliveries. It was found that incidence rates of postpartum hemorrhage were marginally lower in carbetocin group, confirming the non-inferiority of carbetocin as compared to oxytocin in its use

for prophylaxis of post-partum hemorrhage. Need for use of other oxytocics to achieve uterine tone was slightly higher in the oxytocin group, as was the rate of atonic hemorrhage at 1-3 hours post-delivery, however this was not found to be statistically significant. This is consistent with studies showing similar rate of onset with longer action of carbetocin.[10] Post-delivery blood loss, as assessed by decrease in hemoglobin and PCV values showed no significant difference in either group. The safety profile of both drugs was also found to be comparable, with no incidence of adverse effects seen in either group withing the first 24 hours post administration.

Hence, the decision to use carbetocin should be made on basis of convenience in specific settings. In developing nations such as India, atonic post-partum hemorrhage is the most common cause of maternal mortality.[2] Use of oxytocics has been proven to be the most effective tool in the prevention as well as treatment of post-partum hemorrhage, leading to the widespread use of oxytocin.[6] However, effective maintenance of the cold chain required for action of oxytocin is difficult in India, especially in rural settings. In such cases, room temperature stable carbetocin can be especially lifesaving. Moreover, carbitocin has also been found to be effective as a single intravenous/intramuscular dose.[11] Carbetocin has also been shown to be safe for intravenous as well as intramuscular administration, with incidence of adverse effects being rare, allowing it to be used in primary health care centers.[9] The cost of carbetocin in India is higher than that of oxytocin, with 100 mcg carbetocin costing Rs.300 and 10 units oxytocin costing Rs.100. However, the non-requirement of cold chain as well as the efficacy of single dose make carbetocin a useful drug in the Indian setting.

CONCLUSION

This study found carbetocin to be slightly superior to oxytocin in the prevention of post-partum hemorrhage in women undergoing singleton term vaginal deliveries. However, this difference was not found to be statistically significant. Carbetocin is room temperature stable and requires single dose administration, hence it can be used conveniently in developing countries such as India.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Anurag A, Singh S, Kumar S. Comparison of carbetocin and oxytocin in the prevention of atonic post-partum hemorrhage following normal vaginal delivery. Int J Reprod Contracept Obstet Gynecol 2022;11:2665-8.