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Carbetocin versus Oxytocin in the Prevention of Postpartum Haemorrhage after Caesarean Section

Dr E.J.Srinivas
Associate Professor
Dept of Anesthesiology
East point college of medical science and research centre
Bangalore, Karnataka, India

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ABSTRACT
Post partum haemorrhage is one of the major contributors to maternal mortality and morbidity worldwide. There are many pharmacological options for the management of post partum hemorrhage, oxytoc in being the first line choice of treatment. Carbetocin, along acting oxytocin agonist, appears to be a promising agent for the prevention of PPH.
This comparative study was between Carbetocin Versus Oxytocin for the Prevention of Postpartum Haemorrhage in Caesarean Section To determine the safety and effectiveness of carbetocin and oxytocin for the prevention of post-partum haemorrhage in caesarean section. Randomized controlled clinical trial was done in the department of Obstetrics and Gynaecology of East point Medical college and Research centre Bangalore between January to May 2023. Study population were 64 pregnant women admitted for delivery and underwent caesarean section, who were randomly selected. Women in the intervention group(group I) received injection carbetocin abolus of 100µgm diluted in 100ml Normal saline given within3 minutes after delivery; women in the standard treatment group (group II) received 20I Uofoxytocin (10 units IV bolus , 10 units as infusion in 10 minutes) administered immediately after childbirth. Difference of mean age, mean gestational age and indication of C/S were not statistically significant between two groups. Regarding haemodynamic effect, both drugs were almost similar. There was no significant difference in per-operetive blood loss, uterine tone, level of uterine fundus, urine output in urobag and hemoglobin level. Need for additional oxytocics required 0(0.0%) vs 5(16.7%) patients in group I and group II respectively and was found statistically significant. Blood transfusion needed was 0(0.0%) vs 3(10.0%) patients and primary PPH 0(0.0%) vs 3(9.4%), though both were not statistically significant. No significant difference regarding side effects was found. Administration of single bolusdose of carbetocin (100µgIV) after delivery of the baby in caesarean section immediately reduces the need for additional oxytocics, occurrence of primary PPH and further blood transfusion. Side effects are mild and similarin both the groups. Carbetocin can be considered as a good alternative to oxytoc in for the prevention of PPH in Ceserean section.
KEYWORDS- Carbetocin, Oxytocin, PPH, Uterus Atony, Uterotonic agents.

I. INTRODUCTION

Prevention of PPH is a major issue due to its impact on maternal mortality and morbidity. Primary PPH is defined as blood loss morethan 500ml after vaginal delivery and morethan 1000ml after C/S, that occurs in the first 24 hours after delivery.In 2017, World health organization (WHO) has estimated that around 2,95,000[1] maternal deaths occurring each year on a global scale in association with pregnancy and delivery. Among them, 28.37%[1] resulting from postpartum hemorrhage. The main risk of the primary cause of postpartum hemorrhage is uterine at ony which occurin 80.0% cases. The prevalence of PPH in caesarean deliveries is 0.6%.

The decreased prevalence of postpartum hemorrhage in most developed parts of the world is probably due to better management of the third stage of labor. According to, BDHS (2014) MMR is 170/ 100000 live births, BMMS (2016) 196/100000 live births and WHO (2015) 176/100000 live births (NIPORT).

Caesarian section rate is increasing day by day and getting accessible to every level of health care delivery system even in countries with limited facility. Uterine tonicity is the most common cause of PPH. Oxytocic agents are the substances that producer hythmic contraction of uterine muscle following delivery of the fetus and thus cause caesation of bleeding.

Conventional oxytotic agents used include

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oxytocin, ergometrine, syntometrine and prostaglandins. Oxytocin has been used routinely formany years. It is a short acting uterotonic agent.

Carbetocin is a long-acting synthetic oxytocin analogue, 1-deamino-1 monocarbo-(2-0-methyl- tyrosine)- oxytocin firstly described in 1987. The clinical and pharma cological properties of carbetocin are similar to those of naturally occurring oxytocin. It has a half life of 40 mins, around 4-10 times longer than oxytocin. Like oxytocin, carbetocin binds to oxytocin receptors present on the smooth musculature of the uterus, resulting in rhythmic contractions of the uterus, increases frequency of existing contractions and increases uterine tone. In pharmacokinetic studies, intravenous injections of carbetocin produces tetanic uterine contractions within two minutes, lasting six minutes, followed by rhythmic contractions for a further hour. Intra muscular injection produces tetanic contractions in less than twominutes, lasting about 11 minutes and followed by rhythmic contractions for an additional two hours. In comparison to oxytocin, carbetocin induces a prolonged uterine response when administered post partum and also ahead in terms of both amplitude and frequencyofcontractions[2].

Till now it was recommended that Oxytocin should be used as oxytocic agent either in the form of intramuscular injection or I/V bolus or I/V infusion[3].With the use of Carbetocin uterine contractions occur in less than two minutes after intravenous administration of optimal dosage of 100 µg. Several data of literature[4] suggest that prophylactic administration of carbetocin may be a good alternative to oxytoc into prevent post-partum haemorrhage. Aim of this study was to compare the haemodynamic effects of carbetocin and oxytocin, to assess the efficacy of carbetocin and oxytocinin terms of intraoperative blood loss and the need of additional uterotonic in caesarean section for management of post-partum haemorrhage and to compare side effects of them.

II. MATERIALS AND METHOD:

This was a randomized controlled clinical trial from January to May 2023 carried out in the Department of Obstetrics & gynecology at East point medical college and research centre Bangalore. Sixty four pregnant women undergoing C/S were enrolled. Inclusion criteria were women at term pregnancy undergoing elective or emergency caesarean section under spinal anaesthesia in women with risk factors for PPH like multiple pregnancy, two or more previous caes are an section, uterine fibroids, pasthistory of PPH and myomectomy.

Exclusion criteria were hypertension, preeclampsia, eclampsia, placentaprevia, gestation a lageless than 37weeks, cardiac, renalorliverdiseases, epilepsy and general anaesthesia, as well as women with history of hypersensitivity to carbetocin oroxytocin.

A written informed consent was asked from eligible women on admission. 32 pregnant women were recruited in intervention group who received bolus dose of 100 µg of carbetocin intravenously immediately after delivery of the baby and another 32 pregnant women in control group who received bolus dose of 20 IU of oxytocin intravenously immediately after delivery of the baby.

The primary outcome of this study was the evaluation of vitalsigns during and after the operation, estimated blood loss (per operative and within first 24 hours after surgery), difference in preoperative and post operative haemoglobin, uterinetone, uterine position, urinary output, use of additional oxytotics, occurrence of primary PPH, requirement of blood transfusion adverse effects. All patients received spinal anaesthesia.

To evaluate the haemodynamic effects between carbetocin and oxytocin the study was considered the dropin a blood pressure comparing the BP after spinal procedure and 5 minutes after drug administration. Occurrence of nausea, vomiting, flushing, haedache, dyspnea and tachycardia were recorded.

The latter important outcome of this study was the need for additional uterotonic agents and the evaluation of the drop in haemoglobin level by comparing the haemoglobin concentration on admission with the measure at 24 hours after delivery. Also the blood loss is checked immediately after caesarean, defining ashaemorrhage a blood loss in excess of 1000 ml or more[5]. Blood loss were estimated by visual estimation, measuring collected fluid/blood in suction container before and after delivery of the placenta and weight of all blood soaked materials and clots. Calculated by (wet item in gram wt-dryitemingram wt=blood losing ram wt.1gram wt=1ml blood loss)[6]. Blood pressure (in mmHg), uterine tone (standardized as Very good, Good, Sufficient, Atony), uterine position (with respect to the umbilical point, UP) were monitored at 2 hours, 12 hours and 24 hours after caes are an section[7].All patients had the Foley catheter and urobag in situ for 12 hours after caes are an section. Finally, incidence of PPH, requirement of blood transfusion and are measured.

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III. RESULTS:

Total 70 pregnant women were initially recruited in this study. Among them 6 cases were excluded not meeting inclusion criteria. Thus 64 women were included in the final analysis.

Demographic characteristics of the study patients showed- Mean age was found26.5±4.9 years in group I Carbetocin and 27.2±4.8 years in group II Oxytocin. Majority 22 (68.8%) patients were multi gravida in group I and 23 (71.9%) in group II. The meange station a lage was found 38.6±1.6weeksin group I and 38.9±1.6 weeks in group II. The difference were not statistically significant (p>0.05) between two groups. That is the groups were homogenous.

Indications of Ceserean section were not statistically significant (p>0.05) between two groups. P/H/O 1C/S with other obstetrical indication was common in both groups, which was 9(28.1%) in group I and 13(40.6%) in group II. Other indications were CPD, mal- presentation, feotal distress, obstructed labor etc.

Regarding vitals, BP (systolic & diastolic), urine output were more or less similar in both groups.

Though the difference in blood loss between two groups were not statistically significant, loss of blood was 70-100 ml lessin group I.

Uterine tone and level of uterine fundus we real most similar in both groups and diference were not statistically significant (p>0.05).

Haemoglob in level is a proxy indicator of blood loss. The mean difference were not statistically significant (p>0.05) between two groups.

Adminstration of additional oxytocics, blood transfusion & side effects of drugs were less in group I but not statistically significant.

Table-I

Distribution of the study patients by maternal blood loss at different followup (n=64)

Materna lbloodloss(ml)	Group-I(n=32) Mean±SD	Group-II(n=32) Mean±SD	Pvalue
Peroperative	363.3±107.4	441.3±209.6	0.066^{ns}
Range (min-max)	250-650	300-900	
2hrs after caes are an section	389.7±113.8	463.3±238.0	0.120^{ns}
Range (min-max)	270-700	330-1100	
12hrs after caes are an section	423.8±121.2	504.0±243.3	0.100^{ns}
Range (min-max)	290-770	350-1150	
24hrs after caes are an section	452.8±122.8	526.3±234.1	0.121^{ns}
Range (min-max)	300-800	390-1200	

s=significant, ns=not significant

Pvalue reached from unpaired t-test

Table-II

Distribution of the study patients by hemoglobin in different followup(n=64)

Hemoglobin(g/dl)	Group-I(n=32) Mean±SD	Group-II(n=32) Mean±SD	Pvalue
Before administration of drug	10.7±0.9	10.9±0.8	0.351^{ns}
Range (min-max)	9-12.4	9.2-13	
24hrs after caes are an section	10.2-0.8	10.0±0.9	0.351^{ns}
Range (min-max)	8.8±11.8	8.4-12.2	

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Table-III
Distribution of the study patients by outcome(n=64)

Outcome (primary PPH)	Group-I (n=32)		Group-II (n=32)		P value
	n	%	n	%	
Yes	0	0.0	3	9.4	0.119ns
No		32	100.0	29	90.6

The difference was not statistically significant(p>0.05)

IV. DISCUSSION:

This randomized controlled clinical trial was carried out to determine the safety and effectiveness of carbetocin and oxytocin for the prevention of post- partum haemorrhage in caesarean section. Majority of the patients were in 3rd decade, multipara and gestational age belonged to 37 – 40 weeks in both groups. Past history of one Ceserean section with other obstetrical indication, Past history of Ceserean section with scar tenderness, breech presentation with other obstetrical indication and prolonged labour with fetal distress were the commonest indication in both groups. Blood pressure, maternal blood loss, uterine tone, position of uterine fundus to the umbilical point, urine output in urobag and hemoglobin level were almost similar between two groups. Additional oxytocics not needed in carbetocin group (p<0.05). On the other hand, no need of any blood transfusion, side effect and no primary PPH observed in carbetoc in group.

V. CONCLUSION:

A single intravenous injection of carbetocin (100µgm) appears to be more effective than a single intravenous injection of oxytocin (20 IU) for maintaing adequate uterine tone, less blood loss, no need of additional oxytocics and blood transfusion and no incidence of PPH, with a similar safety profile and minor side effects, in the third stage and in the first 24 hours after delivery.

VI. RECOMMENDATION

A single intravenous injection of 100 µgm of carbetocin immediately after birth of the baby in pregnant women undergoing caesarean section under spinal anesthesia can be used effectively and safely to prevent post-partum hemorrhage.

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