Comparison of Carbetocin versus Oxytocin for Decreased Blood Loss from Caesarean Section: A Randomized Clinical Trial

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ABSTRACT

Objectives: *The aim of the present study was to compare the efficacy of oxytocin bolus and infusion to carbetocin bolus followed by oxytocin infusion in reducing operative and postoperative blood loss after caesarean section. Therefore reducing needs for additional uterotonic agents.* ***Methods:*** *Hundred (100) women scheduled for elective caesarean section under spinal anaesthesia, were included in this study and divided into two groups. Group-O; received oxytocin 10 IU bolus, followed by 20 IU oxytocin in each 1000 ml saline for 24 hours. Group-C; received carbetocin 100 µgm bolus followed by 20 IU oxytocin infusion in each 1000 ml saline for 24 hours. The main parameters were evaluated and blood loss was calculated during caesarean delivery along with 24 hours posto-perative period, in addition to the need for additional uterotonic drugs.* ***Results:*** *Blood loss was compared and accepted clinically in two groups but loss was less during caesarean section in carbetocin groups than that of oxytocin groups. Carbetocin groups did not require any other uterotonic drug but oxytocin groups required other uterotonic drugs during operative and postoperative periods.* ***Conclusion:*** *Carbetocin and oxytocin were comparable for reducing blood loss and maintaining tone of the uterus during and after caesarean section. Additional uterotonic use was significantly lower in carbetocin groups with lower incidence of PPH, blood transfusion, Hb%, Hct% changes within 24 hours. of caesarean section.*

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INTRODUCTION

Caesarean section (CS) is the most common operation for the Obstetricians, but has to take challenge to reduce operative and postoperative bleeding. Rate of CS is increasing up by 20% to 30% in most developed countries; up to 40% in China and as high as 70% in some Latin American countries.[1,2] Now-a-days, PPH has still been the common cause of maternal death after delivery-delivery with incidence of 1:1000, specially in developing countries.[3] The most common cause of PPH (postpartum

haemorrhage) is uterine atony.[3, 4] CS delivery-delivery itself is one of the PPH risk factors.[5,6] For this reason, WHO (in 2012) suggested the PPH prevention methods by administration of uterotonic drugs, immediately after child birth by CS, combined with controlled cord traction for placental delivery.[7]

Current strategies for preventing PPH include, the prophylactic use of utertonic agents to enhance natural contraction and retraction following CS.[8,9] Many factors would affect blood loss during and after CS, e.g. maternal cause (weight, parity, H/O previous CS), foetal cause (multiple gestation, polyhydramnios, malpresentation) and technical cause (operation time, type of incision, placental site and separation technique and type of anaesthesia). To reduce maternal morbidity and mortality caused by bleeding, it is important to reduce the amount of bleeding during and after CS. The guidelines of the Royal College of Obstetricians and Gynaecologists (UK) on CS recommended a slow intravenous bolus dose of 5 IU oxytocin after delivery of the baby.[10] This practice is the same in most countries of the Europe and Australia. In UK, a survey of Obstetricians and Anesthesiologists, the use of oxytocin bolus[11] was standard but dose varied between 5 and 10 IU. So, Obstetrician used an additional infusion of oxytocin on a selective or routine basis to high risk cases.[12] In US, they recommended the use of oxytocin infusion instead of a bolus dose.[13] The very recent Canadian guidelines recommended the use of carbetocin instead of oxytocin at CS.[8] Oxytocin is the most widely used uterotonic agent, but has a half life of only 4-10 minutes. Carbetocin is a synthetic analog of oxytocin with a half life 4-10 times longer than oxytocin. It is used as a single dose (100µgm) slowly I/v or I/m injection.[14] Carbetocin is currently appro-ved in 23 countries for prevention of uterine atony and excessive bleeding following caesarean delivery-delivery in spinal or epidural anaesthesia.

METHODS

This is a prospective randomized clinical study conducted from January 2017 to December 2017 at Delta hospital limited at Mirpur-11, Dhaka, Bangla-desh. Written informed consents were taken from 100 women undergoing elective Caesarean section (CS) under spinal anesthesia. The patients were clinically examined and USG of abdomen, Complete Blood Count, coagulation profile, urine analysis, and blood sugar tests were done. Exclusion criteria were women with coagulopathy, fibroid, placenta praevia, anticoagulant and antiplatelet therapy, and ecclampsia. All women were given subara-chnoid block (spinal anesthesia) using 25 G spinocaine B. BRAUN needle, with a dose of 12.5 mg heavy bupivacaine mixed with 25 µgm fentanyl after preloaded with 1000 ml Hartman solution. All CS were done by same Obstetrician with same team. Intraoperative blood pressure was maintai-ned by using inj. Ephedrine intravenously in 5 mg incremental doses. After delivery-delivery of the baby, women were randomly divided into equal two groups: 50 women were in each group.

Group-O received 10 IU oxytocin bolus (diluted to 5 ml normal saline) intravenously over 2 minutes followed by 20 IU oxytocin in each 1000 ml saline for 24 hours.

Group-C received 100 µgm carbetocin diluted to 5 ml normal saline bolus dose intravenously over 2 minutes followed by 20 IU oxytocin infusion in each 1000 ml saline for 24 hours.

Intraoperative blood loss was calculated by the sum of the amounts of blood loss in suction bottle and estimated blood volume from all blood stained swabs, while postoperative blood loss was calculated by weighing all sanitary pads used within 24 hours. All patients' demographic data, amount of blood loss, blood transfusion, and additional uterotonic agents used, Hb%, Hct% changes in 24 hourrs after CS and side effects were collected in data sheet. Statistical analysis was carried out by using the Statistical Package for Social Sciences (SPSS) Version 22.0 for windows (SPSS Inc., Chicago, Illinois, USA). Continuous data were expressed as the mean standard deviation (SD) and categorical variables are expressed as percentages. Chi-square (χ^2) and unpaired t-tests were done for measuring of

p-values for all statistical tests. A '*p*' value <0.05 was considered as statistically significant.

With the changes of Hb% and Hct% at 24 hours post CS, total amount of blood loss was calculated, transfusion depended on the calculated blood loss. During operation, addition of uterotonic drugs were administered if surgeon perceived inadequate uterine contraction and also in the postoperative period.

RESULTS

Demographic characteristics in two groups of the patients were comparable with no significant differences regarding age, weight, height, BMI, parity. There were no significant differences in preoperative Hb% and Hct% values in both the groups (Table I).

Table I: Comparison of demographic characteristics between two groups (n-100)

Demographic characteristics	Oxytocin-O (n-50) Mean ± SD	Carbetocin-C (n-50) Mean±SD	*p* value
Age (years)	26.80±4.04	26.02±3.47	0.303 ^{ns}
Weight (kg)	77.24±4.50	76.08±4.77	0.214 ^{ns}
Height (cm)	157.69±3.73	157.66±4.08	0.970 ^{ns}
BMI(kg/m2)	31.12±2.42	30.64±2.27	0.312 ^{ns}
Parity-primipara	34(68.0%)	41(82.0%)	
multipara	16(32.0%)	9(18.0%)	0.106 ^{ns}
Preoperative Hb%	11.72±0.71	11.92±0.82	0.196 ^{ns}
Preoperative Hct%	35.07±0.73	35.20±0.74	0.397 ^{ns}

Data were expressed as mean±SD, unpaired student t-test was performed to compare between two groups, s= significant, ns= not significant.

Table II shows operative and 24 hours postoperative blood losses were significantly less in carbetocin groups (297.30 ± 88.37) than oxytocin groups (411.20±93.09), *p*<0.001. Postoperative losses were also significantly less in carbetocin groups than oxytocin groups (166.20±58.26 and 312.70±156.32 respectively, *p*<0.001). Regarding postoperative Hb% and Hct% values, carbetocin group had 11.25±0.82 and 34.19±45.04 respectively similar to oxytocin group (11.25±3.30 and 33.90±3.40 (p=0.257).

Table II: Comparison of operative and postoperative variables between two groups (n-100)

Variables	Oxytocin (n-50) Mean ± SD	Carbetocin (n-50) Mean ± SD	*p* value
Operative blood loss	411.20±93.09	297.30±88.37	<0.001 ^{s}
Postoperative 24 hours blood loss	312.70±156.32	166.20±58.26	<0.001 ^{s}
Postoperative Hb%	11.25±3.30	11.25±0.82	0.993 ns
Postoperative Hct%	33.90±3.40	24.19±45.04	0.257 ns

Data were expressed as frequency, percentage and mean ± SD. Unpaired student t-test was performed for quantitative variables and Chi-squared test (χ^2) was done for qualitative variables. S= significant, ns= not significant.

Table III shows comparison of use of other utero-

tonic agents in two groups which was significantly less in carbetocin group than oxytocin group (4.0% vs 24.0%) (p=0.004). Blood transfusion was needed more in oxytocin group than carbetocin group (14.0% vs 4.0%) but not significant.

Table III: Comparison of use of other uterotonic agents and Blood transfusion in two groups (n-100)

Variables	Oxytocin (n-50) Number (%)	Carbetocin (n-50) Number (%)	*p* value
Use of other uterotonic agents	12(24.0%)	2(4.0%)	0.004 [s]
Blood transfusion	7(14.0%)	2(4.0%)	0.081 [ns]

Unpaired student t-test was performed.
S= significant, ns= not significant.

There were no significant differences in side effects between the groups, but carbetocin group had no headache.

Table IV: Comparison of side effects between two groups (n-100)

Side effects	Oxytocin (n-50) Number (%)	Carbetocin (n-50) Number (%)	*p* value
Nausea	14(28.0%)	20(40.0%)	0.205 [ns]
Vomiting	18(36.0%)	11(22.0%)	0.123 [ns]
Headache	3(6.0%)	00(0.0%)	0.079 [ns]

Data were expressed as frequency, percentage and mean±SD. Chi-square (χ^2) Test was done.
s=significant, ns=not significant.

DISCUSSION

Caesarean section (CS) is a very common operation for the Obstetricians but has to take challenge to reduce blood loss during and after 24 hours of operation. Carbetocin a newer drug having eight aminoacid long chain analogues of oxytocin, having longer half life than oxytocin. Carbetocin has been approved for promoting uterine contraction in order to prevent postoperative bleeding in CS. In the present study, operative blood loss was significantly less in carbetocin groups than that of oxytocin groups (p<0.001). Postoperative blood loss was relatively high in oxytocin groups than that of carbetocin groups but the differences are not significant. Our results were similar to that conducted by Attilacos et al,[8] who reported less blood loss with the use of carbetocin when compared to oxytocin bolus.

Borruto et al,[15] compared carbetocin bolus and oxytocin 20 IU infusion and they found equivalent results regarding maintenance of tonic uterine contraction and limitation of blood loss during and after CS which is matched with this study results. Triopon et al,[14] also found that, carbetocin was similarly effective as oxytocin during CS.

Su et al,[16] in the Cochrane of 2007 regarding "Oxytocin agonists for preventing postpartum haemorrhage" and in the Cochrane of 2012 regarding "Carbetocin for preventing postoperative haemorrhage" concluded that the use of carbetocin is more effective than oxytocin for preventing PPH in women undergoing CS, but the data and evidences were still insufficient.[16] The results of clinical study matched with those results. Regarding the literature about carbetocin, D Dan Zerean et al,[17] firstly described a lower additional uterotonic

need for treatment of uterine atony in women who took carbetocin soon after delivery. Also Borruto et al,[15] describe a lower rate of additional oxytocic need in women undergoing CS using carbetocin after delivery-delivery of the baby. In this study, use of other uterotonic agents in carbetocin groups were significantly less (2; 4.0%) (p<0.004), which was matched with above study.

In conclusion, carbetocin and oxytocin are compa-rable drugs for reducing blood loss, maintaining uterine tone during and after CS. Adding oxytocin infusion for 24 hours, postoperatively might decrease blood loss and reduces the need for additional uterotonic agents.

Conflict of Interest: None

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