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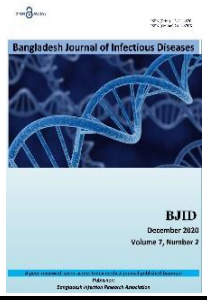

Comparison of Complication and Post-Operative Infection Rate Between Application of Carbetocin and Oxytocin during Management of Post-Partum Hemorrhage after Caesarean Section

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Abstract

Background: Adverse effects can be produced by carbetocin and oxytocin during management of post-partum hemorrhage after caesarean section. **Objective:** The purpose of the present study was to compare the adverse effects among women with post-partum hemorrhage after caesarean section. **Methodology:** This randomized controlled trial was conducted in the Department of Obstetrics and Gynaecology at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from July 2015 to December 2015 for a period of six months. Pregnant women diagnosed on the standard criteria admitted in BSMMU, Dhaka, Bangladesh were selected as study population by consecutive type of sampling. Randomization was performed according to computer generated simple random sampling method. An Uterotonic was an agent used to induce contraction or greater tonicity of the uterus. Then the patients were monitored per operatively and post operatively. All the information was recorded in data collection sheet. Main outcome variables were estimated blood loss. **Results:** A total number of 96 pregnant women were recruited for this study of which 48 cases were enrolled in group I and the rest of 48 case were enrolled in group II. The mean age with SD of the group I and group II were 24.4±4.7 years and 24.7±3.7 years. In blood transfusion of the study patients, 2(4.2%) patients need blood transfusion in group I and 5(10.4%) in group II (p>0.05). One (2.1%) patients had anaemia in group I and 5(10.4%) in group II. Forty-six (95.8%) patients had average menstrual flow in group I and 40(83.3%) in group II (p>0.05). Considering the side effect, 1(2.1%) patients had nausea in group I and 4(8.3%) in group II. Two (4.2%) patients had vomiting in group I and 5(10.4%) in group II. One (2.1%) patients had headache in group I and 4(8.3%) in group II. Four (8.3%) patients had infection rate in group I and 5(10.4%) in group II (p>0.05). **Conclusion:** In conclusion blood transfusion, anaemia, vomiting and infection rate are found less in group I than group II. [*Bangladesh Journal of Infectious Diseases, December 2023;10(2):59-64*]

Keywords: Adverse effects; carbetocin; oxytocin; post-partum hemorrhage; caesarean section

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Introduction

Oxytocin is relatively safe when used at recommended doses, and side effects are uncommon[1]. The hemodynamic effects of an oxytocin bolus consist of systemic vasodilatation, with hypotension, tachycardia, and an increase in cardiac output and pulmonary artery pressure, resulting in brief hypotension and tachycardia in a dose dependent manner[2-4]. It is an effective drug for the control of post-partum hemorrhage, but the disadvantage is its short half-life of 4 to 10 minutes, regularly requiring a continuous intravenous infusion or repeated intramuscular injections[5].

Carbetocin is a long-acting synthetic analog of oxytocin with agonist action and found more effective in reducing the incidence of post-partum hemorrhage because of its ability to induce strong uterine contractions. Its half-life is 40 min, and uterine contractions occur in less than 2 min after intramuscular or intravenous (IV) administration[6]. A single bolus of 100 μg carbetocin has been shown to be as effective as a continuous 16-h infusion of oxytocin in reducing the intraoperative blood loss in women undergoing elective cesarean delivery[7]. Carbetocin also resulted in a significantly lower incidence of additional oxytocin intervention in the carbetocin group compared with the oxytocin group in women undergoing elective cesarean delivery[8-9]. However, another study demonstrated a different result that carbetocin have similar requirements for additional uterotonics at non-elective cesarean section[10-12].

Safety of carbetocin following vaginal births and emergency Cesarean sections has not been established, though studies have suggested efficacy following vaginal births to that following Cesarean sections[11]. Some studies have shown that a 10 to 70 μg dose following vaginal delivery caused contractions and no adverse side effects[13]. The recommended dose for an average adult female is 100 μg, administered slowly over a minute[8].

Adverse reactions may occur like nausea, vomiting, abdominal pain, itching skin, increased body temperature, trembling and weakness in 10.0 to 40.0% patients[9]. However, 1.0% to 5.0% patients may experience back and chest pain, dizziness, anemia, chills and sweating, metallic taste, tachycardia and respiratory distress[10]. The purpose of the present study was to compare the adverse effects among women with post-partum hemorrhage after Caesarean Section.

Methodology

Study Settings and Population: This randomized controlled trial was conducted in the Department of Obstetrics and Gynaecology at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from July 2015 to December 2015 for a period of six months. Pregnant women diagnosed on the standard criteria admitted in BSMMU, Dhaka, Bangladesh were selected as study population by consecutive type of sampling. Patient with risk factors for primary post-partum haemorrhage such as multiple pregnancy, one or more previous caesarean section, presence of uterine fibroids, previous myomectomy, presence of placenta previa, past history of post-partum hemorrhage, fetal macrosomia and fetal malformations associated with polyhydramnios were included in this study. Presence of hypertension, eclampsia, cardiac, renal or liver diseases, epilepsy, general anaesthesia, as well as women with history of hypersensitivity to Carbetocin according to the Br National Formulary or patients unwilling to give consent for this study were excluded from this study.

Randomization and Blinding: Randomization was performed according to computer generated simple random sampling method. Single binding was performed without knowing the drugs to the participants.

Study Procedure: Postpartum haemorrhage was defined as any amount of bleeding from or into the genital tract following birth of the baby up to the end of puerperium, which adversely affects the general condition of the patient evidenced by rise in pulse rate and falling blood pressure, is called postpartum haemorrhage. An Uterotonic was an agent used to induce contraction or greater tonicity of the uterus. Detail history was taken by structured questionnaire. At first the pregnant women were selected according to inclusion and exclusion criteria. Then detailed informed written consent was taken from each patient. The drug that was introduced during caesarean section was allocated by coin tossing. The drug carbetocin will be supplied by Beacon Pharmaceuticals Limited, Dhaka, Bangladesh. Verbal consent was taken from Product Manager (Mr. Tanhar, Product manager for Carbetocin, Beacon Pharmaceuticals Ltd.). Each ampule will contain 100μg of carbetocin, 9 mg sodium chloride, acetic acid-glacial to pH 3.8 and water for injection to 1 mL. It has to be kept in refrigerator at 4^0 C, without any freezing and has to be administered immediately without any delay.

Follow up and Outcomes Measures: Then the patients were monitored per operatively and post operatively. All the information was recorded in data collection sheet. Main outcome variables were Estimated blood loss (Visual estimation, number of used mops, amount of aspirated blood), difference between preoperative and post-operative haemoglobin level, vital sign during and after operation, Uterine tone, Incidence of blood transfusion and Adverse effects like nausea, vomiting, headache and so on.

Statistical Analysis: Statistical analyses were carried out by using the Statistical Package for Social Sciences version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Chi-Square test with Yates correction was used to analyze the categorical variables, shown with cross tabulation. Student t-test was used for continuous variables. P values <0.05 was considered as statistically significant.

Ethical Implications: Ethical clearance was obtained from Institutional Review Board of BSMMU. Written informed consent was obtained from the patient or from her legal guardian. Patient confidentiality was strictly maintained. No name, address or contact details of the patient was divulged.

Results

A total number of 96 pregnant women were recruited for this study of which 48 cases were enrolled in group I and the rest of 48 case were enrolled in group II. The mean age with SD of the group I and group II were 24.4±4.7 years and 24.7±3.7 years. The difference between the mean age of group I and group II were not statistically significant (Table 1).

Table 1: Distribution of the Study Patients by Age Group (n=96)

Age Group	Group I	Group II
≤20 Years	13(27.1%)	9(18.8%)
21 to 30 Years	31(64.6%)	35(72.9%)
More Than 30 Years	4(8.3%)	4(8.3%)
Total	**48(100.0%)**	**48(100.0%)**
Mean±SD	24.4±4.7	24.7±3.7
Range (min, max)	19, 39	19, 33

Chi-Square test was performed; p value was 0.729

In blood transfusion of the study patients, it was observed that 2(4.2%) patients need blood transfusion in group I and 5(10.4%) in group II. The difference was not statistically significant (p>0.05) between two groups (Table 2).

Table 2: Distribution of the Study Patients by Blood Transfusion (n=96)

Blood Transfusion	Group I	Group II
Yes	2(4.2%)	5(10.4%)
No	46(95.8%)	43(89.6%)
Total	**48(100.0%)**	**48(100.0%)**

P value reached from chi square test; P value was 0.218

One (2.1%) patients had anaemia in group I and 5(10.4%) in group II. Forty-six (95.8%) patients had average menstrual flow in group I and 40(83.3%) in group II. The difference was not statistically significant (p>0.05) between two groups (Table 2).

Table 3: Distribution of the Study Patients by Anaemia and Menstrual Flow (n=96)

Variables	Group I	Group II	P value
Anaemia			
Present	1(2.1%)	5(10.4%)	0.101
Absent	47(97.9%)	43(89.6%)	
Total	**48(100.0%)**	**48(100.0%)**	
Menstrual Flow			
Average	46(95.8%)	40(83.3%)	0.045
More than average	2(4.2%)	8(16.7%)	
Total	**48(100.0%)**	**48(100.0%)**	

P value reached from chi square test

Considering the side effect of the study patients, it was observed that 1(2.1%) patients had nausea in group I and 4(8.3%) in group II. Two (4.2%) patients had vomiting in group I and 5(10.4%) in group II. One (2.1%) patients had headache in group I and 4(8.3%) in group II. Four (8.3%) patients had risen of temperature due to infection in group I and 5(10.4%) in group II. The difference was not statistically significant (p>0.05) between two groups (Table 4).

Table 4: Distribution of the Study Patients by Side Effects (n=96)

Side Effects	Group I	Group II	P value
Nausea			
• Yes	1(2.1%)	4(8.3%)	0.181
• No	47(97.9%)	44(91.7%)	

Side Effects	Group I	Group II	P value
Vomiting			
• Yes	2(4.2%)	5(10.4%)	0.218
• No	46(95.8%)	43(89.6%)	
Headache			
• Yes	1(2.1%)	4(8.3%)	0.181
• No	47(97.9%)	44(91.7%)	
Infection Rate			
• Yes	4(8.3%)	5(10.4%)	0.500
• No	44(91.7%)	43(89.6%)	

P value reached from chi square test

Discussion

A total of 96 patients admitted in Gynaecology and Obstetrics Department of Bangabandhu Sheikh Mujib Medical University, Dhaka, for delivery between July 2015 to December 2015 were included in this study. Among them 48 cases treated with Carbetocin was considered as group I and rest 48 treated with Oxytocin was considered as group II. Patient with risk factors for primary post-partum haemorrhage such as multiple pregnancy, one or more previous caesarean section, presence of uterine fibroids, previous myomectomy, presence of placenta previa, past history of PPH, fetal macrosomia and fetal malformations associated with polyhydramnios were enrolled in this study. Presence of hypertension, eclampsia, cardiac, renal or liver diseases, epilepsy, general anaesthesia, as well as women with history of hypersensitivity to Carbetocin according to the British National Formulary and patients unwilling to give consent were excluded from the study.

The present study findings were discussed and compared with previously published relevant studies. In this present study it was observed mean age was found 24.4±4.7 years in group I and 24.7±3.7 years in group II. The mean marital age was found 4.4±4.0 years in group I and 4.1±3.9 years in group II. The difference was not statistically significant (p>0.05) between two groups. Reyes et al.20 found the mean age was 26.52±9.12 years in Carbetocin group and 26.78±8.39 years in Oxytocin group. The difference was not statistically significant (p>0.05) between two groups, which is closely resembled with the present study. On the other hand, Bosilah et al[9] had observed the mean age was 33.0±4.6 years in Carbetocin group and 33.3±4.6 years in Oxytocin group. Similarly, Ahmed et al[13] observed at baseline, there was no significant difference between carbetocin and oxytocin in terms of mean age, where mean was 30 years and 31 years respectively. The higher mean age may be due to geographical variations, racial, ethnic differences, genetic causes, different lifestyle and increased life expectancy may have significant influence in their study patients[11].

In this current study it was observed that 2(4.2%) patients need blood transfusion in group I and 5(10.4%) in group II. The difference was not statistically significant (p>0.05) between two groups, which is similar with Bosilah et al[9] study, where they found 10.3% cases need for blood transfusions in oxytocin group. Similarly, Ahmed et al[13] found that the two groups did not significantly differ in terms of blood transfusion requirements (P>0.05). In another study Hawker and Weeks[14] administrated blood transfusions in 2.2% of the cases in the carbetocin group and 2.7% in the oxytocin group (p>0.05). Larciprete et al[15] found that 3(10.3%) patients needed blood transfusion in Oxytocin group but not needed in Carbetocin group. The difference was not statistically significant (p>0.05) between two groups. In another study Jaffer et al[16] observed that blood transfusion was needed 4(2.1%) in carbetocin group and 39 5(2.6%) in oxytocin group. The difference was not statistically significant (p>0.05) between two groups, which are comparable with the current study. In this series it was observed that 1(2.1%) patients had anaemia in group I and 5(10.4%) in group II. Forty-six (95.8%) patients were average menstrual flow in group I and 40(83.3%) in group II. The difference was not statistically significant (p>0.05) between two groups.

In this study it was observed that 1(2.1%) patients had nausea in group I and 4(8.3%) in group II. Two (4.2%) patients had vomiting in group I and 5(10.4%) in group II. One (2.1%) patients had headache in group I and 4(8.3%) in group II. Four (8.3%) patients had risen of temperature in group I and 5(10.4%) in group II. Side effects were comparatively less in group I but the difference were not statistically significant (p>0.05) between two groups. Jaffer et al[16] found 2 subjects experienced at least one AE with a moderate degree of severity and four subjects experienced a mild AE after carbetocin like nausea, headache, abdominal pain. In those six cases, the relationship with carbetocin was rated as unlikely or none. In the oxytocin group a total of six AEs were experienced by six subjects. Two subjects experienced moderate AEs (fluxus, atony) unrelated to oxytocin. Four subjects experienced mild AEs like hypotension or fluxus, rated as having no, unlike or possible relationship with oxytocin. In another study, Larciprete et al[15] obtained that nausea and vomiting

was found 3.6% cases in Carbetocin group and but not found in Oxytocin group. Fever was found 3.4% in Oxytocin group but not found in Carbetocin group. The difference was not statistically significant ($p>0.05$) between two groups. There weren't any recorded important adverse effects in both study groups, instead nausea and vomiting was observed with similar frequency in both study groups also observed by Larciprete et al[15] and Jaffer et al[16]. The above findings are consistent with the current study.

Conclusion

In conclusion blood transfusion is less needed among the patients in group I than in group II. This difference is not statistically significant between two groups. Again less patients have reported anaemia in group I than in group II. Furthermore, more patients have average menstrual flow in group I than in group II. This difference is not statistically significant between two groups. Vomiting are found less in group I than group II. Infection rate is less than group I than group II. Further large scale study should be carried out to get the real scenario.

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None

Conflict of Interest
The authors have no relevant conflicts of interest to declare.

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Contribution to authors:
Choudhury FH: Conception and design, or design of the research; Choudhury FH, Tanzin ST, Ahmed S: the acquisition, analysis, or interpretation of data; conceptualized and designed the overall study. Noor MS: involved in data collection; Choudhury FH, Tanzin ST, Fatema N: Drafting the manuscript or revising it critically for important intellectual content. Choudhury FH: involved in data input and data cleaning. Noor MS, Tanzin ST: conducted data analysis. Choudhury FH, Tanzin ST, Ahmed S, Fatema N: drafted the manuscript. All authors reviewed and approved the final manuscript.

Data Availability
Any questions regarding the availability of the study's supporti ng data should be addressed to the corresponding author, who can provide it upon justifiable request.

Ethics Approval and Consent to Participate
The Institutional Review Board granted the study ethical approval. Since this was a retrospective study, not every study participant provided formal informed consent.

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References

1. Pheto P. An audit of uterotonic use for the prophylaxis and treatment of haemorrhage at caesarean delivery at Mowbray Maternity Hospital, Cape Town, South Africa (Master's thesis, University of Cape Town).
2. Shetty SS. Comparison of the adequacy of uterine tone with low dose oxytocin infusion versus low dose oxytocin bolus along with the infusion during elective caesarean section a prospective, randomized, double blind study (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)).
3. Al Anwar AM, Abdal Salam HS, Esukni SM, Abdel Rahman MM. Carbetocin versus Oxytocin: A Comparative Study to Prevent Postpartum Hemorrhage in Pre-eclamptic Women Delivered by Caesarean Section. The Egyptian Journal of Hospital Medicine. 2022;89(1):5063-8
4. Zein El Abdeen E. Carbetocin versus oxytocin and ergometrine for prevention of postpartum hemorrhage following caesarean section. Evidence Based Women's Health Journal. 2018;8(1):138-43.
5. Wang BS, Zhou LF, Coulter D, Liang H, Zhong Y, Guo YN, et al. Effects of caesarean section on maternal health in low risk nulliparous women: a prospective matched cohort study in Shanghai, China. BMC pregnancy and childbirth. 2010;10(1):1-0.
6. Sweeney G, Holbrook AM, Levine M, Yip M, Alfredsson K, Cappi S, et al. Pharmacokinetics of carbetocin, a long-acting oxytocin analogue, in non-pregnant women. Current Therapeutic Research-Clinical and Experimental. 1990;47(3):528-40.
7. Fawcus S, Moodley J. Postpartum haemorhage associated with caesarean section and caesarean hysterectomy. Best practice & research Clinical obstetrics & gynaecology. 2013;27(2):233-49.
8. Dey T, Weeks AD. Identification, prevention and management of post-partum haemorrhage. Obstetrics, Gynaecology & Reproductive Medicine. 2020;30(8):231-41.
9. Bosilah AH, Eldesouky E, Alghazaly MM, Farag E, Sultan EE, Alazazy H, et al. Comparative study between oxytocin and combination of tranexamic acid and ethamsylate in reducing intra-operative bleeding during emergency and elective cesarean section after 38 weeks of normal pregnancy. BMC Pregnancy and Childbirth. 2023;23(1):1-1.

10. Elsafty MS, Hassanin AS, Laban M, Ibrahim AM, Ahmed WU, Abou Elnoor AA. Intravenous carbetocin shot is superior to oxytocin infusion for placental delivery in second trimester abortion: a pilot randomized controlled trial. The Journal of Maternal-Fetal & Neonatal Medicine. 2016;29(5):850-4.
11. Ahmed AO. A Comparison of Combined Rectal Misoprostol and Oxytocin with Oxytocin Alone in the Control of Blood Loss during Elective Caesarean Section: A Randomized Controlled Trial. Faculty of Obstetrics and Gynaecology. 2018
12. Steer PJ. Prevention and management of post-operative caesarean section complications. Textbook of Caesarean Section. 2016:117.
13. Ahmed AR, Saleh AA, Abd Elhameid AA, Badr MS. Incidence and outcome of primary postpartum hemorrhage at Zagazig University Hospitals. Zagazig University Medical Journal. 2020;26(6):970-80
14. Hawker L, Weeks A. Postpartum haemorrhage (PPH) rates in randomized trials of PPH prophylactic interventions and the effect of underlying participant PPH risk: a meta-analysis. BMC pregnancy and childbirth. 2020;20(1):1-2.
15. Larciprete G, Montagnoli C, Frigo M, Panetta V, Todde C, Zuppani B, et al. Carbetocin versus oxytocin in caesarean section with high risk of post-partum haemorrhage. Journal of prenatal medicine. 2013;7(1):12.
16. Jaffer D, Singh PM, Aslam A, Cahill AG, Palanisamy A, Monks DT. Preventing postpartum hemorrhage after cesarean delivery: a network meta-analysis of available pharmacologic agents. American journal of obstetrics and gynecology. 2022;226(3):347-65