

Assessment Of The Necessity Of Additional Uterotonics And Blood Transfusion Within 24 Hours Of Delivery After Carbetocin

Jahan MA¹, Ashraf F², Bhuiyan SMAU³

¹Dr. Mahbuba Akhter Jahan, Specialist, Department of Obstetrics and Gynaecology, Mugda Medical College Hospital, Dhaka, Bangladesh

²Dr. Fatema Ashraf, Specialist & Ex-Head, Department of Obstetrics and Gynaecology, Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh

³Dr. Shah Mohammad Ashek Uddin Bhuiyan, Classified Specialist, Department of Psychiatry, Combined Military Hospital, Dhaka, Bangladesh

Abstract

Introduction: The primary purpose of active management of the third stage of labor is to reduce the risk of PPH. Prevention of postpartum hemorrhage is essential in the pursuit of improved health care for women. The need for additional uterotonics reflects the degree of postpartum vaginal bleeding accounted for by uterine atony. This study aimed to analyze the necessity of additional uterotonics and blood transfusion within 24 hours of delivery after carbetocin.

Methods: This cross-sectional observational study was conducted at the Department of Obstetrics and Gynaecology, Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh. The study period was from May 2016 to October 2016. 100 women undergoing normal vaginal delivery were the study subject. A convenient sampling technique was used in this study. Necessary data was collected in the data collection sheet. Women received a bolus of 100 microgram carbetocin IV at delivery of the anterior shoulder. A standardized deliver mat (Quaiyum's mat) was used before placental removal for measuring blood loss. Statistical analysis was carried out by using the Statistical Package for Social Sciences version 19.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated by frequencies and percentages.

Result: In this study, the majority (54, 54.0%) of patients belonged to age 20-25 years, followed by (30, 30.0%) >25 years. The majority of 85(85.0%) patients had a gestational age of 37-40 weeks and the mean gestational age was found 38.9±1.17 weeks. The majority 72(72.0%) patients had fundal height at 36 weeks and their mean fundal height was found 35.4 ±0.9 weeks. It was observed that 93(93.0%) patients had spontaneous and 07(7.0%) had induced. Majority 68(68.0%) patients had Hb% <10.5. Mean Hb% before delivery was 10.3±0.47 gm/dl with a range from 9.40 to 11.20 gm/dl. Additional uterotonics were used in 15(15.0%) and blood transfusion in 07(7.0%) patients.

Conclusion: Carbetocin is a long-acting synthetic analog of oxytocin that combines the safety and tolerability profile of oxytocin with the sustained uterotonic activity of ergometrine. Most of the patients does not need additional uterotonic agents, only 15% needed additional uterotonic drugs. Seven (7.0%) patients required a blood transfusion.

Keywords: Uterotonic, PPH, Carbetocin

Date of Submission: 18-08-2023

Date of Acceptance: 28-08-2023

I. INTRODUCTION

Postpartum hemorrhage (PPH) is defined as a blood loss >500 ml and serious PPH is a blood loss >1,000 ml. PPH is a serious condition remaining the single main cause of maternal morbidity and mortality. [1] The impact of PPH on maternal morbidity and mortality makes active management of the third stage of labor a critical key. [2][3] Some interventions can save thousands of women's lives. AMTSL consists of three basic procedures: the use of oxytocin within one minute following delivery of the baby, delivery of the placenta with controlled cord traction, and massage of the uterus after delivery of the placenta. [4] Postpartum hemorrhage (PPH) is a potentially life-threatening complication of both vaginal and cesarean delivery. The prevalence of PPH

is approximately 6% of all deliveries. The most frequent cause of PPH is uterine atony; therefore, active management of the third stage of labor rather than expectant management is recommended. [5] The need for additional uterotonics is an important outcome variable as it reflects the degree of postpartum vaginal bleeding accounted for by uterine atony. However, very limited published literature is available, which compared the use of carbetocin and oxytocin in low-risk women who delivered vaginally. Limited literature is available to see the outcome of carbetocin in women undergoing vaginal deliveries. [6] The incidence of PPH is 40% after vaginal delivery and 30% after cesarean section. Criteria for PPH are based on the amount of blood loss. In clinical obstetrics, the exact measurement of blood loss is often difficult. The most important treatment of PPH is red blood cell (RBC) transfusion. [7] The use of uterotonics for the prevention of postpartum hemorrhage (PPH) during the third stage of labor is recommended for all births. Although several medications are used for the management of the third stage, carbetocin is an effective drug for the control of such events. Knowledge about the efficacies, risks, and benefits is essential for clinical use, identification of needs, planning, and further strategies. [8] Over the past two decades, several other alternatives have been explored including the use of prostaglandins such as misoprostol and carboprost. The role of various prostaglandins including misoprostol for postpartum hemorrhage prophylaxis is limited. Among the agents that have been studied, oxytocin agonist (carbetocin) appears to be the most promising for this indication. Carbetocin is a long-acting synthetic octapeptide analog of oxytocin with agonist properties. In pharmacokinetic studies, intravenous injections of carbetocin produced tetanic uterine contractions within 2 minutes, lasting 6 minutes, followed by rhythmic contractions for a further hour. Intramuscular injection produced tetanic contractions in <2 minutes, lasting about 11 minutes, and followed by rhythmic contractions for an additional 2 hours. The prolonged duration of activity after intramuscular compared with the intravenous carbetocin was significant. In comparison with oxytocin, carbetocin induces a prolonged uterine response when administered postpartum, in terms of both amplitude and frequency of contractions. [9][10][11][12]

II. OBJECTIVE

General Objective

- To analyze the necessity of additional uterotonics and blood transfusion within 24 hours of delivery after carbetocin.

Specific Objectives

- To know the age distribution of the study subjects.
- To know the distribution of the study patients by gestational age and fundal height.
- To know the distribution of the study patients by Hb% before delivery
- To assess the additional uterotonics and blood transfusion using the third stage of labor.

III. METHODS

This cross-section observational study was conducted at the Department of Obstetrics and Gynaecology, Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh. The study period was from May 2016 to October 2016. 100 women undergoing normal vaginal delivery were the study subject. A convenient sampling technique was used in this study. Necessary data was collected in the data collection sheet. A standardized deliver mat (Quaiyum's mat) was used before placental removal for measuring blood loss, which was also measured by pre weighted sanitary pad. Blood loss was measured from each of the pregnant women within 24 hours of the postpartum period. Women were advised to preserve their soaked pads. Women received a bolus of 100 microgram carbetocin IV at delivery of the anterior shoulder. Blood loss, the uterine contraction was assessed by clinical examination of the uterus per abdominally, the need for additional uterotonics, the need for blood transfusion, and side effects of carbetocin within 24 hours of delivery. Statistical analysis was carried out by using the Statistical Package for Social Sciences version 19.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated by frequencies and percentages. Before the commencement of this study, written and, or verbal approval was taken. All the information and records were kept confidential. Ethical clearance was obtained from the institutional ethics committee.

Inclusion Criteria

- Women of gestational age more than 36 weeks of pregnancy with labor pain.
- Patients who had given consent to participate in the study.

Exclusion Criteria

- Women with multiple pregnancies
- Placenta previa.
- Abruptio placentae.
- Pregnancy with severe anemia
- Known cases of cardiac, renal, or liver disorder
- Hypersensitivity to carbetocin
- Unwilling to participate in the study.

IV. RESULTS

Table 1: Distribution of the study patients by age (N=100)

Age (years)	N	%
<20	16	16.0
20-25	54	54.0
>25	30	30.0
Mean±SD	23.6±4.04	
Range (min-max)	(18-30)	

In this study, the majority (54, 54.0%) of patients belonged to age 20-25 years, followed by (30, 30.0%) >25 years. [Table 1]

Table 2: Distribution of the study patients by gestational age and fundal height (N=100)

Characteristics	N	%
Gestational age (weeks)		
37-40	85	85.0
>40	15	15.0
Mean±SD	38.9±1.17	
Range (min-max)	(37-41)	
Fundal height (weeks)		
34	28	28.0
36	72	72.0
Mean±SD	35.4±0.9	
Range (min-max)	(34-36)	

The majority of 85(85.0%) patients had a gestational age of 37-40 weeks and the mean gestational age was found 38.9±1.17 weeks. The majority 72(72.0%) patients had fundal height at 36 weeks and their mean fundal height was found 35.4 ±0.9 weeks. [Table 2]

Table 3: Distribution of the study patients by nature of the onset of labor pain (N=100)

Nature of onset of labor pain	N	%
Spontaneous	93	93.0
Induced	07	7.0

It was observed that 93(93.0%) patients had spontaneous and 07(7.0%) had induced. [Table 3]

Table 4: Distribution of the study patients by Hb% before delivery (N=100)

Hb% before delivery (gm/dl)	N	%
<10.5	68	68.0
≥10.5	32	32.0
Mean±SD	10.3±0.47	
Range (min-max)	(9.40-11.20)	

The table shows Hb% before delivery, it was observed that the majority 68(68.0%) patients had Hb% <10.5. Mean Hb% before delivery was 10.3±0.47 gm/dl with a range from 9.40 to 11.20 gm/dl. [Table 4]

Table 5: Additional uterotonics and blood transfusion using the third stage of labor (N=100)

	N	%
Additional uterotonics		
Yes	15	15.0
No	85	85.0
Blood transfusion		
Yes	07	7.0
No	93	93.0

Additional uterotonics were used in 15(15.0%) and blood transfusion in 07(7.0%) patients. [Table 5]

V. DISCUSSION

In present study showed the mean age was found 23.6±4.04 years with an age range from 18 to 30 years. Similar results were found in a study by Tasmin et al. [13] they showed the mean age of the study population was 25.8 ± 4.5 years where the minimum age was 18 years and the maximum age was 38 years. In this study, it was observed that the majority of 85(85.0%) patients had a gestational age of 37-40 weeks, and the mean gestational age was found 38.9±1.17 weeks. The majority 72(72.0%) patients had fundal height at 36 weeks and their mean fundal height was found 35.4 ±0.9 weeks. A study by Tasmin et al. [13] showed the mean gestational age at delivery was 38±1.3 weeks. Similar results were also found in the study of Su et al. [9] they showed gestational age was found 39.0±1.2 weeks with a range from 35.7 to 41.6 weeks. Leung et al.¹⁵ study also support our results that gestational age at delivery was found 39.2±1.6 weeks. In this present study, it was observed that 93(93.0%) patients had spontaneous onset of labor and 07(7.0%) had induced. Approximately similar results were found in the study of Leung et al. [14] they showed spontaneous onset of labor was found at 60.0%, and induced labor was 40.0%. In this current study, it was observed that the majority of 68(68.0%) patients had Hb% <10.5. Mean Hb% before delivery was 10.3±0.47 gm/dl with a range from 9.40 to 11.20 gm/dl. Leung et al. [14] study checked for hemoglobin change 48 hours instead of 24 hours after delivery to provide a longer time for hemodynamic equilibrium. In our study, the mean fall in hemoglobin, the incidence of >10% and >20% drop in hemoglobin level, were lower in the carbetocin group compared with that of the syntometrine group, but the difference was insignificant. In this present study, it was observed that additional uterotonics were needed in 15(15.0%) and blood transfusion in 07(7.0%) patients. Tasmin et al. [13] study showed among the study population 94% of patients did not need any additional uterotonics. Leung et al. [14] study showed the incidence of blood transfusion, additional oxytocic injection, the prolonged third stage (≥30 minutes), and manual removal of placenta were similar between the two groups. The proportion of subjects needing additional uterotonic treatment was 3.1% (CI 1.7-5.1%) in the carbetocin group and 7.2% (CI 5.8-8.9%) in the oxytocin group. The relative risk for additional uterotonic treatment after carbetocin versus oxytocin was 0.41 (95% CI 0.19-0.85). [15] Dansereau J et al, Borruto F et al, and Boucher M et al compared with intravenous oxytocin administration for several hours, carbetocin resulted in a more rapid and sustained uterine involution, less need for additional uterotonic medication, and blood transfusion due to mild blood loss. [16][17][18] Similarly, Holleboom CA et al showed that carbetocin was most effective compared with the oxytocin 5 IU bolus subgroup with less need for additional uterotonic medication (3.1 vs. 9.3 %, *p* = 0.0067) and blood transfusions (2.2 vs. 3.6 %, *p* = 0.0357). However, fewer women in the carbetocin arm needed additional uterotonics but perioperative blood loss, severe postpartum hemorrhage, blood transfusion, and operating time were not different according to Razali N et al. [20]

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

VI. CONCLUSION

Carbetocin is a long-acting synthetic analog of oxytocin that combines the safety and tolerability profile of oxytocin with the sustained uterotonic activity of ergometrine. Most of the patients does not need additional uterotonic agents, only 15% needed additional uterotonic drugs. Seven (7.0%) patients required blood transfusion.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

VII. RECOMMENDATION

Some studies demonstrated a lower rate of additional oxytocic usage after carbetocin compared with oxytocin, carbetocin may be more effective in preventing uterus atony and thereby PPH. Still, to get robust data, further studies should be conducted involving a large sample size and multiple centers.

REFERENCES

- [1]. World Health Organization (2009) WHO Guidelines For The Management Of Postpartum Hemorrhage And Retained Placenta
- [2]. Prendiville WJ, Elbourne D, McDonald S (2000) Active Versus Expectant Management In The Third Stage Of Labor
- [3]. Tharakan T, Jha J (2008) Randomized Double-Blind Prospective Trial Of Active Management Of The Third Stage Of Labor. *Arch Med Sci* 4(1):79–82
- [4]. Al-Sabir A, Alam ME, Salim F, Huda N, Ahmed NKJM, Faisal AJ. Assessment On The Availability And Routine Use Of Active Management Of The Third Stage Of Labor. E&R Study. Dhaka: Engender Health Bangladesh Country Office; 2008.
- [5]. Moertl MG, Friedrich S, Kraschl J, Wadsack C, Lang U, Schlembach DJ. Hemodynamic Effects Of Carbetocin And Oxytocin Given As Intravenous Bolus On Women Undergoing Cesarean Delivery: A Randomized Trial. *BJOG: An International Journal Of Obstetrics & Gynaecology*. 2011 Oct;118(11):1349-56.
- [6]. Onwochei DN, Van Ross J, Singh PM, Salter A, Monks DT. Carbetocin Reduces The Need For Additional Uterotonics In Elective Cesarean Delivery: A Systematic Review, Meta-Analysis, And Trial Sequential Analysis Of Randomized Controlled Trials. *International Journal Of Obstetric Anesthesia*. 2019 Nov 1;40:14-23.
- [7]. Jansen AJ, Van Rhenen DJ, Steegers EA, Duvekot JJ. Postpartum Hemorrhage And Transfusion Of Blood And Blood Components. *Obstetrical & Gynecological Survey*. 2005 Oct 1;60(10):663-71.
- [8]. Fawole AO, Sotiloye OS, Hunyinbo KI, Umezulike AC, Okunlola MA, Adekanle DA, Osamor J, Adeyanju O, Olowookere OO, Adekunle AO, Singata M. A Double-Blind, Randomized, Placebo-Controlled Trial Of Misoprostol And Routine Uterotonics For The Prevention Of Postpartum Hemorrhage. *International Journal Of Gynecology & Obstetrics*. 2011 Feb;112(2):107-11.
- [9]. Su L, Rauff M, Chan Y, Mohamad Suphan N, Lau T, Biswas A, Et Al. Carbetocin Versus Syntometrine For The Third Stage Of Labor Following Vaginal Delivery—A Double-Blind Randomized Controlled Trial. *BJOG* 2009;116:1461-1466.
- [10]. Yuen PM, Chan NS, Yim SF, Chang AM. A Randomized Double-Blind Comparison Of Syntometrine And Syntocinon In The Management Of The Third Stage Of Labor. *Br J Obstet Gynaecol* 1995;102:377-80.
- [11]. Gulmezoglu AM, Forna F, Villar J, Hofmeyr GJ. Prostaglandins For Prevention Of Postpartum Hemorrhage (Cochrane Review). In: *The Cochrane Library*, Issue 1. Oxford: Update Software; 2004.
- [12]. Chong YS, Su LL, Arulkumaran S. Current Strategies For The Prevention Of Postpartum Hemorrhage In The Third Stage Of Labor. *Curr Opin Obstet Gynecol* 2003;16:143-50.
- [13]. Tasmin SF, Akhtar MJ, Mondal RN, Yeasmin N, Islam GR. Efficacy And Safety Of Carbetocin In The Active Management Of Third Stage Of Labour Following Emergency Caesarean Section. *Dinajpur Med Col J* 2016; 9 (1):45-52.
- [14]. Leung S, Ng P, Wong W, Cheung T. A Randomised Trial Of Carbetocin Versus Syntometrine In The Management Of The Third Stage Of Labour. *BJOG* 2006;113:1459–1464
- [15]. Holleboom CA, Van Eyck J, Koenen SV, Kreuwel IA, Bergwerff F, Creutzberg EC, Bruinse HW. Carbetocin In Comparison With Oxytocin In Several Dosing Regimens For The Prevention Of Uterine Atony After Elective Caesarean Section In The Netherlands. *Archives Of Gynecology And Obstetrics*. 2013 Jun;287:1111-7
- [16]. Dansereau J, Joshi AK, Helewa ME, Doran TA, Lange IR, Luther ER Et Al (1999) Double-Blind Comparison Of Carbetocin Versus Oxytocin In Prevention Of Uterine Atony After Cesarean Section. *Am J Obstet Gynecol* 180(3 Pt 1):670–676
- [17]. Borruto F, Treisser A, Comparetto C (2009) Utilization Of Carbetocin For Prevention Of Postpartum Hemorrhage After Cesarean Section: A Randomized Clinical Trial. *Arch Gynecol Obstet* 280:707–712
- [18]. Boucher M, Horbay GL, Griffin P, Deschamps Y, Desjardins C, Schulz M Et Al (1998) Double-Blind, Randomized Comparison Of The Effect Of Carbetocin And Oxytocin On Intraoperative Blood Loss And Uterine Tone Of Patients Undergoing Cesarean Section. *J Perinatol* 18(3):202–207
- [19]. Holleboom CA, Van Eyck J, Koenen SV, Kreuwel IA, Bergwerff F, Creutzberg EC, Bruinse HW. Carbetocin In Comparison With Oxytocin In Several Dosing Regimens For The Prevention Of Uterine Atony After Elective Caesarean Section In The Netherlands. *Archives Of Gynecology And Obstetrics*. 2013 Jun;287:1111-7.
- [20]. Razali N, Latar IL, Chan YK, Omar SZ, Tan PC. Carbetocin Compared To Oxytocin In Emergency Cesarean Section: A Randomized Trial. *European Journal Of Obstetrics & Gynecology And Reproductive Biology*. 2016 Mar 1;198:35-9.