

Oxytocin Vs Carbetocin in Preventing Postpartum Haemorrhage Following Vaginal Delivery in A Tertiary Hospital in Manipur**Nongmeikapam Upen¹, Tenshubam Nimmi², Mayanglambam Ronita Devi³, Kharibam Paikhomba Singh⁴**¹PGT (OBG) JNIMS, Imphal, Manipur, India²Senior Resident, JNIMS Imphal, Manipur, India³Assistant Professor, Department of Obstetrics and Gynaecology, JNIMS, Imphal, Manipur, India⁴Associate Professor, Department of Obstetrics and Gynaecology, JNIMS, Imphal, Manipur, India

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Conflict of interest: Nil

Abstract:**Background:** Searching of better and effective uterotonic is required to prevent postpartum haemorrhage [PPH] in pregnancy. This study was conducted to compare the efficacy of Carbetocin and Oxytocin in preventing PPH following vaginal delivery.**Materials & Methods:** An RCT was conducted among 260 singleton pregnancy without complications. Each half received Inj. Oxytocin 10 I.U. intramuscular and Inj. Carbetocin 100µg intravenous immediately after vaginal delivery of the baby. The investigator placed a calibrated drape under the woman's buttock & blood loss was measured for 1 hr or 2 hrs postpartum if the bleeding continued beyond 1 hour. The research team provided (three) pre-weighed standard sanitary pads to each pregnant woman to measure the blood loss in 24 hrs postpartum period. Women were advised to preserve the soaked pads in a sealable container which was provided by the study staff members. The amount of blood was measured in grams by digital postal scale and multiplied by a constant value 1.06 to get the amount of blood loss in milliliters [ml] within 24 hrs. of delivery. Data was analysed using Jamovi Ver. 2.4. Chi-square test was used for categorical data and t-test for continuous data. p-value of <0.05 was taken as significant.**Results:** Oxytocin group had more PPH (37.7%) compared to Carbetocin group (11.5%). Severe PPH was seen only in the Oxytocin group in this study. Mean blood loss was also more in the Oxytocin group (487±204 ml) compared to the Carbetocin group (315±149 ml). There was more use of additional uterotonics and uterine massage in the oxytocin group.**Conclusion:** Carbetocin is more effective in preventing PPH amongst pregnant women with singleton pregnancy following vaginal delivery. Further multicentric and meta-analytic study needs to be performed to increase its robustness.**Keywords:** PPH, Oxytocin, Carbetocin.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

A fair amount of blood loss is expected during vaginal delivery. When the blood loss is more than 500ml within 24 hrs of vaginal delivery or 1000 ml following cesarean section it is defined as Post-Partum Haemorrhage [PPH]. Most maternal deaths due to PPH could be prevented through the use of prophylactic uterotonics during the third stage of labour along with timely appropriate management.[1]

Conventional uterotonics like Oxytocin has been used for preventing PPH but it has its limitations like a short half-life, less contraction time and side effects like fluid overloading, convulsion, arrhythmia and pulmonary odema. Moreover, oxytocin potency deteriorates when it is exposed to temperature >

30°C for a prolonged period of time.[2] Carbetocin is a long-acting synthetic analogue of Oxytocin with agonists property. Its half-life is 40 minutes and uterine contraction occurs in less than 2 minutes after intravenous (IV) administration of optimal dosage of 100 mcg.

Duration of action of Carbetocin is 1 hour and 2 hr. after I.V. and I.M. injection respectively.[3] Carbetocin binds to oxytocin receptors present on smooth musculature of the uterus, resulting in rhythmic contractions of the uterus, increase frequency of existing contraction and increase uterine tone.[4] Moreover, Carbetocin ensures more effective contraction and less adverse effects like headache,

tremor, hypotension, nausea, abdominal pain and pruritus.

The purpose of this study was to compare the efficacy of Carbetocin and Oxytocin in preventing PPH following vaginal delivery.

Materials and Methods

A randomized control trial was conducted on 260 admitted pregnant women during the year 2022-2023 in the Dept. of Obs. & Gynae. JNIMS, Imphal East, Manipur, India. After approval from the Hospital Ethics Committee, written informed consent from the participating patients were taken.

A detailed clinical, obstetrical, medical and surgical history was taken followed by a thorough General & Systemic examination with reference to Cardiovascular System (CVS), Central Nervous System (CNS), Respiratory System (RS), Per Abdomen (PA) & Per Veginum (P/V). Women were allocated randomly into two groups based on a computer generated serial number.

During the study period, the first group of 130 women received Inj. Carbetocin 100µg intravenous and the second group of 130 women received 10 IU of Inj Oxytocin intramuscular immediately after delivery of the baby and prior to the delivery of the placenta. Blood loss was measured for 1 hr or 2 hrs postpartum [if the bleeding continued beyond one hour] from the calibrated drape placed under the woman's buttock. Three pre-weighed standard sanitary pads were provided to each of the pregnant woman to measure the blood loss in 24 hrs postpartum period.

Women were advised to preserve the soaked pads in a sealable container which were provided by study staff members. The amount of blood was measured in grams by digital postal scale and multiplied by a constant value 1.06 to get the amount of blood loss

in milliliters [ml] within 24 hours of delivery. Data collected were entered in Microsoft Excel 360. Data was analysed using Jamovi Ver. 2.4. Chi-square test was used for categorical data and t-test for continuous data. Probability value of < 0.05 was taken as significant.

Inclusion Criteria:

1. Pregnant women undergoing vaginal delivery between 37-40 weeks of gestation (gestational age was recorded according to the last menstruation period and confirmed by ultrasound report).
2. Case willing to participate in the study.
3. Parity ≤ 3
4. Singleton pregnancy
5. Hb% ≥ 11 gm/dL

Exclusion Criteria:

1. Pregnant women with complications like
 - a. Placenta Praevia
 - b. Uterine fibroid.
 - c. Multiple Pregnancy
 - d. Previous uterine incision.
 - e. Malpresentations.
 - f. Medical disorders of pregnancy.
 - g. Hypertensive disorders in pregnancy, Gestational Diabetes
 - h. Known case of cardiac, renal, liver disease, epilepsy and moderate anemia (Hb<9gm/dL).
2. Unwilling to participate in the study.

Input variables were age and parity. Output variables were additional uterotonic therapy, massive blood loss (≥ 500 ml), need for additional uterine massage and blood transfusion.

Results

Table 1a: Baseline characteristics of study participants

Characteristics	Oxytocin group (Mean \pm SD)	Carbetocin group (Mean \pm SD)	t-test, p-value
Age	25.7 \pm 4.5	25.4 \pm 4.7	Value=0.470, p-0.639
Period of gestation	38.6 \pm 1.02	38.5 \pm 1.08	Value=1.174, p-0.243

Table 1b: Baseline characteristics of study participants -Gravida

Gravida	Oxytocin group N (%)	Carbetocin group N (%)	Chi-square test, p-value
One	64(49.2)	54(41.5)	Value=1.575 p-0.45
Two	47(36.2)	55(42.3)	
More than two	19(14.6)	21(16.2)	
Total	130(100.0)	130(100.0)	

Table 1c: Baseline characteristics of study participants- Parity

Parity	Oxytocin group (n %)	Carbetocin group (n %)	Chi-square test, P-value
Zero	70(53.8)	65(50.0)	Value=3.25 p-0.355
One	51(39.2)	60(46.1)	
More than one	9(6.9)	5(3.8)	
Total	130(99.9)	130(99.9)	

Table 2: Comparison of both groups in terms of blood loss

Blood loss in ml	Oxytocin group n(%) / Mean \pm SD	Carbetocin group n(%) / Mean \pm SD	Chi-square test/t-test p-value
≤ 500	77(59.2)	115(88.5)	Value=29.6 p<0.001
>500	49(37.7)	15(11.5)	
>1000	4(3.1)	0(0.0)	
Total	130(100.0)	130(100.0)	
Blood loss in Mean \pm SD	487 \pm 204	315 \pm 149	Value=7.75, p<0.001

Discussion:

The baseline characteristics of the study participants were comparable (no significant difference) as shown in table 1a, 1b & 1c. PPH was seen more in the Oxytocin group (37.7%) compared to the Carbetocin group (11.5%). Severe PPH was seen only in the Oxytocin group. These findings were found to be significant ($p < 0.05$).

Mean blood loss in the Oxytocin group was 487 \pm 204 ml and in the Carbetocin group it was 315 \pm 149 ml which was statistically significant ($p < 0.001$). Additional need for other uterotonic agents and uterine massage was seen more in Oxytocin group in comparison to the Carbetocin group. Need for blood transfusion was not observed in both groups in this study.

In this study, it was seen that oxytocin group had more blood loss (mean = 487 \pm 204 ml) compared to Carbetocin group (mean 315 \pm 149 ml). Also, PPH was seen more among oxytocin group (37.7%) than carbetocin group (11.5%). This study was in concordance with the study by Fahmy NG et al [5] where blood loss among oxytocin group (mean 721 \pm 45 ml) was significantly more than the carbetocin group (Mean 437 \pm 45 ml). Risk of PPH after caesarean section was also lower when carbetocin was used instead of oxytocin (44% vs. 60%) in the study by Gallos ID et al [6]. The need for additional uterotonic agents (assessed subjectively by the attending physician) was higher in the oxytocin group compared to the carbetocin group in the study by Liker IP et al [7]. Same finding was also observed in a systematic review, meta-analysis and trial sequential analysis of randomised controlled trials conducted by Onwochei DN et al [8]. These findings were also found in the studies by Gallos ID et al [6] & Kang et al [9]. But in a meta-analysis conducted by Jin XH et al [3] there were no significant differences between carbetocin and oxytocin in PPH, use of additional uterotonic agents, blood transfusion, uterine massage, and adverse effects.

Ahmed Mohamed Maged et al have randomized 200 women undergoing vaginal delivery. They also showed that there were no significant adverse effects of both groups. [10] In our study there were no major side effects of both drugs. Sufus Rabow et al showed both drugs caused a global vasodilatation with lowering of vascular tonus in both large & small arteries

accompanied by a slight drop in BP but without any compensatory increment in HR. [11]

In our study none of patients in oxytocin group and carbetocin group showed the cardiovascular effect. The known antidiuretic activity of oxytocin is hyponatremia and water intoxication. These are feared side effects of oxytocin. Larciprete et al in their study compared antidiuretic activity of oxytocin & carbetocin with regard to postoperative 12th hour diuresis amount and determined that in the carbetocin group it was 1,300 ml + 250 ml ($P = 0.01$). [12] De Bonis et al the amount of diuresis at the post-operative 24th hour was compared and found to be 2,282.36 + 8.0 ml in the carbetocin group and 2,292.9 + 82.6 ml in the oxytocin group. [16]

One of the most important limitations of drug use is its side effects. Oxytocin is known to cause unwanted cardiovascular side effects such as tachycardia, hypotension and electrographic changes. In addition, oxytocin has also been shown to cause nausea, vomiting, tachycardia, flushing, headache, dizziness, chills, metallic taste, dyspnea, palpitation, itching, chest pain, pulmonary oedema, severe water intoxication and convulsions. [14,15,16,17]

In our study we found none of these side effects. Mahmoud A et al in their study regarding the adverse effect profiles appear reassuringly similar between the two medications the risk of experiencing nausea, vomiting, abdominal pain, itching, metallic taste were similar in women given oxytocin and carbetocin. [19]

These findings were none in our setup studies. Sumangala B. Chikamath et al compared the primary outcome of intramuscular injection of carbetocin 100 μ g vs oxytocin 10 iu intramuscular. [20] They observed that a slightly higher increase in blood loss for the same third stage of labour duration with oxytocin than with carbetocin. The same observation is found in this study. Mahabubal Akhter Jahan et al concluded from their study that carbetocin appears to be an effective new drug in the AMTSL. In our study prevention of blood loss at least 500 ml was better and use of additional uterotonic agents were less in carbetocin group.

Conclusion

In this study, carbetocin is more effective in preventing PPH among singleton women on vaginal delivery. Carbetocin appears to be an ideal effective drug

in AMTSL. Further multicentric and meta-analysis need to be performed to increase its robustness and applicability.

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