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Original Research Paper

COMPARING THE EFFICACY OF OXYTOCIN TO CARBETOCIN IN MANAGING THE THIRD STAGE OF LABOR AT AN INDIAN HEALTHCARE CENTER

Dr. Meena Jain,[1] Dr. Anand Ramdas Tambat,[2] Dr. Shipra Singh,[3] Dr Jharna Sahu[4*]

[1*]Associate Professor, Department of Obstetrics and Gynecology, Shri Balaji institute of medical sciences, Mowa, Raipur, Chhattisgarh
[2]Associate Professor, Department of Obstetrics and Gynecology, A.C.P.M. Medical College, Dhule, Maharashtra
Assistant Professor, Department of Obstetrics and Gynecology, Veerangana Avanti Bai Lodhi, Autonomous State Medical College, Etah, Uttar Pradesh
[4*]Assistant Professor, Department of Pharmacology, Pt Jawahar Lal Nehru Medical College Raipur, Chhattisgarh

Corresponding author
Dr Jharna Sahu[4]
Email gargjharna@yahoo.com

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ABSTRACT

Background: It has been reported globally that many females died of severe bleeding following their delivery with postpartum hemorrhage being a common cause of maternal death. It is mainly caused by uterine atony. To manage this, the third stage of labor needs to be managed actively. Generally, oxytocin is used for uterus contraction following delivery. However, it has a shorter life, more side effects, and less contraction time, hence, recently Carbetocin has been used with lesser side effects and prolonged acting time.

Aim: The present study aimed to assess the safety and efficacy of oxytocin to Carbetocin in managing the third stage of labor at an Indian healthcare center.

Methods: The study assessed 100 subjects based on the inclusion and exclusion criteria of the study. In all the subjects, per abdomen examination was done along with the general examination. An ultrasound examination was also done. The data gathered were analyzed statistically.

Results: Baseline demographics and data were not comparable in the two study groups. In the majority of the subjects from both groups, mild anemia was seen. No side effects were noted in the Carbetocin group. In the oxytocin group, abdominal pain and nausea were seen. Mean blood loss was higher in the oxytocin group compared to Carbetocin group.

Conclusions: The present study concludes that carbetocin has higher efficacy compared to oxytocin as it maintains the tone of the uterus adequately and prevents blood loss and postpartum hemorrhage in females undergoing vaginal delivery. Hence, carbetocin is considered a good alternative to oxytocin in the active management of third-stage labor.

Keywords: Maternal morbidity, postpartum hemorrhage, third-stage labor, uterine tone

INTRODUCTION

In recent times, nearly one female dies every minute from postpartum hemorrhage. It is the major cause of mortality in morbidity and concerns both maternal and child health. Postpartum hemorrhage is seen in nearly 4% of females with normal vaginal delivery. This incidence increases in the developing nations. In nations with low income, maternal deaths due to post-partum hemorrhage contribute to nearly 30% of maternal deaths. The majority of the deaths are seen in 4 hours following delivery depicting that it is a consequence of the third stage of labor.[1,2]

Blood loss of more than 500ml in the vaginal delivery or 1000ml in the Cesarean section is termed Postpartum hemorrhage (PPH). If PPH occurs in the first 24 hours, it is termed primary PPH, after 24 hours and within 6 weeks is termed secondary PPH. Following 2012 data, the WHO recommends active management of the third stage of labor to prevent postpartum hemorrhage. This includes uterotonic oxytocin administration. In addition to WHO recommendations, ACOG also suggests uterine massage.[3]

Oxytocin is a known conventional uterotonic used for preventing postpartum hemorrhage. Oxytocin has a short lifespan, lesser contraction time, and is associated with side effects. The most common side effects are arrhythmia, pulmonary edema, convulsions, and fluid overload. Ergot alkaloids are used at a later stage. However, certain issues are associated with their use including the need for its protection from light for its efficacy and stability which is lost on not maintaining the proper cold chain, oxytocin was still recommended as uterotonic for effective management of the third stage of labor. Oxytocin can be given in both intravenous and intramuscular routes.[4]

As oxytocin has a shorter life, more side effects, and less contraction time, Carbetocin has recently been used with lesser side effects and prolonged acting time. Carbetocin is a synthetic analog of oxytocin and is long-acting. Owing to its prolonged action, it can decrease the adverse effects and increase the contraction time. The adverse effects include headache, nausea, pruritus, abdominal pain, and tremor.[5] The existing literature data is scarce concerning their comparison and efficacy, the present study aimed to assess the safety and efficacy of oxytocin to Carbetocin in managing the third stage of labor at an Indian healthcare center.

MATERIALS AND METHODS

The present hospital-based cross-sectional study aimed to assess the safety and efficacy of oxytocin to Carbetocin in managing the third stage of labor at an Indian healthcare center. The study was done at after the clearance was given by the concerned Institutional Ethical committee. The study subjects were from the Department of Obstetrics and Gynecology of the Institute. Verbal and written informed consent was taken from all the participants before participation.

The study included 100 pregnant females with a gestational age of >37 weeks who were admitted to the labor ward of the Institute. These subjects were divided randomly into two groups where Group I subjects were given Carbetocin as 100 microgram/ml and Group II subjects were given 10 IU oxytocin.

The inclusion criteria for the study were pregnant females with a gestational age of more than 37 weeks, subjects achieving normal vaginal delivery, and subjects that underwent emergency or

elective cesarean section for obstetrics and Gynecological reasons. The exclusion criteria for the study were subjects having epilepsy, hepatic disease, heart disease, hypertension, renal disease, HELLP syndrome, preeclampsia, placenta accrete, placenta previa, anticoagulant therapy, coagulation defects, or bleeding disorders.

For all the subjects, data were gathered using a pre-formed structured proforma questionnaire including demographic data and clinical examination followed by relevant laboratory tests and abdominal examination. A detailed history was recorded for all the pregnant females including the comorbidities, gestational age at the time of delivery, parity, and age. Anthropometric data were also gathered concerning the weight and height of the subjects and general examination. Per abdomen examination was also done to assess presentation, fetal life, and uterine height. Standard techniques were used for assessing anthropometric data.

To assess height subjects were asked to stand erect with no footwear and were assessed for a stadiometer which was rounded to the nearest 0.1 cm. For weight, a digital electronic machine was used after checking standardization. Study subjects were asked to stand on a weighing machine without footwear and heavy clothing. The weight was recorded in kilograms. Ultrasound was done to exclude placenta previa, for retroplacental clots, and placenta localization. Ultrasound also assessed fetal well-being. For postpartum hemorrhage, blood loss of more than 500 ml was considered from the genital tract within 24 hours of vaginal delivery.

The data gathered were analyzed statistically using SPSS (Statistical Package for the Social Sciences) software version 21.0 (IBM Corp., Armonk. NY, USA) for assessment of descriptive measures, independent t-test, Mann Whitney U test, and chi-square test. The results were expressed as mean and standard deviation and frequency and percentages. The p-value of <0.05 was considered statistically significant.

RESULTS

The present hospital-based cross-sectional study aimed to assess the safety and efficacy of oxytocin to Carbetocin in managing the third stage of labor at an Indian healthcare center. The study included 100 pregnant females with a gestational age of >37 weeks who were admitted to the labor ward of the Institute. These subjects were divided randomly into two groups where Group I subjects were given Carbetocin as 100 microgram/ml and Group II subjects were given 10 IU oxytocin. The mean age of the study subjects was 24.4±3.3 and 24.4±3.6 years in the oxytocin and carbetocin group which was statistically comparable with p=0.54. The mean gestational age in the oxytocin and carbetocin groups was 38.4±1.4 and 38.2±1.3 weeks respectively with p=0.34. The mean diastolic and systolic pressure was also comparable in the oxytocin and carbetocin groups with p=0.44 and 0.42 respectively as shown in Table 1.

On comparing anemia of various grades in study subjects, it was seen that 20 subjects from oxytocin and 18 subjects from carbetocin had no anemia. Mild anemia was seen in 26 and 22 subjects respectively from the oxytocin and carbetocin group. Moderate anemia was seen in 2 and 8 subjects from the oxytocin and carbetocin group respectively. From oxytocin and carbetocin group severe anemia was seen in 2 subjects each. The difference in the two groups was statistically non-significant with p=0.9 as summarized in Table 2.

Concerning the comparison of side effects in two study groups, abdomen pain was seen in 4 subjects from the oxytocin group, and headache, vomiting, and nausea were seen in 4, 4, and 2 subjects respectively from the oxytocin group. No subject from the oxytocin group reported hypotension and fever. No subject from the carbetocin group reported any side effects during the study duration. The difference between the two groups was statistically non-significant concerning abdomen pain, hypotension, headache, fever, vomiting, and nausea with p=0.13, 0.3, 0.17, 0.3, 0.13, and 0.37 respectively as depicted in Table 3.

The study results showed that for outcomes of labor in two groups of study subjects, blood transfusion of <600ml was needed in 10 subjects from oxytocin and no subject from the carbetocin group, and of ≥600ml was needed in 42 and 50 subjects from oxytocin and carbetocin groups which were significantly higher in carbetocin group with p=0.02. Additional uterotonics were needed in 16 and 2 subjects respectively from the oxytocin and carbetocin groups which was significantly higher in the oxytocin group with p=0.001. Blood transfusion was needed in 12 and no subjects from oxytocin and carbetocin group which was significantly higher in oxytocin group with p=0.001. Fundal massage was needed in 12 subjects from the oxytocin group which was significantly higher compared to 2 subjects from the carbetocin group with p=0.03 (Table 4). Mean blood loss was significantly higher in the oxytocin group with 443±30 ml compared to 322±22 ml in the carbetocin group with p=0.01 (Table 5).

DISCUSSION

The present study assessed 100 pregnant females with a gestational age of >37 weeks who were admitted to the labor ward of the Institute. These subjects were divided randomly into two groups where Group I subjects were given Carbetocin as 100 microgram/ml and Group II subjects were given 10 IU oxytocin. The mean age of the study subjects was 24.4±3.3 and 24.4±3.6 years in the oxytocin and carbetocin group which was statistically comparable with p=0.54. The mean gestational age in the oxytocin and carbetocin groups was 38.4±1.4 and 38.2±1.3 weeks respectively with p=0.34. The mean diastolic and systolic pressure was also comparable in the oxytocin and carbetocin groups with p=0.44 and 0.42 respectively. These data were similar to the studies of SR Ortiz et al[6] in 2014 and Ramanathan G[7] in 2006 where authors assessed subjects with demographic data comparable to the present study.

The study results showed that on comparing anemia of various grades in study subjects, it was seen that 20 subjects from oxytocin and 18 subjects from carbetocin had no anemia. Mild anemia was seen in 26 and 22 subjects respectively from the oxytocin and carbetocin group. Moderate anemia was seen in 2 and 8 subjects from the oxytocin and carbetocin group respectively. From oxytocin and carbetocin group severe anemia was seen in 2 subjects each. The difference in the two groups was statistically non-significant with p=0.9. These results were consistent with the findings of CAG Holleboom et al[8] in 2013 and Agnes P et al[9] in 2011 reported a non-significant difference in anemia prevalence in the oxytocin and carbetocin group as seen in the results of the present study.

For the comparison of side effects in two study groups, abdomen pain was seen in 4 subjects from the oxytocin group, and headache, vomiting, and nausea were seen in 4, 4, and 2 subjects respectively from the oxytocin group. No subject from the oxytocin group reported hypotension and

fever. No subject from the carbetocin group reported any side effects during the study duration. The difference between the two groups was statistically non-significant concerning abdomen pain, hypotension, headache, fever, vomiting, and nausea with p=0.13, 0.3, 0.17, 0.3, 0.13, and 0.37 respectively. These findings were in agreement with the results of Manal M et al[10] in 2016 and AM Maged et al[11] in 2015 where authors suggested side effects similar to the present study for oxytocin and carbetocin groups in their respective studies.

It was seen that for outcomes of labor in two groups of study subjects, blood transfusion of <600ml was needed in 10 subjects from oxytocin and no subject from the carbetocin group, and of ≥600ml was needed in 42 and 50 subjects from oxytocin and carbetocin groups which were significantly higher in carbetocin group with p=0.02. Additional uterotonics were needed in 16 and 2 subjects respectively from oxytocin and carbetocin groups which was significantly higher in the oxytocin group with p=0.001. Blood transfusion was needed in 12 and no subjects from oxytocin and carbetocin group which was significantly higher in oxytocin group with p=0.001. Fundal massage was needed in 12 subjects from the oxytocin group which was significantly higher compared to 2 subjects from the carbetocin group with p=0.03 (Table 4). Mean blood loss was significantly higher in the oxytocin group with 443±30 ml compared to 322±22 ml in the carbetocin group with p=0.01. These results correlated with the findings of Ahraf F et al[12] in 2022 and Senthihes Let al[13] in 2016 where outcomes and mean blood loss as higher with oxytocin compared to carbetocin reported by the authors in their studies as seen in the results of the present study. Price of carbetocin is 450 rupees, where as price of Oxytocin is 19 rupees only in India. Carletocin has to be administered with 100 ml NS through Iv route and Oxytocin can be given intramuscular.

CONCLUSIONS

The present study, within its limitations, concludes that carbetocin has higher efficacy compared to oxytocin as it maintains the tone of the uterus adequately and prevents blood loss and postpartum hemorrhage in females undergoing vaginal delivery. Hence, carbetocin is considered a good alternative to oxytocin in the active management of third-stage labor.

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TABLES

Characteristics	**Oxytocin (n=50)**	**Carbetocin (n=50)**	**p-value**
Gestational age	38.4±1.4	38.2±1.3	0.34
Diastolic pressure	72.2±10.4	74.4±3.4	0.42
Systolic pressure	110±2.3	114±6.4	0.44
Mean age (years)	24.4±3.3	24.4±3.6	0.54

Table 1: Demographic data of the study participants

Anemia	**Oxytocin**	**Carbetocin**	**p-value**
No anemia	20	18	0.9
Mild	26	22	
Moderate	2	8	
Severe	2	2	

Table 2: Comparison of various grades of anemia in study subjects

Side effects	Oxytocin (n=50)	Carbetocin (n=50)	p-value
Abdomen pain	4	0	0.13
Hypotension	0	0	0.3
Headache	4	0	0.17
Fever	0	0	0.3
Vomiting	4	0	0.13
Nausea	2	0	0.37

Table 3: Comparison of side-effects in oxytocin and carbetocin groups

Variables	Oxytocin (n=50)	Carbetocin (n=50)	p-value
Blood transfusion			
<600	10	0	**0.02**
≥600	42	50	
Additional uterotonics need			
Yes	16	2	**0.001**
No	34	48	
Blood transfusion			
Yes	12	0	**0.001**
No	38	50	
Fundal massage			
Yes	12	2	**0.03**
No	38	48	

Table 4: Outcome of the third stage of labor in two groups of study subjects

Parameters	Oxytocin (n=50)	Carbetocin (n=50)	p-value
Mean blood loss (ml)	443±30	322±22	**0.01**

Table 5: Mean blood loss with post-partum hemorrhage in oxytocin and carbetocin group