The Egyptian Journal of Hospital Medicine (October 2019) Vol. 77 (2), Page 5008-5015

Carbetocin Versus Oxytocin in Prevention of Atonic Postpartum Hemorrhage

Esmael Mohamed Talaat Elgarhy, Ashraf Hamdy Mohamed, Mohamed Mahmoud Mohamed Abdelfatah*
Department of Obstetrics and Gynecology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
* Corresponding author: Mohamed Mohamed Mahmoud Abdelfatah, Mobile: (+20)01068673424, E-mail: dr.mzayed2020@gmail.com

ABSTRACT

Background: Death due to pregnancy remains an important cause of premature mortality of women worldwide. An estimated 500,000 women die from this cause every year with up to quarter of deaths occur due to hemorrhage.

Objective: The aim of this study was to compare the effectiveness and safety of carbetocin versus oxytocin in the prevention of atonic postpartum Hemorrhage (PPH) after vaginal deliveries and cesarean sections.

Patient and Methods: This computerized random cross sectional prospective comparative study included a total of 400 pregnant women who were going to deliver, attending at Obstetric and Gynecological Department at El-Mataria Teaching Hospital in Corporation with Obstetric and Gynecological Department, Faculty of Medicine, Al-Azhar University. This study was conducted between October 2017 to October 2018.

Results: Carbetocin was proved statistically to be more effective in preventing uterus atony and thereby PPH in comparison with oxytocin.

Conclusion: It could be concluded that carbetocin is a better uterotonic agent in comparison with Oxytocin in the management of atonic postpartum hemorrhage after delivery either vaginal or cesarean section as it decreases incidence of occurrence of PPH and post-partum blood loss.

Keywords: Carbetocin, Oxytocin, Atonic Postpartum Hemorrhage

INTRODUCTION

Post-partum hemorrhage is the leading cause of morbidity and mortality among pregnant ladies throughout the world causing 140,000 deaths each year globally. This corresponds to the one woman dying in every 4 minutes and it is the 5th most common cause of maternal mortality throughout the world [(1)].

Postpartum hemorrhage was classified into two types, primary and secondary, ***Primary*** is defined as blood loss of greater than 500 ml due to vaginal delivery and loss of 1000 ml due to C-section within first 24 hours of delivery. ***Secondary*** is defined as excessive vaginal blood loss or heavy lochia discharge occurring at least 24 hours after the end of the third stage of labor [(2)].

Another definition of Primary Postpartum Hemorrhage "PPH" is that blood loss sufficient to cause hypovolemia, a 10% drop in the hematocrit or requiring transfusion of blood products (regardless of route of delivery) [(3)].

Risk factors for PPH include; past history of PPH, multiple pregnancy, fetal macrosomia, primi-gravida, grand multi-parity, older age, preterm births, genital tract injuries, non-use of oxytocics for PPH prophylaxis, labor induction, cesarean birth and intra-uterine fetal deaths [(4)].

It is axiomatic that postpartum hemorrhage occurs unpredictably, and no patient is immune from it, it simply states that it is an equal opportunity killer [(5)]. In many International and local studies, it was revealed that the main cause of PPH is uterine atony which is responsible for at least 80% of cases followed by vaginal hematoma, cervical or vaginal tear, adherent placenta, uterine angle extension and retained placenta [(3)].

Uterotonic drugs increase the tone of the uterine muscles and were initially introduced for the treatment of PPH [(6)].

Oxytocin is the most widely used uterotonic agent but has a half-life of only 4–10 min, that is why it is better administered as a continuous intravenous infusion to achieve sustained uterotonic activity [(7)].

Carbetocin is a synthetic long-acting oxytocin agonistic analogue with prolonged half-life prolonging its pharmacological effects. Its prolonged uterine activity may theoretically offer advantages over oxytocin in the management of the third stage of labor. The side-effect profile of carbetocin was not found to be different from that of oxytocin but may prove to be advantageous when compared to syntometrine [(8)].

The aim of this study was to compare the effectiveness and safety of carbetocin versus oxytocin in the prevention of atonic PPH after vaginal deliveries and cesarean sections.

PATIENTS AND METHODS

This computerized random cross sectional prospective comparative study included a total of 400 pregnant women who were going to deliver, attending at Obstetric and Gynecological Department at El-Mataria Teaching Hospital in Corporation with Obstetric and Gynecological Department, Faculty of Medicine, Al-Azhar University. Written informed consent from all the subjects were obtained. This study was conducted between October 2017 to October 2018.

Ethical approval:

Approval of the Ethical Committee, Faculty of Medicine, Al-Azhar University was obtained.

The included subjects were randomly divided into two groups; **Group I (Carbetocin group)** included 200

Received:13/07/2019
Accepted:13/08/2019

women who received carbetocin and delivered either by cesarean section (CS) or vaginal, **Group II (Oxytocin group)** included 200 women who received oxytocin and delivered either by cesarean section (CS) or vaginal**.**

all patients were subjected to the followings:

I. Full Medical History:

- **Personal history**: Name, Age, occupation, address, special habits, parity, No. of kids etc.
- **Past history**: of abortions, PPH or any medical disease can cause bleeding tendency.
- **Menstrual and Obstetric and history:**
  - Age of menarche, Regularity of the cycle and its durations, and Last menstrual period
  - Gravidity, parity, and pregnancy outcomes.
  - Expected date of delivery
  - Any complication during pregnancy, labor or puerperium.
- **Family history:** systemic diseases, congenital anomalies and history of PPH.

II. Full general examination: including cardiological, chest, abdominal and monitoring vital data (heart rate, systolic and diastolic blood pressure).

III. Obstetrical Examination:

- Fundal level to correlate with GA.
- Obstetric grip (fundal grip, umbilical grip, first pelvic grip and second pelvic grip).
- Obstetric Ultrasound for viability, fetal biometry, placentation, presentation and position.

IV. Vaginal Examination:

For assessing the cervical effacement, dilation, fetal presentation, occipit, and exclude caput succedaneum or any sort of mechanical obstruction. Vaginal examination was done under complete aseptic conditions by sterile gloves.

V. Routine preoperative investigations: Complete blood count (CBC)**,** bleeding and coagulation profile, kidney Function tests (urea and creatinine) and liver function test (AST, ALT, albumin & Total bilirubin).

These investigations were done to exclude patients with abnormal kidney or liver functions or hidden general chronic medical diseases.

VI. Intra Operative:

- **In cases delivered with CS:**

Anesthesia technique was standardized, spinal anesthesia was performed. Patients received an intravenous bolus of 500 mL crystalloid before spinal anesthesia. A size 25G pencil-point needle was used at a suitable lumbar interspace. The patient can be sitting or in the left lateral position for spinal anesthesia. The anesthetic solution consisted of 2 ml 0.5% hypertonic bupivocaine (2.2 ml in the sitting position), 10–20 μg fentanyl and 0.1 mg preservative free morphine. Anesthesia should be to the level of T5, as assessed by touch. The patient was tilted 15° to the left of supine and standard. Monitoring used as per the AAGBI guidelines. Anesthetists replaced blood loss at operation with colloid infusion or blood when deemed necessary. Intravenous crystalloids were continued at 1L/8 hours until the morning after surgery. The surgical approach to cesarean section was standardized. Surgeons were asked to operate to a standard procedure that specifies transverse lower segment cesarean section two layer closure of the uterine incision, and to avoid delivering the uterus for suturing unless clinically indicated.

- **Active management of the third stage of labor as the following:**

Administration of the uterotonic agent with delivery of the anterior shoulder of the baby. Clamping and cutting the umbilical cord soon after birth. Applying controlled cord traction while applying simultaneous counter-pressure to the uterus, through the abdomen to avoid its inversion.

VII. Intervention and giving the study drugs: Selection of the study drug that was given to each patients was done by computerized random sample selection.

1) **Carbatocin group**: patients was given 1ml solution of 100 μg carbatocin by slow intravenous injection over 2 minutes after the C-shaped incision of the uterus is done in CS or after crowning of the fetal head in vaginal delivery.
2) **Oxytocin group:** patients was given 20 IU oxytocin by I.V. infusion over one hour after the C-shaped incision of the uterus is done in CS or after crowning of the fetal head in vaginal delivery.

VIII. Local Examination Following Delivery: To exclude traumatic PPH e.g.: extension of episiotomy, cervical, vaginal, Para urethral tears or retained either placental or membranous parts.

IX. Follow up the patients postoperatively: for 24 hours after delivery.

- Vital data (HR, SBP and DBP)
- Hemoglobin concentration
- Hematocrit percent.

X. Outcomes:

- **Primary outcomes:** The incidences of atonic postpartum hemorrhage between both groups.

Secondary outcomes:

- Calculation of amount of intrapartum and postpartum blood loss and compare between the incidences of major obstetric hemorrhage (≥ 500 – 1000 ml) following use of different uterotonic agents.
- Change in hemoglobin and hematocrit value post versus pre delivery between groups.
- To assess the need for blood transfusion.
- The need for further uterine intervention for treatment of PPH.
- Any fetal or maternal morbidity e.g. development of severe anemia, need for blood transfusion, Hysterectomy…. etc.

Statistical analysis

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (**SPSS version 20.0 for windows; SPSS Inc, Chicago, IL, 2001**). Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

Descriptive Statistics: Mean, Standard deviation (± SD) and range for parametric numerical data, while Median and Interquartile range (IQR) for non-parametric numerical data. Frequency and percentage of non-numerical data.

Analytical Statistics: Student T Test: was used to assess the statistical significance of the difference between two study group means. **Mann Whitney Test (U test):** was used to assess the statistical significance of the difference of a non-parametric variable between two study groups. **Chi-Square test (X^2):** was used to examine the relationship between two qualitative variables. **Paired t-test:** was used to assess the statistical significance of the difference between two means measured twice for the same study group.

P- value: level of significance

- P>0.05: Non significant (NS).
- P< 0.05: Significant (S).
- P<0.01: Highly significant (HS).

RESULTS

Table (1): Comparison between both studied group regarding demographic, anthropometric and obstetric data:

	Variable	Group I Carbetocin) (N = 200)	Group II (Oxytocin) (N = 200)	P-value
Maternal Age: (years)	- mean ± SD - range	28.04 ± 2.9 (20 – 36)	28.74 ± 2.5 (21 – 35)	0.229 (NS)
Body Mass Index: (Kg/m2)	- mean ± SD - range	26.02 ± 2.2 (23 – 32)	25.87 ± 2.15 (22 – 31)	0.237 (NS)
Gestational Age (GA): (weeks)	- mean ± SD - range	38.8 ± 1.3 (37 – 41)	38.61 ± 1.2 (37 – 41)	0.69 (NS)
Parity	- mean ± SD - range	2.08 ± 1.18 (0 – 5)	1.03 ± 2.03 (0 – 4)	MW 0.631 (NS)

No significant difference between both groups of the study regarding maternal age, BMI, GA, and parity with p-value: 0.229, 0.237, 0.690 and 0.631 respectively.

Table (2): Comparison between both studied groups regarding labor and post-labor data:

Variable	Group I (Carbetocin) (N = 200)	Group II (Oxytocin) (N = 200)	P-value
Mode of delivery: - Vaginal Delivery - Cesarean section	97 (48.5%) 103 (51.5%)	102 (51.0%) 98 (49.0%)	X^2 0.617 (NS)
Occurrence of atonic post-partum hemorrhage: - yes - No	9 (4.5%) 191 (95.5%)	24 (12%) 176 (88%)	X^2 *0.006 (S)*
Estimated Blood Loss: (ml) - Mean ± SD - range	520.3 ± 254.1 150 – 1500	587.2 ± 303.7 300 – 1500	*U* *0.019 (S)*
Occurrence of postpartum anemia: - yes - No	5 (2.5%) 195 (97.5%)	12 (6.0%) 193 (94.0%)	X^2 *0.08* (NS)

No significant difference between both groups of the study regarding mode of delivery, occurrence of post-partum anemia and need for blood transfusion with p-value: 0.617, 0.08 and 0.2 respectively. There was a statistically significant difference between both groups of the study regarding incidence of occurrence of atonic PPH and estimated blood loss with p-value: 0.006 and 0.019 respectively.

Table (3): Comparison of vital data, Hb concentration, Hematocrit and percentage of difference pre and post in Carbetocin group:

Variable	Group I (Carbetocin)		p-value
	Pre labor	**Post labor**	
Pulse:	**84.8 ± 7.05**	**85.78 ± 7.14**	**0.168 (NS)**
Systolic Blood pressure:	**110.1 ± 2.3**	**108.9 ± 9.8**	**0.093 (NS)**
Diastolic Blood pressure:	**67.05 ± 1.15**	**65.9 ± 9.7**	**0.097 (NS)**
HB% concentration:	**10.66 ± 0.76**	**9.94 ± 0.80**	**<0.001 (HS)**
HCT	**31.76 ± 2.2**	**29.8 ± 0.32**	**<0.001 (HS)**

There was no statistically significant difference between pre and post 2 hour after administration of therapeutic drugs hemodynamic data including HR, SBP and DBP within carbetocin group with p-value: 0.168, 0.093 and 0.097 respectively. While there was a statistical significant difference between pre- and post-labor hemoglobin concentration and hematocrit percent with the carbetocin group with p-value: <0.001 for each.

Table (4): Comparison of vital data, Hb concentration, Hematocrit and percentage of difference pre and post in oxytocin group:

Variable	Group II (Oxytocin)		p-value
	Pre labor	**Post labor**	
Pulse:	**86.01 ± 7.5**	**87.4 ± 9.7**	**0.110 (NS)**
Systolic Blood pressure:	**110.4 ± 1.26**	**109.9 ± 8.46**	**0.409 (NS)**
Diastolic Blood pressure:	**67.17 ± 0.05**	**66.7 ± 6.5**	**0.307 (NS)**
HB (g/dl):	**10.75 ± 0.83**	**9.7 ± 0.9**	**<0.001 (HS)**
HCT (%)	**31.68 ± 2.1**	**29.2 ± 1.9**	**<0.001 (HS)**

There was no statistical significant difference between pre and post 2 hour after administration of therapeutic drugs hemodynamic data including HR, SBP and DBP within oxytocin group with p-value: 0.110, 0.409 and 0.307 respectively. There was a statistical significant difference between pre- and post-labor hemoglobin concentration and hematocrit percent with the oxytocin group with p-value: <0.001 for each.

Table (5): Comparison between patients delivered by vaginal delivery (VD) in both studied groups:

	Vaginal Delivery	**VD in Group I (N = 97)**	**VD in group II (N = 102)**	
Occurrence of atonic post-partum hemorrhage:	**- yes**	**4 (4.1%)**	**12 (11.8%)**	**X2**
	- No	**93 (95.9%)**	**90 (88.2%)**	**0.095 (NS)**
Estimated Blood Loss: (ml)	**- Mean ± SD**	**337.6 ± 178.5**	**410.5 ± 197.9**	***U***
	- range	**150 – 1200**	**300 – 1150**	***0.001 (S)***
Hemoglobin (g/dl) before Labor:	- **mean ± SD**	**10.6 ± 0.7**	**10.8 ± 0.9**	**0.083**
	- **range**	**9.5 – 12.1**	**9.4 – 12.5**	**(NS)**
Hemoglobin (g/dl) 24 hours after Labor:	- **mean ± SD**	**9.9 ± 0.8**	**9.7 ± 0.6**	**0. 047**
	- **range**	**7.2 – 12.1**	**7 – 11.7**	**(S)**
Hemoglobin difference	- **mean ± SD**	**0.7 ± 0.3**	**1.1 ± 0.4**	**<0.001**
	- **range**	**0.2 – 2.4**	**0.7 – 2.9**	**(HS)**
Hematocrit (%) Before Labor	- **mean ± SD**	**31.9 ± 2.1**	**31.5 ± 2.0**	**0.17**
	- **range**	**28.5 – 36.3**	**28.5 – 36.3**	**(NS)**
Hematocrit (%) 24 hours after Labor	- **mean ± SD**	**30.1 ± 2.2**	**29.2 ± 1.9**	**0.002**
	- **range**	**26.5 – 35.1**	**26.1 – 33.5**	**(HS)**
Hematocrit Difference	- **mean ± SD**	**1.9 ± 0.6**	**2.4 ± 0.5**	**<0.001**
	- **range**	**0.5 – 3.2**	**1.5 – 4.0**	**(HS)**

There was no statistical significant difference between both studied groups regarding occurrence of atonic PPH, pre-labor hemoglobin concentration and hematocrit percent with p-value: 0.095, 0.259 and 0.710 respectively. There was significant difference between both groups of the study regarding post (24 hours) hemoglobin concentration and hematocrit percent with p-value: 0.047 and <0.001 respectively. Also there was significant difference between both of them regarding difference between.

Table (6): Comparison between patients delivered by Cesarean section (CS) in both studied groups:

variable	CS in Group I (Carbetocin) (N = 97)	CS in group II (Oxytocin) (N = 102)	
Occurrence of atonic post-partum hemorrhage:			
- yes	**5 (4.9%)**	**12 (12.3%)**	***X^2***
- No	**98 (95.1%)**	**86 (87.7%)**	***0.059 (NS)***
Estimated Blood Loss: (ml)			
- Mean ± SD	**690.9 ± 196.9**	**771.1 ± 285.4**	***U***
- range	**400 – 1500**	**400 – 1750**	***<0.001 (S)***
Hemoglobin (g/dl) before Labor:			
- mean ± SD	**10.7 ± 0.8**	**10.6 ± 0.8**	**0.407**
- range	**9.5 – 12.8**	**9.5 – 12.4**	**(NS)**
Hemoglobin (g/dl) 24 hours after Labor:			
- mean ± SD	**10.0 ± 0.9**	**9.7 ± 0.9**	***0.019***
- range	**7.4 – 12.1**	**7.1 – 11.6**	***(S)***
Hemoglobin difference			
- mean ± SD	**0.7 ± 0.4**	**1.0 ± 0.5**	***<0.001***
- range	**0.3 – 2.6**	**0.4 – 2.8**	***(HS)***
Hematocrit (%) Before Labor			
- mean ± SD	**31.8 ± 2.1**	**31.7 ± 2.0**	**0.730**
- range	**28.5 – 36.3**	**28.4 – 36.8**	**(NS)**
Hematocrit (%) 24 hours after Labor			
- mean ± SD	**29.7 ± 2.1**	**29.1 ± 1.5**	***0.021***
- range	**26.4 – 34.6**	**26.1 – 34.0**	***(S)***
Hematocrit Difference			
- mean ± SD	**2.1 ± 0.6**	**2.6 ± 0.8**	***0.003***
- range	**0.8 – 4.1**	**1.1 – 5.8**	***(HS)***

There was no statistical significant difference between both studied groups regarding occurrence of atonic PPH, pre-labor hemoglobin concentration and hematocrit percent with p-value: 0.059, 0.407 and 0.730 respectively. There was significant difference between both groups of the study regarding post (24 hours) hemoglobin concentration and hematocrit percent with p-value: 0.019 and 0.021 respectively. Also there was significant difference between both of them regarding difference between.

Table (7): Comparison between both studied groups regarding therapeutic drugs side effects:

Variable	Group I (Carbetocin) (N = 200)	Group II (Oxytocin) (N = 200)	P-value
Occurrence of Side Effects			
- Yes	**20 (10%)**	**28 (14%)**	***X^2***
- No	**180 (90%)**	**172 (86%)**	***0.218***
Nausea	**2**	**1**	
Vomiting	**1**	**1**	
Tachycardia (HR > 100 b/min)	**8**	**10**	
Flushing	**1**	**2**	
Dizziness	**2**	**3**	
Headache	**1**	**1**	
Shivering	**1**	**1**	
Metallic taste	**1**	**2**	
Dyspnea	**1**	**1**	
Palpitations	**0**	**1**	
Itching	**2**	**3**	
	0	**2**	
	20	**28**	

There was no significant difference between both groups of the study regarding side effects of therapeutic drugs.

DISCUSSION

Post-partum hemorrhage is the leading cause of morbidity and mortality among pregnant ladies throughout the world causing 140,000 deaths each year globally [(1)].

The aim of this study was to compare the effectiveness and safety of carbetocin versus oxytocin in the prevention of atonic postpartum Hemorrhage (PPH) after vaginal deliveries and cesarean sections.

The included studied 400 pregnant women were randomly divided into two groups; **Group I (Carbetocin group)** included 200 women who received carbetocin and delivered either by cesarean section (CS) or vaginal, **Group II (Oxytocin group)** included 200 women who received oxytocin and delivered either by cesarean section (CS) or vaginal**.**

Group II (oxytocin group) was found to be associated with significant increase of incidence of atonic postpartum hemorrhage (p: 0.006) and amount of blood loss (p: 0.019) when compared with group I (carbetocin group). Also group II was associated with significantly lower Hemoglobin concentration (p: 0.005) and Hematocrit percent (p: <0.001) that was measure 24 hours after labor, while the difference in Hb and HCT between pre and post-labor findings was significantly higher in group II in comparison with group I (p: <0.001 for each).

Within group I, our result showed that the 24-hour post-labor findings of both Hb concentration and HCT percent was significantly lower in comparison with their pre-labor findings (p:<0.001 for each). Similar findings were reported with group II.

A comparison was done between those delivered vaginally in both studied groups (I and II) showed that patients in group II had a significant higher amount of blood loss (p: 0.001). Also group II was associated with significantly lower hemoglobin concentration (p: 0.047) and hematocrit percent (p: 0.002) that was measure 24 hours after labor, while the difference in Hb and HCT between pre and post-labor findings was significantly higher in group II in comparison with group I (p: <0.001 for each)

Another comparison was done between those delivered by CS in both studied groups (I and II) and our results showed patients in group II had a significant higher amount of blood loss (p: <0.001), also group II was associated with significantly lower Hemoglobin concentration (p: 0.019) and Hematocrit percent (p: 0.021) that was measure 24 hours after labor, while the difference in Hb and HCT between pre and post-labor findings was significantly higher in group II in comparison with group I (p: <0.001 and 0.003 respectively).

From these findings, it could be concluded that Carbetocin may be more effective in preventing uterus atony and thereby PPH in comparison with oxytocin and this could be attributed to that carbetocin causes a tetanic uterine contraction produced 2 min after an intravenous injection of 8-30 mg or intramuscular injection of 10-70 mg, which persists for approximately 1 min. Rhythmic uterine contractions persist for 60 and 120min after intravenous and intramuscular injection respectively which decrease the uterine atony. Also, this can be explained by the known longer half-life of Carbetocin when compared to Oxytocin causing a more uterine response, in terms of frequency and amplitude of uterine contractions [(9)].

Our results were in agree with those of **Maged *et al.*** [(2)] who reported in their A prospective double-blinded randomized study conducted on 200 high risk pregnant women undergoing vaginal delivery that there was a statistically significant difference between the two study groups regarding occurrence of PPH (4% in carbetocin group versus 16% in oxytocin group) with p-value: 0.037. They also reported that there was a statistically significant difference between the two study groups regarding Amount of bleeding (ml) (337.73 ± 118.77 in carbetocin group versus 378 ± 143.2 in oxytocin group) with p-value: 0.03. Regarding Hb concentration, they reported that there was no significant difference between Hb before delivery (g/dl) 11.01 ± 1.3 in carbetocin group versus 11.11 ± 1.24 in oxytocin group with p-value: 0.581. while there was a significant difference between Hb 24 h after delivery(g/dl) 10.51 ± 1.38 in carbetocin group versus 10.13 ± 1.26 in oxytocin group with p-value: 0.04. They also reported that there was a significant difference regarding Hb difference (before and after delivery) (g/dl) 0.55 ± 0.35 in carbetocin group versus 0.96 ± 0.62 in oxytocin group with p-value: <0.001.

Our results were also in agree with those of **Debbie-Lyn** [(11)] who reported in their Randomized single blind controlled trial on 70 pregnant women undergone Cesarean Section, that a significant reduction in the post-operative hemoglobin levels from the baseline preoperative level was noted in the carbetocin group (mean 118 to 108, P<.001). Likewise, the levels were also significantly low post-operative in the oxytocin group (mean 116 to 96, P<.001). Post-operatively, levels in the carbetocin group were statistically higher (mean 108.6 versus 96.03, P=.001). Also, a significant reduction in the post-operative hematocrit levels from the baseline preoperative level was noted in the carbetocin group (mean 0.36 to 0.33, P=.001). Likewise, the levels were also significantly low post-operative in the oxytocin group (mean 0.36 to 0.31, P=.018).

In contrast to our findings regarding amount of blood loss, **Larciprete *et al.*** [12] reported in their study on 102 pregnant women undergoing caesarean section that there was no significant difference in the amount of estimated blood loss and in the incidence of primary post-partum hemorrhage (>1000 ml) in both groups.

In consistence with our findings regarding Hb concentration and HCT percent was **Maged *et al.*** [10] who reported in their prospective randomized study was conducted in which 100 pregnant women undergoing vaginal delivery that there was no significant difference between Hb before delivery (g/dl) 11.45 ± 1.45 in carbetocin group versus 11.27 ± 1.43 in oxytocin group with p-value: 0.55. And there was no significant difference between Hb 24 h after delivery (g/dl) 10.85 ± 1.51 in carbetocin group versus 10.71 ± 1.5 in oxytocin group with p-value: 0.645. They also reported that there was no significant difference regarding Hb difference (before and after delivery) (g/dl) 0.6 ± 0.28 in carbetocin group versus 0.56 ± 0.25 in oxytocin group with p-value: 0.529.

Our results showed that there was no statistically significant difference between both groups Post-labor anemia with p-value: 0.08. Also, regarding need for blood transfusion, no statistical significant difference was reported between both groups with p-avlue:0.2.

In agree with our results **Maged *et al.*** [10] reported that there was no statistically significant difference between the carbetocin group and the oxytocin group regarding the need for blood transfusion (12% vs 18%) with p-value: 0.401.

Attilakos *et al.* [8] reported also in their study on women at term undergoing elective or emergency caesarean section, that there were no significant differences in the number of women requiring blood transfusions between oxytocin and carbetocin groups.

Regarding pre administration of the therapeutic drugs hemodynamic and vital data, our results showed that there was no statistically significant difference between both groups regarding the pre-labor Heart rate, SBP and DBP with p-value: 0.097, 0.107, and 0.141 respectively. Also, regarding the 2 hours after administration of the therapeutic drugs hemodynamic and vital data, our results showed that there was no statistically significant difference between both groups regarding the pre-labor Heart rate, SBP and DBP with p-value: 0.058, 0.275 and 0.333 respectively.

The Comparison between pre and 2 hour after administration of the therapeutic drugs hemodynamic data within both studied groups showed that there was no statistical significant difference between findings regarding HR, SBP and DBP with p-value: 0.168, 0.039 and 0.307 respectively in group I and with p-value: 0.110, 0.409 and 0.097 respectively in group II.

These findings were in agree with **Mannaerts *et al.*** [13] who reported in their A randomized controlled trial in term pregnant women (carbetocin n = 32; oxytocin n = 26) undergoing planned CS, that Both medications had hypotensive effect, difference in BP for carbetocin versus oxytocin: systolic (14.4 ± 2.4 mmHg versus 8.5 ± 1.8 mmHg); diastolic (7.8 ± 1.6 mmHg versus 8.9 ± 3.0 mmHg) without significant difference between the drugs (p = 0.1 and p = 0.7). And Mean heart rate did not change after carbetocin or oxytocin treatment.

Side effects following drug administration was reported in 20 (10%) cases in carbetocin group and in 28 (14%) cases in the oxytocin group with no statistical significant difference between both groups with p-value: 0.218.

Our results were in agree with those of **Maged *et al.*** [10] who reported that there was no significant difference between the 2 groups regarding the occurrence of nausea, vomiting, tachycardia, flushing, dizziness, headache, shivering, metallic taste, dyspnea, palpitations and itching.

Regarding the need for other procedures to achieve control of PPH, our results showed that there was no significant statistical difference between both groups of the study regarding the need for other uterotonic drugs or the need for other intervention e.g. balloon tamponade, uterine artery ligation, internal iliac artery ligation, hysterectomy … etc, with p-value: 0.358 and 0.428. There was no reported mortality or hysterectomy among participating patients.

Similar to our findings was **Maged *et al.*** [10] who reported that regarding different measures needed to control the bleeding after failure of carbetocin and oxytocin. One patient in the oxytocin group had uterine artery ligation but bleeding was not controlled and internal iliac artery ligation was needed. There were no mortalities and hysterectomy was not needed in any patient.

CONCLUSION

It could be concluded that carbetocin was found to be a better uterotonic agent in comparison with Oxytocin in the management of atonic postpartum hemorrhage after delivery either vaginal or cesarean section as it decreases incidence of occurrence of PPH and post-partum blood loss.

REFERENCES

1. **Csorba R (2012):** Management of post-partum hemorrhage. Orvosi Hetilap., 153(17):643.
2. **Maged AM, Hassan AM, Shehata NA (2016):** Carbetocin versus oxytocin for prevention of postpartum hemorrhage after vaginal delivery in high risk women. J Matern Fetal Neonatal Med., 29; 4:532-6.
3. **Knight M, Callaghan W, Berg C *et al.* (2009):** Trends in postpartum hemorrhage in high resource countries: a

review and recommendations from the International Postpartum Hemorrhage Collaborative Group. BMC Pregnancy Childbirth, 9(1):55-59.

4. **Ononge S, Mirembe F, Wandabwa J and Campbell O (2016):** Incidence and risk factors for postpartum hemorrhage in Uganda. Reproductive Health, 13:38-46.
5. **Edhi MM, Aslam H, Naqvi Z and Hashmi H (2013):** Postpartum hemorrhage: causes and management. BMC Research Notes, 6:236-42.
6. **Westhoff G, Cotter AM and Tolosa JE (2013):** Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage. https://www.ncbi.nlm.nih.gov › pubmed
7. **Liabsuetrakul T, Choobun T, Peeyananjarassri K *et al.* (2007):** Prophylactic use of ergot alkaloids in the third stage of labour. Cochrane Database Syst Rev., 2:CD005456.
8. **Attilakos G, Psaroudakis D, Ash J *et al.* (2010):** Carbetocin versus oxytocin for the prevention of postpartum haemorrhage following caesarean section: the results of a double-blind randomised trial. BJOG., 117(8):929–936.
9. **Hunter DJ, Schulz P, Wassenaar W (1992):** Effect of carbetocin, a long-acting oxytocin analog on the postpartum uterus. Clin Pharmacol Ther., 52:60-7.
10. **Maged AM, Hassan AM, Shehata NA (2016):** Carbetocin versus oxytocin in the management of atonic post partum haemorrhage (PPH) after vaginal delivery: a randomised controlled trial. Arch Gynecol Obstet., 293; 5:993-9
11. **Debbie-Lyn Uy, Pangilinan NC, And Ricero-Cabingue C (2013):** Carbetocin Versus Oxytocin for the Prevention of Postpartum Hemorrhage Following Elective Cesarean Section: Rizal Medical Center Experience. Philippine Journal of Obstetrics & Gynecology, 37: 2: 71-116.
12. **Larciprete G, Montagnoli C, Frigo M *et al.* (2013):** Carbetocin versus oxytocin in caesarean section with high risk of post-partum haemorrhage. J Prenat Med., 7(1):12-8.
13. **Mannaerts D, Van der Veeken L, Coppejans H *et al.* (2018):** Adverse Effects of Carbetocin versus Oxytocin in the Prevention of Postpartum Haemorrhage after Caesarean Section: A Randomized Controlled Trial. J Pregnancy, 8:1374-9.