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Carbetocin Compared with Oxytocin in Prevention of Postpartum Hemorrhage in Cases of Uterine Overdistention

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Abstract

Postpartum haemorrhage is defined as blood loss of one thousand millilitres or hypovolemia. It may result from uterine atony, retained placental tissue, maternal genital tract trauma and accidental haemorrhage. Separation of the placenta, uterine contraction, and typical hemostatic mechanisms regulate normal postpartum bleeding. Oxytocin is the best in preventing postpartum haemorrhage. Carbetocin, a long-acting synthetic analogue of oxytocin with agonist action, is injected intravenously as a single bolus over 1 minute to prevent postpartum haemorrhage and decrease the need for further uterotonic medications. The aim of this study is to compare the effectiveness, safety, and tolerability of carbetocin versus oxytocin in prevention of postpartum hemorrhage. This is a prospective clinical trial include 100 pregnant women divided into 2 equal groups in the department of obstetrics and gynecology at Itay Al-Baroud General Hospital. Group (A): Received 100 mcg of carbetocin as a single dose by direct intravenous injection over one minute. Group (B): The women received a continuous intravenous infusion of 10 IU oxytocin in 500 ml 0.9% NaCl solution. The difference was statistically non-significant according to total blood loss. Regarding the need for additional uterotonics drugs and blood transfusion the difference was significantly higher in Oxytocin group. According to the adverse effects of both drugs there was no significant difference between groups except for Pyrexia which was significantly higher in Oxytocin group and Nausea significantly higher in Carbetocin group. Complete blood count data 24 hours after delivery was significantly better in Carbetocin group. women having carbetocin had higher hemoglobin, less blood loss, reduced need for additional uterotonics, and reduced need for blood transfusion.

Keywords: Postpartum Hemorrhage, Carbetocin, Oxytocin, Uterine Overdistention.

1. Introduction

Postpartum hemorrhage is defined as blood loss of at least 1000 cc or blood loss associated with symptoms of hypovolemia. Early (primary) postpartum hemorrhage is defined as blood loss occurring in the first 24 hours postpartum. Late (secondary)

postpartum hemorrhage is defined as blood loss occurring between 24 hours and 12 weeks postpartum [1]. Postpartum hemorrhage is an important cause of maternal mortality and morbidity, with a worldwide prevalence of 6%, accounting for 27.1% of all maternal deaths and the majority occurring within 24 hours following birth [2]. Following delivery of the baby, normal bleeding is controlled by separation of the placenta, uterine contraction with constriction of placental bed vessels, and normal hemostatic pathways [1]. Postpartum hemorrhage can result from uterine atony, retained placental tissue including that from abnormal placentation, maternal genital tract trauma, pre-eclampsia and gestational hypertension and previous postpartum hemorrhage (PPH). In addition, other causes include obesity (BMI >35), anemia (<9 g/dl), advanced maternal age, prolonged labor (> 12 hours), coagulopathies, big baby (> 4 kg), polyhydramnios and all cases of over distended uterus as twin pregnancy. Also, it may occur in women with no identifiable risk factors [3]. Uterine atony is the major cause of hemorrhage accounting for up to 80% of postpartum hemorrhage (PPH) cases [4]. Therefore, inducing a rapid and effective uterine contraction following delivery is an important issue [5]. Active management of third-stage labor helps to reduce the rate of severe primary postpartum hemorrhage (PPH) [6]. Several uterotonics agents are used to prevent postpartum hemorrhage (PPH) because of uterine atony, including oxytocin, ergot alkaloid and prostaglandin. Oxytocin is the most widely used and effective uterotonic agent for prevention of postpartum hemorrhage (PPH) [7], but it has a rapid onset and short duration of action. So, it is better administered intravenously to achieve sustained uterotonic activity [8]. Carbetocin , a long-acting synthetic analog of oxytocin with agonist action, which is given as a single intravenous bolus over 1 min, instead of a continuous oxytocin infusion, for the prevention of postpartum hemorrhage (PPH) and decrease the need for additional uterotonic agents [9].

2. Patients and Methods

This is a prospective comparative clinical study include one hundred pregnant women presented with uterine over distention between the ages of 18 and 40 years, chosen according to specific criteria and divided into 2 equal groups in the department of obstetrics and gynecology at Itay Al-Baroud General Hospital from October 2020 till October 2021.

2.1 Inclusion Criteria

Women undergoing delivery by vaginal or cesarean section after 28 weeks of gestation and had any case of uterine over distention during pregnancy: Multiple pregnancies: Twins, Trible, Polyhydramnios, Fetal macrosomia and fibroid with pregnancy.

2.2. Exclusion Criteria

Any medical disorder with pregnancy that carry risk factors for postpartum hemorrhage as (PET, anemia, thrombocytopenia, placenta previa), chorioamnionitis, prolonged labor, cardiac, renal, and liver diseases. For all patients included in the study, on the day of delivery all patients were subjected to: Complete history taking: Personal history e.g., Name, Age, Occupation, Address, Menstrual history especially, last menstrual period (LMP), Full obstetric history and the accurate expected date of delivery, Medical and surgical history and Family history. Examination: Full general examination, Obstetric examination, vaginal examination if there isn't contraindication and Ultrasonography examination for assurance of diagnosis and evaluation of fetal condition. Laboratory examination: Mainly complete blood counting (CBC), RH factor and Coagulation profile. All patients were informed about the study, aims and all information about it and written consent was obtained. A total

number of 100 pregnant women presented with uterine over distention between the ages of 18 and 40 years, chosen according to specific criteria and divided into 2 equal groups each group involved 50 cases. Group (A): Received 100 mcg of carbetocin (Pabal 100 mcg Ferring Pharmaceuticals: Saint-Prex, Switzerland) as a single dose by direct intravenous injection over one minute. Group (B): Women received a continuous intravenous infusion of 10 IU oxytocin (Syntocinon; Novartis, Basel, Switzerland) in 500 ml 0.9% NaCl solution. All women received their drug immediately before delivery of the placenta and after delivery of second twin in twin pregnancy or the third one in triplet. The need for additional uterotonics agents (misoprostol, methylergometrine) and frequency of the additional since administration of study dose till 24 hours after delivery is reported. Duration of the operation, blood transfusion, maternal pulse rate, blood pressure and the newborn body weight also recorded. Uterine tone was assessed immediately after delivery of the placenta and then every 5 minutes until the end of delivery. Estimation of blood loss was beginning after suction of amniotic fluid and discarding it by the double jar suction apparatus after suction of amniotic fluid, discarding it and delivery of the placenta. After delivery of the placenta, the volume of blood loss was assessed by weight by subtracting the dry weight of absorbing materials (pads, sponges, etc.) from the weight of blood-containing materials and using the conversion 1 gm weight = 1 ml to quantify the blood volume contained in the materials [10]. Also, by the number of towels used and to which degree they were stocked (soaked towel = 150 cc and semi-soaked towel = 75 cc). Then, confirmation was done by measuring the difference in hemoglobin concentration 24 hours after delivery and the change in concentration was compared to the baseline level of hemoglobin. Finally, data was collected and classified according to NCBI. Vital signs of the patients were measured every 30 minutes in the first two hours after delivery then every two hours during hospitalization. Complete blood count examination was done 24 hours after delivery. Normal amount of blood loss ≤ 500 ml for vaginal delivery and ≤ 1000 ml for cesarean section delivery in absence of clinical signs of hypovolemic symptoms. Post-Partum haemorrhage was characterized by blood loss > 500 ml for vaginal delivery and > 1000 ml for cesarean section delivery. According to the amount of blood loss and the clinical symptoms of the case, the degree of shock was determined. So, Post-Partum haemorrhage (PPH) degree was classified in to mid, moderate and sever. In mild PPH the amount of blood loss is about 10001500 ml which represent (15-25%) of the patient total blood, moderate PPH blood loss is about 1500-2000 ml (25-35%) of the patient total blood and sever PPH blood loss > 2000 ml which represent about (3550%) of the patient total blood [11]. Women's that suspected or diagnosed with postpartum hemorrhage were treated by repeating the dose of uterotonic agents or giving adjuvant therapy for controlling and preventing more blood loss as Misoprostol (Misotac),Methergine (methylergonovine maleate), Tranexamic Acid (kapron) and Ethamsylate (Dicenon). Blood transfusion was given according to hemoglobin level and clinical assessment of cases.Women were also evaluated for adverse effects of drugs within 24h after delivery like shivering, fever, tachycardia, skin rash and blood reaction. (methylergonovine maleate), Tranexamic Acid (kapron) and Ethamsylate (Dicenon). Blood transfusion was given according to hemoglobin level and clinical assessment of cases.Women were also evaluated for adverse effects of drugs within 24h after delivery like shivering, fever, tachycardia, skin rash and blood reaction.

3. Data collection and statistical analysis:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM

Corp) Qualitative data were described using number and percent. Shapiro-Wilk test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the results obtained was judged at the 5% level. The tests used were Chi-square test, for categorical variables, to compare between different groups. Fisher's Exact or Monte Carlo correction, Correction for chi-square when more than 20% of the cells have expected count less than 5. Student t-test, For normally distributed quantitative variables, to compare between two studied groups. Mann Whitney test for abnormally distributed quantitative variables, to compare between two studied groups.

- P-value >0.05 was considered insignificant.
- P-value <0.05 was considered significant.
- P-value <0.001 was considered as highly significant.

3. Results

As shown in Table 1, comparison between the two groups is studied according to different demographic data. Regarding Age (years), obstetric history, gestational age (weeks), Rh factor and BMI, the difference was statistically nonsignificant between the two studied groups. As shown in table 2 regarding mode of delivery 18 % of cases in Group (A) undergo Spontaneous Vaginal delivery, 82 % do Caesarean section (CS). Group (B) 12% delivered by Spontaneous Vaginal delivery and 76 % undergo Caesarean section (CS). As shown in table 3 regarding the total blood loss, 52.0 % of cases showed PPH (uterine atony) in Group A: Carbetocin and 66.0 % in Group B: Oxytocin showed PPH (uterine atony), the difference was statistically non-significant between the two studied groups. As show in table 4 regarding need for additional uterotonics drugs, need for blood transfusion and need for uterine massage the difference was statistically significant. But, regarding need for surgical intervention, the difference was statistically non-significant between the two studied groups. As show in table 5 regarding the adverse effect of medications about 10 % of Group A developed adverse effect and about 18 % of Group B developed adverse effect of the drug the difference was statistically non-significant between the two studied groups. As show in table 6 regarding HB (mg/dl), Platelet count and HCT% before and 24 hours after delivery, the difference was statistically significant between the two studied groups.

Table 1: Demographic data distribution between the two studied groups**.**

	Personal data	Group A (n=50)		Group B (n=50)		Test of sig.	P
		No.	%	No.	%		
1.		Age (years)					
	Min. – Max.	19.0 – 38.0		18.0 – 37.0		t= 1.401	0.164
	Range	19		20			
	Mean ± SD	27.80 ± 5.96		26.14 ± 5.89			
	Median (IQR)	26.50 (23.0–34.0)		25.0 (22.0–31.0)			
2.		Obstetric History					
	-Parity						
	Nullipara Multipara	12	24.0	13	26.0	□□□□ □□□□□	0.783
		38	76.0	37	74.0		
	-Previous abortion						
	No Yes	37	74.0	44	88.0	□□□□ □□□□□	0.074
		13	26.0	6	12.0		
	-Previous PPH						
	No Yes	42	84.0	38	76.0	□□□□ □□□□□	0.263
		8	16.0	12	24.0		
	-Recurrent PPH	6	75	9	75	= 75 %	
3.		Current GA (weeks)					
	Preterm cases Full-term cases	29	58.0	27	54.0	□□□ 0.162	0.687
		21	42.0	23	46.0		
4.		Rh Factor					
	Negative Positive	8 42	16.0 84.0	15 35	30.0 70.0	□□□ 2.767	0.096
5.		BMI (kg/m/2)					
	Min. – Max. Range Mean ± SD. Median (IQR)	20.30 – 36.70		22.0 – 35.40		t= 1.508	0.135
		16.40		13.4			
		29.94 ± 3.83		28.84 ± 3.41			
		29.90(27.20–33.20)		28.20(26.90–30.70)			

Group A: Carbetocin (Pabal) Group B: Oxytocin

Table 2: Distribution of the two studied groups according to mode of delivery

Mode of delivery	Group A (n=50)		Group B (n=50)		□2	P
	No.	%	No.	%		
Spontaneous Vaginal delivery	9	18.0	12	24.0		
Caesarean section (CS) Elective CS Emergency CS	41 22 19	82.0 44.0 38.0	38 17 21	76.0 34.0 42.0	0.542	0.461
Duration of operation in Caesarean section (min.)	(n=41)		(n=38)			
Min. – Max. Mean ± SD Median	25.0 – 120.0 53.78 ± 21.55 55.0		45.0 – 200.0 105.24 ± 85.13 75.0		U=363.0	<0.001*

Table 3: Distribution of the two studied groups according to amount of blood loss

Total Blood Loss	Group A (n=50)		Group B (n=50)		□2	P
	No.	%	No.	%		
Normal amount of blood loss	24	48.0	17	34.0	2.026	0.155
PP hemorrhage (uterine atony)	26	52.0	33	66.0		
Mean of estimated blood loss ± SD.	871 ± 305		922.8 ± 430			0.06
Mild	10	20.0	11	22.0	0.060	0.806
Moderate	5	10.0	7	14.0	0.379	0.538
Severe	11	22.0	15	30.0	0.832	0.362

Table 4: Comparison between the two studied groups according to need for intervention

		Group A (n=50)		Group B (n=50)		□□	P
		No.	%	No.	%		
1.	Need for additional uterotonics drugs	40	80.0	50	100.0	11.111*	0.001*
2.	Need for blood transfusion No Yes	 34 16	 68.0 32.0	 26 24	 52.0 48.0	4.421*	0.039*
3.	Need for surgical intervention No Yes	 47 3	 94.0 6.0	 45 5	 90.0 10.0	2.412	0.487
4.	Need for uterine massage No Yes	 24 26	 48.0 52.0	 17 33	 34.0 66.0	6.250	0.012*

*Surgical intervention as: B-Lynch suture, traumatic repair, internal iliac artery ligation and hysterectomy.

Table 5: Distribution of the two studied groups according to adverse effect of medications

		Group A (n=50)		G (	roup B n=50)	□□□(p)
		No	%	No	%	
Adverse effect of medications	Yes	5	10.0	9	18.0	1.329 (FEp= 0.388)
	No	45	90.0	41	82.0	
Shivering	Yes	2	4.0%	7	14.0%	3.053 (FEp= 0.160)
	No	48	96.0%	43	86.0%	
Pyrexia	Yes	2	4.0%	8	16.0%	4.000* (FEp= 0.046*)
	No	48	96.0%	42	84.0%	
Nausea	Yes	8	16.0%	2	4.0%	4.000* (FEp= 0.046*)
	No	42	84.0%	48	96.0%	
Vomiting	Yes	4	8.0%	1	2.0%	1.895 (FEp= 0.362)
	No	46	92.0%	49	98.0%	
Skin rash	Yes	-	-	1	2.0%	1.010 (FEp= 1.000)
	No	50	100.0	49	98.0%	

Table 6: Comparison between the two studied groups according to complete blood count (CBC) before and 24 hours after delivery.

CBC		Group A (n=50)	Group B (n=50)	U	P
HB (g/dl)	Before delivery				
	Min. – Max. Range Mean ± SD. Median (IQR)	10.40 – 13.90 3.5 11.71 ± 0.79 11.50 (11.20–12.20)	10.40 – 12.90 2.5 11.27 ± 0.64 11.20 (10.80–11.70)	838.50*	0.004*
	After delivery				
	Min. – Max. Range Mean ± SD. Median (IQR)	4.30 – 12.10 7.8 10.03 ± 1.57 10.15 (9.60–11.0)	4.50 – 11.60 7.1 8.98 ± 2.50 9.55 (8.70–10.50)	864.0*	0.008*
Platelet x103 /µL	Before delivery				
	Min. – Max. Range Mean ± SD. Median (IQR)	100.0 – 595.0 495 226.6 ± 84.31 211.50	105.0 – 326.0 221 182.16 ± 57.14 169.30	941.50*	0.032*
	After delivery				
	Min. – Max. Range Mean ± SD. Median (IQR)	55.0 – 370.0 315 198.54 ± 79.90 189.0 (140.0–269.0)	31.0 – 283 252 155.80 ± 89.39 145.0 (104.0–180.0)	843.50*	0.005*
HCT%	Before delivery				
	Min. – Max. Range Mean ± SD. Median (IQR)	21.02 – 39.50 18.48 32.29 ± 5.35 33.0 (31.02–35.10)	20.20 – 39.0 18.8 32.06 ± 3.03 32.05 (30.40–34.0)	1047.0	0.162
	After delivery				
	Min. – Max. Range Mean ± SD. Median (IQR)	21.0 – 35.0 14 29.66 ± 5.84 31.25 (27.0–34.0)	14.0 – 36.0 22 26.69 ± 7.57 27.05 (25.60–32.0)	902.0*	0.016*

4. Discussion

Postpartum hemorrhage (PPH) accounts for nearly one quarter of all maternal deaths worldwide [12] and was the second frequent cause of maternal death in the UK between 2000 and 2017 [13]. In developing countries, Postpartum hemorrhage (PPH) is estimated to be responsible for about 30% of maternal deaths [12]. Uterine atony is the most common cause of immediate heavy postpartum hemorrhage. The administration of oxytocin after delivery of the neonate reduces the likelihood of postpartum hemorrhage and administration of 5 IU oxytocin by slow intravenous injection is currently recommended for all caesarean sections. However, the use of additional uterotonic drugs is common, to arrest bleeding, or prophylactically if there are risk factors for postpartum hemorrhage [7]. The prophylactic use of uterotonics reduces mean blood loss and therefore maternal morbidity and mortality. Although oxytocin has been long the product of first choice, carbetocin has found its place in modern obstetrics. Up till now, the best product for prevention remains subject for discussion [14]. Both products are believed to have a similar mechanism of action; that is, oxytocin and carbetocin bind to the same receptor [15].Oxytocin is a receptor agonist and carbetocin is a long working variant. A study by Cole et al., compared the in vitro effect of oxytocin and carbetocin on the contractility of myometrium samples obtained during elective caesarean section and found the former to be more effective [16]. The aim of our study is to compare effectiveness, safety, and tolerability of carbetocin versus oxytocin in prevention of postpartum hemorrhage (PPH) in women with uterine over distention undergoing both vaginal and cesarean delivery. In the present study, 100 pregnant women were randomly divided into two groups; Group A: Carbetocin (Pabal), included 50 women ranged in age between 19.0 – 38.0 years with a mean age of 27.80 ± 5.96 years who received carbetocin and delivered either by cesarean section (41 cases) or vaginal delivery (9 cases). Group B: Oxytocin included 50 women ranged in age between 18.0 – 37.0 years with a mean age 26.14 ± 5.89 years who received oxytocin and delivered either by cesarean section (38 cases) or vaginal delivery (12 cases). In agreement with our findings Zein El Abdeen et al., studies were done on 200 pregnant ladies who had an elective caesarean section at a gestational age ≥ 37 weeks. Two groups were formed, 100 women in Group A (Carbetocin) with mean age was (29.73±6.27) years, as well as 100 pregnant women in group B with mean age (29.57±6.19) received a mixture of intravenous oxytocin and intramuscular ergometrine. There were no significant differences in age between the study groups. In another study done by Maged et al., 300 women admitted to Kasr Aini hospital were divided into 2 groups: group 1 (150 women) was given carbetocin, while group 2 (150 women) was given oxytocin and methergine, mean age in Group (A) was (24.6 ± 5.2) years while in Group (B) was (26.4 ± 6.1) years. The differences between the two groups were not statistically significant [18].

Regarding body mass index (BMI) (kg/m/2), Group A was 29.94 ± 3.83 kg/m/2 and Group B was 28.84 ± 3.41 kg/m/2, the difference was statistically nonsignificant (p=0.135). in agreement with our study Abdrabo reported in his study that the average age (years) for the carbetocin group was 25.84±2.76 as well as for the oxytocin and ergometrine group was 27.02±3.38, while the average BMI for the carbetocin group was 27.58±3.04 and for the oxytocin and ergometrine group was 27.04±2.83, with no significant statistical differences between the two groups [19]. Regarding Rh factor, Group A showed 84.0 % + ve Rh and Group B showed 70.0 % +ve Rh. The difference was statistically non-significant between the two studied groups. But when we compare Rh factor in total sample, we found that postpartum hemorrhage (PPH) cases showed higher negative Rh factor than normal cases. The difference was statistically significant ($p<0.002$*). Regarding number of cases who had

previous postpartum hemorrhage in both groups (8 cases in Group A and 12 cases in Group B), the difference was statistically non-significant between them (p=0.263). However, 75.0% of cases who had a history of previous postpartum hemorrhage (6 cases in Group A and 9 cases in Group B) developed a recurrent postpartum hemorrhage in our study. This result was in accordance with several more recent studies. Linde et al., who compare the recurrence of postpartum hemorrhage resulted in mothers with a history of postpartum hemorrhage (PPH) having three- and six-fold higher risks of postpartum hemorrhage (PPH) in their second and third deliveries respectively [20]. In this study, we found that the incidence of primary postpartum hemorrhage (PPH) is high, 52.0 % showed postpartum hemorrhage (uterine atony) in Group A: Carbetocin (Pabal) and 66.0 % in Group B: Oxytocin showed postpartum hemorrhage (uterine atony). The lower amount of blood loss we observed in the carbetocin group may have been due to the strong uterine contraction induced by the carbetocin injection, which may mean that the blood loss decreased during the operation, even though there was not statistically significant. In addition, regarding HB (mg/dl) 24 hours after delivery, Group A: Carbetocin (Pabal) was 10.03 ± 1.57 and Group B: Oxytocin was 8.98 ± 2.50. The difference was statistically significant (p=0.008*). Regarding Platelet count (x103 /µL) 24 hours after delivery, Group A: Carbetocin (Pabal) was 198.54 ± 79.90 and Group B: Oxytocin was 155.80 ± 89.39, the difference was statistically significant (p=0.005*). This result was in accordance with Seow et al., who compared the efficacy and safety of carbetocin with those of oxytocin infusion in women with twin pregnancy undergoing elective cesarean delivery [5]. The mean estimated blood loss during surgery was lower in the carbetocin group compared with the control group, but the difference was not statistically significant. This result is similar to other studies that carbetocin is associated with less blood loss compared to syntometrine in the prevention of postpartum hemorrhage [9]. Concerning pre- and postoperative HB, some authors found that the estimated blood loss in women who underwent cesarean deliveries was more in the oxytocin group. This agreed with our study which showed statistical difference between both groups [21]. Jin et al. found that there is no difference in efficacy between oxytocin and carbetocin regarding mean blood loss which is in line with our study [14].In the past, several studies looked for the most effective agent for prevention of postpartum hemorrhage (PPH), although need for additional uterotonics was essential.

In the present study, regarding need for blood transfusion, 32.0 % need for blood transfusion in Group A: Carbetocin (Pabal) and 48.0 % need for blood transfusion in Group B: Oxytocin. The difference was statistically significant (p=0.039*). Oxytocin group showed a trend of a higher incidence of blood transfusion and need for additional uterotonic agents compared with the carbetocin group. Regarding need for additional uterotonics drugs, 80.0 % need additional uterotonics drugs in Group A: Carbetocin (Pabal) and 100.0 % in Group B: Oxytocin needs additional uterotonics drugs. The difference was statistically significant (p=0.001*). Borruto F et al., And Dansereau J et al., were in agreement with our study concerning need for additional uterotonic drugs. Regarding Duration of operation (min.), Group A: Carbetocin (Pabal) was 53.78 ± 21.55 min and Group B: Regarding Platelet count (x103 /µL) 24 hours after delivery, Group A: Carbetocin (Pabal) was 198.54 ± 79.90 and Group B: Oxytocin was 155.80 ± 89.39, the difference was statistically significant (p=0.005*). This result was in accordance with Seow et al., who compared the efficacy and safety of carbetocin with those of oxytocin infusion in women with twin pregnancy undergoing elective cesarean delivery [5]. The mean estimated blood loss during surgery was lower in the carbetocin group compared with the control group, but the difference

was not statistically significant. This result is similar to other studies that carbetocin is associated with less blood loss compared to syntometrine in the prevention of postpartum hemorrhage [9]. Concerning pre- and postoperative HB, some authors found that the estimated blood loss in women who underwent cesarean deliveries was more in the oxytocin group. This agreed with our study which showed statistical difference between both groups [21]. Jin et al. found that there is no difference in efficacy between oxytocin and carbetocin regarding mean blood loss which is in line with our study [14]. In the past, several studies looked for the most effective agent for prevention of postpartum hemorrhage (PPH), although need for additional uterotonics was essential.

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Regarding the side effects of the medications, Oxytocin group showed a statistical difference for pyrexia with p value (0.046), Carbetocin group showed a statistical difference for nausea with p value (0.046) and the difference was statistically nonsignificant between the remnant side effects between both groups. Since the surgical skill of the surgeon can also affect operation time, all procedures in this study were performed by the same surgeon.

Our study has similar aspects regarding the effect of carbetocin on the uterus in comparison with oxytocin to that of Ortiz et al. who found that carbetocin was more effective than oxytocin following caesarean section (CS) with at least one risk factor for prevention of postpartum hemorrhage [23]. We found that women having carbetocin had higher hemoglobin, less blood loss, reduced need for additional uterotonics, and reduced need for blood transfusion when compared with the oxytocin group [23], this result is similar to other studies that carbetocin is associated with less blood loss compared with syntometrine in the prevention of postpartum hemorrhage [24]

6. Conclusion

According to the results of this study, Carbetocin shows superiority above Oxytocin in prevention of post-partum haemorrhage as carbetocin causes better uterine tone for a relatively longer duration with the same safety and tolerability as

oxytocin, and it enables us to obtain a perfect result with a single IV injection. Carbetocin is solely efficient in controlling postpartum hemorrhage as it is associated with less need for further uterotonic agents or surgical haemostatic measures in comparison to Oxytocin. It combines the safety and tolerability profile of oxytocin with sustained uterotonic activity over oxytocin for a relatively long duration.

7. Recommendation

Finally, we prefer further research with higher volume samples to assess whether the prophylactic effect of Carbetocin is superior to the prophylactic effect of the conventional uterotonic agents or not, as the using of Carbetocin is still limited due to its high cost.

References

1. Paul Lyons and Nathan McLaughlin (2020): Obstetrics in Family Medicine: A Practical Guide, 3rd Edition, Kindle Edition, March 2020, California University of Science and Medicine, CA, USA.

2. Yu W 2020: A meta-analysis of the effects of intramuscular and intravenous injection of oxytocin on the third stage of labor. Archives of Gynecology and Obstetrics, 109(2): p. 173–177.

3. Royal College of Obstetrician & Gynaecologists (RCOG) (2017): Shoulder dystocia guideline no. 42. Green top guidelines. London: RCOG

4. Sentilhes L, Vayssière C, Deneux-Tharaux C (2016): Postpartum Haemorrhage guidelines. Eur J Obstet Gynecol Reprod Biol.198:12–21.

5. Seow KM, Chen KH, Wang PH, Lin YH, Hwang JL (2017): Carbetocin verses oxytocin for prevention of postpartum hemorrhage in infertile women with twin pregnancy undergoing elective cesarean delivery. Taiwan J Obstet Gynecol.56 (3):273-275. doi: 10.1016/j.tjog. 04.001.

6. Adnan N, Conlan-Trant R, McCormick C, Boland F, Murphy DJ. (2018): Intramuscular versus intravenous oxytocin to prevent postpartum haemorrhage at vaginal delivery: randomized controlled trial. Bmj 362: k3546.

7. Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ (2018); Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database Syst Rev. 12:CD011689 Cochrane network met analysis supports use of carbetocin.

8. Gallos I, Williams H, Price M, Pickering K, Merriel A, Tobias A, Lissauer D, Gee H, Tuncalp O, Gyte G, Moorthy V, Roberts T, Deeks J, Hofmeyr J, Gulmezoglu M, Coomarasamy A. (2019): Uterotonic drugs to prevent postpartum haemorrhage: a network meta-analysis. Health Technol Assess. 2019; 23:1–356.

9. El Behery MM, El Sayed GA, El Hameed AA, Soliman BS, Abdelsalam WA, Bahaa A (2016): Carbetocin verses oxytocin for prevention of postpartum hemorrhage in obese nulliparous women undergoing emergency cesarean delivery. J Matern Fetal Neonatal Med.29 (8):1257e60.

10. Chaudhuri P, Biswas J, and Mandal A (2012): Sublingual misoprostol versus intramuscular oxytocin for prevention of postpartum hemorrhage in low-risk women. Int J Gynaecol Obstet., 116: 138-142.

11. Federación Latinoamericana (2018): de Asociaciones de Sociedades de Obstetricia y Ginecología. Hemorragia

postparto. Donde estamos y hacia donde vamos? Paitilla: FLASOG.

12. World Health Organization (2019): WHO Recommendations for the Prevention and Treatment of Postpartum Haemorrhage. Availableonline:http://www.who.int/reproductiv ehealth/publications/maternal_perinatal_health/9 789241548502/en/ (accessed on 23 October 2019).

13. Trends in maternal mortality (2019): 2000 to 2017: estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division. Geneva: World Health Organization.

14. B. Jin, Y. Du, F. Zhang, K. Zhang, L. Wang, and L. Cui (2016): "Carbetocin for the prevention of postpartum hemorrhage: A systematic review and meta-analysis of randomized controlled trials, "The Journal of Maternal-Fetal and Neonatal Medicine, vol. 29, no. 3, pp. 400–407.

15. WHO 2021: The Global Prevalence of Anemia in 2021.

16. Cole NM, Carvalho JC, Erik-Soussi M, Ramachandran N, Balki M (2016): In vitro comparative effect of carbetocin and oxytocin in pregnant human myometrium with and without oxytocin pretreatment. Anesthesiology. 124(2):378–86.

17. Zein El Abdeen 2018: Carbetocin verses oxytocin and ergometrine for prevention of postpartum hemorrhage following caesarean section. Evidence Based Women's Health Journal. 8(1), 138.

18. Maged AM, Hassan AM and Shehata NA (2016): Carbetocin versus oxytocin in the management of atonic postpartum haemorrhage (PPH) after vaginal delivery: a randomized controlled trial. Arch Gynecol Obstet.293: 5:993-9.

19. Abdrabo HA 2016: Comparative Study between Carbetocin versus Oxytocin and Ergometrinein Prevention of Post-Partum Haemorrhage, Nature and Science; http://www.sciencepub.net/nature.

20. Linde LE, Ebbing C, Moster D (2022): Recurrence of postpartum hemorrhage, maternal and paternal contribution, and the effect of offspring birthweight and sex: a populationbased cohort study. Arch Gynecol Obstet. https://doi.org/10.1007/s00404-021-06374-3 - DOI - PubMed.

21. Askar AA, Ismail MT, El-Ezz AA, Rabie NH (2011): Carbetocin versus syntometrine in the management of third stage of labor following vaginal delivery. Archives of Gynecology and Obstetrics. 284(6):135965.

22. Moertl MG, Friedrich S, Kraschl J, Wadsack C, Lang U, Schlembach D (2011): Haemodynamic effects of carbetocin and oxytocin given as intravenous bolus on women undergoing caesarean delivery: a randomized trial. BJOG.118:1349e56.

23. Rosales Ortiz SR, Perez RA, Hernandez RS, Castorena MIY, Cristobal FGL, Gonzalez MAC (2014): Carbetocin versus oxytocin for prevention of postpartum hemorrhage: a randomized controlled trial. Eur J Obstet Gynecol Reprod Biol . 383:1–7.

24. Maged AM, Ragab AS, Elnassery N, AI Mostafa W, Dahab Sh, Kotb A (2017): Carbetocin versus syntometrine for prevention of postpartum hemorrhage after cesarean section. J Matern Fetal Neonatal Med.30:962–966.