

Carbetocin Or Oxytocin To Prevent Postpartum Haemorrhage Due To Uterine Aony In Cases Of Elective Caesarean Section

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ABSTRACT

Background: Despite the technological advancement made in the past few decades, postpartum haemorrhage (PPH) remains one of the principal causes of maternal deaths in developing nations. The administration of uterotonic drugs widely prevents the PPH; therefore, it is the main point of active management. Among uterotonics, oxytocin has proven to be very effective in reducing the incidence of PPH. One prophylactic drug which has been introduced in recent times is carbetocin, a synthetic long-acting oxytocin analogue. It has a longer half life of 41 min, allowing it to stimulate a prolonged uterine response of up to an hour after a single intravenous dose, obviating the need for infusion. **Methods:** A total of 120 pregnant women divided into two groups; Group I (Carbetocin group) included 60 women who received carbetocin and delivered by caesarean section (CS), Group II (Oxytocin group) included 60 women who received oxytocin and delivered by caesarean section (CS). **Results:** Our result showed that, there was a statistically significant difference for the prevention of atonic postpartum hemorrhage between the two groups ($p < 0.01$), for carbetocin group. There was also a statistically significant difference between the two groups ($p < 0.01$), according to need to additional procedures, such as need to modified B-lynch sutures and need to bilateral uterine arteries ligation for carbetocin group. **Conclusion:** We concluded that carbetocin was a better alternative to traditional oxytocin in the prevention of PPH after elective caesarean section.

INTRODUCTION

Despite the technological advancement made in the past few decades, postpartum haemorrhage (PPH) remains one of the principal causes of maternal deaths in developing nations⁽¹⁾.

PPH is responsible for one – fourth of maternal deaths worldwide. PPH is defined as postpartum blood loss 500ml after vaginal delivery and blood loss > 1000 ml after caesarean delivery. Uterine atony is the most common cause of PPH. Active management of the third stage of labor (AMTSL) is recommended for prevention of PPH⁽²⁾.

Administration of uterotonic agents is an essential component of AMTSL, as this prophylactic strategy has decreased the incidence of PPH by nearly the half⁽³⁾.

The administration of uterotonic drugs widely prevents the PPH; therefore, it is the main point of active management. Among uterotonics, oxytocin has proven to be very effective in reducing the incidence of PPH(4).

A single dose of carbetocin has been hypothesised to act as a 16 hours intravenous oxytocin infusion regarding the increase in uterine tone and the reduction of the risk of PPH in elective caesarean section(5).

One prophylactic drug which has been introduced in recent times is carbetocin, a synthetic long-acting oxytocin analogue. It has a longer half life of 41 min, allowing it to stimulate a prolonged uterine response of up to an hour after a single intravenous dose, obviating the need for infusion(6).

Meta-analysis has shown that when compared to oxytocin, carbetocin reduced the need for additional uterotonics. This may translate into savings in terms of lower staffing time taken to monitor and administer the additional medication(7).

Aim of the work

Our study was conducted to compare which is more effective for the prevention of atonic PPH, during elective caesarean section, oxytocin or carbetocin.

PATIENTS AND METHODS

This prospective randomized clinical trial was conducted at Department Of Obstetrics And Gynaecology, Benha Teaching Hospital, Egypt. A total of 120 pregnant women attending the delivery unit in the period from January 2019 to January 2020 were enrolled in the study.

Patients were eligible if they were scheduled for an elective caesarean section through a lower – segment transverse incision under spinal anaesthesia. Only term pregnancies (after 37 weeks) with singleton fetuses were included from primgravida (PG) to para 4. Patients were excluded from the study if they have any known risk factor for PPH (severe anemia, antepartum haemorrhage, polyhydramnios, multiple gestation or history of PPH). Patients having any medical disorder contraindicating the use of carbetocin (hepatic disease, renal disease, serious cardiovascular disorder, preeclampsia, eclampsia or epilepsy) were also excluded from the study. Patients meeting the above inclusion criteria were counseled about the study, and an oral informed consent was obtained.

Abdominal ultrasound was performed for all participants for confirmation of the fetal life, maturity (37), and for exclusion of multiple gestation, polyhydramnios, placenta previa or the presence of uterine fibroids.

The included subjects were randomly divided into two groups; Group I (Carbetocin group) included 60 women who received carbetocin and delivered by caesarean section, Group II (Oxytocin group) included 60 women who received oxytocin and delivered by caesarean section.

By the anaesthetists, after cord clamping, cases in the carbetocin group, were given 1 ml of carbetocin (Pabal, 1 ml ampoule – 100 g/ml, Ferring Pharmaceuticals, Kiel, Germany) containing

100 g of carbetocin/ml as a single direct slowly intravenous (IV) injection and cases in the oxytocin group were given, 10 international units (IU) of oxytocin (Syntocinon, Novartis Pharma AG, Basel, Switzerland) slowly direct intravenous (IV) injection.

Need to additional procedures such as modified B-lynch sutures or Bilateral Uterine Arteries Ligation were done, in cases progressed to PPH, due to uterine atony inspite of giving the uterotonics carbetocin or oxytocin. These additional procedures were recorded in both groups.

Maternal blood pressure was measured before CS and checked immediately after giving the uterotonic drug, then 30 minutes and 60 minutes later. Pulse was measured before CS and rechecked 60 minutes after the end of CS. Blood was sampled for haemoglobin and platelet count before CS and then rechecked 24 hours after CS. For the safety of both drugs used on liver and kidney functions, blood was withdrawn for AST, ALT and creatinine 24 hours after the end of CS.

Statistical analysis was performed using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to describe variables; percent, proportion for qualitative variables. Mean, SD, range for Quantitative variables. Comparison between groups was done using Chi-Square test for qualitative variables, independent t – test for quantitative variables p values with significance of less than 0.05% were considered statistically significant.

RESULTS

Table (1): Shows that, there were no statistically significant difference between the two groups for all demographic variables.

Variable	Drug		Mean $\pm$ (SD) (no) or (%)	P value
Age (years)	Carbetocin		30.68 $\pm$ (8.41)	0.965
	Oxytocin		30.78 $\pm$ (8.46)	
Parity	Carbetocin	Nulliparous	29 (48.3 %)	0.714
		Multiparous	31 (51.7 %)	
	Oxytocin	Nulliparous	27 (45.0 %)	
		Multiparous	33 (55.0 %)	
BMI (kg/m ²)	Carbetocin		20.997 $\pm$ (4.791)	0.933
	Oxytocin		21.280 $\pm$ (4.876)	
Gestational age (weeks)	Carbetocin		38.29 $\pm$ (0.92)	0.877
	Oxytocin		38.31 $\pm$ (0.93)	
Birth weight (grams)	Carbetocin		2959.83 $\pm$ (387.71)	0.981
	Oxytocin		2963.67 $\pm$ (339.53)	

Table (2): Shows that, there was a statistically significant difference between the two groups for the prevention of postpartum haemorrhage (p < 0.01) for carbetocin group.

Variable	Drug	(no) or (%)	P value
Postpartum hemorrhage	Carbetocin	3 (5 %)	0.01
	Oxytocin	12 (20 %)	

In table (3) there was a statistically significant difference between the two groups according to success rate, need to modified B – lynch sutures or need to bilateral uterine arteries ligation ($p < 0.01$) for carbetocin group.

Table (3): Final outcome for the two groups.

Variable	Drug	(no) or (%)	P value
Success rate	Carbetocin	57 (95 %)	0.01
	Oxytocin	48 (80 %)	
Failure rate	Carbetocin	3 (5 %)	0.01
	Oxytocin	12 (20 %)	
Need to modified B-lynch sutures	Carbetocin	2 (3.3 %)	0.01
	Oxytocin	8 (13.3 %)	
Need to Bilateral Uterine Arteries ligation	Carbetocin	1 (1.6 %)	0.01
	Oxytocin	4 (6.6 %)	

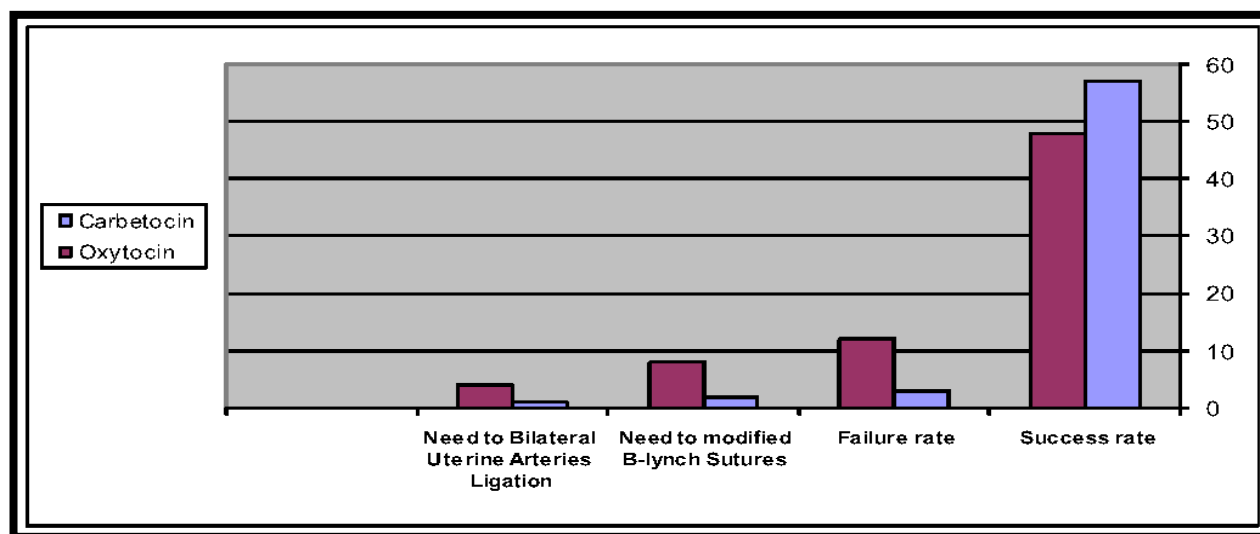


Fig. (1) : Final outcome for the two groups

DISCUSSION

The third stage of labor is defined as the time between delivery of the baby and delivery of the placenta. It is potentially the most dangerous part for the mother. The main risk is the occurrence of postpartum hemorrhage⁽⁸⁾. Around the world, one maternal death every 4 minutes occurs as result of PPH which considers a potentially life – threatening complication and is one of the major contributors to maternal mortality and morbidity.

Active management of the third stage of labor has three components; use of an uterotonic agent, early cord clamping and controlled cord traction. Use of a uterotonic agent is the key for prevention of PPH⁽⁹⁾. Several studies have shown that the use of uterotonic agents can reduce the incidence of PPH up to 30% - 40% and use of these drugs for PPH prevention is approved by all researchers⁽¹⁰⁾.

The study aimed at evaluation of effect of carbetocin in preventing PPH compared with oxytocin in elective caesarean section.

Our study showed that, there was a statistically significant difference for success rate the in the prevention of atonic PPH between the two drugs ($p < 0.01$) for carbetocin group. There was also a statistically significant difference between the two groups according to need to additional procedures such as need to modified B-Lynch sutures or need to Bilateral Uterine Arteries Ligation, for carbetocin group.

Dansereau et al., compared the effectiveness of 100 mcg of IV carbetocin with continuous infusion of oxytocin for 8 hours (25 IU of oxytocin in 1000 mL of Ringer's lactate, 125 mL per hour) among women undergoing elective caesarean section. Carbetocin group had benefit of decreased need for therapeutic oxytocics (4.7% vs. 10.1%; $p < 0.05$)⁽¹¹⁾.

Boucher et al., compared the effectiveness of 100 mcg of intramuscular carbetocin to 2h of 10 I.U of intravenous oxytocin infusion administrated immediately after placental delivery among women with high risk pregnancies after vaginal delivery. The authors reported that the carbetocin need significantly less uterine massage than oxytocin (43.4% versus 62.3%; $P = 0.02$), with no significant difference between the agents regarding the need for additional uterotonic drugs, the amount of bleeding, the prevention of PPH and the haemoglobin difference before and after delivery⁽¹²⁾.

Attilakos et al., compared carbetocin 100 mcg or oxytocin 5 IU administrated intravenously after the delivery of the baby in women undergoing caesarean sections. The carbetocin group needed significantly less additional uterotonics (33.5% versus 45.5%). On the other hand, they found no significant difference in the blood loss, PPH and fall in haemoglobin⁽¹³⁾.

Larciprete et al., compared the effectiveness of 100 mcg IV carbetocin to 20 IU of oxytocin in 1000ml of 0.9% NaCL solution IV (150 mL/hour) administrated to women with high risk pregnancies undergoing caesarean sections. More women needed additional uterotonic agents in the oxytocin group (23.5% versus 0%, $P < 0.01$), though there was no significant difference in estimated blood loss and in the drop of haemoglobin level⁽¹⁴⁾.

Maged et al., compared carbetocin 100mcg or oxytocin 5 IU administrated intramuscularly after the delivery of the baby in women with at least 2 risk factors for PPH undergoing vaginal delivery. The authors found that the carbetocin was superior to oxytocin regarding postpartum blood loss (337.73 ± 118.77 versus 378 ± 143.2), occurrence of PPH (4% versus 16%), need for additional uterotonics (23% versus 37%) and the change in haemoglobin level (0.55 ± 0.35 versus 0.96 ± 0.62). There was no significant difference between the two groups regarding occurrence of major PPH. Regarding drugs side effects, the incidence of tachycardia was significantly higher in the carbetocin group⁽¹⁵⁾.

Amornpetchakul et al., compared carbetocin 100 mcg to oxytocin 5 IU administrated intravenously after the placental delivery in women with high risk pregnancies undergoing vaginal delivery. The carbetocin group had less postpartum blood loss (146.7 ± 90.4 vs. 195.1 ± 146.2 mL; $P < 0.01$), a lower incidence of atonic PPH (0 % vs. 6.3%; $P < 0.01$), less usage of additional uterotonic drugs

(9.1% vs. 27.6%; $P < 0.01$), and a lower incidence of postpartum anaemia than the oxytocin group. No significant differences regarding the side effects⁽¹⁶⁾.

Reyes and Gonzalez, performed a prospective study in women with severe preeclampsia who were randomized to receive either oxytocin or carbetocin during the third stage of labor. They found that carbetocin was as effective as oxytocin in the prevention of PPH. Carbetocin had a safety profile similar to that of oxytocin, and it was not associated with the developement of oliguria or hypertension. They concluded that carbetocin is a appropriate alternative to oxytocin for the prevention of PPH in women with severe preeclampsia⁽¹⁷⁾.

Samimi et al., study carried out on pregnant women received intramuscular syntometrine (containing 5 I.U of oxytocin and 0.2 mg ergometrine) or intramuscular carbetocin after placental delivery. The mean fall in haemoglobin level in the carbetocin group was significantly lower than the syntometrine group (0.41 ± 0.36 versus 1.04 ± 0.78 , $P < 0.001$). The carbetocin group needed significantly less additional uterotonic (1% versus 11%, $P = 0.002$). Moreover systolic blood pressure and uterine tone immediately and 30 minutes after drug administration were significantly different. Incidence of tachycardia is higher in the carbetocin group⁽¹⁸⁾.

CONCLUSION

From our study, there is a good over all agreement that carbetocin appears to be more effective than oxytocin in prevention of uterine atony during elective caesarean section.

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