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COMPARATIVE STUDY BETWEEN CARBETOCIN VS COMBINATION OF ERGOMETRINE AND OXYTOCIN IN THE PREVENTION OF POST-PARTUM HEMORRHAGE AFTER CESAREAN SECTION

Mohamed Algharib
Obstetrics and gynecology Alazh er university, amedawad72@yahoo.com

ISMAIL EL GARHEY
Obstetrics and Gynecology Department, Faculty of Medicine, Al-Azhar University, Egypt, ismailtalatelgarhey@gmail.com

ADEL ELBOGHDADY
Obstetrics and Gynecology Department, Faculty of Medicine, Al-Azhar University, Egypt, adelalyelboghdady@yahoo.com

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Comparative Study Between Carbetocin Vs Combination Of Ergometrine And Oxytocin In The Prevention Of Post-Partum Hemorrhage After Cesarean Section

Obstetrics and Gynecology

Mohamed Awad Almetwally Algharib[1,*] M.B.B.CH, Ismail Talat El Garhey[1] MD, Adel Aly Elboghdady[1] MD

Corresponding Author:

Mohamed Awad Almetwally Algharib
amedawad72@yahoo.com

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[1]*Obstetrics and Gynecology Department, Faculty of Medicine, Al-Azhar University Cairo, Egypt.*

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ABSTRACT

Background: Caesarean section is a known risk factor for Postpartum hemorrhage5, and the rate of caesarean births is on the rise around the world. The cesarean section is a bloody process; most surgeries lose between 750 and 1000 mL of blood and a postpartum hemorrhage (PPH) occurs when more than 1000 mL of blood is lost.

Aim of the work: there is difference between carbetocin vs combination of ergometrine and oxytocin in the prophylaxis of (PPH) following cesarean section.

Patients and methods: The study had been conducted at Obstetrics and Gynacology department, El-Hussein universal hospital included 200pregnant women All cases were selected from Obstatric and Gynacology department , El-Hussein universal hospital from January 2021 - June 2021.

Results: Estimated blood loss in Group (A) was ranged between 532-821 with mean ±S.D. 688.98±58.363 while in Group (B) was ranged between 834-1301 with mean ±S.D. 1026.97±65.379. P<0.001 indicated statistically significant differences across groups. The requirement for additional uterotonics in Group (A) is 4 (4.0 %), while in Group (B), the requirement is 67 (67.0 %). P<0.001 indicated statistically significant differences across groups.

Conclusion: Carbetocin has been shown to be effective in preventing atonic post-partum haemorrhage after cesarean section. It has the same potency as I.V. syntocinon and ergometrine combined. In comparison to the mixture of syntocinon and ergometrine, carbetocin alone had fewer maternal side effects such as increased blood pressure, nausea and vomiting. The carbetocin group uses less extra uterotonic medications than the syntocinon and ergometrine group. Compared to syntocinon and ergometrine, carbetocin causes less blood loss. It's also linked to smaller reductions in hemoglobin levels after surgery.

Keywords: *Caesarean; carbetocin; ergometrine; oxytocin; postpartum hemorrhage*.

INTRODUCTION

Excessive bleeding at or after delivery, known as postpartum hemorrhage (PPH), is a potentially life-threatening condition that is one of the leading causes of maternal morbidity and mortality globally [1]. Due to irreversible shock, maternal mortality happens often in a short time period [2]. Anemia, tiredness, and depression are among the maternal morbidity effects [3].

Despite significant improvements in treatment in recent years, it is now recognized to account for about half of all postpartum maternal deaths in low- and middle-income nations. As a result, preventing PPH is critical in the quest for better women's health care [4]

With an estimated death rate of 140 000 annually, or one mother death each four minutes, PPH is the greatest reason of maternal mortality globally. PPH happens in 5% of all deliveries and accounts for a significant portion of maternal deaths [5]. The most of such fatalities happen within four hours of birth, implying that they are caused by the third stage of labor. [6]

PPH has been defined as a loss of blood of 500 ml or more in the 3rd stage of labor, while severe PPH has been defined as a loss of blood of 1000 ml or more. It has been demonstrated that active therapy of the 3rd stage of labor is effective in preventing PPH [7]. Using a uterotonic drug, early cord clamping, and controlled cord traction are three components of active treatment of the 3rd stage of labor. Currently, oxytocin and ergometrine are the most often used pharmacologic drugs. When oxytocin alone is compared to syntometrine (a combination of oxytocin and ergometrine), there is a statistically significant decrease in the risk of PPH for loss of blood greater than 500 ml but less than 1000 ml [8].

Nevertheless, the unpleasant negative impacts of nausea, vomiting, and raised blood pressure in

previously normotensive ladies were well reported as being significantly higher in syntometrine recipients [8]. In the 3rd stage of labor, prophylactic usage of ergot alkaloids reduces loss of blood and PPH [9].

PATIENTS AND METHODS

The study had been conducted at Obstetrics and Gynacology department, El-Hussein universal hospital included 200 pregnant women all cases were selected from Obstatric and Gynacology department , El-Hussein universal hospital from January 2021 - June 2021.

Inclusion criteria: More than 37 weeks gestation: the gestational age would be established depending on the starting day of the last normal menstrual cycle and verified via ultrasound scanning during the first trimester.

Exclusion criteria: Vaginal delivery, Ladies having cesarean section under general anaesthetic would be excluded because carbetocin is only licensed to be used with regional anaesthetic in Egypt, gestational age less than 37 weeks and exclusion of any risk factor for postpartum hemorrhage for examples: Placenta previa, pregnancy induced hypertension, marked anemia, multiple pregnancy and accidental hemorrhage

Operational design: Explanation of the procedure to all women participating in the study. Before starting the study, all patients were asked to sign a written consent form and were counseled on the risks and benefits of the study.

The ladies who took part in the study have been separated into two groups: Group (A): 100 women who received a carbetocin ampoule 100 µg I.V drip on 200 cc glucose after the fetal head was delivered. Group (B): 100 women who received a combination of intraoperative oxytocin 10 I.U. and ergometrine 0.2 mg after fetal head delivery.

Methods

The following procedures were carried out on the patients: Complete history taking: Personal history, including name, age, marital status, and address, as well as menstrual history: including age of Menarche, menstrual disturbance, dysmenorrhea, related symptoms, obstetric history including parity and mode of delivery, present history: of chronic diseases and medication, past history of HTN, DM, family history of similar condition or diabetes, history of allergy to any medication and surgical history of operation, laparoscopic interference, treatment of hirsutism by Laser.

Examination: General examination: Evaluation of vital signs and measurement weight, height (BMI). Abdominal and local clinical examination: to assess fundal level and gestational age, scar of previous operation, mass, tenderness or rigidity and any abdominal or pelvic clinically detectable pathology. Bimanual pelvic examination of both adenexa, and uterus for detection of any abnormality of female genitalia. Vaginal examination: Cervical assessment including cervical dilatation, consistency, effacement and position. Investigations: Laboratory investigations, Complete blood count, Rh typing, And coagulation profile: Prothrombin time, Partial Thromboplastin Time, INR, liver function testsand renal function tests. Ultrasound scan using trans abdominal ultrasound scan to: Confirm gestational age. Detect any risk factors for postpartum hemorrhage as placenta previa. In all cases, approved ethical committee taken, information sheet completed included Age, Parity, Gestational age at delivery, also the Blood pressure, Pulse, Temperature and Hemoglobin concentration hematocrite value noted before cesarean sections and 24 hours post-partum. The differences between pre- and post C.S values were calculated in each group. The uterine tone and size were determined by palpating the front wall of the uterus with a hand lying on the fundus. A boggy uterus combined with severe vaginal hemorrhage or an increase in uterine size may indicate uterine atony. Need for additional uterotonic drug in each group population were reported and tabulated. Incidence of postpartum hemorrhage was reported and tabulated

Study drug administration: The study drug (carbetocin or oxytocin) was delivered slowly (over 30– 60 secs) intravenously by the anesthetist after the infant was born during CS. It was demonstrated that slow delivery reduces the potentially deleterious hemodynamic impacts of oxytocin (and, likely, carbetocin) (Tektook et al., 2019 and Kwon et al., 2020). Additional oxytocics were administered at the surgeon's discretion.

Ethical Consideration: Informed verbal consent had been obtained from each participant sharing in the study.

Statistical analysis of the data: Data was uploaded into the computer and analyzed with the IBM SPSS software program version 20.0. (Armonk, NY: IBM Corp). Numbers and percent were used to describe qualitative data. To ensure that the distribution was normal, the Kolmogorov-Smirnov test was applied. Ranges (minimum and maximum), mean, and standard deviation were used to describe quantitative data. The significance of the obtained findings was determined at a 5% level of significance.

RESULTS

Age in Group (A) was ranged between 27-43 years with mean ± S.D. 34.85±5.034 years while in Group (B) was ranged between 26-41 years with mean ± S.D. 33.71±4.522 years. P=0.103 indicated no statistically significant differences across groups. Table (1)

Age	Group (A) (n=100)	Group (B) (n=100)	U	P Value
Min.-Max.	27-43	26-41	4335.00	0.103
Mean± S.D	34.85±5.034	33.71±4.522		

U: Mann-Whitney test
p: p value for comparing the two groups under study
*: Statistically significant at P <0.05

Table 1: Comparison of two groups with regard to patient age (years)

Gestational age in Group (A) was ranged between 37-40 weeks with mean ± S.D. 38.54±1.176 weeks while in Group (B) was ranged between 37-40 weeks with mean ± S.D. 38.59±1.111 weeks. Where P=0.754, there were no statistically significant differences across groups. Table (2)

Gestational Age	Group (A) (n=100)	Group (B) (n=100)	U	P Value
Min.-Max.	37-40	37-40	4876.00	0.754
Mean± S.D	38.54±1.176	38.59±1.111		

U: Mann-Whitney test
p: p value for comparing the two groups under study
*: Statistically significant at P <0.05
Table 2: Comparison of two groups with regard to patient gestational age (weeks)

Estimated blood loss in Group (A) was ranged between 532-821 with mean ± S.D. 688.98±58.363 while in Group (B) was ranged between 834-1301 with mean ± S.D. 1026.97±65.379. P<0.001 indicated statistically significant differences across groups. Table (3)

Estimated blood loss	Group (A) (n=100)	Group (B) (n=100)	U	P Value
Min.-Max.	532-821	834-1301	0.00	<0.001*
Mean± S.D	688.98±58.363	1026.97±65.379		

U: Mann-Whitney test
p: p value for comparing the two groups under study
*: Statistically significant at P <0.05
Table 3: Comparison of two groups with regard to patient estimated blood loss

Uterine tone in Group (A) show that 5(5.0%) had soft uterine tone and 95(95.0%) had firm uterine tone while in Group (B) 16(16.0%) had soft uterine tone and 84(84.0%) had firm uterine tone. P=0.019 indicated statistically significant differences across groups. Table (4)

Uterine tone	Group (A) (n=100)		Group (B) (n=100)		P Value
	No.	%	No.	%	
Soft	5	5.0	16	16.0	0.019*
Firm	95	95.0	84	84.0	
Total	100	100	100	100	

p: p value for comparing the two groups under study
*: Statistically significant at P <0.05
Table 4: Comparison of two groups with regard to patient uterine tone

Need for additional uterotonics in Group (A) show that 4(4.0%) need for additional uterotonics while in Group (B) 67(67.0%) need for additional uterotonics. P<0.001 indicated statistically significant differences across groups. Table (5)

Need for additional Uterotonics	Group (A) (n=100)		Group (B) (n=100)		P Value
	No.	%	No.	%	
No	96	96.0	33	33.0	<0.001*
Yes	4	4.0	67	67.0	
Total	100	100	100	100	

p: p value for comparing the two groups under study
*: Statistically significant at P <0.05
Table 5: Comparison of two groups with regard to patient need for additional uterotonics

Adverse effect in Group (A) show that 3(3.0%) had adverse effect while in Group (B) 5(5.0%) had adverse effect. There were no statistically significant differences between groups where P=0.721. Table (6)

Adverse effect	Group (A) (n=100)		Group (B) (n=100)		P Value
	No.	%	No.	%	
No	97	97.0	95	95.0	0.721
Yes	3	3.0	5	5.0	
Total	100	100	100	100	

p: p value for comparing the two groups under study
*: Statistically significant at P <0.05
Table 6: Comparison of two groups with regard to patient adverse effect

Complications in Group (A) show that 28(28.0%) had headache, 4(4.0%) had Nausea and vomiting, 1(1.0%) had sweating and 9(9.0%) had fever while in Group (B) 36(36.0%) had headache, 24(24.0%) had Nausea and vomiting and 28(28.0%) had sweating. In terms of nausea and vomiting, sweating, as well as fever, there was a statistically significant difference across groups. Table (7)

Complications	Group (A) (n=100)		Group (B) (n=100)		P Value
	No.	%	No.	%	
Headache	28	28.0	34	36.0	0.289
Nausea and vomiting	4	4.0	24	24.0	<0.001*
Sweating	1	1.0	28	28.0	<0.001*
Fever	9	9.0	0	0	0.003*

p: p value for comparing the two groups under study
*: Statistically significant at P <0.05
Table (7): Comparison of two groups with regard to patient complications

DISCUSSION

Primary postpartum hemorrhage (PPH) is defined by the World Health Organization (WHO) as a loss of blood of 1000 mL after a cesarean section (CS). It is responsible for one-quarter of the leading direct reasons of maternal fatalities worldwide, and approximately one-third of maternal deaths in Africa and Asia [10].

Those who had a CS had a higher risk of postpartum complications than ladies who had a vaginal delivery (VD) or vaginal birth after cesarean section (VBAC). One of the challenges being advanced to reduce the high number of cesarean section cases is (VBAC). CS has the highest prevalence of major surgical intervention in various portions of the world. Previous CS delivery is one of the most important factors of an increasing rate of a repeated CS [11].

In the present study, Age in Group (A) was ranged between 27-43 years with mean± S.D. 34.85±5.034 years while in Group (B) was ranged between 26-41 years with mean± S.D. 33.71±4.522 years. The differences between the groups were not statistically significant. Residence in Group (A) show that 61(61.0%) were from urban places and 39(39.0%) were from rural places while in Group (B) 53(53.0%) were from urban places and 47(47.0%) were from rural places. Where P=0.317, there were no statistically significant differences between groups.

In agreement with our findings, Zein El Abdeen et al., [12] studies were done on 200 pregnant ladies who had an elective caesarean section at a gestational age ≥ 37 weeks. Two groups of women were formed. Carbetocin was given intravenously to 100 women in Group A. Their mean age was (29.73±6.27) years, as well as 100 pregnant women (≥ 37 weeks) (group B) who received a mixture of intravenous oxytocin and intramuscular ergometrine. Their mean age, (29.57±6.19). There were no significant differences in age between the study groups.

In another study done by Maged et al., [10], The 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, Age in Group (A) was years with mean± S.D. 24.6 ± 5.2 years while in Group (B) was with mean± S.D. 26.4 ± 6.1 years. The differences between the groups were not statistically significant.

Abdrabo, [13] reported in his study that the average age (yrs) for the carbetocin group at 25.84±2.76 as well as for the oxytocin and ergometrine group at 27.02±3.38, while the average BMI for the carbetocin group at 27.58±3.04 and for the oxytocin and ergometrine group at 27.04±2.83, with no significant statistical differences between the two groups.

In the current study, we found that gestational age in Group (A) was ranged between 37-40 weeks with mean ± S.D. 38.54±1.176 weeks while in Group (B) was ranged between 37-40 weeks with mean ± S.D. 38.59±1.111 weeks. Where P=0.754, there were no statistically significant differences between groups.

This comes in comparison with the study of Amornpetchakul et al., [14] which reported that gestational age in Group (Oxytocin) was with mean ± S.D. 38.4±1.2 weeks while in Group (Carbetocin) was with mean ± S.D. 38.5±1.3 weeks. Between groups, there were no statistically significant differences.

In another study of Zein El Abdeen et al., [12] gestational age in Group (carbetocin) was with mean ± S.D. was (38.61±1.11weeks), and in (group B) who received a combination of intravenous oxytocin and intramuscular ergometrine; their mean ± S.D. of GA was (38.31±1.11weeks).

In the current research, we discovered that Estimated blood loss in Group (A) was ranged between 532-821 with mean ± S.D. 688.98±58.363 while in Group (B) was ranged between 834-1301 with mean ± S.D. 1026.97±65.379. P<0.001 indicated statistically significant differences between groups.

Similar to our results, the study of Zein El Abdeen et al., [12] reported that estimated blood loss in Carbetocin group was 448.50±85.11, while in Oxytocin+ Ergometrine group was 505.05±111.05, P<0.001 indicated statistically significant differences between groups. The average of HB 24 hours after operation in carbetocin group was (11.18±0.94); while in the other group, the mean was (10.98±0.91) with no significant association. In carbetocin group the mean regarding HB difference was (0.51±0.26) while in oxytocin group the mean was (0.54±0.30) with no significant association.

In contrast to our findings, the study of Maged et al., [10] reported that Mean blood loss intraoperative 578 ± 178 in group who received carbetocin, and mean blood loss was 602 ± 213 in oxytocin and methergine group, with no significant association between them.

Moreover, Boucher et al., [15] reported that Mean blood loss 413.3 ± 197.5 in group who received carbetocin, and mean blood loss was 410.4 ± 194.1 in oxytocin group, with also non-significant association between them.

Concerning pre- and post-operative HB, some authors found that the estimated blood loss in women who had cesarean deliveries was more in the oxytocin group. This agreed with our study. This group had a higher drop in HB. In contrary to our research, Attilakos et al., [16] in which HB difference between both groups showed no significant association. This difference from our study may be because all above authors used more patients making difference in sample size.

This is also in line with the findings of a prior research by Askar et al. [17] at Al-Azhar University Hospital, which comprised 240 healthy ladies with viable normal singleton pregnancies and normal vaginal birth at or after 37 weeks' gestation. Among the carbetocin and syntometrine groups, there were statistically significant differences in estimated mean loss of blood, with the syntometrine group losing 81.5 ml more. The average decline in hemoglobin concentration was 0.8 g/dl in the carbetocin group and 1.1 g/dl in the syntometrine group 24 hours

following birth, with the difference statistically significant.

In addition to above findings, the present study, we found that uterine tone in Group (A) showed that 5(5.0%) had soft uterine tone and 95(95.0%) had firm uterine tone while in Group (B) 16 (16.0%) had soft uterine tone and 84(84.0%) had firm uterine tone. P=0.019 indicated statistically significant differences between groups.

In a harmony with our results, the study of Zein El Abdeen et al., [12] which reported that uterine atony occurred more in women in the group who received oxytocin with ergometrine (39%) in comparison to carbetocin group (21%). It was obvious that oxytocin group needed more oxytocics than carbetocin group. In terms of uterine atony, there was a significant association between the two groups with a P value of 0.005.

On the other hand, in terms of the demand for additional uterotonics, Group (cabergolin) has a 4(4.0%) need, but Group (B) has a 67(67.0%) need. P<0.001 indicated statistically significant differences between groups.

As per Attilakos et al., [18] 377 ladies who had cesarean sections have been randomly assigned to receive either intravenous carbetocin 100 µg or intravenous oxytocin 5 IU following the baby was delivered. The carbetocin group required fewer uterotonic drugs that are consistent with our results.

Our findings were consistent with those of Samimi and Abedzadeh-Kalahroudi [19,] who randomly assigned 200 ladies having vaginal birth to take carbetocin or syntometrine to avoid PPH. They discovered that the carbetocin group had a lesser need for extra uterotonics. Carbetocin is more efficient than syntometrine in preventing PPH, according to the researchers.

Our findings are likewise consistent with those of Maged et al., [10] who randomly assigned 100 ladies who delivered vaginally and had at least two risk factors for atonic PPH to receive either 100 µg intravenous carbetocin or 5 IU intramuscular oxytocin. They discovered that in the carbetocin group, hemorrhage, PPH, and the requirement for further uterotonics were all much lower.

Abdrabo, [13] reported that seven instances (14%) in the carbetocin group require extra uterotonic, whereas twenty one instances (42%) in the oxytocin and ergometrine group require extra uterotonic. As a result, the oxytocin and ergometrine group required significantly more uterotonics.

Su et al., [20] included four studies with a total of 1037 ladies in their meta-analysis (one study on VD and three studies on CS). In both CS and VDs, carbetocin is linked to a lower demand for uterine massage (RR 0.38, 95% CI 0.18–0.80; RR 0.70, 95% CI 0.51–0.94), respectively.

In the study on our hands, we found that as regard adverse effect in Group (A) showed that 3(3.0%) had adverse effect while in Group (B) 5(5.0%) had adverse effect. No statistically significant differences between groups were found at P=0.721.

In agreement with our findings, the study of Maged et al., [10] reported no significant difference in the incidence of nausea, vomiting, and shivering between the two study groups. Metallic taste, flush, headaches, dizzy, breathlessness, and itch were more common in the carbetocin group than in the oxytocin methergine group, whereas palpitations were more common in the oxytocin methergine group than in the carbetocin group.

In a study comparing the efficiency of intravenous carbetocin against intravenous oxytocin for the avoidance of atonic postpartum hemorrhage (PPH), Amornpetchakul et al., [14] found no significant difference in side effects between the two groups. There were no patients in either group who had a severe bleeding (EBL >1000 mL), had a transfusions, or had peripartum hysterectomy

In the current study, we demonstrated that as regard complications; in Group (A) 28(28.0%) had headache, 4(4.0%) had Nausea and vomiting, 1(1.0%) had sweating and 9(9.0%) had fever while in Group (B) 36(36.0%) had headache, 24(24.0%) had Nausea and vomiting and 28(28.0%) had sweating. In terms of vomiting and nausea, sweating, and fever, statistically significant differences existed across groups.

On the other hand, Abdrabo, [13] reported that in terms of complications, 4 patients in the carbetocin group had primary PPH, 3 of whom were transfused with blood, whereas 5 patients in the oxytocin and ergometrine groups had primary PPH, 4 of whom were transfused with blood, and one patient had a hysterectomy for intractable postpartum hemorrhage. These results were statistically non-significant.

CONCLUSION

Carbetocin has been shown to be effective in preventing atonic post-partum haemorrhage after cesarean section. It has the same potency as I.V. syntocinon and ergometrine combined. In comparison to the mixture of syntocinon and ergometrine, carbetocin alone had fewer maternal side effects such as increased blood pressure, nausea and vomiting. The carbetocin group uses less extra uterotonic medications than the syntocinon and ergometrine group. Compared to syntocinon and ergometrine, carbetocin causes less blood loss. It's also linked to smaller reductions in hemoglobin levels after surgery.

REFERENCES

1. Shennan AH, Green M, Chappell LC. Maternal deaths in the UK: pre-eclampsia deaths are avoidable. *The Lancet*. 2017; 389(10069):582-4.
2. Metwally AM, Abdel-Latif GA, Mohsen A, El Etreby L, Elmosalami DM, Saleh RM, et al. Strengths of community and health facilities-based interventions in improving women and adolescents' care seeking behaviors as approaches for reducing maternal mortality and improving birth outcome among low income communities of Egypt. *BMC Health Services Research*. 2020; 20(1):1-4.

3. Zhu C, Estrada M, White J, Lal M. Heat-stable sublingual oxytocin tablets as a potential needle-free approach for preventing postpartum hemorrhage in low-resource settings. *Drug delivery and translational research.* 2018; 8(3):853-6.

4. Oyeneyin L, van den Akker T, Durojaiye O, Obaado O, Akanbiemu F, Olagbuji Y, et al. Confidential enquiries into maternal deaths in Ondo State, Nigeria–a comparative analysis. *BMC Pregnancy and Childbirth*. 2019; 19(1):514.

5. Butwick A, Lyell D, Goodnough L. How do I manage severe postpartum hemorrhage? *Transfusion*. 2020; 60(5):897-907.

6. Andrikopoulou M and D'Alton ME. Postpartum hemorrhage: early identification challenges. *InSeminars in perinatology* 2019; 43(1): 11-7.

7. Begley, C. M., Gyte, G. M., Devane, D., McGuire, W., Weeks, A., & Biesty, L. M. Active versus expectant management for women in the third stage of labour. *Cochrane database of systematic reviews*. 2019; (2).

8. Adnan N, Conlan-Trant R, McCormick C, Boland F, Murphy DJ. Intramuscular versus intravenous oxytocin to prevent postpartum haemorrhage at vaginal delivery: randomised controlled trial. *bmj*. 2018; 362.

9. Liabsuetrakul T, Choobun T, Peeyananjarassri K, Islam QM. Prophylactic use of ergot alkaloids in the third stage of labour. *Cochrane Database of Systematic Reviews*. 2018; (6).

10. Maged M, Ahmed R, Ahmed E, Noura A, Walaa D, Sherif; K. Carbetocin versus syntometrine for prevention of postpartum hemorrhage after cesarean section. *The Journal of Maternal-Fetal & Neonatal Medicine*. 2016; 1–5. doi:10.1080/14767058.2016.1192601.

11. Bangal VB, Giri PA, Shinde KK, Gavhane SP. Vaginal birth after cesarean section. *North Am J Med Sci*. 2013; 5:140. https://doi.org/10.4103/1947-2714.107537.

12. Zein El Abdeen, E. Carbetocin versus oxytocin and ergometrine for prevention of postpartum hemorrhage following caesarean section. *Evidence Based Women's Health Journal*. 2018; 8(1), 138-43.

13. Abdrabo HA, Comparative Study between Carbetocin versus Oxytocin and Ergometrinein Prevention of Post-Partum Haemorrhage, *Nature and Science* 2016;14(5) http://www.sciencepub.net/nature.

14. Amornpetchakul P, Tripop L, Dittakarn B, Jarunee L, Ratree S, Ratchada J. Intravenous carbetocin versus intravenous oxytocin for preventing atonic postpartum hemorrhage after normal vaginal delivery in high‐risk singleton pregnancies: a triple‐blind randomized controlled trial, Springer-Verlag GmbH Germany, *part of Springer Nature*, 2018.

15. Boucher M, Carl A, Georges F, Tracy A., Ruth E. Comparison of Carbetocin and Oxytocin for the Prevention of Postpartum Hemorrhage Following Vaginal Delivery: A Double-Blind Randomized Trial. *Journal of Obstetrics and Gynaecology Canada*. 2004; 26(5), 481–488. doi:10.1016/S1701-2163(16)30659-4.

16. Attilakos G, Psaroudakis D, Ash J, Buchanan R, Winter C, Donald F, et al. Can a new oxytocin analogue reduce the need for additional oxytocics after caesarean section? The results of a double-blind randomized trial. Archives of Disease in Childhood. *Fetal and Neonatal Edition* 2008;93

17. Askar AA, Ismail MT, El-Ezz AA, Rabie NH. Carbetocin versus syntometrine in the management of third stage of labor following vaginal delivery. *Archives of Gynecology and Obstetrics*. 2011; 284(6):1359–65.

18. Attilakos G, Psaroudakis J, Ash R, Buchanan C, Winter F, Donald A. Carbetocin versus oxytocin for the prevention of postpartum haemorrhage following caesarean section: the results of a double-blind randomised trial. *BJOG*. 2010; 117:929–36.

19. Samimi MIA, Abedzadeh-Kalahroudi M. Carbetocin vs. syntometrine in prevention of postpartum hemorrhage: a double blind randomized control trial. *Iran Red Crescent Med J*. 2013; 15:817–22.

20. Su, L. L., Chong, Y. S., & Samuel, M. Oxytocin agonists for preventing postpartum haemorrhage. *Cochrane database of systematic reviews*. 2007; (3).