MEDICINE UPDATES JOURNAL
Faculty of Medicine Port Said University
Volum: 15 No:4 PP:46 - 59

"Comparison between Intravenous Carbetocin and Rectal Misoprostol as prophylaxis for postpartum hemorrhage in lower segment caesarean section among low-risk patients"

Rasha Abdelaziz Mostafa El Mammoun 1 Walid Elsayed Elrefaie 2 Mohamed Hafez Younis 2 Ibrahim Arafa Reyad 2

1 Resident of obstetrics & gynecology Port Said obstetrics and gynecology hospital

2 Obstetric and gynecology faculty of medicine port said university

Submitted: 03/09/2023
Accepted:25/09/2023

DOI: 10.21608/MUJ.2023.233801.1146

ISSN : 2682-2741

https://muj.journals.ekb.egdean@med.psu.edu.eg
vice_dean_postgraduate@med.psu.edu.eg

ABSTRACT:

Background: Post-partum hemorrhage (PPH)is a noteworthy reason for maternal death in underdeveloped countries, virtually all fatalities coming about (PPH) happen within the initial 24 hours after birth. Most of these could be avoided by using prophylactic uterotonics during the third phase of parturition, by ideal, fitting administration.

Aim: To realize which medication is more valuable as prophylaxis of P.P.H Carbetocin or misoprostol in elective lower segment caesarean segment.

Materials and Methods: This randomized controlled study comprised eligible 100 low-risk patients and 50 women who received 1 ampoule of carbetocin diluted with 100 ml distilled water and received IV after delivery of the baby (group A). The patient in the(group B) received two tablets of misoprostol rectally after insertion of the urinary catheter directly before sterilizing the patient during lower segment CS.

Result: There was a significant difference in atony of the uterus during surgery in patients who received rectal misoprostol than in patients who received IV carbetocin {15 (30%) versus 5 (10%) P-value 0.012}, respectively. and the necessity for transfused blood {23 (46%) versus 9 (18) P-value 0.003 necessity for another uterotonic medication was statistically significantly higher in misoprostol group {32 (64%) vs 15 (30%) P-value 0.001}, different on Hb and HcT measure after born higher in misoprostol group with high statistic significant {9.08 ± 0.72 vs 10.01 ± 0.75, P-value: <0.0001} {29.26 ± 2.13 vs 32.56 ± 2.33, P-value <0.001}.

Conclusion: IV of 100 ug carbetocin minimized bleeding during CS more than 400 ug misoprostol per rectum.

Key Words: Carbetocin, CS, oxytocin, PPH, misoprostol.

Introduction:

One of the most common women's procedures is caesarean sections, which are becoming more common globally [(1)]. Postpartum hemorrhage (PPH) after a CS is a crucial issue and a critical factor in mother death.[(2)] PPH is described by the WHO as lost blood of at least 500 mL in twenty-four hours[(3)]. Minimizing surgical blood loss during CS benefits patients by lowering postsurgical death and reducing susceptibility to blood transfusion-related problems. It was noticed that AMTSL, as opposed to expectant management, is preferable during delivery, the atonic uterus is the master source of hemorrhage during delivery [(4)]. Controlled cord traction of placenta delivery during caesarean section, as well as intramuscular or intravenous syntocinon administration, are active third-stage labor management techniques [(5)(6)].

Syntocinon can be replaced by other uterotonic medications like Misoprostol, a(PGE1) analogue with strong uterotonic activity, low price, stable in room temperature, and minimal side effects. There are numerous ways to administer it, including orally, vaginally, sublingually, rectally, or buccally [(7)(8)].

An industrial counterpart of human syntocinon, carbetocin has modifications of its components that lengthen its half-life and effects [(9)]. infusion of carbetocin intravenously caused regular contraction of the uterus lasting 60 min, IM injection considerably extends its duration of action to 120 minutes [(10)].

Patient and method:

This open-label, randomized trial was approved by Research Ethic Committee of Port-Said Faculty of Medicine in 18/1/2022 and carried out at the Obstetrics & Gynecology special hospital at Port Said during the period between July 2020 to July 2021 and included 100 pregnant ladies admitted for lower segment caesarian section and categorized as low risk for PPH. Following receiving the nod from the faculty's ethics committee, Port said University's College of Medicine. All patients are eligible to participate in this study after giving written informed consent regarding the nature and the aim of the study. Each patient had the right to withdraw from the study at any phase, without any adverse impact on her medical or ethical management.

All low-risk patients will be a random selection made from each of the two groupings.

The patients listed below were not included in the study.:

1. Who had experienced PPH in prior pregnancies
2. Uterine fibroids
3. Diseases (e.g., DM, coagulation disorders, anemia, heart affection, hepatic or kidney injury).

4. Patients had a history of antepartum bleeding.
5. Multi-fetal pregnancies.
6. Patient with polyhydramnios.
7. Patient taking anticoagulant drugs.

Each participant will be allocated into either two groups using simple random sample 1:1 randomization in which a computerized random sample is taken from the study population, each one receives a sealed envelope containing digitally produced numbers then the patient picks one and these are provided to a patient by a nurse in the outpatient clinic or the delivery word.

All patients were delivered by CS with spinal anesthesia, group A ladies were given one ampoule of carbetocin IV diluted in 10 ml of distilled water after baby birth, while patients of group B were given 400 mg misoprostol rectally after insertion of urinary catheter, The study's outcome variables included the necessity for blood transfusions, the length of the procedure, any operational problems (such as uterine atony), a hemoglobin level deficiency and hospital stay.

Statistical analysis:

Quantitative results are expressed as numbers and percentages. The qualitative result was presented as mean and standard deviation (mean ± SD), The Chi-Square-test (X2) was used to compare qualitative data, and the Student's "t" test was used to compare quantitative data of two independent samples of normal released data, the Mann Whitney test used to compare quantitative data of two independent samples of non-normal released data, and the ANOVA test was used to compare quantitative data of more than two independent samples. Using the "Pearson correlation" correlation coefficient, the link between the variables was studied.

The coefficient interval was set to 95%. The level of significance is calculated according to the following probability (P) values:

- $P<0.05$ was considered statistically significant.
- $P<0.001$ was highly significant.
- $P>0.05$ was considered non-significant.

Results:

100 women who underwent CS were incorporated into the research. In which 50 women were included in group A and given carbetocin 100 milligram IV during operative soon after fetus extraction and 50 ladies were included in group B and given misoprostol 400 ug per rectum soon before sterilizing lady during CS, no statistically significant difference between patients receiving IV carbetocin and patients receiving rectal misoprostol as regards the age, parity, BMI and gestational age. The demographic characteristics of both groups are presented (age, parity, and gravidity).

uterine atony through surgery was significantly high in misoprostol group 5 (10%) versus 15 (30%) in carbetocin IV with P-value 0.012 required for blood transfusion was significantly higher in misoprostol group 9 (18%) versus 23 (46%) in carbetocin with P-value 0.003 as presented in table(I).

Extra uterotonic medications needed to be taken were significantly higher in misoprostol group 15 (30%) versus 32 (64%) in carbetocin with a P-value 0.001 as presented in Table (II).

A statistically significant decline in post-operative hemoglobin was recorded. and also, post-operative statistically significantly higher Hematocrit dropped by more than 10% in patients receiving rectal misoprostol compared to those receiving IV carbetocin, with mean and standard deviation values of 10.01 and 32.56, and P-values of 0.0001 and 0.0001, sequentially, as shown in Table(III).

As apparent in Table(IV), a statistically significant increase in the operative and post-operative blood loss in patients who received rectal misoprostol compared to patients who received IV carbetocin. The mean and standard deviation were respectively: 295.80 102.82 versus 390.40 138.50 and Mean SD: 457.50 114.50 versus 546.00 118.31 versus 0.0001.

As illustrated in Table(V), patients who received rectal misoprostol experienced statistically significantly further operation time and further hospital stays than those who received IV carbetocin. The mean and standard deviation were respectively 43.70 10.92 versus 48.30 11.68 and 1.48 0.71 versus 1.90 0.79 with P-value of 0.006 and 0.006 sequencely**.**

There was statistically significant decrease in the post-operative systolic and diastolic blood pressure in patients received rectal misoprostol than patients received IV carbetocin{ Mean ± SD: 116.72 ± 4.57 versus 108.36 ± 6.89 with P-value: <0.0001 and Mean ± SD: 76.86 ± 6.32 versus 70.74 ± 8.02 with P-value: <0.0001}respectively as located in table(VI).

Concerning the prior to operation blood pressure, no statistical significant difference across patients who received IV carbetocin and patients who received rectal misoprostol (Mean SD: 118.72 4.57 versus 117.04 6.49 with P-value: 0.138 and Mean SD: 79.70 4.96 versus 78.82 4.47 with P-value: 0.367, respectively).

Concerning the prior to surgery hemoglobin and hematocrit, the no statistical significant difference across patients who received IV carbetocin and patients who received rectal misoprostol (Mean SD: 11.31 0.57 versus 11.23 0.52 with P-value: 0.464 and Mean SD: 35.56 2.33 versus 34.76 2.12 with P-value: 0.076, respectively).

Discussion:

With a vaginal or cesarean delivery, PPH is an obstetric emergency that may arise. It is an extremely prevalent cause of delivery-related complications, and shock, kidney injury, syndrome of acute respiratory distress, coagulopathy, and Sheehan syndrome can make it worsen. PPH is one of the main five factors that trigger maternal deaths, similarly in nations that are industrialized and developed Uterus atony is the primary reason for PPH **(Ahmed R. et al., 2020)[11].**

With the goal to trigger uterine contractions, lower blood loss, and avoid PPH, it is imperative to provide uterotonic drugs, Primary postpartum hemorrhage is outlined as blood loss across the initial 24 hours of delivery. Uterine atony, accounting for 70% of the reasons for 1ry PPH, arises when the uterus malfunctions to contract after giving birth to a fetus. **(RCOG, 2016)[12].**

Our research's primary objective is to evaluate the efficacy of rectal misoprostol and intravenous carbetocin in order to prevent postpartum hemorrhage throughout elective lower-segment caesarean sections (L.S.C.S.) in low-risk individuals.

This randomized control study was conducted on 100 ladies, all patients were delivered by CS with spinal anesthesia, The ladies in group A received one ampoule of carbetocin diluted with 10 mL of distilled water via intravenous after the baby's birth. Patients in group B took misoprostol two tablets retally after the insertion of a urinary catheter during a lower segment caesarean section. All patients were evaluated according to uterine atony, blood loss, blood transfusion, hospital stay, post-operative hemoglobin, and hematocrit level.

In our study, we compared the obstetric data of the analyzed groups and reported no statistically significant differences according to age, parity, BMI, or gestational age across patients who obtained IV carbetocin and patients who obtained rectal misoprostol.

Our study agreed with **Sameer Abd El-Wahab et al. (2020)[13]** Considering age and parity, no statistically significant difference between the assessed groups (P>0.05).

In this research, we show no statistically significant difference in preoperative blood pressure across patients taking IV carbetocin and patients taking rectal misoprostol.

Al Anwar et al. (2022)[14], who hoped to enhance the clinical outcomes of carbetocin contrary to oxytocin to minimize postpartum hemorrhage in patients with pre-eclampsia undergoing Caesarean Section (CS), agreed with the outcomes of the study, no statistically significant difference on presystolic and diastolic blood pressure through the tested groups (P>0.05).

Concerning preoperative hemoglobin and hematocrit, we notice no statistically significant difference in the results of our research amongst patients administering IV carbetocin and patients administering rectal misoprostol.

The study of **Elomda F et al. 2023**[15]**,** who compared the use of carbetocin infusion, rectal misoprostol, and intravenous oxytocin bolus and infusion for reducing blood loss after elective cesarean section, approved our research. Examining pre-operative Hb and hematocrit, no statistically significant difference between the two groups (P>0.05).

We show a statistically significant decrease in the postoperative systole and diastole blood pressure in patients who received rectal misoprostol than in patients who received iv carbetocin with mean 116.72 ± 4.57 & 108.36 ± 6.89 between group A & B respectively with p-value: < 0.0001 SBP and 76.86 ± 6.32 & 70.74 ± 8.02 between group A & B respectively, P-value < 0.0001 DBP.

Al Anwar et al. (2022)[14] discovered N0 statistically significant difference in post-surgical SBP and post-surgical t-DBP between the analyzed groups (P>0.05), which was contrary to the findings of our investigation.

As regards the comparison of post-operative Hb and hematocrit of the studied groups, we found that As regarding to comparison of post-operative Hb and hematocrit of the studied groups it was observed it was a significant decline in the postoperative HB and statistically significant post-operative hematocrit higher drop of>10% in patients who received rectal misoprostol compared to patients who received IV carbetocin with mean±sd for hemoglobin 10.01 ± 0.75 & 9.08 ± 0.72 between group A & B respectively, P-value <0.0001 and hematocrit with mean±sd 32.56 ± 2.33 & 29.26 ± 2.13 between group A &B respectively with P-value: <0.0001, and for hematocrit drop >10% 5 (10%) 5 patient in carbetocin group versus 21 (42%) 21 patient in misoprostol group, P-value <.0001.

Our research is on par with that **of Abd El Aziz et al., 2022**[16], who sought to investigate the success rate and security of misoprostol vs. carbetocin in cesarean sections: They assessed that among the three studied groups

of the study, hemoglobin and hematocrit levels 24 hours postoperatively revealed a reasonably moderate decrease. Thus, post-CS hemorrhagic anemia is avoided or reduced when carbetocin is introduced.

Our study experienced a statistically significant rise in during-surgery and following-surgery blood loss in patients who received rectal misoprostol compared to patients who received IV carbetocin, with during-surgery blood loss with mean±sd for intraoperative blood loss of about 295.80 ± 102.82 & 390.40 ± 138.50 between group A&B respectively & P-value: <0.0001 while post-surgery loss of blood mean±sd was 457.50 ± 114.50 % & 546.00 ± 118.31 respectively, with P-value <0.0001.

In accordance with **Ismail et al.'s 2019**[17] study, which compared the security and success of carbetocin as well as misoprostol to the avoidance of atonic PPH in high-risk ladies, it found a statistically significant difference in blood loss on groupings being evaluated (P-value = 0.004), with greater bleeding taking place in the misoprostol group.

Elgazayerli, W. S. (2019) [18] concurred with our study that rectal misoprostol seemed less efficient than carbetocin for dropping intraoperative and postoperative lost blood and atony of the uterus in patients undergoing caesarean deliveries**.**

In opposing **Zein El Abdeen's 2018** [19] research, their studies on 2014 prospective randomized observational study involved 200 pregnant ladies who experienced an elective cesarean section while under regional anesthetic. Considering vaginal bleeding, HB estimation before and after the procedure, or HB difference, no statistically significant correlation to either of the study groups.

In our research, we noticed that uterine atony developed more frequently in the misoprostol group. in 5(10%) patients in the carbetocin group versus 15 (30%) in the misoprostol group with P-value 0.012.

In accordance with **Ismail et al.'s 2019**[17] study results, there existed a statistically significant difference in analyzed groupings with respect to uterine tone (P= 0.016), with greater tone (cases not included in PPH) in the carbetocin group. mean uterine tone 44 (88%) in carbetocin versus 34 (68%) in the misoprostol group.

In the present research, we showed that the misoprostol group notably required blood transfusion as opposed to the carbetocin group, with 9 (18%) participants in the carbetocin group needing transfusion against 23 (46%) participants in the misoprostol group, with a P-value of 0.0003.

Our research matched the results of **Moustafa et al., 2020**[20], who tested the misoprostol efficacy against carbetocin in controlling PPH following CS in people with minimal risk. a statistically significant difference (P-

value = 0.018) in blood transfusion rates among the reviewed groups, the incidence of transfusions was greater in the misoprostol group.

In contrary to **Sameer Abd El-Wahab et al.'s** [21] study from 2020, which stated that actually no statistically significant difference across the groupings under examination with respect to blood transfusion (P-value = 0.245), our research shows a difference across the groups.

We notice a statistically significant greater chance for the need for another tonic (oxytocin) and in the evaluated ladies groups it was higher in the misoprostol group but The oxytocin dose did not vary statistically significantly between the two groups,

In conformity with **Ismail et al.'s 2019**[17] research, which demonstrated a statistically significant difference among the checked groupings in how much demand for uterotonics (P-value = 0.016), the need for uterotonics diminished in the carbetocin group.

As stated by **Moustafa et al. (2020)**[20], a statistically significant difference among checked groups with respect to the Oxytocin dose (P=0.001). Our investigation contradicted what they found.

The hospital stay appeared much lengthier in the misoprostol group comparison to the carbetocin group in our research with a mean of 1.80 ± 0.76 in the misoprostol group & 1.42 ± 0.64 in in carbetocin group respectively with P-value: 0.008 on our study.

Our study was consistent with **Sun et al., 2022**[22] who aimed to study the efficacy of carbetocin on blood loss during surgery and diameter of myometrium during CS with the uterus with previous scare at term pregnancy and difference in stay of hospital, as a statistic significance different on the studied groups on a hospital stay (P-value: = 0.006).

In contrast with **Abd El Aziz et al,2018**[16] who found that ladies who took carbetocin and ladies who took misoprostol did not have considerably different mean hospital stays (MD O.12, 95% CI O.O3 to O.27, 185 participants, study)[2O].

Conclusion:

In patients post caesarean deliveries who are at low risk for getting postpartum hemorrhage, carbetocin seemed to be a better option than misoprostol at sustaining sufficient uterine tone and minimizing excessive blood loss.

In further research, though, various administration methods and doses will be used and their effects will be assessed, a larger sample size would be needed. Therefore, carbetocin can be regarded as one of the uterotonic drugs that reduce PPH frequency and, therefore, maternal mortality in reproductive age.

Table (I):

Comparison of the study groups' uterine atony and blood transfusion requirements

		IV carbetocin	Rectal misoprostol	t/x^2	P-value	Sig.
		No.= 50	No.=50			
Uterine atony	No	45 (90%)	35 (70%)	6.250•	0.012	HS
	Yes	5 (10%)	15 (30%)			
blood transfusion	No	41 (82%)	27 (54%)	9.007*	0.003	HS
	Yes	9 (18%)	23 (46%)			

P-value > 0.05: Non-significant (NS); P-value < 0.05: Significant (S); P-value < 0.01: highly significant (HS) *Chi-square test

Table (II): difference in the dose and demand for tonics (oxytocin) in the groups under study

		IV carbetocin	Rectal misoprostol	t/x^2	P-value	Sig.
		No.= 50	No.=50			
Use of tonics (oxytocin)	No	35 (70%)	18 (36%)	11.602•	0.001	HS
	Yes	15 (30%)	32 (64%)			
Oxytocin dose (IU)	Range	10 - 20	10 - 30	-1.089•	0.282	NS
	Mean ± SD	32.56 ± 2.33	29.26 ± 2.13			

P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) • independent student t test, *Chi squaare test

Table (III): Comparison of post-operative Hb & hematocrit of the studied groups

		IV carbetocin	Rectal misoprostol	t/x^2	P-value	Sig.
		No.= 50	No.=50			
Post-operative Hb (gm/dl)	Range	8 - 12	7 - 10	6.238•	<0.0001	HS
	Mean ± SD	10.01 ± 0.75	9.08 ± 0.72			
Post-operative hematocrit	Range	26 - 36	25 - 35	6.587•	<0.0001	HS
	Mean ± SD	32.56 ± 2.33	29.26 ± 2.13			
Post-operative hematocrit drop >10%	No	45 (90%)	29 (58%)	13.306*	<0.0001	HS
	Yes	5 (10%)	21 (42%)			

p-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) • independent student t-test, *chi square test

Table (IV): Comparison of operative and post-operative blood loss in the studied groups

		IV carbetocin	Rectal misoprostol	t/x^2	P-value	Sig.
		No.= 50	No.=50			
Intra-operative blood loss (ml)	Range	100 - 510	200 - 580	-3.878•	<0.0001	HS
	Mean ± SD	295.80 ± 102.82	390.40 ± 138.50			
Post-operative blood loss (ml)	Range	270 - 665	365 - 850	-3.801•	<0.0001	HS
	Mean ± SD	457.50 ± 114.50	546.00 ± 118.31			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) • Mann whiney test

Table (V): Comparison of the time required for the operation and the extent of the hospital stay in the evaluated groups:

		IV carbetocin	Rectal misoprostol	t/x^2	P-value	Sig.
		No.= 50	No.=50			
Operative duration (min)	Range	25 - 70	30 - 70	-2.035•	0.045	S
	Mean ± SD	43.70 ± 10.92	48.30 ± 11.68			
Hospital stay (days)	Range	1 - 3	1 - 3	-2.804•	0.006	HS
	Mean ± SD	1.48 ± 0.71	1.90 ± 0.79			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) • independent student t test

Table (VI): Comparison of post-operative blood pressure amongst the groups pursuant to the study:

		IV carbetocin	Rectal misoprostol	t/x^2	P-value	Sig.
		No.= 50	No.=50			
Post-operative systolic blood pressure(mmHg)	Range	98 - 119	93 - 113	7.150•	<0.0001	HS
	Mean ± SD	116.72 ± 4.57	108.36 ± 6.89			
Post-operative diastolic blood pressure (mmHg)	Range	58 - 85	58 - 82	4.237•	<0.0001	HS
	Mean ± SD	76.86 ± 6.32	70.74 ± 8.02			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: high significanc (HS) • independent student t test

References:

1.Feduniw, S., Warzecha, D., Szymusik, I., & Wielgos, M. *Epidemiology, prevention and management of early postpartum hemorrhage - a systematic review. Ginekologia polska, (2020), 91(1), 38–44. https://doi.org/10.5603/GP.2020.0009.*

2. ***Butwick, A. J., Ramachandran, B., Hegde, P., Riley, E. T., El-Sayed, Y. Y., & Nelson, L. M.*** *Risk Factors for Severe Postpartum Hemorrhage After Cesarean Delivery: Case-Control Studies. Anesthesia and analgesia, (2017), 125(2), 523–532. https://doi.org/10.1213/ANE.0000000000001962.*

3. **WHO** Recommendations for the Prevention and Treatment of Postpartum Hemorrhage. *World Health Organization* (2012).

4. **Yefet, E., Yossef, A., Suleiman, A.** Hemoglobin drop following postpartum hemorrhage. Sci Rep (2020), 10, 21546.

5. ***Baird E. J.*** *Identification and Management of Obstetric Hemorrhage. Anesthesiology clinics, (2017). 35(1), 15–34.*

6. ***Gallos I., Williams H., Price M., Pickering K., Merriel A., Tobias A., Lissauer, D., et. al.*** *Uterotonic drugs to prevent postpartum haemorrhage: a network meta-analysis. Health technology assessment (Winchester, England), (2019), 23(9), 1–356.*

7. ***American College of Obstetricians and Gynecologists Committee on Obstetric Practice****Delayed umbilical cord clamping after birth: ACOG committee opinion number 814.*

8.American College of Obstetricians and Gynecologists *Practice bulletin no. 183: Postpartum hemorrhage.Obstetrics & Gynecology. 2017; 130: 168-186*

9.Attilakos G., Psaroudakis D., Ash J., Buchanan R., Winter C., Donald F., Hunt L., & Draycott T. Carbetocin versus oxytocin for the prevention of postpartum haemorrhage following caesarean section: the results of a double-blind randomised trial. *BJOG: an international journal of obstetrics and gynaecology, (2010), 117(8), 929–936.*

10. **Ali A., Nasr A., Ahmed H., Rasheedy M., & Badawy M.** Carbetocin versus Oxytocin and Misoprostol in prevention of atonic post-partum hemorrhage in high-risk patients planed for cesarean delivery. *Int J Reprod Contracept Obstet Gynecol. 2018 Jan;7(1):10-14.*

11. **Ahmed A., Saleh A., Abd Elhameid A., & Badr M.** Incidence and outcome of primary postpartum hemorrhage at Zagazig University Hospitals. *Zagazig University Medical Journal, (2020), 26(6), 970-980.*

12. **RCOG.** Prevention and management of postpartum haemorrhage. *Bjog, (2016), 124, e106-e149.*

13. **Sameer Abd El-Wahab A., Khalil Ahmed A., & Marai A.** The effect of Carbetocin compared to rectal misoprostol in the management of blood loss during the third stage of vaginal delivery in low risk patients for postpartum hemorrhage. *Al-Azhar Medical Journal, (2020), 49(4), 1673-1682.*

14. **Al Anwar A., Abdal Salam H., Esukni S., & Abdel Rahman M.** Carbetocin versus Oxytocin: A Comparative Study to Prevent Postpartum Hemorrhage in Pre-eclamptic Women Delivered by Caesarean Section. *The Egyptian Journal of Hospital Medicine, 89(1), 5063-5068. doi: 10.21608/ejhm.2022.261171.*

15. ***.Elomda F. A., Said A. M., & Sahloul W. H.*** *Comparison between oxytocin intravenous bolus, oxytocin intravenous bolus and infusion, rectal misoprostol and carbetocin infusion for the control of blood loss at elective cesarean section. Al-Azhar International Medical Journal, (2023) 4(2), 3.*

16. ***Abd El Aziz, M. A., Iraqi, A., Abedi, P., & Jahanfar, S.*** *The effect of carbetocin compared to misoprostol in management of the third stage of labor and prevention of postpartum hemorrhage: a systematic review. Systematic Reviews, (2018), 7, 1-8.*

17. **Ismail I., Fahmy M., & Farouk H.** Carbetocin versus misoprostol in prevention of postpartum hemorrhage in high-risk patients. *The Egyptian Journal of Hospital Medicine, (2019), 77(2), 4913-4919.*

18. Elgazayerli W. S. *Comparison between syntocinon, misoprostol and carbetocin in reducing blood loss in elective caesarean section. Journal of Evidence Based Women's Health, (2019), 9, 482-6.*

19. **.Zein El Abdeen E. & Shehata N.** Carbetocin versus oxytocin and ergometrine for prevention of postpartum hemorrhage following caesarean section. *Evidence Based Women's Health Journal, 8(1), 138-143. doi: 10.21608/ebwhj.2018.6218.*

20. ***A. Moustafa, S. Abd Elhady, H. Shalaby, & W. Elrefaie***. *Carbetocin versus Misoprostol in Reducing Blood Loss during Cesarean Section in low-risk patients. A Randomized Controlled Trial. Evidence Based Women's Health Journal, (2020), 10(3), 209-215.*

21. **.Sameer Abd El-Wahab A., Khalil Ahmed A., & Marai A.** The effect of Carbetocin compared to rectal misoprostol in the management of blood loss during the third stage of vaginal delivery in low risk patients for postpartum hemorrhage. *Al-Azhar Medical Journal, (2020), 49(4), 1673-1682.*

22. **Sun D.** Carbetocin Controls Intraoperative Blood Loss and Thickness of Myometrium in Scar Uterus Cases. *Evidence-based complementary and alternative medicine: eCAM, 2022, 5477432. https://doi.org/10.1155/2022/5477432 (Retraction published Evid Based Complement Alternat Med. 2023 Jun 21; 2023:9813924).*