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Original Research Article

Comparison between Haemodynamic Effects of Oxytocin and Carbetocin in Women Undergoing Elective LSCS under Spinal Anaesthesia

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Abstract:

Background: Postpartum hemorrhage, or excessive bleeding at or after childbirth, is a potentially life-threatening complication of both vaginal delivery and cesarean section, and it is one of the leading causes of maternal morbidity and mortality worldwide. The primary cause of this hemorrhage is uterine atony. Oxytocin has proved to be very effective in reducing PPH incidence, thus making it a routinely used uterotonic agent. However, many women experience nausea, vomiting, chest pain, and discomfort attributed to the dose-dependent effects of oxytocin. Many alternatives, such as prostaglandin analogs, have been tested in the past; however, none have surpassed the efficacy of oxytocin. Carbetocin is a longer-acting oxytocin analog that works along the same molecular pathways and has a longer half-life of around 40 min. Carbetocin's lack of relative gastrointestinal and cardiovascular side effects should make it a better alternative than oxytocin and other ergot alkaloids.

Aim and Objectives: The aim of this study is to compare the hemodynamic effects of carbitocin with oxytocin and evaluate the efficacy of carbitocin versus oxytocin in preventing PPH.

Material and Methods: This prospective randomized, double-blind study was conducted in a tertiary hospital associated with a medical college; 60 patients undergoing elective cesarean section under spinal anesthesia were randomly allocated to one of the two groups. Group I received 5 IU oxytocin in 10ml NS followed by 15 IU in 500ml NS infusion. Group II 100 mcg of Carbitocin in 10ml NS after delivery of right shoulder. Patients were assessed for SBP, DBP, heart rate, and SpO2 at 1,5,10 and 15 minutes, respectively. Total blood loss was evaluated at the end of surgery, and Hb was repeated after 24 hours to assess the effectiveness of the drugs in controlling PPH. Students' t-tests and chi-square tests were used per the requirement, and a P value of <0.05 was considered statistically significant.

Result: Out of 60 patients, 30 patients received oxytocin, and the remaining 30 received Carbitocin; Oxytocin group demonstrated significant tachycardia after 1 minute of drug administration compared to carbitocin Group, heart rate remained significantly higher in oxytocin group at 5,10 and 15 minutes compared to carbitocin Group, Both SBP & DBP remained significantly stable in Carbitocin group compared to oxytocin group at 1,5,10 & 15 minutes. The amount of blood loss and post-operative Haemoglobin Intraoperative SpO2 remained similar in both groups. Both groups were comparable in terms of side effect profile. The Carbitocin group was marginally better, showing a lesser incidence of Nausea, Vomiting & chest pain.

Conclusion: Our study's findings suggest that carbetocin is an equivalent drug to oxytocin in terms of uterotonic action and has a significantly better hemodynamic profile than oxytocin in patients undergoing LSCS under regional anesthesia.

Keywords: Postpartum Hemorrhage, Carbetocin, Oxytocin, Lower Segment Cesarean Section, Spinal Anesthesia.

Introduction

Postpartum hemorrhage, or excessive bleeding at or after childbirth, is a potentially life-threatening complication of both vaginal delivery and cesarean section, and it is one of the leading causes of maternal morbidity and mortality worldwide [1], with a prevalence of 6% of all deliveries [2]. PPH

is defined as blood loss of more than 1000 ml after cesarean section that occurs in the first 24 hours. [3] The effects on maternal morbidity include fatigue, Sheehan's syndrome, anemia, coagulopathy, and shock. [4,5]

The primary cause of this hemorrhage is uterine atony; therefore, active management of the third stage of labor (AMTSL) has become a recommended protocol. [6,7]

Among other uterotonic agents, oxytocin has proven to be very effective in reducing the incidence of PPH, making oxytocin a routinely used uterotonic agent during every cesarean section to aid in the contraction of the uterus and prevent blood loss. However, many women experience nausea, vomiting, chest pain, and discomfort attributed to the dose-dependent effects of oxytocin. [8]

Significant hemodynamic changes like tachycardia, increased stroke volume, cardiac output, decreased systemic vascular resistance and arterial blood pressure, and ST depression on ECG are also associated with oxytocin [9]. Many alternatives, such as prostaglandin analogs, have been tested in the past. However, another review concluded that intramuscular prostaglandins are not preferable to conventional injectable uterotonics as part of the active treatment of the third stage of labor. [10]

Carbetocin is a longer-acting oxytocin analog that works along the same molecular pathways as oxytocin but with a longer half-life of around 40 min. [11,12] A single IV dose of carbetocin 100 µg results in uterine contraction within 2 min, with a duration of around 60 min, compared with 16 min for oxytocin. [13,14] Although oxytocin is the most widely accepted uterotonic agent, a lot of data from the literature suggest that prophylactic administration of carbetocin can turn out to be a better alternative to oxytocin in the prevention of PPH; however, which uterotonic agent is ideal for prophylactic use is still debatable. [15]

Carbetocin's lack of relative gastrointestinal and cardiovascular side effects should confirm its recommendation to be used compared to Syntometrine and other ergot alkaloids. [14]

Keeping this background in mind, the aim of this study was to compare both drugs regarding effectiveness, safety, and hemodynamic effects in pregnant women during cesarean sections under spinal anesthesia.

Material and Methods

After obtaining Institutional Ethical Committee approval and informed consent from the patients, a prospective randomized, double-blind clinical study was conducted. Sixty consenting patients belonging to the American Society of Anaesthesiology (ASA) class I and II between the age group of 20-35 years planned for elective LSCS under spinal anesthesia were selected and included in the study. These patients were randomly divided into two groups consisting of 30 patients each.

Inclusion criteria: Consenting patients, ASA class I and class II patients, patients aged between 20 and 35, and patients undergoing surgeries requiring spinal anesthesia.

Exclusion criteria: Patient's refusal of regional anesthesia, patients who have arthritis or scoliosis or peripheral neuropathy, infection at injection sites, any contraindication to regional anesthesia, ASA class III and above, participants with a known history of allergy to any of the study drugs, anticipated difficult airway, cardiac disease, significant hepatic or renal insufficiency, patient diagnosed with diabetes, hyperthyroidism or hypothyroidism were not included in the study.

Group I (n=30) received 5 IU of oxytocin in 10 ml normal saline and 15 IU in 500 ml NS infusion.

Group II (n=30) received 100 mcg of carbitocin in 10 ml normal saline bolus.

Technique: On arrival in the operation theatre, the patient's body weight was recorded. All routine monitoring devices (NIBP, pulse oximeter, ECG) were attached. An 18G i/v cannula was inserted at the dorsum of the left hand and connected to a 500ml Ringer Lactate drip and preloaded with 500ml fluid and NIBP cuff on the right hand. Baseline readings of mean arterial blood pressure (MAP), heart rate (HR), and peripheral oxygen saturation (SPO2) were recorded; all the patients received 4mg of ondansetron before administering spinal anesthesia.

Under all aseptic precautions, a 25-gauge spinal needle (Quincke's type) was inserted at the lumbar at L2-L3 or L3-L4 inter-vertebral space, the free flow of clear CSF confirmed correct needle placement; after confirming the needle's location 2.5ml heavy 0.5% bupivacaine was administered intrathecally. Patients were assessed for onset and levels of sensory block & motor block. Surgery was started after achieving a T8 dermatomal level of sensory block. The sensory block level was assessed bilaterally using the pinprick method at the midclavicular line.

Vital parameters like systolic and diastolic blood pressure, heart rate, and oxygen saturation were recorded at 1, 5, 10, and 15 minutes after injecting the study drugs, and total blood loss during the surgery was assessed at the end of surgery.

All the patients were monitored for adverse effects like headache, nausea, bradycardia, vomiting, hypotension, and chest pain for the next hour.

Patients suffering from hypotension were treated with 6mg mephentermine bolus doses intravenously, and all episodes of bradycardia were treated with 0.3mg intravenous atropine sulfate.

Result

Demographics- Both the groups were demographically similar.

Table 1: Comparison of demographic profile between both groups.

Parameter	Oxytocin (n = 30)	Carbetocin (n = 30)	P-Value
Age(years)	26.43 ± 5.73	25.76 ± 5.33	0.640
Weight(kilograms)	69.73 ± 12.67	71.13 ± 12.23	0.664
Gestational Age (Weeks)	38.20 ± 1.11	38.33 ± 1.05	0.643
Systolic Blood Pressure	128.82 ± 15.11	129.93 ± 13.81	0.767
Diastolic Blood Pressure	80.97 ± 12.5	83.01 ± 12.13	0.523
Heart Rate	93.08 ± 10.27	91.11 ± 9.38	0.441
Oxygen Saturation	98.71 ± 1.02	98.77 ± 0.92	0.811
Postoperative Hb (g/dl)	8.91 ± 0.84	8.75 ± 0.73	0.434

Abbreviations: GA-gestational age; Hb-haemoglobin, P-Value <0.05 considered significant.

Table 2: Comparison of heart rate between both the groups at different time intervals

Heart Rate	Oxytocin (n = 30)	Carbetocin (n = 30)	P-Value
Pre-intervention	93.08 ± 10.27	91.11 ± 9.38	0.441
1 minute	110.62 ± 12.56	100.21 ± 10.32	0.009
5 minutes	97.33 ± 10.9	88.33 ± 9.38	0.001
10 minutes	86.15 ± 7.91	80.15 ± 6.71	0.002
15 minutes	78.42 ± 7.63	75.40 ± 6.67	0.108

A P-value <0.05 is considered significant.

Patients in the Oxytocin group experienced statistically significant tachycardia at 1,5,10, and 15-minute time intervals compared to the Carbitocin group.

Table 3: Comparison of systolic blood pressure between both the groups at different time intervals

SBP	Oxytocin (n = 30)	Carbetocin (n = 30)	P-Value
Pre-intervention	128.82 ± 15.11	129.93 ± 13.81	0.767
1 minute	102.85 ± 11.28	110.12 ± 11.73	0.015
5 minutes	107.53 ± 10.29	115.33 ± 10.54	0.005
10 minutes	112.90 ± 9.35	118.70 ± 10.62	0.028
15 minutes	116.33 ± 9.43	121.47 ± 10.21	0.047

p-Value <0.05 is considered significant.

Patients in the Oxytocin group experienced a statistically significant fall in systolic blood pressure at 1,5,10 and 15 minutes compared to the Carbitocin group.

Table 4: Comparison of diastolic blood pressure between both groups at different time intervals

DBP	Oxytocin (n = 30)	Carbetocin (n = 30)	P-Value
Pre-intervention	80.97 ± 12.5	83.01 ± 12.13	0.523
1 minute	64.85 ± 10.21	71.72 ± 8.04	0.005
5 minutes	68.42 ± 9.7	75.17 ± 8.74	0.006
10 minutes	71.7 ± 9.88	77.03 ± 8.92	0.032
15 minutes	77.03 ± 10.51	82.33 ± 9.54	0.045

p-Value <0.05 is considered significant.

Patients in the Oxytocin group experienced statistically significant falls in diastolic blood pressure at 1,5,10 and 15-minute time intervals compared to the Carbitocin group.

Table 5: Comparison of oxygen saturation between both the groups at different time intervals

O_2 saturation	Oxytocin (n = 30)	Carbetocin (n = 30)	P-Value
Pre-intervention	98.71 ± 1.02	98.77 ± 0.92	0.811
1 minute	98.32 ± 1.13	98.63 ± 0.93	0.250
5 minutes	98.43 ± 1.11	98.62 ± 0.96	0.709
10 minutes	98.56 ± 1.01	98.67 ± 1.21	0.703
15 minutes	98.75 ± 1.05	98.66 ± 0.1.3	0.769

p-Value <0.05 is considered significant.

Oxygen saturation remained comparable between both the groups at 1,5,10 and 15 minutes.

Table 6: Comparison of side effects and safety profile between both groups

Parameter	Oxytocin (n = 30)	Carbetocin (n = 30)	P-Value
Nausea & Vomiting	6(20%)	3(10%)	0.278
Chest Pain	5(16.6%)	2(6.6%)	0.227
Vasopressor Requirement	7(23.3%)	3(10%)	0.165
Uterotonic Supplementation	6(20%)	3(10%)	0.469
Blood Loss During Surgery(ml)	856.25 ± 93.32	849 ± 88.64	0.758

p-Value <0.05 is considered significant.

Patients belonging to the Oxytocin group experienced a higher incidence of nausea, vomiting, chest pain, vasopressor requirement, and additional uterotonic supplementation compared to patients in the carbetocin Group, but these differences were not statistically significant. The amount of blood loss remained comparable in both groups.

Discussion

This study was designed to compare oxytocin with carbetocin in terms of the hemodynamic effects of the drugs and their ability to prevent postpartum hemorrhage.

It is known that the hemodynamic effects of an oxytocin bolus include increased cardiac output and pressure of the pulmonary artery, hypotension, systemic vasodilation, and tachycardia, depending on the dose and rate of administration [16,17,18]. Such hemodynamic impact, especially on patients with cardiovascular diseases or hypovolaemia, could result in myocardial ischemia. [19]

A recent study by Moertl et al. shows that patients treated with oxytocin have more pronounced hypotension and hemodynamic rebound than patients treated with carbetocin, with comparable effects on the cardiovascular system. [20]

In addition, this study indicated that more patients needed additional doses of oxytocin in the oxytocin group (20%) compared to the carbetocin group (10%). Dansereau et al. reported similar findings with lower additional uterotonics doses for treating uterine atony in females taking carbetocin after delivery. [21]

The present study's findings of the safe hemodynamic effects with less need for more uterotonics and the previous findings that repeated oxytocin administration led to significant hemodynamic changes reinforce the notion that carbetocin might become the treatment of choice as a more effective uterotonic drug than oxytocin for preventing PPH in females with preeclampsia, hypertension, or cardiac problems. [15,20]

We found a lack of additional uterotonic need after CS in the carbetocin group (10%) compared to the oxytocin group (20%), and we did not demonstrate any difference in the amount of blood loss after cesarean section and in the drop of hemoglobin level after 24 hours of surgery. Previous studies have shown that carbetocin could induce maternal tachycardia, but it was significantly less than oxytocin at 1,5,10 and 15-minute intervals. [22,23,24]

Su et al. in the Cochrane of 2007 regarding "*Oxytocin agonists for preventing postpartum hemorrhage*" and in Cochrane 2012 regarding *"Carbetocin for preventing postpartum hemorrhage*," conclude that the use of carbetocin is more effective than oxytocin for preventing PPH in women undergoing cesarean section. However, the data and the evidence were still insufficient. [14] In this study, we observed carbitocin and oxytocin to be comparable in efficacy of prevention of PPH, carbitocin being marginally better.

Oxytocin briefly tends to cause hypotension accompanied by marked increases in cardiac output and HR in healthy females undergoing a C-section under spinal anesthesia. It is assumed that the primary hemodynamic effect of oxytocin is vasodilation action via receptors on vascular endothelium that trigger the nitric oxide pathway [13,17]. In our study, we observed a statistically significant drop in both systolic and diastolic blood pressures in the Oxytocin group at 1,5, 10, and 15 minutes of drug administration compared to the carbetocin group.

We observed statistically significant tachycardia in the oxytocin group at 1-minute time intervals compared to the carbetocin group, whereas the heart rate was significantly higher in the oxytocin group at 5, 10, and 15 minutes, respectively, compared to the carbetocin Group.

We observed oxygen saturation comparable in both groups at 1,5,10 and 15 minutes.

Therefore, despite carbetocin being a synthetic oxytocin analog, the slight difference in the molecular structure determines a significantly safer hemodynamic profile with statistically comparable side effects and a similar uterotonic potency.

Conclusion

The findings of our study suggest using carbetocin instead of oxytocin as a uterotonic drug with equipotent uterotonic action and a significantly less hemodynamic impact than oxytocin in patients undergoing LSCS under regional anesthesia. The

minimal effect of carbetocin on patients' hemodynamics could be utilized in patients suffering from preeclampsia, risk factors of hemorrhage, and hypotension.

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