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HEMODYNAMIC EFFECTS OF OXYTOCIN AND CARBETOCIN DURING EMERGENCY CAESAREAN SECTION UNDER SPINAL ANAESTHESIA: AN OBSERVATIONAL STUDY

Anaesthesiology

Dr. Masumi Ahmed Department of Anaesthesiology, Post-graduate Trainee, Assam Medical College, Dibrugarh, Assam.

Dr. Swastika Saikia Department of Anaesthesiology, Post-graduate Trainee, Assam Medical College, Dibrugarh, Assam.

Dr. Monjit Shyam Associate Professor, Department of Anaesthesiology, Assam Medical College, Dibrugarh, Assam.

Dr. Debashis Bora Department of Anaesthesiology, Post-graduate Trainee, Department of Anaesthesiology, Assam Medical College, Dibrugarh, Assam.

Dr. Karuna Kumar Das Professor and Head of Department, Department of Anaesthesiology, Assam Medical College, Dibrugarh, Assam

ABSTRACT

Introduction: Oxytocin is a first line uterotonic medication used to decrease post-partum hemorrhage. However it is associated with serious side effects such as hypotension, tachycardia and occasional signs of myocardial ischemia. Carbetocin is a synthetic analog of oxytocin with prolonged duration of action thus abolishing the need of repeated oxytocin infusion. However there isn't enough data reflecting the hemodynamic effects of carbetocin. **Objectives:** The aim of this study was to compare the hemodynamic side effects of oxytocin and carbetocin in patients undergoing emergency LSCS under spinal anaesthesia. **Methods:** 80 patients(40 patients per group) in the age group 18 to 35 years undergoing emergency caesarean section under spinal anaesthesia were included in this study. By consecutive sampling method, 40 patients who received oxytocin were included in group "O" and 40 patients who received carbetocin were included in group "C" respectively. The patients in group "O" received 10 IU oxytocin in 500ml normal saline over 30 minutes and the patients in group "C" received 100 micrograms Carbetocin in 50 ml normal saline over 1 minute. Systolic blood pressure(SBP) , diastolic blood pressure(DBP), mean arterial pressure(MAP), heart rate(HR) and oxygen saturation(SpO2) were assessed preoperatively and at 1,5,10 and 15 minutes after administering both drugs. Number of patients who required additional use of vasopressor intraoperatively in each group were recorded. Incidence of other side effects such as nausea, vomiting, tremors, headache and chest pain in the intraoperative period were documented in each group. **Results:** Based on intragroup comparison, there was a significant increase in heart rate and reduction in blood pressure at 5,10 and 15 minutes after administration of both drugs. However based on intergroup comparison , there was a significant increase in Heart rate and decline in blood pressure in oxytocin group than in carbetocin group. In our study we didn't observe any significant drop in oxygen saturation in both groups. In the oxytocin group 35% patients complained of nausea, vomiting and 22.5% patients complained of chest pain which was significantly higher than in carbetocin group. **Conclusion:** Carbetocin as a uterotonic drug in comparison to oxytocin has high therapeutic potential and minimum haemodynamic impact on parturients undergoing LSCS under spinal anaesthesia.

KEYWORDS

INTRODUCTION:

Postpartum hemorrhage (PPH) stands as a predominant contributor to maternal morbidity and mortality within developing nations[1]. Uterine atony stands out as the primary causative factor for hemorrhage in a majority of cases. The deliberate administration of uterotonics subsequent to the delivery of the fetal anterior shoulder assumes a pivotal role in eliciting uterine contraction, thereby diminishing the likelihood of substantial blood loss during the perioperative timeframe. Over the past four decades, a comprehensive array of uterotonic agents has undergone rigorous examination with the overarching objective of proactively addressing the incidence of postpartum hemorrhage (PPH).

Currently oxytocin is the most commonly used uterotonic agent for prevention of post partum haemorrhage. Oxytocin, characterized by its potent vasoactive properties and intricate hormonal profile, exhibits specific receptor distribution across diverse organ systems, encompassing the myocardium, blood vessels, central nervous system, lactating glands, and myometrium. The peptide exerts a direct relaxant impact on vascular smooth muscle, culminating in a reduction in systemic vascular resistance, thereby inducing hypotension and tachycardia .Additionally, tachycardia may be incited through the direct activation of specific oxytocic receptors within the myocardium, influencing both atrioventricular conduction and myocardial repolarization[2,3]. However the half life of oxytocin is very short , ranging from 4-10 minutes that necessitates continuous or frequent administration of oxytocin. This prevailing uterotonic agent is associated with a spectrum of adverse effects encompassing nausea, vomiting, chest pain, hypotension, coronary artery spasm, and, in rare instances, intracerebral haemorrhage. These side effects mainly results from ergometrine component. Although the hemodynamic changes after oxytocin administration are generally well tolerated in healthy patients, they cannot be used in a significant proportion of the obstetric population due to coexisting comorbidities, such as preeclampsia and cardiac diseases.

Carbetocin, a synthetic oxytocin analog has an extended half-life, 4- 10 times longer half life than oxytocin. Thus carbetocin obviates the necessity for additional oxytocin administration. Carbetocin produces a longer uterine response when administered following childbirth. Carbetocin has relatively less gastrointestinal and cardiovascular side effects and can be recommended to be used in comparison to oxytocin. Nevertheless, the hemodynamic implications of carbetocin remain inadequately elucidated. Consequently, a comprehensive assessment of the hemodynamic profiles of both oxytocin and carbetocin is imperative, particularly in their roles as uterotonic agents, and especially in high-risk parturients afflicted by pre-existing or pregnancy-related cardiovascular conditions.

This observational study was done to compare the hemodynamic side effects of carbetocin and oxytocin during emergency caesarean section under spinal anaesthesia.

AIM AND OBJECTIVE

AIM:

To compare the effect of carbetocin and oxytocin on patient's hemodynamics during emergency caesarean section under spinal anaesthesia.

OBJECTIVES:

To compare the requirement of vasopressor in patients who received oxytocin and carbetocin

To compare the incidence of side effects such as nausea, vomiting, headache, tremors and chest pain intraoperatively with carbetocin and oxytocin

MATERIALS AND METHODS:

Place Of Study:
The present study was carried out in Assam Medical College and Hospital.

Type Of Study: Hospital based observational study

Sample Size:
Sample size was calculated at 95% confidence limit and absolute precision was taken as 10. For the present study sample size is calculated to be 80. In each group 40 patients were included.

Ethical Clearance:
Ethical clearance was taken from Institutional Ethical Committee(H) of Assam Medical College and Hospital.

Consent:
Written and informed consent is taken from all patients. Any cost incurred during the study is borne by the researcher.

Inclusion and Exclusion Criteria
Inclusion Criteria:
Parturients aged more than 18 years and less than 35 years posted for emergency LSCS under spinal anaesthesia.

Exclusion Criteria:
Patients/ family members who have not given consent
Contraindication for regional anaesthesia (eg; coagulopathy)
Parturients with pregnancy related complications (eg. Gestational diabetes, hypertensive disorders of pregnancy, pre existing diabetes mellitus or hypertension, cardiovascular or renal diseases , hypothyroidism and hyperthyroidism) as these conditions might interfere with the hemodynamic parameters.
Conditions with increased risk of PPH (eg; placenta previa, placental abruption and multiple gestation)

METHODOLOGY
A detailed history was taken and a detailed physical examination was carried out for all patients preoperatively. After shifting the patients to operation theatre, continuous monitoring of electrocardiogram, noninvasive arterial Blood pressure and pulse oximetry was carried out. An intravenous cannula was inserted and fluid preloading was done with 500ml ringer's lactate solution. Under all aseptic and antiseptic conditions spinal anesthesia was performed in left lateral or sitting position at lumbar level L3-L4 or L4-L5 space with 2.5 ml bupivacaine heavy (12.5 mg) and the patients were put in supine position immediately after spinal anesthesia. All patients were supplemented with oxygen via facemask @5-6 L/min.

By consecutive sampling method, 40 patients who received oxytocin were included in group "**O**" and 40 patients who received carbetocin were included in group "**C**" respectively.

The patients in group "O" received 10 IU oxytocin in 500ml normal saline over 30 minutes and the patients in group "C" received 100 micrograms Carbetocin in 50 ml normal saline over 1 minute.

Blood pressure (BP)was considered as the primary outcome encompassing mean BP, systolic blood pressure (SBP), and diastolic blood pressure (DBP). This study included additional hemodynamic parameters, such as heart rate (HR) and oxygen saturation, both preoperatively and at designated intervals of 1, 5, 10, and 15 minutes subsequent to the commencement of the operative procedure.

Systemic manifestations indicative of myocardial ischemia, namely chest pain, dyspnea, and/or sensations of chest heaviness, as well as the occurrence of hypotension (defined as BP < 90/60 mmHg) following the administration of the drugs were recorded in each group. Additionally, the research examined the intraoperative utilization of vasopressor (mephentermine) in each group.

Statistical Analysis:
The statistical analysis of data was performed using the computer program, Statistical Package for Social Sciences (SPSS for Windows, version 20.0. Chicago, SPSS Inc.) and Microsoft Excel 2010.

Results on continuous measurements are presented as mean ± standard deviation are compared using student t test.

Discrete data are expressed as number (%) and are analyzed using Chi square test and Fischer's exact test (where the cell counts were <5 or 0).

Pearson's correlation coefficient (r) was used to measure the associations among continuous variables. For all analyses, the statistical significance was fixed at 5% level (p value <0.05).

RESULTS:

The observations made in our study are shown in various tables and graph.

Table – 1: Characteristics of the included patients

Parameter	Oxytocin (n = 40)		Carbetocin (n = 40)		p-value
	MEAN	SD	MEAN	SD	
AGE	24.13	3.01	23.475	3.86	0.4040
WEIGHT	53.40	6.36	52.10	6.35	0.3630
GA (WEEKS)	38.08	0.69	38.1	1.06	0.9008

Table – 2:Comparison of mean values of HR at study intervals and pre intervention value

HR	Oxytocin (n = 40)		Carbetocin (n = 40)		p-value
	MEAN	SD	MEAN	SD	
Preintervention	84.18	14.93	83.45	13.55	0.8207
1 MIN	85.38	15.32	83.9	13.78	0.6520
5 MIN	99.60	16.71	92.15	13.48	0.0312
10 MIN	98.58	15.74	91.7	14.15	0.0433
15 MIN	96.75	15.79	88.55	15.47	0.0215

Table – 3: Comparison of mean values of SBP at study intervals and pre intervention value

SBP	Oxytocin (n = 40)		Carbetocin (n = 40)		p-value
	MEAN	SD	MEAN	SD	
Preintervention	130.58	19.56	130.05	16.36	0.8968
1 MIN	127.55	16.71	128.45	16.22	0.8075
5 MIN	107.70	14.48	122.05	15.99	0.0001
10 MIN	107.00	14.68	120.6	15.27	0.0001
15 MIN	112.50	13.30	123.95	15.36	0.0006

Table – 4: Comparison of mean values of MAP at study intervals and pre intervention value

MAP	Oxytocin (n = 40)		Carbetocin (n = 40)		p-value
	MEAN	SD	MEAN	SD	
Preintervention	90.65	6.72	92.68	15.47	0.4498
1 MIN	89.98	7.68	91.13	6.26	0.4650
5 MIN	80.38	9.45	86.03	14.98	0.0471
10 MIN	79.53	8.56	85.38	15.32	0.0382
15 MIN	84.80	14.51	90.45	6.61	0.0279

Table – 5: Comparison of mean values of DBP at study intervals and pre intervention value

DBP	Oxytocin (n = 40)		Carbetocin (n = 40)		p-value
	MEAN	SD	MEAN	SD	
Preintervention	82.30	11.45	82.18	9.75	0.9582
1 MIN	82.23	11.24	82.93	11.29	0.7818
5 MIN	70.05	8.71	71.50	8.74	0.4596
10 MIN	68.20	7.33	69.10	7.04	0.5771
15 MIN	70.90	7.13	72.33	8.96	0.4336

Table 6: Comparison between mean values of Oxygen saturation at different time intervals

Oxygen saturation	Oxytocin (n = 40)		Carbetocin (n = 40)		p-value
	MEAN	SD	MEAN	SD	
Preintervention	99.10	o.93	99.18	0.87	0.7108
1 MIN	99.05	1.04	99.1	0.93	0.8208
5 MIN	98.90	0.96	99.025	0.95	0.5584
10 MIN	98.825	0.93	98.95	0.90	0.5442
15 MIN	99.075	1.00	99.2	0.94	0.5655

Table 7:Comparison of vasopressor requirement in both groups

Vasopressor requirement	Oxytocin (n = 40)		Carbetocin (n = 40)	
	Number	%	Number	%
Yes	17	42.5	6	15
No	23	57.5	34	85

Table 8: Comparison of side effects in both groups

Symptoms	Oxytocin (n = 40)		Carbetocin (n = 40)	
	Number	%	Number	%
Nausea/vomiting	14	35	7	17.5
Chest pain	9	22.5	2	5
Tremors	5	12.5	1	2.5
Headache	12	30	6	15
Pruritus	0	0	0	0

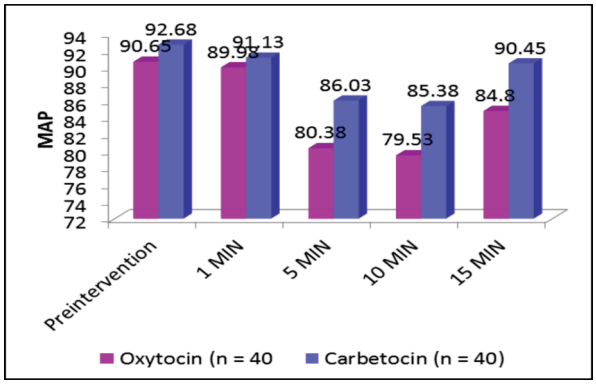

FIG: Comparison of MAP at different time intervals between Oxytocin and Carbetocin group

The patient demographic characteristics, including age, weight, and gestational age at delivery, exhibited no notable differences between the studied cohorts. However, upon conducting independent group analyses, notably elevated systolic blood pressure (SBP) and mean arterial pressure (MAP) were discerned at 5, 10, and 15 minutes post-administration in the carbetocin cohort compared to the oxytocin cohort.

Intergroup comparisons further elucidated a significant elevation in SBP and MAP at corresponding time intervals in the carbetocin group, albeit both cohorts experienced a decrease in diastolic blood pressure (DBP) without discernible intergroup disparities.

Furthermore, employing paired t-tests for intergroup comparisons revealed a marked increase in heart rate post-administration for both carbetocin and oxytocin, with a more pronounced elevation observed at 5, 10, and 15 minutes post-administration in the oxytocin cohort.

Noteworthy observations also encompassed stable oxygen saturation levels, maintained between 97% and 100% throughout the procedural timeline for both groups, with no statistically significant alterations following drug administration ($p > 0.05$).

Additional administration of mephentermine was necessitated in 17 patients (42.5%) within the oxytocin cohort and 6 patients (15%) within the carbetocin cohort.

Moreover, adverse events reported included nausea, vomiting, chest pain, and tremors, with varying frequencies between the two cohorts. Specifically, headaches were notably more prevalent in the oxytocin group, accounting for 30% of cases, compared to 15% in the carbetocin group.

Conclusively, our investigation underscores superior hemodynamic attributes associated with carbetocin vis-à-vis oxytocin, particularly regarding heart rate and mean blood pressure fluctuations subsequent to uterotonic administration.

DISCUSSION:

The aim of the study was to compare the hemodynamic effects of carbetocin and oxytocin. Nonetheless, a persistent discourse exists concerning the optimal uterotonic agent for prophylactic purposes, and the existing literature lacks definitive conclusions on this issue.

The hemodynamic effects of oxytocin bolus are profound as described in various studies such as increased cardiac output, severe hypotension, systemic vasodilation and tachycardia depending on the dose and rate of administration[2] .Such hemodynamic effects can result in myocardial ischemia especially in patients with preexisting cardiovascular diseases or hypovolemia.

Moertl MG et el [4]conducted a study on hemodynamic effects of carbetocin and oxytocin on women undergoing caeserean section in 2011 and concluded that females treated with oxytocin have more pronounced hypotension and hemodynamic rebound than carbetocin treated females . Our study revealed similar findings**. Moertl MG** also described in their study that both carbetocin and oxytocin groups reported almost equal incidence of nausea, vomiting, flushing and headache.

In their investigation**, Borruto et al**[5] documented a diminished occurrence of necessitating supplementary oxytocic agents among women subjected to carbetocin during cesarean section (CS) and thus decreasing the hemodynamic side effects of uterotonics. In the present study, we haven't compared the efficacy of the drugs as uterotonic agents, but we have observed the hemodynamic parameters were more stable in carbetocin group.

Mannaerts and L. Van der Veeken et al[6] in their study found that even with lower dose of oxytocin, it has an hypotensive effect and it was comparable to carbetocin and after initial drop in BP ,majority of patients remained stable. However in our study we have compared the effect of 10 units oxytocin in 500ml Normal saline and 100micrograms of carbetocin and we have observed that patients belonging to oxytocin group had more profound fall in BP and increase in HR than oxytocin group, but there was no significant difference(p value >0.5) between oxygen saturation between both groups.

In a study done by **Robabeh Taheripanah et al**[7] , it was documented that pulse rate was significantly higher in oxytocin group compared to carbetocin group(p value <0.05) but BP and respiratory rate were comparable between both groups. They have observed in their study that side effects such as headache, tremor, dizziness were more common in oxytocin group (p value<0.05) but nausea and vomiting were comparable across groups. Their study also reported that 27% patients in carbetocin group reported pruritus whereas the incidence of pruritus was 0 in oxytocin group. In our study we have observed 35% patients in oxytocin group and 17.5% in carbetocin group complained of nausea, vomiting. We have also observed that more patients complained of chest pain in oxytocin group. However in our study no patients reported pruritus in both groups.

Mannaerts et al[6] demonstrated both carbetocin and oxytocin produced fall in BP without significant difference in HR and BP between groups. **Larciprete et al**[8] has also observed similar results. After initial drop in BP , majority patients remained stable until end of procedure.

But our study has revealed that fall in MAP, SBP was more significant at 5,10, 15 mins with oxytocin group and HR was significantly increased in oxytocin group compared to carbetocin group. Our study findings were similar to results of the study done by **Viayaka Jannu et al**[9] that demonstrated stable hemodynamic responses of carbetocin over oxytocin.

CONCLUSION:

In this prospective observational study, findings were obtained after documenting the hemodynamic changes following the administration of oxytocin or carbetocin in parturients undergoing emergency LSCS under spinal anesthesia. The study demonstrated a favorable and safe hemodynamic profile in the carbetocin group. However, both interventions resulted in a significant increase in heart rate (HR) and a decrease in blood pressure (BP), including systolic (SBP), diastolic (DBP), and mean BP. Notably, the carbetocin group exhibited a return to normal SBP and mean BP levels after 15 minutes, whereas the oxytocin group did not. Furthermore, the oxytocin group experienced a greater increase in HR and a more pronounced reduction in BP compared to the carbetocin group.

The findings of the current study shows that Carbetocin as a uterotonic drug in comparison to oxytocin has a minimum haemodynamic impact on parturients undergoing LSCS under spinal anaesthesia.

Limitations:

a) We studied haemodynamic effect of study drugs for brief duration of surgery and significant effects could still be expected during period of oxytocin infusion
b) In our settings, we included only patients admitted for emergency caesarean section to study the hemodynamic side effects;

efficiency of drugs on uterine contraction and blood loss was not studied that may impact the hemodynamic parameters.

c) In our investigation, we incorporated individuals undergoing emergency lower segment cesarean section (LSCS) under spinal anesthesia. Nevertheless, it is imperative to acknowledge that spinal anesthesia autonomously induced hypotension and bradycardia, potentially eliciting reflex tachycardia. This phenomenon could have exerted an impact on the findings and observations within the scope of our study

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