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Original Article

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Comparative Study of Prophylactic Phenylephrine Bolus with Combined Phenylephrine and Glycopyrrolate Bolus in Maintaining the Haemodynamic in Caesarean Section under Spinal Anaesthesia

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ABSTRACT

Background and Aim: Airway difficulty is common in pregnancy than in the general population due to anatomical and physiological changes during pregnancy. Spinal anaesthesia in pregnant women is associated with greater incidence of having hypotension. Although glycopyrrolate has been investigated previously as an adjunctive agent for preventing hypotension during caesarean section, few data are available for its use specifically when phenylephrine is used as the primary vasopressor. Our study aims to determine the effectiveness of prophylactic combined glycopyrrolate and phenylephrine boluses in maintaining the haemodynamics as compared to prophylactic phenylephrine bolus alone during spinal anaesthesia in caesarean section. **Method**: A prospective, double-blinded clinical study was conducted in the Department of Anaesthesia in collaboration with the Department of Obstretrics and Gynaecology from June 2020 to July 2022. Ninety respondents undergoing cesarean section were allocated into two groups. Group A (n = 45) received prophylactic injection of bolus glycopyrrolate 0.2mg immediately after spinal anaesthesia followed by prophylactic bolus of phenylephrine 75 mcgs intravenously (IV) and Group B (n = 45) received prophylactic bolus of normal saline 1ml immediately after spinal anaesthesia and bolus of injection phenylephrine 75mcgs IV. Then, for every 3 min, systolic blood pressure, diastolic blood pressure, and heart rate (HR) were measured for 30 min, and APGAR scores were measured. **Result**: There was no difference between systolic pressure upto 6mins between the two groups. But from 9mins, lowering of blood pressure was recorded more in group B. For diastolic pressure, it was found to be significantly lower in Group B. However, maintenance of pulse rate was observed better in Group A. **Conclusion**: Incidence of bradycardia was found to be reduced in group A as compared to group B. Haemodynamic stability was found to be more in the group where prophylactic glycopyrrolate was used.

Key Words: *Glycopyrrolate, Phenylephrine, Hypotension, Caesarian section.*

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INTRODUCTION

Caesarean Section (CS) is amongst the most frequently performed surgical procedures in India with a rate of 21.5% according to National Family Health Survey (NFHS-5) [1] and spinal anaesthesia is a commonly used technique in obstetric and gynaecological procedures. Airway difficulty is common in pregnancy than in the general population due to anatomical and physiological changes during pregnancy.[2] However, spinal anaesthesia in pregnant women is associated with greater incidence of having hypotension (70%- 80%) compared to non-pregnant women despite fluid pre-loading or co-loading.[3]

Spinal anaesthesia results in sympathetic vasomotor blockade leading to decreased systemic vascular resistance, primarily from arterial dilation but with some venodilation and compensation are mediated via baroreceptors which results in increased heart rate (HR) as well as stroke volume and vasoconstriction in the unblocked segments.[4] But, in the termed pregnant woman, baseline HR, stroke volume (SV), and cardiac output (CO) are already increased to meet the metabolic demands ofthe fetus, impairing the ability of the cardiovascular system to compensate. Further, supine position causes the gravid uterus to compress the inferior vena cava, reducing venous return and cardiac output.[5]

Maternal symptoms like nausea, vomiting, dyspnea, and adverse fetal effects including depressed APGAR scores have been correlated with the severity and duration of hypotension. According to the International consensus statement on the management of hypotension with vasopressors, the aim should be to maintain the baseline systolic arterial pressure (SAP) at ≥90% of the baseline before spinal anesthesia and avoid a baseline decrease of <80%.[6]

Although glycopyrrolate has been investigated previously as an adjunctive agent for preventing hypotension during caesarean section, few data are available for its use specifically when phenylephrine is used as the primary vasopressor.[7] Few of the studies show conflicting results thereby necessitating further studies. So, the objective of our study was to determine the effectiveness of prophylactic combined glycopyrrolate and phenylephrine boluses in maintaining the haemodynamics as compared to prophylactic phenylephrine bolus alone during spinal anaesthesia in caesarean section.

MATERIALS AND METHODS

This was a prospective, double-blinded clinical study conducted in the Department of3 Anaesthesia in collaboration with the Department of Obstretrics and Gynaecology, JNIMS Imphal Manipur, from November 2020 to October 2022. Institutional Ethics Committee (IEC JNIMS, No. Ac/IEC/JNIMS/2018, 2nd November 2020) approval was taken for the study and written informed consent was obtained from all participants. Patients undergoing elective caesarean section under spinal anaesthesia and fulfilling the inclusion criteria were enrolled. The study was carried out in accordance with the principles of the Declaration of Helsinki, 2013.

Inclusioncriteria*:*

1. Patients having American Society of Anaesthesiologists (ASA) physical status-II.
2. Patients scheduled for elective caesarean delivery aged between 18-40 years under spinal anaesthesia.
3. Patients who had signed the written informed consent.

Exclusioncriteria*:*

1. Patient refusal.
2. Patients having history of any allergy to study drugs.
3. Patients with medical complications like hypertension, diabetes, cardiovasculardiseases, severe anaemia, BMI>30, Addision disease, kidney disease.
4. Patients with obstetric complications like pre-eclampsia, antepartum haemorrhage, gestational diabetes mellitus, foetal malpresentations and malformations, cord prolapse.
5. Patients with local infection at the site of spinal to be given, spinal deformities, other neurological diseases, coagulation abnormalities.

Sample size:a sample size of 45 in each group was taken.

SAMPLE SIZE:

$n=2\{(Z1-\alpha/2+Z1-\beta)/\delta o\}^2S^2$

where $Z1-\alpha/2$= standard normal value at 5%=1.96

$Z1-\beta$ = standard normal value at 80% power=0.8416 δo = A clinical acceptable margin=4.67

S^2= polled Sd of groups

=7.56

Based on a reference study, with mean Systolic blood pressure 121.34+/- 7.91 and 122.11+/-7.20 the estimated effect size at the power of 80% and α value of 0.05, the calculated sample size was found to be 41 in each group. Keeping some room for adjustment the ultimate sample size will be 45 in each group.

Procedure:

Pre anaesthetic check was done in all patients in the study.After taking consent from the patient, a detailed clinical history, medical records, physical examination findings (blood pressure, pulse, respiration, temperature, jaundice, pallor, cyanosis, clubbing, oedema) and medical reports were noted. All patients were kept nil per orally at least 8 hours before induction of spinal anaesthesia. Oral premedication with Tab. Ranitidine 300mg was given the night before the surgery.

An 18G cannula was placed in the peripheral vein in the patient's arm and all the patients were preloaded with IV Ringer lactate solution at the minimal rate to keep thevein open. After preloading, Pulse rate, Systolic and Diastolic Blood Pressure were recorded thrice and the mean value was taken as baseline value before giving spinal anaesthesia in the operation theatre. Monitoring was achieved with pulse oximeter, electrocardiography, noninvasive blood pressure device and a temperature monitor and then Inj.Ondansetron 4mg having volume of 2ml was given intravenously prior to performance to intrathecal block.

Intrathecal block was achieved in all patients under all aseptic precautions using a 25G Quinkes Babcock needle at L2-L3 or L3-L4 interspace in right lateral position using a standard midline approach and once free flow of cerebrospinal fluid is obtained, hyperbaric Inj.Bupivacaine 0.5% 2ml was injected over 10-15 sec. Patients were placed in supine position with left uterine displacement.

One of the study drugs was injected intravenously soon after giving spinal anaesthesia as specified in the group allocation mentioned above. SpO2, electrocardiography, non-invasive blood pressure device, temperature were recorded immediately after giving spinal anaesthesia, then continued to record the same after every 3mins until the delivery of the baby or maximum upto 15mins and then every 5mins till the end of the surgery. Continuous electrocardiography monitoring was continued till the end of the operation. The level of sensory block was assessed by pin prick method and motor block was assessed by Modified Bromage scale. Urine output was measured by keeping a urinary catheter in situ which was removed after 24hrs. Complications of spinal anaesthesia like hypotension, bradycardia, pruritis, nausea and vomiting, shivering were recorded and managed accordingly. Whenever hypotension occurs (fall in systolic blood pressure just below from baseline value) phenylephrine was given intravenously as rescue boluses according to body weight as specified in group allocation. The number of boluses given and the time taken for optimization of blood pressure to baseline value were also noted.

The patients received oxygen 5L/min through oxygen face mask till the delivery of the baby. After the delivery of the baby, Inj. oxytocin 10U IM and 10U slow IV in 500ml Ringer lactate were given. APGAR scores was assessed at 1 and 5 minutes and also umbilical arterial blood sample from a segment of clamped umbilical cord in heparinized syringe will be taken, which was analysed using a blood gas analyser.

Any significant event on the mother and fetus both intraoperatively and post-operatively were noted particularly bradycardia, tachycardia, nausea and vomiting.

Statistical Analysis: Data entry was done in MS Excel and analysis was done using SPSS 23.0.

RESULTS

In our study, ninety respondents undergoing cesarean section were allocated into two groups. Group A (n = 45) received prophylactic injection of bolus glycopyrrolate 0.2mg immediately after spinal anaesthesia followed by prophylactic bolus of phenylephrine 75 mcgs intravenously (IV) and Group B (n = 45) received prophylactic bolus of normal saline 1ml immediately after spinal anaesthesia and bolus of injection phenylephrine 75mcgs IV. Then, for every 3 min, systolic blood pressure, diastolic blood pressure, and heart rate (HR) were measured for 30 min, and APGAR scores were measured. There was no difference between systolic blood pressure upto 6min among the two groups. But from 9min lowering of blood pressure is more in group B. Difference was observed upto 15min as shown in **Figure 1.** For diastolic blood pressure, it was found to besignificanly lower in 3rd, 6th, 9th and 12th min. And a significant difference was observed from 18min to 30min as summarised in **Figure 2.** There was significant dip in pulse rate among group B at 6min to 24min as shown in **Figure 3.** APGAR score <9 was more among group B as shown in **Table 1**. However, it was found to be insignificant.

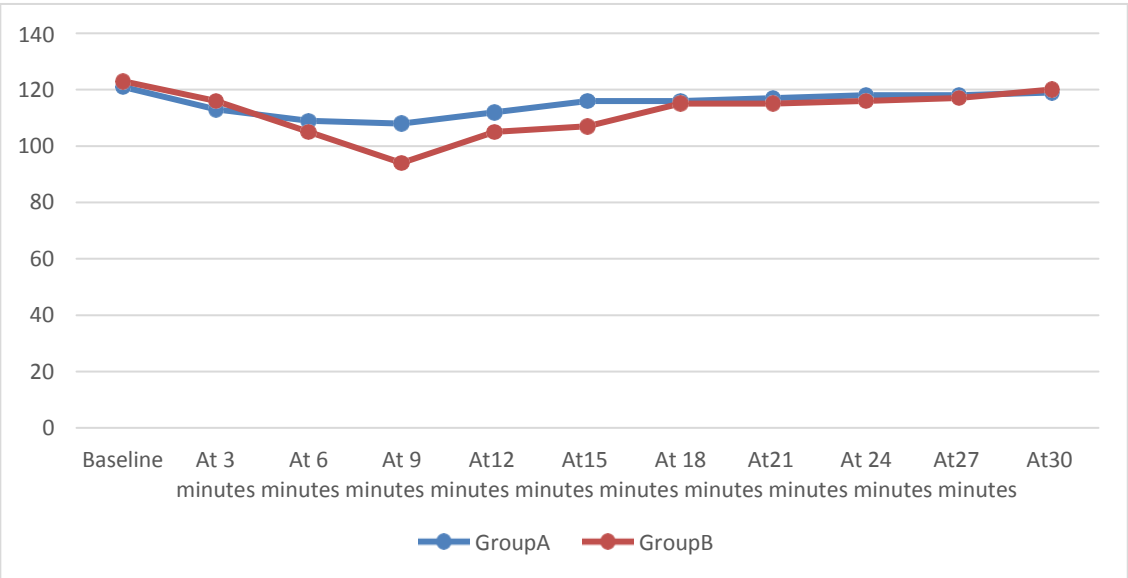

Figure 1: Line diagram showing systolic blood pressure at various minutes comparing two groups.

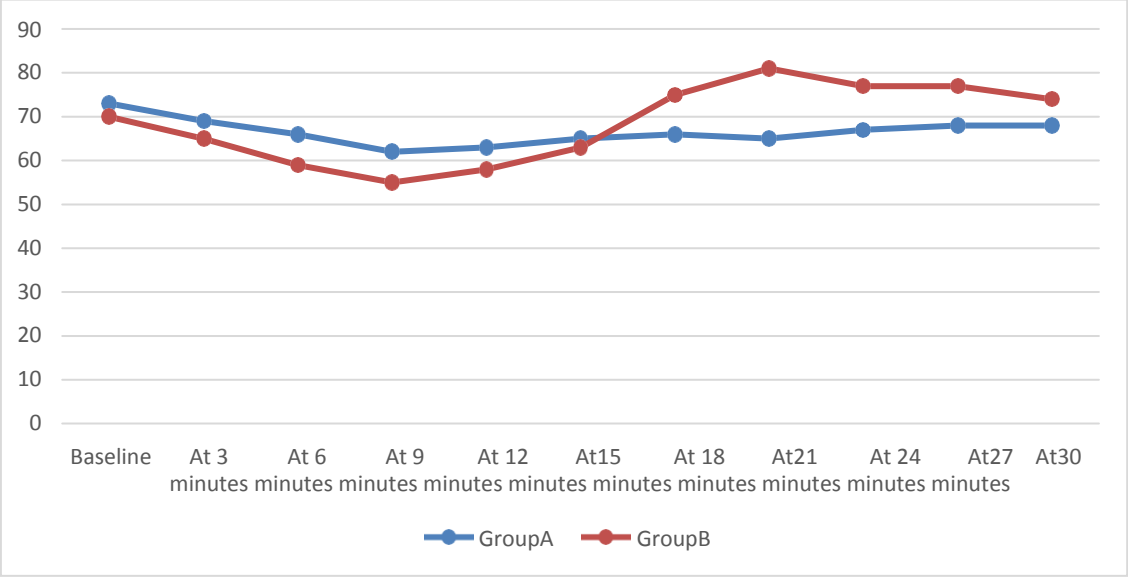

Figure 2: Line diagram showing diastolic blood pressure at various minutes comparing two groups.

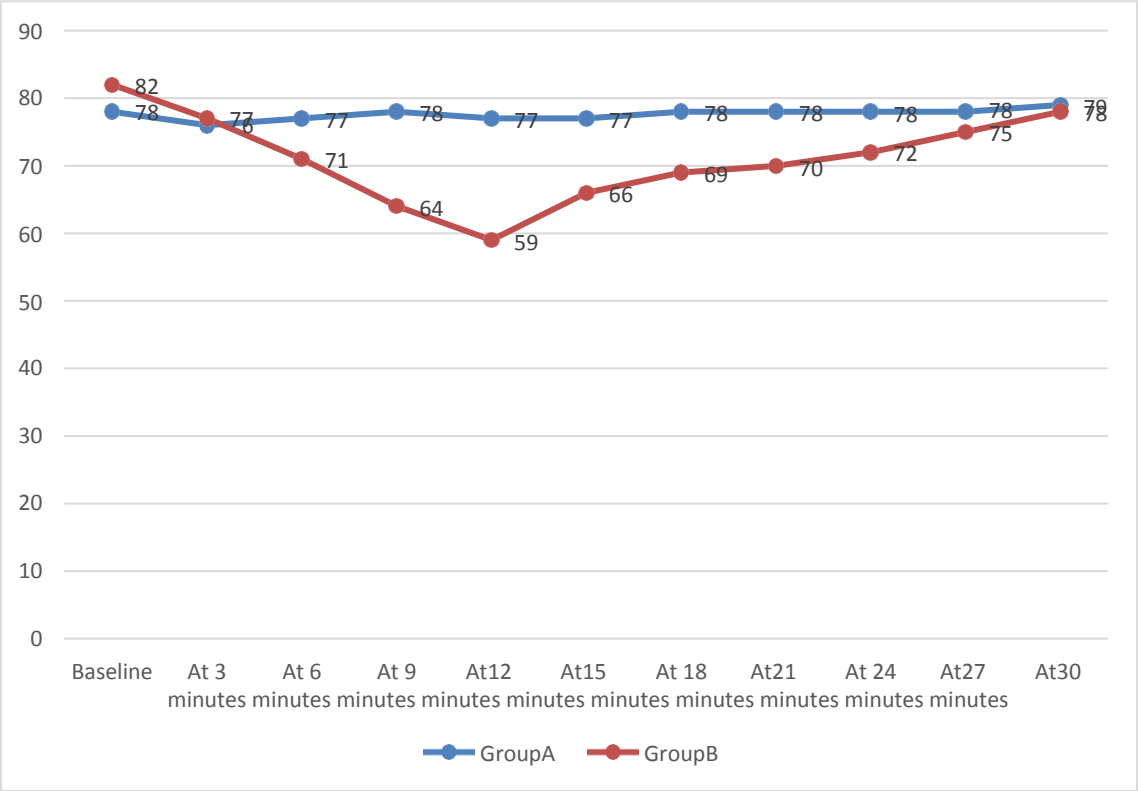

Figure 3: Line diagram showing pule rate at various minutes comparing two groups.

Table 1: APGAR score

APGARscore	**GroupA N(%)**	**GroupB N(%)**	**Chi-squaretest**
<9	6 (13.3)	8 (17.7)	Value=0.338 p-0.56
≥9	39 (86.7)	37 (82.3)	

Total	45 (100.0)	45 (100.0)	

DISCUSSION

A prospective double-blinded clinical study was conducted in the Department Anaesthesiology to determine the effectiveness of prophylactic combined glycopyrrolate (45 respondents) and phenylephrine boluses in maintaining the haemodynamics as compared to prophylactic phenylephrine bolus alone (45 respondents) during spinal anaesthesia in caesarean section.

In this study there was a significant dip in systolic blood pressure from 9th to 15th minute and for diastolic blood pressure from 3rd minute to 12 minutes in group B compared to group A. Systolic hypotension was observed in 9th minute but for diastolic hypotension was observed in 6-9th minute in the control group. Systolic and diastolic blood pressure was maintained in the glycopyrrolate group. This finding is in concordance with finding by Rucklidge MWM et al[8] where glycopyrrolate was used to reduce hypotension following subarachnoid block in parturients. In the study by Hwang J et al[9](done on elderly patients), twenty-three of 33 (70.0%) patients in control group experienced hypotension compared with nine of 33 (27.3%) patients in glycopyrrolate group. So, glycopyrrolate use reduce incidence of hypotension. In the study by Piya R et al[10] also, prophylactic glycopyrrolate before spinal anaesthesia for caesarean section reduced the severity of maternal hypotension. The mean arterial pressure was significantly higher with glycopyrrolate than without. Malem A et al[11] study also showed the incidence of hypotension was less in the glycopyrrolate group compared to the saline group.In some studies[12],[13] the incidence of hypotension was unaffected by glycopyrrolate, butthe ephedrine requirement was significantly higher.

In our study, there was significant dip in pulse rate among the control group from 6th minute to 24th minute. Mean pulse rate below 60/min was seen at 12th minute in the control group. Bradycardia was not seen in the glycopyrrolate group in this study.

Similarly in the study by Piya R et al[10], there was no bradycardia, but the lowest mean HR was higher in the glycopyrrolate group which is almost similar to this study. Another study reported that glycopyrrolate caused increased maternal heart rate and cardiac index which was observed 8-15 mins after induction.[14] The Glycopyrrolate group showed a significant increase in HR than the placebo group in many studies. [13],[15],[16], Bradycardia was significantly less in the glycopyrrolate group compared to the ondansetron group and thus, glycopyrrolate decreased the incidence of bradycardia by30% in the study by Jain R et al17. Heart rate was higher in the study group than the control group in the study by Vadhanan P et al.[18]

The maximal HR achieved in the glycopyrrolate group was significantly higher compared to controls however, the incidence of bradycardia was not statistically different in the study by Patel SD et al19. Three (9.1%) patients in group C experienced bradycardia compared with 1 (3.0%) patient in group G in the study by Hwang J et al.[9]

Limitation of the study:

1. In this study, the level of the sensory block was not compared between the two groups.
2. The rescue boluses of phenylephrine given were also not compared.

CONCLUSION

Systolic and diastolic blood pressure was maintained throughout the study in the glycopyrrolate group (Group A). Similarly, no bradycardia was seen in the glycopyrrolate group. Haemodynamic stability was found to be more in the group where prophylactic glycopyrrolate was used.

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