

ORIGINAL RESEARCH

Effect of prophylactic Glycopyrrolate on the maternal hemodynamics and vasopressor requirement during spinal anesthesia for caesarean delivery

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ABSTRACT

Background and Aims: Spinal anesthesia is a popular technique for caesarean delivery. The occurrence of hypotension and bradycardia induced by spinal anesthesia in parturients undergoing caesarean section can pose risks to both the fetus and the mother. Administering vasopressors prophylactically can mitigate hypotension and bradycardia, thus preserving uteroplacental blood flow. The aim of the study is to determine if Glycopyrrolate reduces the incidence of hypotension and total vasopressor dose required during elective caesarean delivery under spinal anaesthesia. **Materials & Methods:** 60 parturients scheduled for elective LSCS under spinal anaesthesia were randomly allocated into 2 groups of 30 each, Group G received iv Glycopyrrolate 0.2mg (1ml) and Group S received iv Saline (1ml), 5mins before subarachnoid block. The primary outcome like total amount of Ephedrine used to maintain blood pressure intra-operatively and secondary outcomes like maternal hypotension, bradycardia, tachycardia, intra-operative nausea and vomiting, dryness of mouth were also recorded. **Results:** 11 out of 30 parturients (36%) developed hypotension in group G whereas 23 out of 30 parturients (76%) developed hypotension in group S (p= 0.001). Tachycardia occurred in 20% (Group G) and 23% (Group S), whereas there was Bradycardia in 3.33% in Group S and nil in Group G. The median dose of vasopressor requirement was 5mg in Group S and nil in Group G. Significant dryness of mouth was noted in group G (p= 0.002). **Conclusion:** Prophylactic intravenous Glycopyrrolate in spinal anesthesia for caesarean section reduces the incidence and severity of hypotension and the need for vasopressor.

Keywords: Glycopyrrolate; Hypotension; Subarachnoid block.

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INTRODUCTION

Spinal anesthesia has become a popular technique for caesarean delivery because it is deemed to be a safe, quick, and reliable option that also offers postoperative analgesia. However, hemodynamic changes such as hypotension and bradycardia remain common complications associated with spinal anesthesia in the obstetric population. Spinal induced hypotension occurs due to a reduction in systemic vascular resistance, with the effect being more pronounced in the obstetric population due to increased local anesthetic sensitivity and aortocaval compression¹. Bradycardia occurs with spinal

anesthesia for caesarean delivery due to sympathetic blockade of cardiac accelerator fibers that arise at T1-T4—to prevent the development of reflex tachycardia², reduced venous return, and α -agonist vasopressor use¹. Maternal hypotension is associated with severe distress to the mother in the form of nausea and vomiting, dizziness etc. Also, it can lead to placental hypoperfusion that can cause adverse neonatal outcomes. Traditional intravenous (IV) crystalloid preloading or co-loading might help in decreasing the severity of this hypotension but cannot completely prevent its incidence³. If left untreated, spinal-induced hypotension and bradycardia can have

detrimental effects for both mother and fetus including maternal cardiovascular collapse and fetal acidosis. Previous work has shown maternal heart rate (HR) and cardiac output (CO) to be strongly correlated; therefore, minimizing spinal-induced hemodynamic changes with anti-cholinergic drugs may be of interest¹. Sympathomimetics are usually administered “Reactively” i.e. administration of drugs after the appearance of hypotension. A more logical approach is “Proactive” i.e. giving vasopressors pre-emptively to prevent the occurrence of hypotension following subarachnoid block. This pre-emptive or proactive approach has reduced the incidence and severity of spinal anesthesia induced hypotension in many studies conducted worldwide³. Atropine is an anti-cholinergic drug that possesses a tertiary amine structure, allowing it to readily cross the blood-brain barrier and placenta. Glycopyrrolate however, is an anti-cholinergic with a quaternary amine structure, thereby limiting its ability to cross these membranes and making it the popular choice for obstetric patients¹. Glycopyrrolate increases HR by blocking the effects of acetylcholine on the sinoatrial node hence, helps in the prevention of post-spinal hypotension⁴. The use of Glycopyrrolate for reducing hemodynamic changes after spinal anesthesia for caesarean delivery has been investigated; however, results from these studies are conflicting. The primary objective of this study was to determine if prophylactic Glycopyrrolate reduces the incidence of hypotension and total vasopressor dose to maintain hemodynamic stability during elective caesarean delivery under spinal anesthesia¹.

MATERIALS & METHODS

A prospective randomized comparative hospital-based study was conducted on 60 parturients scheduled for elective LSCS under spinal anaesthesia in the Department of Anaesthesia, Doddaballapur district hospital, during May-July 2023, after obtaining approval from institutional ethical committee and patient consent. The sample size was arrived based on formula $1 + Z^2 \times P(1-P) / e^2 N$ where N= Population size;

e = margin of error; Z = z score; P = standard deviation. Parturients belonging to ASA physical status II and III, aged between 18-35 years with a Body Mass Index between 19-30 kg/m², scheduled for elective LSCS were included in the study. Patients with cardiac, pulmonary, cerebrovascular diseases, coagulopathy, local infection, severe spinal deformity, and other known contraindications for spinal anesthesia, known hypersensitivity to any of the study medications were excluded from the study. Selected patients were premedicated with inj Ranitidine 50mg; inj Ondansetron 4mg and preloaded with 500ml RL. They were assigned by sealed envelope method into two groups. Group G who received 0.2 mg (1ml) Glycopyrrolate and Group S received 1ml normal saline IV 5minutes before Spinal anaesthesia. All patients were subjected to spinal anaesthesia with 2ml 0.5% Bupivacaine heavy at L3-L4 space using 25G Quincke's needle through the midline approach and positioned supine with left lateral tilt [15 degree]. Monitoring consisted of frequent recording of ECG, HR, BP, SPO₂, MAP at regular intervals. Surgery was allowed after establishment of adequate sensory block. All patients were specifically observed perioperatively for incidence of hypotension [20% fall from baseline reading], bradycardia [<55bpm], tachycardia [>120bpm], requirement of vasopressor, nausea, vomiting, dryness of mouth. Hypotension was treated with increment of 6mg Ephedrine. When bradycardia was associated with hypotension, IV inj Atropine 0.6mg was administered. The amount of Ephedrine used was noted. The primary outcome was the incidence of hypotension, the total dose of vasopressor (iv Ephedrine) used to maintain blood pressure intra-operatively. Secondary outcomes included, bradycardia, tachycardia, intra-operative nausea and vomiting, dry mouth. The collected data was analysed using SPSS software 22.0. Mean and standard deviation was calculated for all the parameters. Chi-square test was used to find the statistical significance. P value of <0.05 was considered as statistically significant.

RESULTS

TABLE 1: DEMOGRAPHIC DATA

Parameters	Group G	Group S	P value
Mean Age (years)	28 ± 2.10	29 ± 2.12	0.34
Mean Height (cm)	151	152	0.13
Mean Weight (kg)	67 ± 6.2	65 ± 6.12	0.53
BMI (kg/m ²)	28.9	28.4	0.604

TABLE 2: BASELINE PARAMETERS AND INCIDENCE OF HYPOTENSION

	BASELINE PARAMETERS			INCIDENCE OF HYPOTENSION (no. of patients / percentage)		P value
	Mean HR	Mean SBP	Mean DBP	Yes	No	
Group G	104 ± 18	121.83 ± 10.56	75.4 ± 13	11 (36%)	19 (63%)	0.001*
Group S	100 ± 16.8	120.21 ± 8.02	78.6 ± 11.2	23 (76%)	7 (23%)	

36% developed hypotension in group G whereas 76% developed hypotension in group S (p= 0.001).

Table 3 shows The median dose of vasopressor requirement was 5mg in Group S and nil in Group G. (p value 0.007).

TABLE 3: COMPARISON OF TOTAL DOSE OF VASOPRESSOR (MG) USED BETWEEN GROUPS

	Group G	Group S	P value
Mean	3.9	8.6	0.007*
Median	0	5	

There was no statistically significant difference in incidence of complications such as bradycardia, tachycardia and reactive hypertension, percentage change in mean arterial pressure, incidence of nausea and vomiting in both the groups (Tables 5). Symptom of dry mouth was statistically significant between the groups with $p < 0.05$ ($P=0.002$)

TABLE 4: COMPARISON OF COMPLICATIONS BETWEEN THE GROUPS

Complications	Group G (%)	Group S(%)	P value
Bradycardia Yes	- (0%)	1 (3.33%)	0.92
No	30 (100%)	29 (96.6%)	
Tachycardia Yes	6 (20%)	7 (23%)	0.62
No	24 (80%)	23 (76%)	
Percentage change MAP	22.7 (mean) 8.8 (SD)	25.4 (mean) 8.7 (SD)	0.56

TABLE 5: INCIDENCE OF NAUSEA, VOMITING, AND DRY MOUTH BETWEEN GROUP G AND GROUP S

Variables	Group G	Group S	P value
Nausea	3	6	0.39
Vomiting	0	2	0.000*
Dry mouth	16	2	0.002*

DISCUSSION

In the present study, we found that prophylactic use of IV Glycopyrrolate in the elective caesarean section showed significant difference in the vasopressor requirement compared to the normal saline group. Similarly, use of the IV Glycopyrrolate resulted in a significant difference in the incidence of post-spinal hypotension.

In a study conducted by Hwang J et al., Glycopyrrolate proved to be a potent agent, when given prophylactically via intramuscular route, to prevent post spinal hypotension in elderly patients receiving spinal anesthesia for elective lower limb orthopedic surgeries.

Similarly in another study conducted by Piya, R et al, Glycopyrrolate reduced the incidence of hypotension but not bradycardia and decreased the need for vasopressor⁴. Abhinaya Manem et al concluded Pre-emptive treatment with intramuscular Glycopyrrolate reduces the incidence and severity of hypotension in parturients undergoing caesarean sections under spinal anesthesia³.

Taking these findings into consideration and changing the study population, this prospective, randomized study was undertaken to study the efficacy of prophylactic intravenous Glycopyrrolate as a potential preventive agent against spinal anesthesia induced hypotension in elective caesarean sections. In our study, the mean age, weight, height and BMI were comparable between both the groups.

Eleven out of thirty patients in group G developed hypotension. This constitutes to 36% incidence of hypotension. On the contrary, 23 patients out of 30 patients who were in group S, had developed episodes of hypotension requiring treatment with vasopressors. This constitutes to an astonishing 76% incidence of hypotension. There was a clinically as well as statistically significant difference in the incidence of hypotension between the two groups with a p value showing 0.001. These results were quite similar to study done by Hwang J et al. in elderly population undergoing lower limb orthopedic surgeries under spinal anesthesia, which showed that Glycopyrrolate could minimize the incidence of hypotension when given prophylactically².

But there was a study done by Ure D et al., in which it has been observed that there was similar incidence of hypotension in both the groups but the severity of hypotension was less in Glycopyrrolate group⁸.

Similar observations were recorded in the studies done by Yentis et al. and Rucklidge et al., who concluded that there was statistically no significant difference in the incidence and severity of hypotension with Glycopyrrolate pretreatment in pregnant patients undergoing LSCS under spinal anaesthesia^{6,7}. Deshar, R et al concluded prophylactic use of Glycopyrrolate does not decrease the requirements of vasopressor to prevent hypotension in non-elective caesarean section under spinal anesthesia⁵.

In our study, the Median dose of rescue vasopressor used for treatment of hypotensive episodes was used as surrogate marker for assessing the severity of hypotension. Lesser the vasopressor requirement, lesser the severity of hypotension. Mean dose of rescue vasopressor used in Glycopyrrolate group was 3.9 mg and 8.6 mg in saline group. Median dose used was calculated to be 0 mg in Glycopyrrolate group versus 5 mg in saline group. This difference in total rescue vasopressors used between the two groups was statistically significant with a p value of 0.007. Our study results have reinforced the results of many previous studies that, prophylactic Glycopyrrolate administration reduces the requirement of vasopressors after subarachnoid block, thereby reducing the severity of hypotension. Similar results were observed in study by Hwang J et al., though the study population was elderly⁸.

A meta-analysis conducted by Selina D Patel et al., taking into consideration 5 Randomized control trials (RCTs), showed that though the reduction in the incidence of hypotension was not significant with pre-emptive Glycopyrrolate treatment before subarachnoid block, there was a “modest reduction” in severity of hypotension in patients who received Glycopyrrolate. They suggested that larger study populations and further research is required to recommend routine prophylaxis with Glycopyrrolate¹.

3 patients who received Glycopyrrolate had episodes of nausea and or vomiting. 6 patients in saline group complained of nausea and or vomiting. Though the number of patients who developed nausea and vomiting were less in number to conclude that Glycopyrrolate was associated with lesser incidence of nausea and vomiting, results obtained from other studies have shown that Glycopyrrolate administration reduces the incidence and severity of perioperative nausea and vomiting in pregnant females undergoing lower segment caesarean sections under spinal anaesthesia⁹.

16 out of 30 in Group G complained of dryness of mouth with p value Of 0.002 which is both clinically and statistically significant.

CONCLUSION

Prophylactic intravenous Glycopyrrolate in spinal anaesthesia for caesarean section reduced the incidence and severity of hypotension and the need for vasopressor.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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