

Title: The Effect Of Prophylactic IM Inj.Glycopyrrolate In Pregnant Patients For Prevention Of Hypotension Under Spinal Anaesthesia Posted For Lscs”

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ABSTRACT

introduction

Delivery by caesarean section has become very common nowadays. Lower segment caesarean sections (LSCS) are now commonly performed using spinal anaesthesia. In parturients, hypotension is aggravated by compression of the inferior vena cava by gravid uterus. Its incidence has been reported as high as 40-70% and affects 90% women. For reducing the severity of maternal hypotension, many pharmacological and non-pharmacological methods are employed.

Glycopyrrolate, an anticholinergic drug with a quaternary amine structure that limits its ability to cross the blood-brain barrier and placenta and therefore has no effect on the variability of foetal heart rate (FHR) and maternal heart rate (HR). During spinal anaesthesia glycopyrrolate is expected to attenuate hemodynamic changes which makes it a popular choice for obstetric patients.

Material and methods

100 parturient posted for LSCS under spinal anaesthesia were randomised into 2 groups of 50 patients each. Patients in Group G received intramuscular injection glycopyrrolate 0.2mg (1ml) and Patients in Group S received intramuscular injection 0.9% normal saline (1ml) 15 minutes prior to subarachnoid block. Incidence and severity of hypotension, heart rate and blood pressure changes, incidence of nausea and vomiting and APGAR score were observed.

Results

The demographic profile, level of block achieved and duration of the surgery were comparable between the groups. The average heart rate after 2 minutes was significantly higher in Group G. Intraoperatively better haemodynamic stability was observed in Group G compared to Group S. The use of rescue vasopressor was more in Group S compared to Group G (Group G:3 patients, Group S:9 patients).

Conclusion

Prophylactic use of intramuscular injection of glycopyrrolate provides better haemodynamic stability in parturients posted for caesarean section under spinal anaesthesia.

Keywords: Caesarean section, glycopyrrolate, hypotension, parturients, subarachnoid block

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INTRODUCTION

Delivery by caesarean section has become very common nowadays. Serious injury to the baby can be avoided by foregoing a difficult mid-forceps or vaginal breech delivery and instead performing a caesarean section. Because of the availability of electronic and biochemical monitoring for the foetus before and during labour, it has become easier today to recognise a foetal distress and deliver the baby via abdominal route ^[1].

Lower segment caesarean sections (LSCS) are now commonly performed using spinal anaesthesia as it is simple and quick procedure with fast onset of action providing superior quality of block ^[2].

August Bier introduced spinal anaesthesia into clinical practise in 1898, well before Franz Kuhn's breakthrough in oro-tracheal intubation in 1901 ^[3]. For surgeries involving abdomen and lower extremities, regional techniques are the preferred anaesthetic procedure. The various advantages include reduced surgical stress, avoiding airway handling, reduced intraoperative bleed, lower incidence of postoperative thromboembolic events, early resumption of gastrointestinal function.

Spinal anaesthesia for caesarean section has less risk of systemic toxicity due to local anaesthetic agents, lesser transfer to foetus and is cost effective. An inevitable sequence of spinal anaesthesia is blockade of sympathetic preganglionic efferents causing peripheral venous pooling and hypotension.

In parturients, hypotension is aggravated by compression of the inferior vena cava by gravid uterus ^[4]. Its incidence has been reported as high as 40-70% and affects 90% women ^[5]. Maternal hypotension causes nausea, vomiting and dizziness which leads to maternal distress. It can lead to placental hypoperfusion that can cause adverse neonatal outcomes. Spinal-induced hypotension, if left untreated can have deleterious effects on both the mother and the foetus, which may include maternal cardiovascular collapse and foetal acidosis ^[6].

For reducing the severity of maternal hypotension, many pharmacological and non-pharmacological methods are employed. This include leg end elevation and wrapping, use of inflatable boots, intravascular volume expansion using a fluid 'preload', uterine displacement in parturient and administration of vasopressor drugs. Despite these measures hypotension may still occur ^[5,7].

No single method is adequate or conclusively superior.

Glycopyrrolate, an anticholinergic drug with a quaternary amine structure that limits its ability to cross the blood-brain barrier and placenta and therefore has no effect on the variability of foetal heart rate (FHR) and maternal heart rate (HR). It has chronotropic effect through the antimuscarinic activity ^[8]. By inhibiting the action of acetylcholine through its action on muscarinic receptors, it reduces the volume and acidity of gastric secretions and decreases the secretions of the pharynx, trachea, and bronchi. It also has antispasmodic property. During spinal anaesthesia glycopyrrolate is expected to attenuate hemodynamic changes which makes it a popular choice for obstetric patients. Its safety and lack of serious side effects make it an ideal agent for study in this context ^[9].

Hence, this study had been carried out to evaluate the effect of prophylactic intramuscular

	Group G		Group S		p-value
	Mean	SD	Mean	SD	
Age(years)	24.84	4.74	24.78	3.73	0.944
BMI(Kg/m ²)	24.66	1.41	24.31	2.35	0.369
Duration of surgery(mins)	59.18	7.83	56.82	8.95	0.164

glycopyrrolate on the hypotensive response in pregnant patients undergoing LSCS under spinal anaesthesia.

MATERIAL AND METHOD

After obtaining institutional ethics committee clearance, we conducted this prospective randomized double blinded study on hundred parturients belonging to ASA status I and II, aged between 18-35 years posted for lower segment caesarean section under spinal anaesthesia. They were randomised into two equal groups of 50 patients each. Patients in Group G received intramuscular injection glycopyrrolate 0.2mg (1ml) and patients in Group S received intramuscular injection 0.9% normal saline (1ml) 15 minute prior to subarachnoid block. The time of intramuscular injection was taken as T₀₀ and time of spinal anaesthesia was taken as T₀ the following parameters were observed: PR, SBP, DBP, MAP and SPO₂ were recorded every 2 minutes for the first 10 minutes and then every 5 minutes thereafter. Intraoperatively the following data was recorded:

- Level of block
- Incidence of nausea and vomiting
- Total dose of rescue vasopressors given
- Presence of dry mouth
- Any untoward effect of the drug
- Foetal outcome using APGAR Score

RESULTS:

In this study, the demographic profile of the study subjects, duration of the surgery, level of block achieved, and ASA classification were comparable as shown in Table no 1 and Table no 2.

Table 1: Demographic data

(Group G: Glycopyrrolate, Group S: Saline, SD: Standard Deviation)

Table 2: Comparison of Level of block achieved and ASA Classification between the groups

		Group G(n=50)		Group S(n=50)		p-value	χ^2
		Count	%	Count	%		
Level of Block	T4	9	18	6	12	0.697	0.723
	T5	6	12	6	12		

	T6	35	70	38	76		
ASA	I	36	72	33	66	0.517	0.421
	II	14	28	17	34		

Haemodynamic parameters observed revealed that the average heart rate after 2 minutes was significantly higher in glycopyrrolate group(Fig.1). Intraoperatively the average systolic blood pressure was significantly higher in glycopyrrolate group at intra-operative time intervals 0, 2nd, 4th, 6th and 35th minutes (Fig.2). There was less fall in SBP and DBP in glycopyrrolate group compared to saline group (Fig.3). The average mean arterial pressure was significantly higher in glycopyrrolate group compared to saline group(Fig.4).

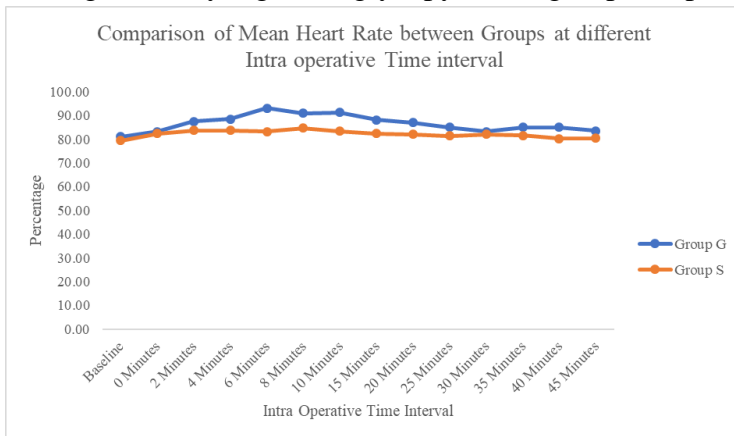


Fig. 1: Comparison of mean heart rate between the groups

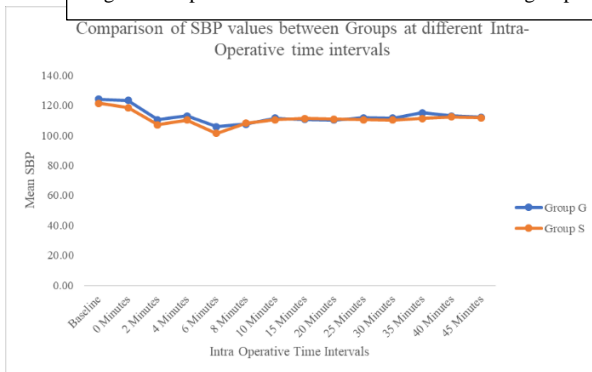


Fig. 2: Comparison of SBP between groups

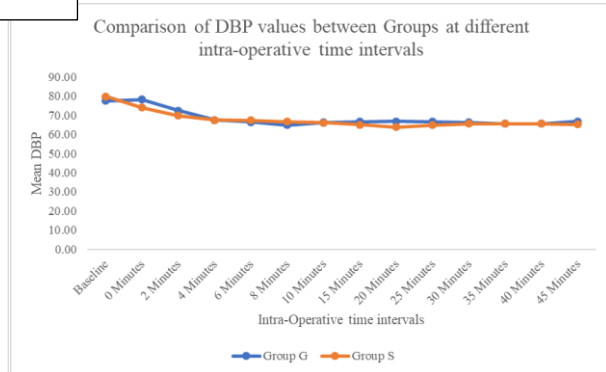


Fig. 3: Comparison of DBP between groups

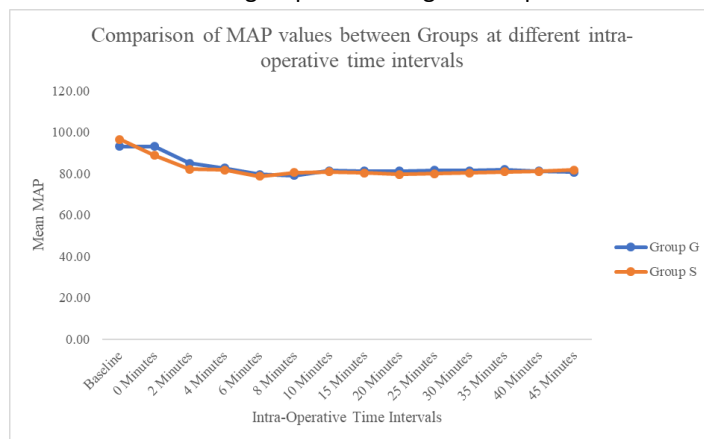


Fig. 4: Comparison of MAP between groups

None of the patients in both groups had any significant respiratory depression (fall in $SPO_2 < 95\%$ or increase in $RR > 20/\text{min}$) needing intervention, at all intervals observed.

Out of 50 patients in Group G, only 3 patients (6%) required vasopressor intraoperatively, while in Group S out of the total 50 patients 9 patients (18%) required rescue vasopressor as shown in table no 3. There were no statistically significant difference in usage of rescue vasopressor between two groups

Table no. 3: Requirement of rescue vasopressor between groups

Rescue Vasopressor	Groups				χ^2 Value	p Value
	Group G		Group S			
	n	%	n	%		
Yes	3	6.0	9	18.0	3.409	0.065
No	47	94.0	41	82.0		
Total	50	100.0	50	100.0		

Out of 50 patients in Group G, 4 patients (8%) had complaints of dryness of mouth and 3 patients (6%) had complaints of nausea and vomiting. While in Group S out of the total 50 patients, 12 patients (24%) had complaints of nausea and vomiting, 5 patients (10%) had episodes of dizziness and 3 patients (6%) had episodes of bradycardia intraoperatively. In Group S the incidence of nausea and vomiting was significantly higher compared to Group G ($p < 0.05$) (Table no 4)

Table no. 4: comparison of side effects between the groups

Complications	Groups				χ^2 Value	p Value
	Group G		Group S			
	N=50	%	N=50	%		
Nausea and Vomiting	3	6.0	12	24.0	5.020	0.025*
Dry Mouth	4	8.0	0	0.0	2.344	0.126
Dizziness	0	0.0	5	10.0	3.368	0.066
Bradycardia	0	0.0	3	6.0	1.375	0.241

We observed that the study drug had no effect on APGAR Score.

DISCUSSION:

Subarachnoid block has become the anaesthetic procedure of choice for caesarean section due to its ease of use and long track record of success. Though spinal anaesthesia has many benefits like fast onset of action, ease of use, and minimal postoperative complications, it has few physiological side effects on the various systems^[2]. The most common side effect following SAB in caesarean delivery is hypotension due to sympatholysis which is seen in up to 85% cases. This is despite the fact that full-term pregnant patients have 40-50% more blood volume than other patients. Hypotension is harmful to both mother and foetus and is better avoided than treated. In presence of post spinal vasodilation, venous return is reduced to the point where cardiac output cannot be increased and is associated with severe hypotension, uteroplacental hypoperfusion, and low APGAR score^[10].

The degree of uteroplacental hypoperfusion is directly proportional to degree of hypotension from baseline value. Spinal-induced hypotension is managed physiologically by increasing venous return, which increases preload and thus restores cardiac output^[5]. Studies have

proven beyond doubt that preloading with colloids are no better than crystalloids in preventing the incidence of hypotension^[11] and have a number of disadvantages, including:

- o Higher cost when compared to crystalloids^[12].
- o Anaphylactic responses^[12]
- o Suppression of the clotting process^[13]

To reduce the incidence of hypotension crystalloids are administered in large quantities (>15ml/kg)^[14]. This can have negative consequences such as:

- o Raised central venous pressure
- o Haemodilution resulting in decreased oxygen-carrying capacity
- o Diuresis due to release of atrial natriuretic peptide lessens the effect of volume load on blood pressure^[15]

Thus, we can draw the conclusion that pre-emptive use of a pharmacologic agent is more effective in preventing hypotension than preloading.

In our study, we have evaluated the effect of prophylactic intramuscular injection of glycopyrrolate in the reduction of incidence and severity of hypotension associated with spinal anaesthesia in pregnant patients.

Total of 100 parturients belonging to ASA I and II with age between 18-35 years posted for lower segment caesarean section under spinal anaesthesia were chosen for our study. Institutional ethics committee approval was obtained, informed and written consent was taken from every case selected for the study, a randomized double-blinded study was conducted with two groups of 50 patients each.

Group G - parturients received an intramuscular injection of 1ml (0.2mg) glycopyrrolate 15 minutes prior to spinal anaesthesia.

Group S - parturients received an intramuscular injection of 1ml 0.9% normal saline 15 minutes prior to spinal anaesthesia.

The time of intramuscular injection was considered as T00 and time of spinal anaesthesia was considered as T0 the following parameters were observed

PR, SBP, DBP, MAP and SPO2 were recorded every 2 minutes for the first 10 minutes and then every 5 minutes till 45 minutes.

Hypotension was treated with intravenous 6mg mephentermine till the arterial blood pressure increases above the threshold value. If bradycardia occurred (less than 50 bpm) without hypotension it was treated with IV atropine 0.6mg.

Other intraoperative parameters observed include: level of block achieved, incidence of nausea and vomiting, total dose of rescue vasopressors used, presence of dry mouth and foetal outcome using APGAR Score.

In our study, the demographic profile of the study subjects, level of block achieved and duration of the surgery were comparable.

Haemodynamic parameters observed revealed that the average heart rate after 2 minutes was significantly higher in Group G throughout the surgery except at 30th minute as compared to Group S. The p-value is < 0.05 for all time interval except 30th minute which is statistically significant. These results were quite similar to study done by Chamchad et al^[16] on the effect of glycopyrrolate in preventing bradycardia after spinal anaesthesia for caesarean section which showed that compared to placebo group glycopyrrolate group had lower incidence of spinal induced bradycardia.

Intraoperatively the average systolic blood pressure was significantly higher in Group G compared to Group S with means 123.24 ± 6.17 , 110.44 ± 6.34 , 113.06 ± 5.58 , 115.16 ± 4.73 at intra-operative time intervals 0, 2nd, 4th, 6th and 35th minutes respectively ($p < 0.05$). Similarly, intraoperatively the average diastolic blood pressure was significantly higher in Group G compared to Group S with means 78.22 ± 5.45 , 72.42 ± 5.26 , 66.56 ± 4.29 at intra-operative time intervals 0, 2nd and 20th minutes respectively ($p < 0.05$). There was less fall in SBP and DBP in glycopyrrolate group compared to saline group. The average mean arterial pressure was significantly higher in glycopyrrolate group compared to saline group. Similar observations were recorded by Ure D et al^[17] and Kamoltip Prasopsuk et al^[18] who concluded that pretreatment with intramuscular glycopyrrolate reduced the incidence of hypotension when compared to the placebo group. But in a study done by Rucklidge et al^[19] it was observed that pretreatment with intramuscular glycopyrrolate prior to SAB does not reduce the incidence of hypotension.

None of the patients in both groups had any significant respiratory depression (fall in $SPO_2 < 95\%$ and increase in $RR > 20/\text{min}$) needing intervention, at all intervals observed.

The incidence of adverse effects was more in saline group compared to glycopyrrolate group (Group G: nausea & vomiting-3, dry mouth 4; Group S: nausea & vomiting-12, dizziness-3, bradycardia-3). Our observations were consistent with a study done by Jain et al^[20] on the effect of glycopyrrolate and ondansetron for preventing nausea and vomiting in caesarean section under spinal anaesthesia and found that glycopyrrolate is an effective substitute for ondansetron for reducing intraoperative and postoperative nausea and vomiting. Similar results were observed in a study done by Hwang J et al^[21] on the effect of prophylactic glycopyrrolate in reducing the hypotensive responses in elderly patients during spinal anaesthesia and concluded that in saline group the incidence of nausea and vomiting was higher than in glycopyrrolate group.

In our study Out of 50 patients in Group G, only 3 patients (6%) required vasopressor intraoperatively, while in Group S out of the total 50 patients 9 patients (18%) required rescue vasopressor. There were no statistically significant difference in usage of rescue vasopressor between two groups. Similar results were observed in a study by Rajesh et al^[22] on the effect of glycopyrrolate on vasopressor requirements for non-elective caesarean section under spinal anaesthesia and found that in emergency caesarean sections performed under spinal anaesthesia, the prophylactic use of glycopyrrolate does not reduce the need for vasopressor for prevention of hypotension.

we found that prophylactic administration of intramuscular glycopyrrolate had no significant effect on the neonatal APGAR score. Our findings were consistent with a study by Biswas et al^[23] on the effect of glycopyrrolate, dexamethasone and metachlopramide in control of post-operative nausea and vomiting after spinal anaesthesia for caesarean delivery were they observed that the neonatal APGAR score between the two groups had no difference. But in another study done by Amatya et al^[24] on effect of glycopyrrolate on nausea, vomiting and neonatal outcome during spinal anaesthesia for elective caesarean section it was found that the neonatal outcome determined by APGAR score was significant statistically in glycopyrrolate group than in normal saline group but was clinically insignificant because both groups had satisfactory APGAR scores.

In this study, we have analysed the effect of prophylactic intramuscular glycopyrrolate in the reduction of frequency and severity of hypotension associated with spinal anaesthesia in parturients. We observed that parturients in glycopyrrolate group had better haemodynamic stability compared with those in saline group. There was less fall in heart rate, systolic blood pressure and diastolic blood pressure in glycopyrrolate group compared to saline group. Mean arterial pressure was significantly higher in glycopyrrolate group. The use of rescue vasopressor was more in the saline group. None of the parturients in either groups had any significant respiratory depression. Parturients belonging to saline group had higher incidence of complications like nausea, vomiting, dizziness, bradycardia. But four patients in the glycopyrrolate group had complaints of dryness of the mouth.

Hence we conclude that the prophylactic use of intramuscular injection of glycopyrrolate provides better haemodynamic stability in parturients posted for caesarean section under spinal anaesthesia.

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