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# COMPARISON OF HEMODYNAMIC STABILITY OF GLYCOPYRROLATE AND ONDANSETRON IN ELECTIVE LSCS UNDER SPINAL ANAESTHESIA

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**Abstract**

***Objective:*** *The purpose of the research is to find out the comparison of hemodynamic stability of glycopyrrolate and ondansetron in elective LSCS under spinal anesthesia.*

***Study Design:*** *Randomized control trial*

***Study Duration:*** *06 months from Nov 2024-Apr 2025*

***Study Place:*** *Anesthesia department of Combined Military Hospital, Kharian*

***Methods:*** *It was a prospective, randomized, and double-blind clinical trial that involved 100 pregnant women who had undergone elective LSCS under spinal anesthesia. The participants were chosen randomly to be treated with either glycopyrrolate (0.2 mg, Group G) or ondansetron (4mg, Group O) as an intravenous drug 5minutes before anesthetizing the spine. Hemodynamic values, hypotension, bradycardia, nausea, vomiting, and vasopressor were monitored. The SPSS 26 was used to analyze data, where p<0.05 was taken to be significant.*

***Results:*** *Among 100 patients undergoing elective LSCS, glycopyrrolate (Group G) had better hemodynamic stability than ondansetron (Group O) with less SBP and MAP changes, higher heart rate, and less hypotension (12% vs 32%) and bradycardia (6% vs 18%). There was low use of ephedrine and atropine in Group G. The safety of both drugs was good towards the mother and the neonate, similar maternal satisfaction and Apgar scores.*

***Conclusion:*** *Prophylactic glycopyrrolate offers superior stability in hemodynamics in case of elective LSCS surgery under spinal anesthesia with a reduction in the incidences of hypotension and bradycardia, and decreased vasopressor.*

## INTRODUCTION

Neuraxial block It is believed that spinal anaesthesia is the most preferred neuraxial technique used in lower segment caesarean section (LSCS) due to its rapidity, successful sensory block, motor block, less maternal risk, and low dose to the newborn as compared to general anaesthesia. Nevertheless, maternal hypotension is a frequent and clinically relevant complication of subarachnoid block and it could result in impaired uteroplacental perfusion, fetal acidosis, maternal nausea, vomiting, and

reduced patient satisfaction. This hypotension is mainly caused by sympathetic blockade below the level of the block which causes vasodilation and decreased systemic vascular resistance due to which is added the aortocaval compression of the gravid state.[1]

Several measures have been explored to reduce hemodynamic instability that is caused by spinal anaesthesia. The classic ones are fluid loading, the administration of vasopressors (phenylephrine or ephedrine), leg compressors, and maneuvers. Nevertheless, the rates of maternal hypotension have been high, which is why the pharmacologic control of the reflexes, which are expressed in the regulation of blood pressure, is of interest. Bezold Jaarisch reflex (BJR) is one of such mechanisms, a cardioinhibitory reflex that happens with the help of serotonin receptors, and that can worsen bradycardia and hypotension in the course of spinal anaesthesia.[2]

One such selective 5 HT3 receptor antagonist that has elicited interest is Ondansetron which is an antiemetic, but which has the potential to reduce the BJR and consequently the ability to stabilise blood pressure and heart rate during spinal anaesthesia. Multiple studies have shown that prophylactic ondansetron can help to prevent an occurrence of spinal induced hypotension and the use of vasopressors, but outcomes are inconsistent between populations and regimens. By contrast, other studies found no significant difference in the ondansetron hypotension rates with placebo, which suggests there is still a need to conduct additional comparative studies.[3]

Glycopyrrolate is an anticholinergic agent that is a synthetic drug that accelerates heart rate by inhibiting the action of the vagal and has been investigated as a premedication to prevent bradycardia and hypotension following spinal surgery. It has a quaternary structure that restricts placental transfer, which is very appealing in obstetric practice. Meta analyses indicate that glycopyrrolate can lower the need of vasopressor and decrease bradycardia, but inconsistent effects are observed on the occurrence of hypotension.[4]

There are few direct comparisons on glycopyrrolate versus ondansetron on the basis of hemodynamic stability in elective LSCS when using spinal anaesthesia due to the significant pharmacologic differences and action mechanisms of these two drugs. This knowledge of their relative efficacy may be relevant to optimised prophylactic measures to improve maternal and fetal outcomes in spinal anaesthesia to perform a caesarean section.

**Methodology:**

The study was a prospective, randomized, double-blind, controlled, clinical trial that was carried out in the Department of Anaesthesiology, CMH Rawalpindi during 06 months between Novemeber 2024 to April 2025. The Institutional Ethics Committee provided ethical clearance and all participants provided written informed consent before enrolment. The principles of the Declaration of Helsinki and Good Clinical Practice guidelines were followed in the study. The sample consisted of 100 expectant mothers who were to have elective lower segment cesarean section (LSCS) done under spinal anaesthetic operation.

**Inclusion criteria:**

1. Age 18–40 years
2. American society of anesthesiologists (asa) physical status iii-ii.
3. Singleton pregnancy
4. Gestational age ≥37 weeks.

**Exclusion criteria:**

1. Preexisting cardiovascular, hypertension, diabetes mellitus, coagulopathy.
2. Hypersensitivity to study drugs known.
3. Multiple pregnancies
4. Fetal anomalies
5. Spinal anaesthesia contraindications.

A randomization table of 50 was created using a computer and randomly assigned the study participants to two equal groups (n=50 each). Group G was given intravenous glycopyrrolate (0.2 mg) 5 minutes prior to spinal anaesthesia and Group O was given intravenous ondansetron (4mg) 5 minutes prior to spinal anaesthesia. The patients as well as the anesthesiologists administering drugs and recording data were blinded on group assignment. The preparation of study drugs was done by a nurse that was not directly involved in patient management. Patients were all fasted (at least 8

hours) and received normal preoperative examination. Vital parameters such as the heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and oxygen saturation (SpO 2) were measured. Intravenous access was made using an 18G cannula, preloading was accomplished using Ringer's lactate 10 mL/kg in 1520 minutes. Spainal anaesthesia under strict aseptic conditions using 25G Quincke spinal needle was done in sitting position at L3, L4 or L4,L5 at the level of interspace. Hyperbaric bupivacaine 0.5 (10-12mg) was injected intrathecally. This was followed by immediate placement of the patients in supine position with a 15 degree left lateral tilt to avoid aortocaval compression. The parameters measured were hemodynamic parameters (HR, SBP, DBP, MAP, SpO 2) at baseline, immediately after spinal injection, and 2, 5, 10, 15, 20, 30, 45 and 60 minutes after spinal anaesthesia. Hypotension was considered as a decrease in SBP above 20 percent of baseline or under 90 mmHg, and it was treated using intravenous ephedrine 510mg on-bolus. Incremental intravenous atropine 0.3-0.6mg was administered to correct Bradycardia (HR less than 50 bpm). The occurrence of nausea, vomiting, and adverse effects were also reported. The main outcome was the hemodynamic stability measured in the SBP, DBP, MAP, and HR modifications. Secondary outcomes were incidence of hypotension and bradycardia, nausea, vomiting and total vasopressor requirement.

The analysis of data was done using SPSS 26. Testing was done using the Student t-test of means using the standard deviation to compare continuous variables represented as mean. Chi-square or Fisher exact test was used to analyse categorical variables. The p-value of less than 0.05 was regarded as statistically significant.

**Results**

One hundred patients were involved in the research and were randomly allocated to Group G (glycopyrrolate, n=50) and Group O (ondansetron, n=50). The two groups were similar in demographic factors such as age, weight, height, body mass index (BMI) and gestational age (p>0.05), which provided baseline homogeneity. There was no difference in the ASA physical status distribution between the two groups with the majority of them as ASA I.

There was a statistically similar mean between the baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) in both groups (p>0.05). After spinal anaesthesia, the reduction in SBP and MAP was experienced in both groups but the degree of fall was vastly different in magnitude. HR in Group G rose a little above baseline (85 ± 8 bpm) to 92 ± 10 bpm at 5 minutes and was indicative of the chronotropic effect of glycopyrrolate. Group O, on the other hand, exhibited the least HR change (84 plus 9 bpm to 86 plus 10 bpm, p less than 0.05).

Group O showed a stronger fall in SBP and MAP within the initial 10 minutes after administration of the spinal injection (SBP: 118 means 96; MAP: 85 means 70) as compared to Group G (SBP: 117 means 104; MAP: 84 means 76) (p<0.05). Hemodynamic parameters got steady after 20 minutes in both groups though Group G had some higher SBP and MAP values all over intraoperative time. Hypotension was found to be much less in Group G (12% vs. 32% in Group O) and bradycardia in 6% of Group G vs. 18% of Group O.

The total intake of ephedrine was much lesser in Group G (mean 6 + 4mg) than in Group O (mean 14 + 6mg, p=0.001), which meant that the hemodynamic stability was better with the prophylaxis of glycopyrrolate. The use of atropine was needed in 3 patients in Group G and 9 patients in Group O to control the bradycardia (p=0.02).

Ondansetron showed a prophylactic antiemetic effect which had less cases of nausea and vomiting (nausea: 6% vs 14; vomiting: 4% vs 10) but not statistically significant (p>0.05). The scores concerning maternal satisfaction (9-point Likert scale) did not differ between the groups (Group G: 8.6) and (Group O): 8.4), (p=0.21).

The 1 and 5 minutes neonatal Apgar scores were not different between the two groups, and there was no indication that the drug had an adverse effect on the infants. Group G and Group O had a mean Apgar of 8.7 ± 0.4 and 8.6 ± 0.5 at 1-minute and 5-minutes respectively (p>0.05).

All in all, glycopyrrolate was associated with better blood circulation stability in spinal anaesthesia in elective LSCS and fewer cases of hypotension,

bradycardia, and vasopressor usage. Although effective as an antiemetic, Ondansetron had less impact on maternal hemodynamics. Neither of the drugs was unsafe, and there were no severe maternal or neonatal adverse outcomes.

**Table 1.1: Hemodynamic Changes After Spinal Anaesthesia**

| Parameter | Group G | Group O |
|---|---|---|
| Baseline HR (bpm) | 85 ± 8 | 84 ± 9 |
| HR at 5 min (bpm) | 92 ± 10 | 86 ± 10 |
| Baseline SBP (mmHg) | 117 | 118 |
| SBP at 10 min (mmHg) | 104 | 96 |
| Baseline MAP (mmHg) | 84 | 85 |
| MAP at 10 min (mmHg) | 76 | 70 |
| Hypotension (%) | 12% | 32% |
| Bradycardia (%) | 6% | 18% |

**Table 1.2: Vasopressor and Atropine Requirement**

| Parameter | Group G | Group O |
|---|---|---|
| Ephedrine (mg, mean ± SD) | 6 ± 4 | 14 ± 6 |
| Atropine (patients requiring) | 3 | 9 |

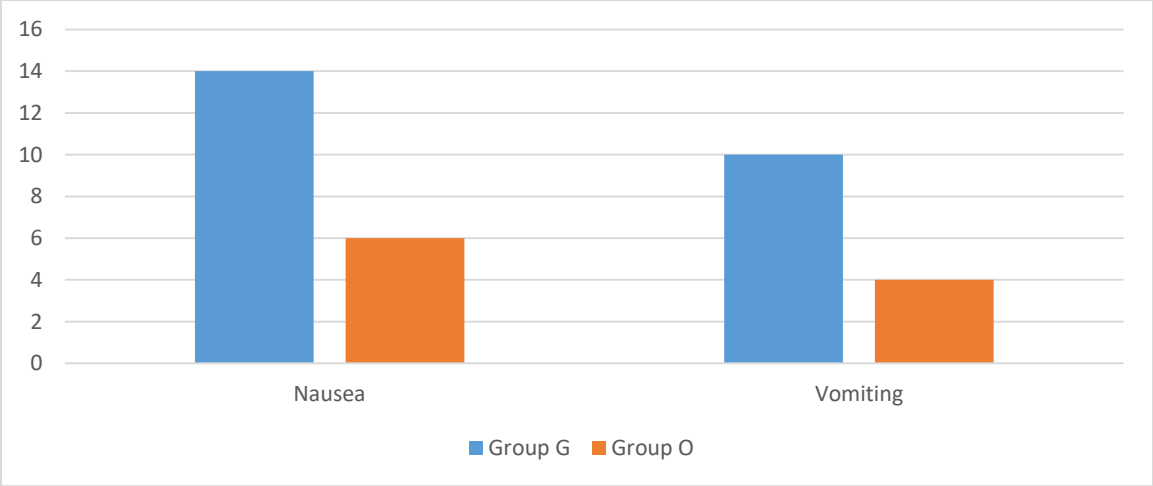
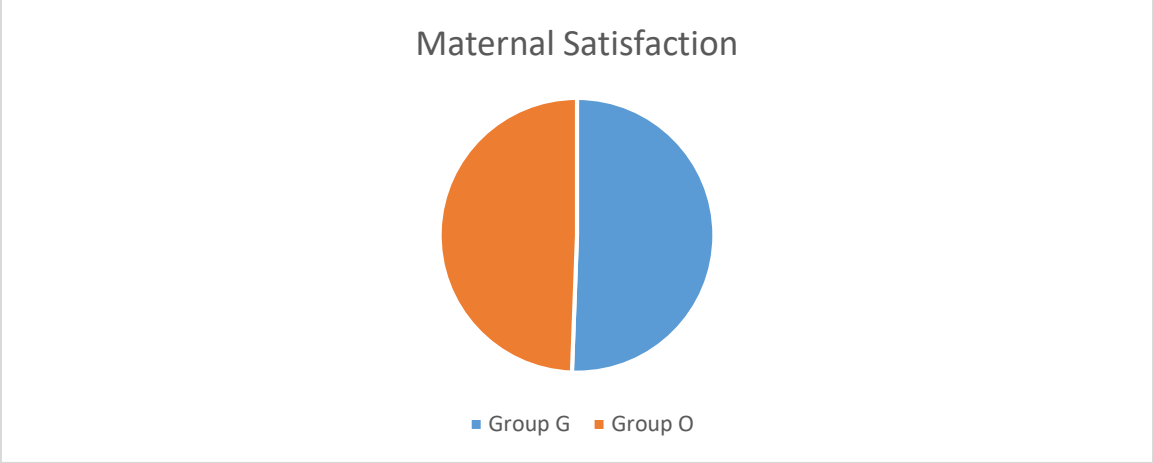



**Chart 1.3: Antiemetic Effects between two groups**




**Pie chart 1.4: Maternal Satisfaction comparison between groups**

**Table 1.5: Neonatal Outcomes (Apgar Scores) between groups**

| Time | Group G | Group O |
|---|---|---|
| 1 min | 8.7 ± 0.4 | 8.6 ± 0.5 |
| 5 min | 8.7 ± 0.4 | 8.6 ± 0.5 |

**Discussion:**

Spinal anesthesia has become common in elective lower segment cesarean section (LSCS) because it has a quick onset and a marked sensory and motor block. It is however frequently linked with maternal hypotension and bradycardia which can interfere with maternal and fetal safety. The objective of the current research was to evaluate the hemodynamic stability associated with the use of prophylactic glycopyrrolate and ondansetron as a part of the spinal anesthesia in the elective LSCS.[5]

We selected two groups consisting of 100 patients each (Group G (glycopyrrolate, n=50) and Group O (ondansetron, n=50) and assigned them at random to each of the groups. The baseline demographics, age, weight, height, body mass index (BMI), gestational age, and ASA physical status ($p>0.05$) were similar in both groups, which resulted in the homogeneity of the baseline.[6]

After the spinal anesthesia, systolic blood pressure (SBP) was reduced in both groups and mean arterial pressure (MAP) was reduced. Group G, however, proved to be more hemodynamically stable with a smaller decrease in SBP (117 to 104 mmHg) and MAP (84 to 76 mmHg) than Group O (SBP: 118 to 96 mmHg and MAP: 85 to 70 mmHg, $p<0.05$). Group G had a slight increase in heart rate (HR) at 5 minutes (85 ± 8 bpm to 92 ± 10 bpm) which is the anticipated chronotropic effect of glycopyrrolate, but there was no significant change in this variable in Group O (84 ± 9 bpm to 86 ± 10 bpm, $p<0.05$). Moreover, Group G (12% and 6%, respectively) had less hypotension and bradycardia as compared to Group O (32% and 18%).[7]

The superiority of glycopyrrolate in vasoactive support was further demonstrated by the poor hemodynamic profile. The average dose of ephedrine needed in Group G was much less than Group O (6 ± 4mg vs 14 ± 6mg, $p=0.001$), and there were fewer patients who needed atropine administration (3 vs 9, $p=0.02$). The present results highlight the effectiveness of glycopyrrolate in counteracting the hypotensive and bradycardic impact of the effects of spinal anesthesia in cesarean section.[8]

Besides its slight effect on the hemodynamics, Ondansetron also showed a small prophylactic antiemetic effect. Group O had fewer cases of nausea and vomiting (Group O vs. Group O (nausea: 6 vs. 14; vomiting: 4 vs. 10) but this was not found to be statistically significant ($p>0.05$). The level of maternal satisfaction (measured on a 9-point Likert scale) did not differ between the groups (Group G: 8.6, Group

O: 8.4; p=0.21), which is an indication of the good tolerability of both drugs by the maternal side.[9]

Notably, there was no significant difference in neonatal outcome in the two groups with no variation between 1- and 5 minutes Apgar scores differing significantly (Group G: 8.7 ± 0.4; Group O: 8.6 ± 0.5, p>0.05), which implies no negative impact of the two drugs on the babies.

These results are in line with other past studies that prove that glycopyrrolate is effective in ensuring hemodynamic stability of the mother by avoiding hypotension and bradycardia caused by spinal anesthesia, without any adverse effects on the fetus. Although ondansetron is a good antiemetic, it does not offer much protection against the ondansetron effects on hemodynamic changes during spinal anesthesia. The findings also substantiate the prophylactic application of glycopyrrolate in elective LSCS to minimize the need of vasopressors and anticholinergics hence enhancing the safety and stability in intraoperative.[10,11]

This time around we attempted to investigate the relative effectiveness of 5-HT3 selective antagonists ondansetron and glycopyrrolate as anticholinergic agent with chronotropic effect when applied in prophylaxis to counter the effects of spinal anesthesia-induced hemodynamic instability in elective LSCS.

We were able to find that prophylactic glycopyrrolate was correlated with better hemodynamic stability in comparison to ondansetron. The fall in systolic blood pressure (SBP) and mean arterial pressure (MAP) when using spinal anesthesia were lower in group G-which is also consistent with the tendency to maintain vascular tone and heart output better. Namely, Group G had 104 mmHg and 76 mmHg of SBP and MAP at 10 minutes, respectively, versus 96 mmHg and 70 mmHg of Group O (p<0.05). Also, after spinal block, the heart rate in Group G also showed a slight rise (85±8 to 92±10 bpm), which supports the chronotropic action of glycopyrrolate. In contrast, Group O showed little variations in its heart rate, which indicated that ondansetron did not have a direct effect on cardiac chronotropy (p<0.05).[12]

Such findings are consistent with the prior studies that postulated that anticholinergic agents like glycopyrrolate have the potential to reduce bradycardic effect of spinal anesthesia through inhibition of parasympathetic response. When hyoscine butyl bromide, an anticholinergically active drug, which has the potential to stabilize heart rate during spinal anesthesia, was used prophylactically in a randomized trial comparing hyoscine butyl bromide and placebo, the rates of bradycardia were significantly lower in the hyoscine butyl bromide group, showing that vagal activity is a viable method of stabilizing heart rates during spinal anesthesia.[13]

Although certain previous studies have provided contradictory findings on the effects of glycopyrrolate on the occurrence of hypotension, numerous larger studies have shown that it has the capacity to decrease vasopressor demand although there is no significant alteration in the incidence of hypotension. This is consistent with our observation that the prophylactic glycopyrrolate group necessitated significantly less ephedrine (6±4 mg vs. 14±6mg, p=0.001) and atropine was also administered significantly less (3 vs. 9, p=0.02) suggesting that hemodynamic control was generally better in the glycopyrrolate group.[14]

In the case of ondansetron its described effect of reducing hypotension induced by spinal anesthesia, is associated with the 5-HT3 receptor inhibiting BezoldJarisch reflex which ought to inhibit bradycardia and vasopressor response caused by cardiac mechanoreceptors. Similar results have been obtained in non-obstetric surgery, which found ondansetron prophylaxis to reduce the incidence of hypotension and Vasopressor use significantly over placebo, indicating a protective effect on spinal-induced changes in hemodynamics. but other researchers have found ondansetrom to have only a protective effect on the changes in blood pressure without any significant effect on the overall incidence of hypotension. These contradictions could be due to differences in sample size, dose, population differences, or interactions between ondansetrom and fluid preloading.[15]

Group O in our study did exhibit a higher decrease in SBP and MAP than Group G, and it would be reasonable to conclude that ondansetron alone may not provide effective hemodynamic protection in the obstetric environment. However, ondansetron had a tendency towards few cases of nausea and vomiting (nausea 6% vs. 14; vomiting 4% vs. 10), but this was

not statistically significant ( p>0.05). This is consistent with the known action of ondansetron as an antiemetic and confirms clinical experience and literature that showed it reduced post-spinal nausea and vomiting. The 2022 review also identified the benefits of ondansetron in the prevention of hypotension, bradycardia, and shivering and concluded that it has a good safety ratios when preventively used during cesarean sections.[16]

A very crucial factor in obstetric anesthesia is that of safety of both the mother and the baby. Our cohort did not find any significant differences in neonatal Apgar score at 1 and 5 minutes between the two groups (both approximately 8.6 to 8.7, p>0.05), indicating that none of the two drugs had negative effects on immediate neonatal outcomes. This observation is consistent with general clinical evidence suggesting that both glycopyrrolate and ondansetron are overall safe during pregnancy with no significant incidence of neonatal depression or other significant congenital malformations in the literature of large populations.[17,18]

The similarity in maternal satisfaction between the intervention groups (Likert scores of 8.6 vs. 8.4, p=0.21) suggests that in spite of the statistically significant differences in the hemodynamic parameters, there was a comparable level of maternal satisfaction in both groups with the respective perioperative care. The findings point to the fact that even over and above statistical significance, clinical relevance and patient-centered outcomes are also the key to the evaluation of pharmacologic interventions in obstetric anesthesia.

**Limitation of study:**

its single-center design and relatively modest sample size, which may limit the external validity of the findings. Nevertheless, the current data provide valuable insights into the comparative hemodynamic effects of glycopyrrolate and ondansetron during spinal anesthesia for elective cesarean section and underscore the importance of individualized patient management. To get more better results, a multi center trial and with increase number of sample population is required.

**Conclusion**:

Prophylactic glycopyrrolate seems to offer better hemodynamic stability than ondansetron in elective LSCS during the use of spinal anesthesia with fewer incidences of severe hypotension and bradycardia and less vasopressor demand. Ondansetron is still an effective antiemetic with a potential smaller impact on hemodynamics but has lesser efficacies as a primary agent in the prevention of the changes in circulation induced by spinal anesthesia. The two drugs showed fair maternal and neonatal safety profile.

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