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Original Article

# Comparison of Phenylephrine Infusion Versus Boluses for Management of Blood Pressure in Elective Caesarean Section

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## ABSTRACT

***Objective:*** To compare the efficacy of intravenous phenylephrine infusion versus boluses for blood pressure management in elective caesarean sections.

***Study Design***: Quasi-experimental study.

***Place and Duration of Study***: Anaesthesia Department, Combined Military Hospital, Rawalpindi Pakistan, from Feb to Jul 2022.

***Methodology:*** Three hundred ninety patients requiring elective caesarean section were divided into an Infusion Group (n=195) and a Bolus Group (n=195). The Infusion Group received phenylephrine with 100 mcg/ml titration immediately after spinal anaesthesia as per weight and height at a 1 ml/minute rate and continued for 5 minutes. Infusion stopped if MAP at 5 minutes was above baseline and restarted if dropped below baseline in subsequent readings. In the case of bradycardia, 600mcg of Glycopyrrolate was administered. Parameters recorded at 1, 5, 10 and 15-minute intervals. In the bolus group, total numbers of 100mcg boluses at the end of fifteen minutes were recorded. Protocol for bradycardia and data record intervals was the same. The primary variables were mean arterial pressure (MAP), heart rate(HR), the total dose of phenylephrine used, and nausea and vomiting.

***Results***: Primary outcome variables showed consistent improvement in maintaining MAP in the Infusion Group versus the Bolus Group ($p$<0.05). A similar trend was seen with heart rate between both groups ($p$<0.05). However, the infusion group had an average fall in heart rate compared to the bolus group at all-time intervals.

***Conclusion***: Phenylephrine infusion offers better hemodynamic stability, requiring less ephedrine support than when given in boluses.

**Key Words:** Blood pressure, Bolus, infusion, Caesarean section, Phenylephrine.

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## INTRODUCTION

Caesarean section delivery remains one of the most common surgical modalities for the anaesthesiologist. With the incidence of caesarean deliveries on the rise worldwide,[1] the prevalence has increased to 22% in expecting mothers globally.[2] Spinal anaesthesia remains the modality of choice for delivery in expecting mothers, and complications and side effects of the procedure need to be addressed for good patient care.[3]

Hypotension remains one of the major side effects of spinal anaesthesia after pain, followed by bradycardia.[4,5] This calls into question the safety of the mother and the baby once administered. Various methods have been proposed to decrease the incidence of hypotension, including fluid pre-load,[6] low-dose spinal, blunting the Bezold-Jarisch reflex and vasopressor support. While fluid pre-load and low-dose spinal tend to improve the hemodynamic profile, patients still develop hypotension during the first 15 minutes of spinal anaesthesia. This requires the use of vasopressor agents as the next rescue procedure.[7,8]

Vasopressor agents have found their place in the treatment of spinal-induced hypotension in recent years when used both prophylactically as well as per requirement. Among the most used agents, phenylephrine is preferred as a first-line agent.[9] However, its role in maintaining a hemodynamic profile and spinal-induced hypotension needs to be studied when using it as a continuous infusion versus a bolus agent. While sufficient literature is available when comparing its effects in addressing the baroreceptor reflex and maintenance of cardiac output, further studies are required to see whether it offers a stable hemodynamic profile with regard to mean arterial pressure (MAP), heart rate (HR), incidence of nausea and vomiting when used as a continuous infusion versus as a bolus regimen.[10]

This study aims to compare the efficacy of intravenous phenylephrine infusion versus intravenous phenylephrine boluses for managing blood pressure in

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elective caesarean sections, with any added benefit seen in the hemodynamic profile of the patients.

## METHODOLOGY

The quasi-experimental study was conducted at the Department of Anaesthesiology, Combined Military Hospital, Rawalpindi Pakistan, from January to December 2021, after IERB approval. The WHO sample size calculator was used to sample size estimation, keeping the population proportion of spinal induced hypotension during caesarean delivery at 50%.[11]

**Inclusion Criteria:** Patients of either gender, aged 18-30 years with a weight between 50-90 kg presenting for scheduled elective caesarean delivery under spinal anaesthesia, were included.

**Exclusion Criteria**: Patients unwilling to spinal anaesthesia, known cases of hypertension or pregnancy-induced hypertension (PIH), diabetes (excluding subjects with gestational diabetes), patients with a known cardiac disease, allergy to phenylephrine or ephedrine, or contraindication to the administration of spinal anaesthesia were excluded.

The patients were divided into the Infusion Group and the Bolus Group. This was a double-masked study, and once the patients were divided into two groups, the anaesthetist on duty in the operating room, unaware of the study protocol, received sealed envelopes containing instructions on how and when to administer Phenylephrine in both groups (Figure).

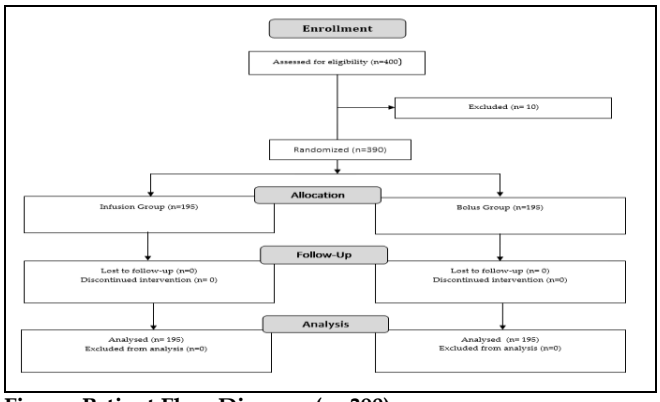


**Figure: Patient Flow Diagram (n=390)**

Both groups received 500 ml of normal saline in the patient holding bay 15 minutes before being shifted to the operating room. Standard monitoring, including non-invasive blood pressure, heart rate, capnography and ECG, was attached to participants in both groups. Bradycardia was defined as a heart rate of <60 beats per minute and hypotension as MAP <50 mm Hg.[12,13]

The attending anaesthetist in the infusion group received a 50 ml infusion syringe with 100 mcg/ml phenylephrine titration. The infusion was started as soon as the patient received spinal anaesthesia based on weight and height at a rate of 1 ml/minute and was continued for the next 5 minutes. If the MAP at 5 minutes was above the baseline, the infusion was stopped, and the dose administered was recorded. Mean arterial pressure was calculated after every minute for fifteen minutes, and the infusion was started if the MAP drooped below the baseline. In the case of bradycardia, 600 mcg of Glycopyrrolate was administered and repeated if necessary. Parameters were recorded for fifteen minutes at 1, 5, 10 and 15-minute intervals after spinal anaesthesia and the total dose of phenylephrine was documented.

The Bolus Group was prepped according to the same protocol but received a bolus dose of 100 mcg of phenylephrine instead of a continuous infusion. The total number of boluses needed at the end of the fifteen-minute period was recorded. The protocol for bradycardia was the same in the group as well, and the data documented followed the same time intervals.

Statistical Package for Social Sciences (SPSS) version 25.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Paired sample t-test was applied to explore the inferential statistics. The *p*-value of ≤0.05 was considered statistically significant.

## RESULTS

Three hundred ninety patients were studied and divided into the Infusion Group (n=195) and Bolus Group (n=195). Both groups were comparable in age. The mean weight in the Infusion Group was 74.10±9.11 kg, with the Bolus Group having a mean weight of 75.55±9.50 kg (Table-I).

When the primary outcome variables were seen, it was observed that there was a consistent improvement in maintaining the MAP stability in the Infusion Group versus the Bolus Group ($p$<0.0001 at 1min, $p$<0.030 at 5 min, $p$<0.0001 at 10 min, $p$<0.0001 at 15min) (Table-II). A similar trend was seen while observing the heart rate between both groups. However, patients in the Infusion Group had an average fall in heart rate than in the Bolus Group at all

time intervals of data collection ($p$<0.001 at 1 min, $p$<0.003 at 5 min, $p$<0.002 at 10 min, $p$<0.212 at 15 min) (Table-III). Other variables measured showed that the total dose of phenylephrine used in the Infusion Group was significantly higher owing to continuous infusion compared to the bolus group. The mean dose used in the Infusion Group was 1433.34±41.02 mcg versus 520.51±68.03 mcg in the Bolus Group. However, the use of ephedrine was considerably less in patients in the Infusion Group: 28(14.4%) patients versus 56(28.7%) patients in the Bolus Group. The frequency of nausea and vomiting in both groups was comparable. The frequency was 52(26.7%) patients in the infusion group versus 60(30.8%) patients in the Bolus Group.

**Table-I Demographic Variables (n=390)**

| Variables | Infusion Group (n=195) | Bolus Group (n=195) |
|---|---|---|
| Age (years) Mean±SD | 24.20±2.21 | 24.36±2.27 |
| Weight (kg) Mean±SD | 74.10±9.11 | 75.55±9.50 |

**Table-II Mean Arterial Pressure and Heart Rate Readings in Both Groups (n=390)**

| Variables | Infusion Group (n=195) | Bolus Group (n=195) | *P*-Value |
|---|---|---|---|
| **Mean Arterial Pressure (MAP) mmHg** | | | |
| MAP AT 1 min | 61.89±6.18 | 58.33±7.48 | <0.001 |
| MAP AT 5 min | 63.04±6.50 | 62.44±6.82 | <0.030 |
| MAP AT 10 min | 64.21±4.44 | 63.26±5.01 | <0.001 |
| MAP AT 15 min | 64.04±4.64 | 62.07±5.89 | <0.001 |
| **Heart Rate (HR) bpm** | | | |
| HR at 1 min | 78.61±6.74 | 77.89±6.61 | <0.001 |
| HR at 5 min | 67.89±9.31 | 69.21±10.11 | <0.003 |
| HR AT 10 min | 64.77±8.48 | 65.79±8.68 | <0.002 |
| HR AT 15 min | 66.85±8.79 | 66.98±8.88 | 0.212 |

**Table-III Total Drugs Requirement and Frequency of Nausea and Vomiting (n=390)**

| Variables | Infusion Group (n=195) | Bolus Group (n=195) |
|---|---|---|
| Total Dose Of Phenylephrine Used (mcg) | 1433.34±41.02 | 520.51±68.03 |
| Ephedrine Used In Patients n(%) | 28(14.4%) | 56(28.7%) |
| Nausea and Vomiting n(%) | 52(26.7%) | 60(30.8%) |

## DISCUSSION

The study was carried out at a tertiary care hospital which receives a major burden of obstetric patients from the city and throughout the country. The main aim to assess whether one modality was superior to the other in the case of vasopressor support was the fact that a lot of obstetric patients land in an emergency in the obstetric emergency centre and are poorly optimized with respect to fluid pre-load with prolonged NPO (nil per oral). Therefore, these patients inadvertently require vasopressor support, which calls into question the best modality that provides the best hemodynamic stability.

A study by George *et al*. showed that phenylephrine infusion is better at maintaining good hemodynamic stability, especially the MAP, compared with other vasopressors, including nor-epinephrine and bolus phenylephrine.[14] The same was seen in the study carried out at our setup. In our studies, however, we saw a steady but slight decline in heart rate that was well within range. This is attributed to the activation of baroreceptor reflex[15] with alpha receptor agonism alone.[16]

When observing the other parameters in the study, the total dose of Phenylephrine in the Infusion Group was approximately double the dose used in the Bolus Group. This may be attributable to tachyphylaxis being observed more in the infusion form, but more studies are needed to confirm this difference.[17] When observing the required dose of ephedrine, the Bolus Group patients needed more doses than the Infusion Group. This is due to better hemodynamic stability provided by the infusion form in contrast to the bolus doses. It was also seen that since the infusion was started as soon as the block was done, it resulted in better MAP control and lesser requirement. A study carried out by AM Sharkey *et al*. also confirmed this. However, they also concluded that the dose can be further reduced if neither estrogen nor epinephrine is used. 18 When talking about the nausea and vomiting, the frequency was comparable in both groups, with no difference in the frequency of nausea. This was also comparable with international studies.[14] It is recommended that phenylephrine be used in the infusion form, especially in poorly optimized patients, when vasopressor support is required.

## LIMITATION OF STUDY

The study was limited to a single centre. A multicenter study would cover a wider demographic area and produce more confirmative results.

## CONCLUSION

We conclude that phenylephrine infusion offers better hemodynamic stability, requiring less ephedrine support than in the bolus form.

**Conflict of Interest:** None.

**Authors' Contribution**

Following authors have made substantial contributions to the manuscript as under:

MMR & SQAS: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

MSS & WT: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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