The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 3, 2025

COMPARISON BETWEEN INTRAVENOUS PHENYLEPHRINE INFUSION AND FLUID CO-ADMINISTRATION VERSUS FLUID PRE-LOADING ONLY ON SPINAL INDUCED HYPOTENSION

Dr Smiya Qayyum[*1], Dr Sami Wahid[2], Dr Sehrish Jabeen[3], Dr Muhammad Imran[4], Dr Tehreem Tahir[5], Dr Iqra Iqbal[6]

*[*1]PGR Anesthesia, CMH Kharian*
[2]Consultant Anesthesiologist CMH Kharian
[3,4] PGR Anesthesia, CMH Kharian
[5,6] House Officers, CMH Lahore

DOI: https://doi.org/10.5281/zenodo.18029977

Keywords
Fluid, hypotension, phenylephrine, pre-loading, co-loading, spinal, caesarian

Article History
Received: 01 January 2025
Accepted: 21 February 2025
Published: 18 March 2025

Corresponding Author: *
Dr Smiya Qayyum

Abstract

Objective: *To compare the incidence of hypotension seen after spinal anesthesia during lower section caesarian section (LSCS) when pre-loading with intravenous infusion of phenylephrine with fluid co-administration versus pre-loading with fluid co-administration alone*

Study Design: *Quasi-experimental study*

Place and Duration of Study: *Anesthesia department of Combined Military Hospital, Kharian from June 2024-November 2024.*

Methodology: *The patients were divided into Group P (n=150), to receive IV Phenylephrine with fluid co-administration and Group F (n=150) receiving fluid pre-loading only. Primary variable studied was the incidence of hypotension between both groups and the total dose of IV Phenylephrine used as rescue analgesia. Secondary variables measured were mean values for arterial pressure and heart rate between both groups.*

Results: *Incidence of hypotension was seen in 42 (28%) patients immediately after spinal in Group P versus 76 (50.7%) patients in Group F (p<0.001). Total mean dose used in both groups was 346.19±27.29 mcg in Group P versus 444.33±90.40 mcg in Group F (p<0.001). The highest mean value for arterial pressure was 88.01±1.97 mm Hg in Group P versus 87.86±1.13 in Group F (p=0.432) while the lowest mean arterial pressure values were 70.15±4.78 mm Hg in Group P versus 61.84±5.23 mm Hg in Group F (p<0.001).*

Conclusion: *We conclude that IV Phenylephrine co-administration as an infusion with fluid results in better hemodynamic stability, less use of rescue vasopressor and decreased incidence of post-spinal hypotension*

INTRODUCTION

Spinal anesthesia is the predominant form of regional anesthesia given worldwide. It offers various advantages over general anesthesia with less complications[1]. Its superior in providing adequate analgesia, decreasing the need for added pain control, results in less blood loss in surgeries below the diaphragm and provides a superior degree of muscle relaxation[2]. Even with all its merits, it has its

fair share of de-merits. The commonest complication encountered with the procedure is the incidence of hypotension and bradycardia[3]. The incidence of hypotension after spinal anesthesia during LSCS is around 64% in female patients[4]. This is a considerable number and the loss of fluid and blood (approx. 1000 ml) during the delivery process requires good control on blood pressure to avoid any complications both for the mother and the baby[5].

Standard methods to prepare a patient for an elective Caesarian section include pre-loading with crystalloid 30 minutes before the procedure to prevent volume depletion and maintain the intravascular fluid compartment after spinal anesthesia administration[6]. Recent literature suggests the use of prophylactic administration of phenylephrine added to fluid co-administration given at the time of spinal anesthesia administration to prevent the incidence of hypotension[7]. This is a safe, cost-effective and easy method to standardize in our resource limited settings if the results are statistically significant. Phenylephrine is a selective alpha-1 agonist and causes vasoconstriction of both venules and arterioles resulting in increasing the mean arterial pressure[8]. The resultant baroreceptor inhibition and firing results in reflex bradycardia and we want to see whether the incidence of bradycardia and prevention of hypertension are profound enough to recommend its use as a standard procedure in our obstetric setups[9].

Our study aims to compare the incidence of hypotension seen after spinal anesthesia during lower section caesarian section (LSCS) when pre-loading with intravenous infusion of phenylephrine with fluid co-administration versus pre-loading with fluid co-administration alone.

METHODOLOGY:

This quasi experimental study was carried out at the Department of Anesthesiology, Combined Military Hospital Kharian from June 2024 to November 2024 after approval form the ethical review board vide letter no. Minimum sample size to be taken was calculated using the WHO calculator keeping the confidence interval at 95%, power of test at 80% with the anticipated decrease in the incidence of hypotension with phenylephrine co-administration with fluid being 24% from 39% when using fluid pre-loading alone[10]. Minimum sample size comparing the two proportions came out to be 147 patients for one group. We included 150 patients in each group making the final study sample of 300 patients divided into Group P (n=150) and Group F (n=150) according to the inclusion criteria. Patients were added to one of the two groups using non-probability consecutive sampling via lottery method.

Inclusion criteria included all ASA-II, female patients presenting for elective Lower Segment Caesarian Section (LSCS) under spinal anesthesia.

Exclusion criteria included patients with advanced cardiac or respiratory disease, patchy or failed spinal requiring general anesthesia, patients allergic to bupivacaine or phenylephrine, patients with history of gestational diabetes and/or pregnancy induced hypertension, patients with abnormal placentation with anticipated massive blood loss and patients unwilling to be included in the study.

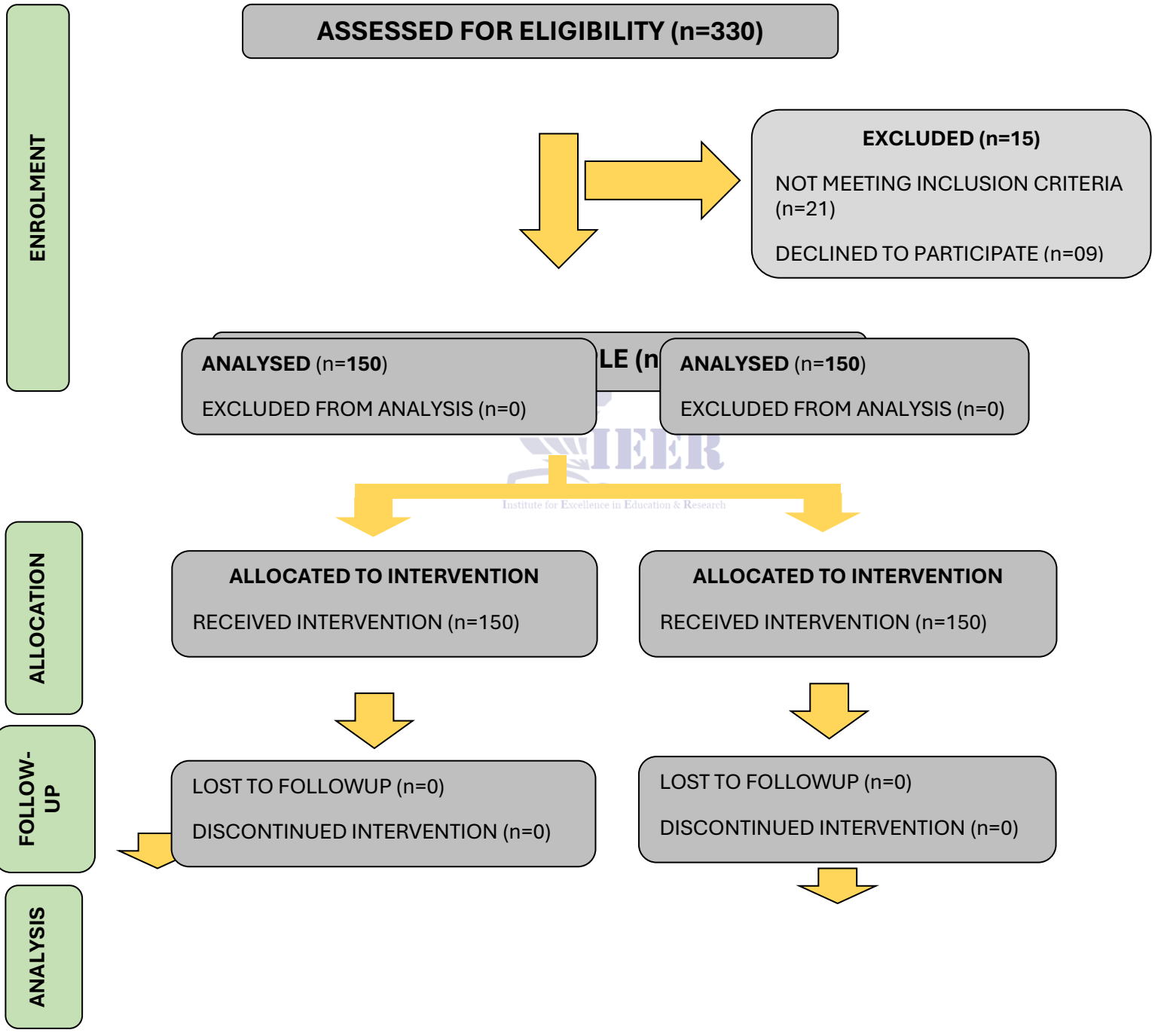
The patients were divided into Group P (n=150), to receive IV Phenylephrine with fluid co-administration and Group F (n=150) receiving fluid pre-loading only. Patients in both groups were thoroughly counselled regarding the study protocol and its possible complications and a written informed high risk consent was taken. Patients were taken to the operating room and standard monitoring was attached and initial values of MAP (mean arterial pressure) and heart rate were taken. Standard 18 G Braun IV cannula was passed in all patients in the right brachial vein.

Patients in Group F received pre-loading with IV Ringer lactate at 15 ml/kg (maximum 1000 ml) in the recovery room before shifting to the operating room. Patients in Group P received no fluid pre-loading, and at the time of spinal administration, co-loading with IV Ringer lactate 1000 ml with IV Phenylephrine 5000 mcg added to the fluid was started at full speed through an 18 G cannula inserted in the brachial vein. Maintenance fluid in both groups was started as IV Ringer lactate at a rate of 1.5 ml/kg/hr. Spinal anesthesia was administered using a 25 G pencil point needle in all patients in the L3-L4 spinal space and 2.5 ml of 0.5% hyperbaric spinal bupivacaine was administered. Quality of the motor block was assessed using the Bromage score and sensory sensation loss was confirmed using cold spray and a level of T6

dermatome for loss of sensation was achieved in all patients[11]. Hypotension was defined as a MAP < 70 mm Hg or a systolic blood pressure less than 90 mm Hg or diastolic blood pressure less than 60 mm Hg[12]. Bolus doses of phenylephrine 50 mcg were given for each episode of hypotension if heart rate > 70 beats per minute. Bradycardia was defined as heart rate < 60 bpm and was corrected with IV Atropine 0.5 mg stat[13]. The infusion of phenylephrine was continued till the delivery of the baby and only stopped if the blood pressure was 20% above the initial baseline value or heart rate was < 60 bpm. The episodes of hypotension and bradycardia were noted as was the total dose of added IV Phenylephrine used as a bolus recue in both groups.

Primary variable studied was the incidence of hypotension between both groups and the total dose of IV Phenylephrine used as rescue analgesia.
Secondary variables measured were mean values for arterial pressure and heart rate between both groups. Demographic data were statistically described in terms of mean and SD, frequencies, and percentages when appropriate. T-test was used to compare statistically significant means between both groups. Chi-square test was used for secondary variables. The p value of <0.05 was considered statistically significant. All statistical calculations were performed using Statistical Package for Social Sciences 26.0.

FIGURE-I: PHASES OF THE STUDY PROTOCOL



RESULTS:

A total of 300 patients were analyzed in the final study protocol. Mean age of patients in Group P was 25.69±2.79 years versus 25.67±2.80 years in Group F (p=0.951). Mean weight was 80.66±3.98 kg in Group P versus 80.47±3.88 kg in Group F (p=0.681). Mean duration of surgery was 56.42±1.87 minutes in Group P versus 56.41±1.87 minutes in Group F (p=0.951) (Table-I).

When analyzing the primary and secondary variables, incidence of hypotension was seen in 42 (28%) patients immediately after spinal in Group P versus 76 (50.7%) patients in Group F (p<0.001). Total mean dose of phenylephrine by infusion given was 268.19±15.13 mcg in Group P versus 0.00±0.00 mcg in Group F (p<0.001). Mean total dose of rescue IV Phenylephrine used was 78.00±24.90 mcg in Group F versus 444.33±90.40 mcg in Group F (p<0.001). Total mean dose used in both groups was 346.19±27.29 mcg in Group P versus 444.33±90.40 mcg in Group F (p<0.001) (Table-II).

Values for mean arterial pressure (MAP) pre-spinal in both groups were 86.35±1.07 mm Hg in Group P versus 86.52±1.16 mm Hg in Group F (p=0.182), values immediately after spinal administration were 76.87±1.78 mm Hg in Group P versus 68.97±3.43 mm Hg in Group F (p<0.001) and tabulated 5 min after spinal administration were 81.89±3.74 mm Hg in Group P versus 70.56±1.84 mm Hg in Group F (p<0.001). Similar values for heart rate were also tabulated. Pre-spinal values between both groups were 87.81±1.20 bpm versus 87.68±1.25 bpm (p=0.349), values immediately after spinal were 94.81±3.80 bpm versus 94.35±3.86 bpm (p=0.300) and 5 minutes after spinal were 70.66±4.69 bpm in Group P versus 69.17±3.37 in Group F (p=0.002). The highest mean value for arterial pressure was 88.01±1.97 mm Hg in Group P versus 87.86±1.13 in Group F (p=0.432) while the lowest mean arterial pressure values were 70.15±4.78 mm Hg in Group P versus 61.84±5.23 mm Hg in Group F (p<0.001) (Table-II).

TABLES

TABLE-I AGE AND HEIGHT CHARACTERISITICS BETWEEN BOTH GROUPS (n=300)

VARIABLE	GROUP P (n=150)	GROUP F (n=150)	p VALUE
MEAN AGE (YEARS)	25.69±2.79	25.67±2.80	0.951
MEAN WEIGHT (KG)	80.66±3.98	80.47±3.88	0.681
MEAN DURATION OF SURGERY (MIN)	56.42±1.87	56.41±1.87	0.951

TABLE-II COMPARISON OF PRIMARY AND SECONDARY VARIABLES BETWEEN BOTH GROUPS (n=300)

VARIABLE	GROUP P (n=150)	GROUP F (n=150)	p VALUE
INCIDENCE OF HYPOTENSION (%)	42 (28%)	76 (50.7%)	<0.001
TOTAL MEAN DOSE OF IV PHENYLEPHRINE BY INFUSION (MCG)	268.19±15.13	00.00±0.00	<0.001
TOTAL MEAN DOSE OF RESCUE IV PHENYLEPHRINE USED (MCG)	78.00±24.90	444.33±90.40	<0.001
TOTAL MEAN IV PHENYLEPHRINE USED (MCG)	346.19±27.29	444.33±90.40	<0.001
MEAN ARTERIAL PRESSURE (MM HG)			
• PRE-SPINAL	86.35±1.07	86.52±1.16	0.182
• IMMEDIATELY AFTER SPINAL	76.87±1.78	68.97±3.43	<0.001
• 5 MIN POST-SPINAL	81.89±3.74	70.56±1.84	<0.001

HEART RATE (BPM)			
• **PRE-SPINAL**	87.81±1.20	87.68±1.25	**0.349**
• **IMMEDIATELY AFTER SPINAL**	94.81±3.80	94.35±3.86	**0.300**
• **5 MIN POST-SPINAL**	70.66±4.69	69.17±3.37	**0.002**
HIGHEST VALUE FOR MEAN ARTERIAL PRESSURE (MM HG)	88.01±1.97	87.86±1.13	**0.432**
LOWEST VALUE FOR MEAN ARTERIAL PRESSURE (MM HG)	70.15±4.78	61.84±5.23	**<0.001**

DISCUSSION:

The use of phenylephrine as a prophylactic measure to counter intra-operative hypertension has been advocated in various surgeries[14]. It has been successfully used to limit the incidence of hypotension in patients with anticipated increased blood loss as well. Many centers nationally are now employing this method by adding phenylephrine to the co-administration of maintenance fluid to achieve hemodynamic stability[15, 16]. The sympathectomy that follows spinal administration results in vasodilation below the level of spinal administration. This change is irreversible till the time the effect of spinal wears off. Another way to counter the effect is to fill the intravascular compartment with fluid which is the basis of fluid pre-loading and other is the use of vasopressors[17]. Phenylephrine is an alpha-1 agonist at both arterioles and venules. It has a rapid onset and short duration making it ideal for per operative management of hypotension. The use of phenylephrine in infusion form is only hindered by its reflex bradycardia which may need to be monitored vigilantly. Our study also aimed to see whether the bradycardia induced was profound enough to warrant cessation of therapy. We found no statistical differences in bradycardia between both groups and no patient required cessation of phenylephrine infusion. But we did find that the decrease in heart rate was more profound when bolus doses of phenylephrine were given rather than when continuous infusion was started in the study groups. This effect has been studied in detail in various national and international studies as well[18].

The primary endpoint of our study was the incidence of hypotension and mean total dose of phenylephrine used. The incidence in the fluid pre-loading group was around 50% while that in the infusion group was decreased to around 28%. The hemodynamic stability offered by the co-administration of IV Phenylephrine also resulted in better mean arterial pressure and heart rate values both immediately after and 5 minutes into the procedure after spinal administration. These findings have been supported by studies done internationally as well[19].

RECOMMEDATIONS:

The study recommends that IV Phenylephrine should be added as an adjunct to fluid co-administration to better counter post-spinal hypotension

CONCLUSION:

We conclude that IV Phenylephrine co-administration as an infusion with fluid results in better hemodynamic stability, less use of rescue vasopressor and decreased incidence of post-spinal hypotension

LIMITATIONS:

The limitations are that the study is single center only.

CONFLICT OF INTEREST:

None.

REFERENCES

1. Ferré F, Martin C, Bosch L, Kurrek M, Lairez O, Minville V. Control of spinal anesthesia-induced hypotension in adults. Local and regional anesthesia. 2020:39-46. https://doi.org/10.2147/LRA.S240753

2. Capdevila X, Aveline C, Delaunay L, Bouaziz H, Zetlaoui P, Choquet O, et al. Factors determining the choice of spinal versus general anesthesia in patients undergoing ambulatory surgery: results of a multicenter observational study. Advances in Therapy. 2020;37:527-40. https://doi.org/10.1007/s12325-019-01171-6
3. Fletcher J, Cockerham R. Spinal-induced hypotension at caesarean section. Anaesthesia & Intensive Care Medicine. 2022;23(6):328-30. https://doi.org/10.1016/j.mpaic.2022.02.025
4. Shitemaw T, Jemal B, Mamo T, Akalu L. Incidence and associated factors for hypotension after spinal anesthesia during cesarean section at Gandhi Memorial Hospital Addis Ababa, Ethiopia. PloS one. 2020;15(8):e0236755. https://doi.org/10.1371/journal.pone.0236755
5. Wang X, Mao M, Zhang S-S, Wang Z-H, Xu S-Q, Shen X-F. Bolus norepinephrine and phenylephrine for maternal hypotension during elective cesarean section with spinal anesthesia: a randomized, double-blinded study. Chinese medical journal. 2020;133(05):509-16.
6. Hunie M, Wubishet T, Fenta E, Teshome D, Kibret S, Desse T, et al. The Effect of Preloading and Co-Loading in the Prevention of Hypotension among Mothers Who Underwent Cesarean Delivery under Spinal Anesthesia: A Prospective Cohort Study. Systematic Reviews in Pharmacy. 2022;13(2).
7. MeenaKumari R, Sathyanarayana V. A study of phenylephrine administration for the prevention and treatment of hypotension in cesarean section during spinal anaesthesia. Journal of Cellular & Molecular Anesthesia. 2021;6(3):240-8. https://doi.org/10.22037/jcma.v6i3.34213
8. Al-Khrasani M, Karadi DA, Galambos AR, Sperlagh B, Vizi ES. The Pharmacological Effects of Phenylephrine are Indirect, Mediated by Noradrenaline Release from the Cytoplasm. Neurochemical Research. 2022;47(11):3272-84. https://doi.org/10.1007/s11064-022-03681-2
9. de Queiroz DV, Velarde LGC, Alves RL, Verçosa N, Cavalcanti IL. Incidence of bradycardia during noradrenaline or phenylephrine bolus treatment of postspinal hypotension in cesarean delivery: A randomized double-blinded controlled trial. Acta Anaesthesiologica Scandinavica. 2023;67(6):797-803. https://doi.org/10.1111/aas.14225
10. Buthelezi A, Bishop D, Rodseth R, Dyer R. Prophylactic phenylephrine and fluid co-administration to reduce spinal hypotension during elective caesarean section in a resource-limited setting: a prospective alternating intervention study. Anaesthesia. 2020;75(4):487-92. https://doi.org/10.1111/anae.14950
11. Karnina R, Rahayu NS, Faruk M. Factors influencing Bromage score in post-spinal anesthesia patients. Bali Medical Journal. 2022;11(3):1146-50. https://doi.org/10.15562/bmj.v11i3.3435
12. Saugel B, Sessler DI. Perioperative blood pressure management. Anesthesiology. 2021;134(2):250-61. https://doi.org/10.1097/ALN.0000000000003610
13. Sidhu S, Marine JE. Evaluating and managing bradycardia. Trends in cardiovascular medicine. 2020;30(5):265-72. https://doi.org/10.1016/j.tcm.2019.07.001
14. Khanna AK, Saha AK, Segal S. Association of the exclusive use of intraoperative phenylephrine for treatment of hypotension with the risk of acute kidney injury after noncardiac surgery. Anaesthesia Critical Care & Pain Medicine. 2023;42(5):101224. https://doi.org/10.1016/j.accpm.2023.101224
15. Riaz MM, Shah SQA, Sikander MS, Tariq W. Comparison of Phenylephrine Infusion Versus Boluses for Management of Blood Pressure in Elective Caesarean Section. Pakistan Armed Forces Medical Journal. 2024;74(2):442-5. https://doi.org/10.51253/pafmj.v74i2.9242

16. Iqbal A, Javed HM, Ahmad K, Ashfaq MA, Butt MR, Khalid M. Phenylephrine Boluses Vs Noradrenaline Boluses for Hypotension after Spinal Anesthesia in LSCS. Pakistan Journal of Medical & Health Sciences. 2022;16(07):775-. https://doi.org/10.53350/pjmhs22167775
17. Massoth C, Töpel L, Wenk M. Hypotension after spinal anesthesia for cesarean section: how to approach the iatrogenic sympathectomy. Current Opinion in Anesthesiology. 2020;33(3):291-8. *DOI:* 10.1097/ACO.0000000000000848
18. Kumar N, Jacob M, Taank P, Singh S, Tripathi N. Clinical comparison of prophylactic phenylephrine infusion vs. bolus regimens on maternal hemodynamics and neonatal outcomes during cesarean section. Journal of Obstetric Anaesthesia and Critical Care. 2020;10(2):118-22. *DOI:* 10.4103/joacc.JOACC_43_20
19. Singh D, Yadav JBS, Singh AK, Rai MK. Comparing the Effect of Phenylephrine Bolus and Phenylephrine Infusion for Maintaining Arterial Blood Pressure During Cesarean Delivery Under Spinal Anesthesia: A Randomized Prospective Study. Cureus. 2023;15(7). https://doi.org/10.7759%2Fcureus.42713