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Original Article

Use of Intravenous Ephedrine in Crystalloid Preload to Decrease the Preload Volume Requirement Before Spinal Anesthesia in Elective Cesarean Section

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ABSTRACT

Objective: To determine the use of intravenous Ephedrine in crystalloid preload before spinal anesthesia in elective cesarean section to prevent hypotension to avoid detrimental effects of hypotension in obstetric patients.
Study Design: Quasi-experimental study.
Place and Duration of Study: Combined Military Hospital, Rawalpindi Pakistan, from Sep 2021 to Feb 2022.
Methodology: A total of (250) full-term parturients (>36 weeks gestation) with an age range of 20 to 35 years, scheduled for elective cesarean section belonging to the American Society of anaesthesiologists classification II were included in the study. Bradycardia and tachycardia were endorsed as <30% or >30% of baseline respectively whereas <20% decline in systolic blood pressure was labeled as hypotension. Hemodynamic profile, nausea, vomiting, and Appearance, Pulse, Grimace, Activity and Respiration scores were recorded.
Results: A total of 250 full-term pregnant patients with a mean age of 25.23±4.15. belonging to American Society of anaesthesiologists II in enrolled in the study. Among Group–E 18(14.4%) experienced hypotension whereas 67(53.6%) participants had a frequency of hypotension in Group–F (*p*-value <0.001), hence greater number of parturients in Group–F 67(53.6%) were administered ≥ 10 mg rescue Ephedrine bolus as compared to 18(14.4%) participants of Group–E (*p*-value <0.001).
Conclusion: This study concluded that prophylactic administration of intravenous Ephedrine as a bolus dose can significantly alleviate the frequency of hypotension in obstetric patients with negligible adverse effects profile on the mother and neonate.

Keywords: Bolus, Ephedrine, Gestation, Hypotension, Normal saline.

How to Cite This Article: *Jadoon AK, Tarar HM, Jadoon M, Bashir S, Abbas S, Jadoon A. Use of Intravenous Ephedrine in Crystalloid Preload to Decrease the Preload Volume Requirement before Spinal Anesthesia in Elective Cesarean Section. Pak Armed Forces Med J 2024; 74(4): 1169-1172. DOI: https://doi.org/10.51253/pafmj.v74i4.8553*

INTRODUCTION

Globally, spinal anesthesia is a standard procedure in elective cesarean section, but 70% reported hypotension which creates complications to maternal and fetal health such as cardiac arrest, death, loss of consciousness, and a decrease in blood flow in the placenta, to mitigate which, prophylactic vasopressor, intravenous fluid administration, and patient positioning have been used, however, more than 40% of hypotensive women suffered adverse effects after fluid loading, such as, coagulopathy, volume overload, and anaphylaxis.[1] Spinal anesthesia cause sympathectomy, which decreases the systematic vascular resistance, increases the vascular venous capacitance, and secondary hypovolemia. To decrease the systematic vascular resistance and preserve arterial blood pressure, cardiac output must be maximized. Among all the pre-spinal intravenous fluid administration, crystalloid and colloid are acknowledged as the best method to prevent post-spinal anesthesia-induced hypotension.[2,3] Colloid's half-life in blood is longer in blood circulation, effectively stabilizing the hemodynamic changes; however, pulmonary edema can occur in addition to anaphylactic shock, which can cause death in severe cases.[4] A previous study reported that 85%-60% of cases of crystalloid preload cause hypotension while 59.3%-36% of cases of crystalloid co-load occurred with hypotension[5] besides allergic reactions and high cost.[6] Ahmed *et al.* mentioned various studies' results and concluded that Ephedrine is the best choice since it maintains uteroplacental blood flow.[7] In literature, prophylactic Ephedrine IV administration via multiple bolus or infusion on arterial pressure (last 10-15 min) has been declared a standard gold method in the prevention and treatment of hypotension.[8-10]

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Received: 14 Apr 2022; revision received: 15 May 2022; accepted: 18 May 2022

Our aim was to determine the use of IV Ephedrine in crystalloid preload before spinal anesthesia in elective cesarean section.

METHODOLOGY

The quasi-experimental study was carried out at Combined Military Hospital, CMH, Rawalpindi Pakistan, from September 2021 to February 2022, after taking approval from Ethics Research Committee of the institute (ERC-211). The sample size was calculated considering an 80% prevalence of post spinal hypotension in obstetric patients.[11]

Inclusion Criteria: Full-term parturients (>36 weeks gestation) with an age range of 20-35 years, scheduled for elective cesarean section belonging to the American Society of Anaesthesiologists (ASA) classification II, were included.

Exclusion Criteria: Patients with a history of any chronic systemic diseases, chronic hypertension, heart Failure and receiving beta-blocker treatment, hematological disease or receiving anticoagulant therapy, preeclampsia or eclampsia, allergic to any medicine or opioids, failed spinal anesthesia or combination of spinal and general anesthesia, were excluded.

With non-probability consecutive sampling technique, 250 participants were enrolled with uniform segregation into two groups: Group-F (equal volume of 0.9% normal saline) and Group-E (10mg bolus dose of prophylactic Ephedrine IV) (Figure). The data was collected on a pre-designed proforma with patients' consent and anonymity. Patients were randomly assigned groups via lottery method. History, age, height, BMI, ASA classification, gravidity, and history of the caesarean section was taken at the time of enrollment. All patients were subjected to pre-anaesthetic evaluation and nil per oral for 8 hours pre-operatively. Premedication was done with intravenous ondansetron 4mg. The first two consecutive measurements i.e. within 10 minutes of attaching monitoring were referred to as baseline blood pressure interpreted as mean arterial blood pressure (MAP). A preload of 500ml Ringer's solution for 20 minutes was necessitated for all participants. Intrathecal anesthesia was performed with the patients in a sitting position in lumbar space L3/L4 or L4/L5 with 10mg 0.5% hyperbaric injection of Bupivacaine.[12]

Either 10 mg of intravenous Ephedrine in the prefilled syringe (30mg diluted in 3ml normal saline hence 10mg/ml prepared) or an equal volume of normal saline were injected into randomly assigned participants after the supine position was made. Systolic Blood Pressure recorded after spinal anesthesia (a), at 1 minute (b), 5 minutes (c), 20 minutes (d) and 40 minutes (e). <20% decline in systolic blood pressure (SBP) was labelled as hypotension. Rescue doses of 10mg Ephedrine were given in the instance of hypotension.

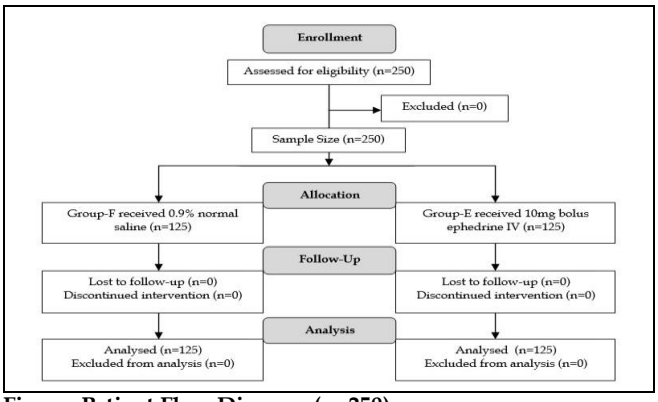

Figure: Patient Flow Diagram (n=250)

Statistical Package for Social Sciences (SPSS) version 24.0 was used for the data analysis. Quantitative variables with normal distribution were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test and Independent sample t-test were applied to explore the inferential statistics.

RESULTS

A total of 250 full-term pregnant patients with a mean age of 25.23±4.15 years (20-35 years), belonging to ASA I and II, 165(66%) and 85(34%) respectively, enrolled in the study. The demographic profile is elaborated in Table-I. Bradycardia was not recorded in Group-E whereas in Group-F, 12(9.6%) patients had bradycardia. Hemodynamic parameters recorded at various intervals between two groups are elucidated in Table-II. Among Group-E 18(14.4%) experienced hypotension whereas 67(53.6%) participants had a frequency of hypotension in Group-F (p-value <0.001), hence greater number of parturients were administered with a rescue IV bolus of 10 mg Ephedrine. In Group-F, 67(53.6%) patients were administered ≥10mg rescue Ephedrine bolus as compared to 18(14.4%) participants of Group E (p-value <0.001) (Table-III). An early advent of the hypotensive episode was observed in Group F when compared with Group E and it was statistically significant (p-value <0.001). No statistically different influence on APGAR score at 0, 1 and 5

minutes was recorded in either of the groups. Frequency of nausea and vomiting among both study groups is elaborated in Table-IV.

Table-I: Demographic Profile (n=250)

Parameters	Group-E (n=125)	Group-F (n=125)	*p*-value
Age (years)	26.23±3.2	25.7±2.7	0.30
Weight (Kg)	58.5±4.0	57.2±4.11	0.18
Hemoglobin (gm.%)	10.31±1.05	10.21±1.14	0.21
Gestation (days)	272.50±9.243	267.93±8.646	0.26
Delivery time (minutes)a	10.17±2.606	11.53±4.840	0.72
Surgery time (minutes)b	39.03±8.71	40.07±10.51	0.55

Table-II: Hemodynamic Parameters (n=250)

Parameters	Group-E (n=125)	Group-F (n=125)	*p*-value
Baseline Systolic Blood Pressure	125.9±14.3	127.01±14.2	0.60
Baseline Mean Arterial Pressure	97.13±12.65	98.12±12.11	0.56
Systolic Blood Pressure (a)	122.11±4.38	121.92±4.46	0.73
Systolic Blood Pressure (b)	121.98±4.24	119.71±9.08	0.012*
Systolic Blood Pressure (c)	121.95±4.21	117.17±10.69	<0.001*
Systolic Blood Pressure (d)	121.83±4.20	116.72±11.69	<0.001*
Systolic Blood Pressure (e)	119.20±8.26	119.20±9.25	0.59

Table - III: Frequency of Hypotension, Rescue Ephedrine, and Tachycardia (n=250)

Parameter	Group-E (n=125)	Group-F (n=125)	*p*-value
Hypotension	18(14.4%)	67(53.6%)	<0.001*
Rescue intravenous Ephedrine	18(14.4%)	67(53.6%)	<0.001*
Tachycardia	29(23.2%)	36(28.8%)	0.38

Table -IV: Adverse Effects (n=250)

Parameters	Group-E (n=125)	Group-F (n=125)	*p*-value
Nausea	1(0.8%)	8(6.4%)	0.04*
Vomiting	8(6.4%)	38(30.4%)	<0.001*

DISCUSSION

A decline of mean arterial pressure/systolic blood pressure is one of the most usually encountered adverse manifestations of spinal anaesthesia, with an anticipated frequency of 80% in literature with a value below 20% of baseline systolic blood pressure referred to as defining criterion.[13] Pre-emptive administration of fluids or vasopressors are suggested for hypotension prevention to avoid detrimental effects on the mother and fetus.

The proposed mechanism of action of Ephedrine for maintenance of blood pressure is via enhancing myocardial contraction which in turn elevates cardiac output and ensues tachycardia.[14] In the current study, participants in both groups were matched in terms of baseline parameters. No statistically significant results were inferred in terms of bradycardia (*p*-value 0.4) and tachycardia (*p*-value 0.2), similar to previous studies.[14] Kee *et al* conducted a study employing various doses of Ephedrine (10mg, 20mg, and 30mg intravenous) in addition to the control group(normal saline) to establish the most optimal prophylactic dose for the prevention of hypotensive spells. Minimal variations of heart rate were recorded in their study which is consistent with our study findings. Interpretations regarding adverse effects of nausea and vomiting were similar among all groups hence, however, greater proportion presented with nausea and vomiting in our study.[15]

Tsen *et al*. compared 10mg Ephedrine prophylactic administration with normal saline. They recorded significant tachycardia, alterations in mean arterial pressure, and vascular resistance index in the drug group after administration of subarachnoid block. Moreover, they quoted a similar frequency of hypotensive episodes around 70% between the drug and control groups.[16] In our study, the most significant decline in blood pressure was observed in the initial 20 minutes necessitating the administration of vasopressor to ensure hemodynamic stability of spinal anesthesia explained by sympathetic block ensued after spinal anesthesia thus emphasizing the prophylactic regime. Iqra *et al* compared two vasopressors Ephedrine and phenylephrine in doses of 10mg (rescue bolus 5mg) and 100mcg (rescue bolus 50mcg) respectively. Both drugs were declared efficient to overcome hypotensive episodes however phenylephrine group had a higher frequency of bradycardia.[17] Khan *et al*. compared preload and co load modalities to alleviate intra operative hypotension in non obstetric patients undergoing surgeries in spinal block and concluded decreased requirements of vasopressors in patients administered.[18] Hypotension causes more detrimental effects on uteroplacental blood flow when compared with vasoconstriction properties of Ephedrine.[19] Neonatal well-being is of utmost concern in all obstetric patients, and our study supported homogenous APGAR scores of 9,9 and 10 at 0,1 and 5 minutes respectively.

LIMITATION OF STUDY

Other contributory factors of hypotension not taken into accounts such as blood loss and surgical expertise of the

operating surgeon in taking hold of bleeders to prevent blood loss, ensuring left lateral with a wedge in obstetric patients undergoing cesarean delivery could have baffled results. Variations in block height and turn in dose-response could have overshadowed results to an extent.

CONCLUSION

Prophylactic administration of intravenous Ephedrine as a bolus dose can significantly alleviate the frequency of hypotension in obstetric patients with negligible adverse effects profile on the mother and neonate.

Conflict of Interest: None.

Authors' Contribution

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

AKJ & HMT: Conception, study design, drafting the manuscript, approval of the final version to be published.

MJ & SB: Data acquisition, critical review, approval of the final version to be published.

SA & AJ: Data acquisition, data analysis, data interpretation, 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.

REFERENCES

1. Yu C, Gu J, Liao Z, Feng S. Prediction of spinal anesthesia-induced hypotension during elective cesarean section: a systematic review of prospective observational studies. Int J Obstet Anesth 2021; 47(1): 103175. https://doi.org/10.1016/j.ijoa.2021.103175
2. Kilinç N, Deniz MN, Erhan E. Crystalloid preload versus crystalloid coload during spinal anesthesia for ureterorenoscopy: A randomized controlled trial. Ege Tip Derg 2020; 59(3): 181-187. https://doi.org/10.19161/etd.789190
3. Gousheh M, Akhondzade R, Asl Aghahoseini H, Olapour A, Rashidi M. The effects of pre-spinal anesthesia administration of crystalloid and colloid solutions on hypotension in elective cesarean section. Anesth Pain Med 2018; 8(4): 45. https://doi.org/10.5812/aapm.69446
4. Fan QQ, Wang YH, Fu JW, Dong HL, Yang MP, Liu DD, et al. Comparison of two vasopressor protocols for preventing hypotension post-spinal anesthesia during cesarean section: a randomized controlled trial. Chin Med J 2021; 134(7): 792-799. https://doi.org/10.1097/CM9.0000000000001404
5. Ni H, Liu H, Zhang J, Peng K, Ji F. Crystalloid coload reduced the incidence of hypotension in spinal anesthesia for cesarean delivery, when compared to crystalloid preload: A meta-analysis. Biomed Res Int 2017; 2017: 1-10. https://doi.org/10.1155/2017/3462527
6. Artawan I, Sarim B, Sagita S, Etty Dedi M. Comparison of the effect of preloading and co-loading with crystalloid fluid on the incidence of hypotension after spinal anesthesia in cesarean section. Bali J Anesthesiol 2020; 4(1): 3. https://doi.org/10.4103/bjoa.bjoa_15_19
7. Ahmed H, Hossam M, Adel A. Volume preload versus ephedrine infusion for prevention of hypotension due to spinal anesthesia for cesarean section. Open J Anesthesiol 2016; 6(3): 37-44. https://doi.org/10.4236/ojanes.2016.63007
8. Chooi C, Cox JJ, Lumb RS, Middleton P, Chemali M, Emmett RS, et al. Techniques for preventing hypotension during spinal anesthesia for cesarean section. Cochrane Database Syst Rev 2020; 7(7): CD002251. https://doi.org/10.1002/14651858.CD002251.pub4
9. Higgins N, Fitzgerald PC, van Dyk D, Dyer RA, Rodriguez N, McCarthy RJ et al. The effect of prophylactic phenylephrine and ephedrine infusions on umbilical artery blood pH in women with preeclampsia undergoing cesarean delivery with spinal anesthesia: a randomized, double-blind trial. Anesth Analg 2018; 126(6): 1999-2006. https://doi.org/10.1213/ANE.0000000000002524
10. Gousheh MR, Akhondzade R, Asl Aghahoseini H, Olapour A, Rashidi M. The effects of pre-spinal anesthesia administration of crystalloid and colloid solutions on hypotension in elective cesarean section. Anesth Pain Med 2018; 8(4): e69446. https://doi.org/10.5812/aapm.69446
11. Šklebar I, Bujas T, Habek D. Spinal anesthesia-induced hypotension in obstetrics: prevention and therapy. Acta Clin Croat 2019; 58(Suppl 1): 90-95. https://doi.org/10.20471/acc.2019.58.s1.13
12. Shitemaw T, Aregawi A, Fentie F, Jemal B. Prophylactic ephedrine to prevent postspinal hypotension following spinal anesthesia in elective cesarean section: a prospective cohort study in Ethiopia. J Obstet Anaesth Crit Care 2019; 9(2): 75. https://doi.org/10.4103/joacc.JOACC_14_19
13. Salama A, Goma H, Abdel-Hamid B. Fluid preloading versus ephedrine in the management of spinal anesthesia-induced hypotension in parturients undergoing cesarean delivery: a comparative study. Ain-Shams J Anaesthesiol 2016; 9(1): 72. https://doi.org/10.4103/1687-7934.174750
14. Jabalameli M, Soltani HA, Hashemi J, Behdad S, Soleimani B. Prevention of post-spinal hypotension using crystalloid, colloid, and ephedrine with three different combinations: A double-blind randomized study. Adv Biomed Res 2012; 1(1): 36. https://doi.org/10.4103/2277-9175.100129
15. Ngan Kee WD, Khaw KS, Lee BB, Lau TK, Gin T. A dose-response study of prophylactic intravenous ephedrine for the prevention of hypotension during spinal anesthesia for cesarean delivery. Anesth Analg 2000; 90(6): 1390-1395. https://doi.org/10.1097/00000539-200006000-00024
16. Tsen LC, Boosalis P, Segal S, Datta S, Bader AM. Hemodynamic effects of simultaneous administration of intravenous ephedrine and spinal anesthesia for cesarean delivery. J Clin Anesth 2000; 12(5): 378-382. https://doi.org/10.1016/s0952-8180(00)00176-8
17. Nazir I, Bhat MA, Qazi S, Buchh VN, Gurcoo SA. Comparison between phenylephrine and ephedrine in preventing hypotension during spinal anesthesia for cesarean section. J Obstet Anaesth Crit Care 2012; 2(2): 92-97. https://doi.org/10.4103/2249-4472.104780
18. Khan MU, Memon AS, Ishaq M, Aqil M. Preload versus coload and vasopressor requirement for the prevention of spinal anesthesia induced hypotension in nonobstetric patients. J Coll Physicians Surg Pak 2015; 25(12): 851-855. https://doi.org/10.2016/jcpsp.501853
19. Shang Y, Li H, Ma J, Tan L, Li S, Li P, et al. Colloid preloading versus crystalloid preloading to prevent hypotension after spinal anesthesia for cesarean delivery: A protocol for systematic review and meta-analysis. Medicine 2021; 100(7): e24607. https://doi.org/10.1097/MD.0000000000002460