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Efficacy of Phenylephrine and Ephedrine for Treatment of Hypotension Encountered During Caesarean Section

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ABSTRACT

***Objective*:** To compare the efficacy of Phenylephrine and Ephedrine in treating hypotension encountered during spinal anaesthesia for caesarean section.

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

***Place and Duration of Study*:** Department of Anaesthesia, Combined Military Hospital, Rawlakot Pakistan, from Sept 2020 to Aug 2021.

***Methodology*:** Hundred (50 in each Group) patients were observed. All patients were preloaded with 15ml/kg Hartmann's solution ten minutes before giving spinal anaesthesia. Baseline blood pressure was recorded just before administration of spinal anaesthesia, at 1-minute intervals up to 5 minutes, and then every 5 minutes afterwards. When hypotension developed, vasopressors were administered, and blood pressure was noted every minute for three minutes following drug administration. The spinal block using 2ml of 0.75% hyperbaric bupivacaine was given at L3-L4 interspace with a 27G spinal needle (Quinke). Group-E patients were given 5mg bolus injection of Ephedrine if mean arterial pressure fell below 20% from baseline. Group-P patients were given a 50ug bolus of Phenylephrine if mean arterial pressure fell below 20% from baseline.

***Results*:** Demographic data was comparable in both groups. There was an insignificant difference between Phenylephrine and Ephedrine in terms of treating hypotension, with a *p*-value of 0.249. Ephedrine was effective in 41(82%) patients and was not effective in 9(18%) patients, whereas Phenylephrine was effective in 45(90%) patients and was not effective in 5(10%) patients.

***Conclusion*:** Our study concluded that Phenylephrine and Ephedrine are equally effective for treating hypotension encountered during spinal anaesthesia.

Keywords: Caesarean section, Ephedrine, Hypotension, Phenylephrine.

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INTRODUCTION

Spinal Anaesthesia is the most frequently used regional anaesthesia technique employed for patients undergoing caesarean deliveries. However, there is a very high incidence of hypotension encountered during spinal anaesthesia if no prophylactic management is employed.[1,2] There are mainly two reasons for hypotension that occur after spinal anaesthesia, i.e., sympathetic blockade and aorto-caval compression by the gravid uterus due to the supine positioning of the patient. It can put life at risk for both mother and fetus if it goes untreated.[3,4]

Hypotension may decrease placental circulation as well as circulation to vital organs.[5] Hypotension encountered during spinal anaesthesia usually manifests as restlessness, anxiety, chest tightness, nausea and vomiting; these all can interfere with the optimal surgical conditions.[6] Spinal-induced hypotension can usually be prevented by preloading the patients with crystalloids, lateral tilting the patient with wedge placement, using vasopressors, and using compression stockings and leg binders.[7] The prophylactic use of vasopressors for spinal-induced hypotension during lower segment caesarean section (LSCS) is well-known. Various drugs have been successfully used in the past, e.g. epinephrine, norepinephrine, Ephedrine and phenylephrine.[8] Preloading with colloids is efficacious, but they are more expensive and carry the risk of adverse effects.

Ephedrine is a direct and indirect-acting sympathomimetic agent. It indirectly stimulates the adrenergic receptors by enhancing noradrenaline activity at the post-synaptic α and β-receptors.[9] Although several studies historically favoured Ephedrine because of its low tendency to decrease uteroplacental blood flow, they recently favour α-

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agonists like phenylephrine. Phenylephrine is a pure α-1 agonist. It is a selective α1-adrenoceptor agonist which directly acts on these receptors, and unlike Ephedrine, it does not cause the release of endogenous catecholamines.[10]

In our setup, we are using Ephedrine as a vasopressor. Ephedrine causes tachyphylaxis after multiple doses, but as far as Phenylephrine is concerned, we can use it as much as we want and achieve adequate mean arterial pressure (MAP). Very few studies have been conducted in our local population to establish its effects. The different results in local and international studies are due to demographic changes. The rationale of this study is to determine the efficacy of Ephedrine compared to Phenylephrine for the management of hypotension during elective caesarean section and to develop a protocol to use it for control of hypotension during anaesthesia.

METHODOLOGY

The quasi-experimental study was conducted at the Anaesthesia Department of the Combined Military Hospital, Rawlakot Pakistan, from September 2020 to August 2021. Prior approval from the Ethical Review Board was sought (Certificate no:102/05/Trg/Adm). WHO sample size calculator was used for sample size calculation, with the anticipated population proportion 1 of 70% and population proportion 2 of 93%.[11]

Inclusion Criteria: Patients age range between 20 to 35 years, having American Society of Anesthesiology status II, undergoing planned elective caesarean section and developed hypotension intra-operatively were selected for this study.

Exclusion Criteria: Patients with cardiovascular, hypertension, diabetes mellitus, renal, pulmonary or liver disease were excluded. Patients with twin pregnancies, patients reporting for emergency caesarean and patients with a history of allergy to the drug under study were also excluded.

All willing patients signed a written consent before recruiting them for the study. All patients were counselled, and the study and procedure were explained in detail during the pre-anaesthesia clinic. Patients willing to participate in this study were randomly divided into two equal Groups. All patients were preloaded with 15ml/kg Hartmann's solution ten minutes before giving spinal anaesthesia. Baseline blood pressure was recorded just before administration of spinal anaesthesia, at 1-minute intervals up to 5 minutes, and then every 5 minutes afterwards. When hypotension developed, vaso-pressors were administered, and Blood pressure was noted every one minute for three minutes following drug administration. The spinal block was given 2ml of 0.75% hyperbaric Bupivacaine at L3-L4 interspace with a 27G spinal needle (Quinke). Group-E patients were given a 5mg bolus injection of Ephed-rine if MAP fell below 20% from baseline. Group-P patients were given a 50ug bolus of Phenylephrine if MAP fell below 20% from baseline (Figure).

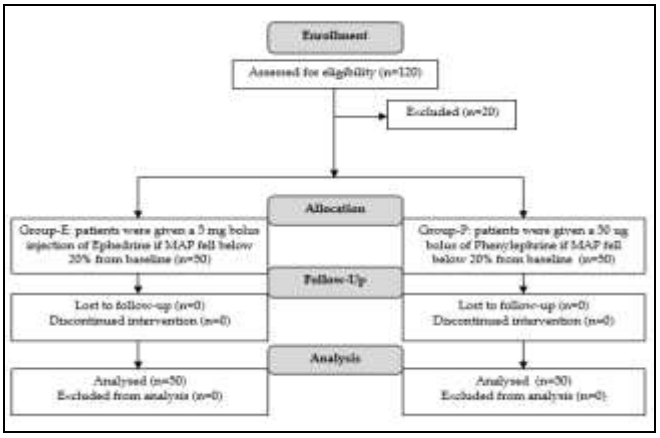

Figure: Patient Flow Diagram (n=100)

The specially designed proforma was used to collect data, which was analyzed using the Statistical Package for Social Science (SPSS) version 23. Mean±SD was calculated for quantitative variables like age, systolic, diastolic, and MAP. Frequency and percentage were calculated for qualitative variables like efficacy. The Chi-square test was used to compare the efficacy in both groups. The *p*-value of 0.05 or less was taken as significant.

RESULTS

In this study, we compared the two groups with respect to age, BMI, baseline blood pressure, and drug efficacy. The mean age in the ephedrine group was 28.04±3.78 years, whereas in the phenylephrine group, the mean age was 26.80±3.00 years. There wasn't any significant difference in both Groups in terms of age, with a *p*-value of 0.072. A detailed comparison is shown in Table-I.

Table-I: Age Distribution of the Patients (n=100)

Age Groups	Group-E (n=50)	Group-P (n=50)
20-25 years	16(36%)	15(30%)
26-30 years	21(42%)	27(54%)
31-35 years	13(22%)	8(16%)

Body mass index (BMI) was comparable in both groups, with a p-value of 0.126. The mean BMI for group-E was 32.29±5.21, whereas 30.92±3.50 for group-P. In the Ephedrine group, the baseline MAP was 93.5±8.59 mmHg. Whereas in the Phenylephrine Group baseline mean MAP was 91.24±7.97 mmHg. A detailed comparison is shown in Table-II.

Table-II: Baseline Blood Pressure (n=100)

	Group-E (n=50)	Group-P (n=50)	*p*-value
Systolic Blood Pressure (Mean±SD)	126.08±12.08	122.14±10.81	0.104
Diastolic Blood Pressure (Mean±SD)	77.1±7.43	75.76±7.27	0.364
Mean Arterial Pressure (Mean±SD)	93.5±8.59	91.24±7.97	0.176

There was an insignificant difference between Phenylephrine and Ephedrine in terms of treating hypotension, with a *p*-value of 0.249. Ephedrine was effective in 41(82%) patients and was not effective in 9(18%) patients, whereas Phenylephrine was effective in 45(90%) patients and was not effective in 5(10%) patients.

DISCUSSION

Our study shows that there was an insignificant difference between Phenylephrine and Ephedrine in terms of treating hypotension with a *p*-value of 0.249. Ephedrine was effective in 41(82%), whereas Phenylephrine was effective in 45(90%) patients. Similar results were found in a study done by Fassaert et al.[12] In another study conducted by Dusitkasem et al.[13] reported that Phenylephrine and Ephedrine are both suitable selections for treating and preventing hypotension, which is induced by sympathetic blockade during spinal anaesthesia. There is no conclusive evidence that either drug is more efficient than the other in terms of safety profile and maintaining maternal blood pressure.

A local study conducted at Khyber Teaching Hospital Peshawar by Aziz et al.[14] had reported that Phenylephrine demonstrated lower efficacy (28.4%) for the treatment of spinal-induced hypotension than Ephedrine (34.3%). Another local study conducted by Siddiqui et al.[15] at Agha Khan Hospital Karachi revealed that Phenylephrine and Ephedrine are equally effective in treating maternal hypotension induced by spinal anaesthesia.

Phenylephrine is more effective at maintaining blood pressure, but it can result in reflex bradycardia and reduce cardiac output.[16] Hence, it may reduce the uteroplacental blood flow.[17] Magalhaes et al.[18] reported more episodes of hypotension in the phenylephrine Group than in the ephedrine Group. This could be due to the fact that Phenylephrine has a shorter duration of action than Ephedrine. A quantitative systematic review by Lee et al.[19] supported Ephedrine over Phenylephrine for the prevention and treatment of maternal hypotension.

In any study by Cooper et al.,[20] the results favouring Phenylephrine over Ephedrine contradicted our results. They also found that phenylephrine results in lesser fetal acidosis and a decreased incidence of maternal nausea and vomiting than Ephedrine.

CONCLUSION

Our study concluded that Phenylephrine and Ephedrine are equally effective for treating hypotension encountered during spinal anaesthesia.

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Authors' Contribution

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

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

AH & AAM: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

SR & SR: Conception, data acquisition, drafting the manuscript, 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. Ferré F, Martin C, Bosch L, Kurrek M, Lairez O, Minville, V. Control of spinal anesthesia-induced hypotension in adults. Local Reg Anesth 2020; 13(1): 39-46. https://doi.org/10.2147/lra.s240753
2. Hasanin A, Mokhtar AM, Badawy AA, Fouad R. Post-spinal anesthesia hypotension during cesarean delivery, a review article. Egypt J Anaesth 2017; 33(2): 189-193. https://doi.org/10.1016/j.egja.2017.03.003
3. Tatikonda C, Rajappa G, Rath P, Abbas M, Madhapura V, Gopal N. Effect of intravenous ondansetron on spinal anesthesia-induced hypotension and bradycardia: A randomized controlled double-blinded study. Anesth Essays Res 2019; 13(2): 340. https://doi.org/10.4103/aer.aer_22_19
4. Zelop C, Einav S, Mhyre J, Martin S. Cardiac arrest during pregnancy: Ongoing clinical conundrum. Obstetric Anesthesia Digest. 2019; 39(2): 70-72. https://doi.org/10.1097/01.aoa.0000557653.70376.8c
5. Ke J, George R, Beattie W. Making sense of the impact of intraoperative hypotension: From populations to the individual patient. Br J Anaesth 2018; 121(4): 689-691. https://doi.org/10.1016/j.bja.2018.07.003

6. Wang X, Mao M, Liu S, Xu S, Yang J. A comparative study of bolus norepinephrine, Phenylephrine, and ephedrine for the treatment of maternal hypotension in parturients with Preeclampsia during cesarean delivery under spinal anesthesia. Med Sci Monit 2019; 25(1): 1093-1101. https://doi.org/10.12659/msm.914143
7. Massoth C, Töpel L, Wenk M. Hypotension after spinal anesthesia for cesarean section: How to approach the iatrogenic sympathectomy. Curr Opin Anaesthesiol 2020; 33(3): 291-298. https://doi.org/10.1097/aco.0000000000000848
8. Ryu C, Choi GJ, Park YH, Kang H. Vasopressors for the management of maternal hypotension during cesarean section under spinal anesthesia: A Systematic review and network meta-analysis protocol. Medicine 2019; 98(1): e13947. https://doi.org/10.1097/MD.0000000000013947
9. Stohs SJ, Shara M, Ray SD. P -synephrine, ephedrine, P -octopamine and M -synephrine: Comparative mechanistic, physiological and pharmacological properties. Phytoth Res 2020; 34(8): 1838-1846. https://doi.org/10.1002/ptr.6649
10. Mohta M, Garg A, Chilkoti GT, Malhotra RK. A randomised controlled trial of phenylephrine and noradrenaline boluses for treatment of postspinal hypotension during elective caesarean section. Anaesthesia 2019; 74(7): 850-855. https://doi.org/10.1111/anae.14675
11. Magalhães E1, Govêia CS, de Araújo Ladeira LC, Nascimento BG, Kluthcouski SM. Ephedrine versus phenylephrine: prevention of hypotension during spinal block for cesarean section and effects on the fetus. Rev Bras Anestesiol 2009; 59(1): 11-20.
12. Fassaert L, Jan de Borst G, Immink R. Effect of Phenylephrine and ephedrine on cerebral (Tissue) oxygen saturation during carotid Endarterectomy (PEPPER): A randomized controlled trail. Eur J Vasc Endovasc Surg 2019; 58(6): e92. https://doi.org/10.1016/j.ejvs.2019.06.625
13. Dusitkasem S, Herndon BH, Somjit M, Stahl DL, Bitticker E, Coffman JC. Comparison of Phenylephrine and ephedrine in treatment of spinal-induced hypotension in high-risk pregnancies: A narrative review. Frontiers in Medicine 2017; 4(2): 1-8. https://doi.org/10.3389/fmed.2017.00002
14. Aziz N, Bangash R, Khan P. Comparison between ephedrine and phenylephrine in the prevention of post spinal hypotension during elective cesarean section. J Med Sci 2013; 21(1): 27-30.
15. Siddiqui SA, Salim B, Siddiqui SZ. Comparison of phenylephrine and ephedrine for treating hypotension after spinal anesthesia for cesarean section: A Randomized double-blind clinical trial. Anesthesia Pain Intensive Care 2015; 19(1): 44-49.
16. Swenson K, Rankin S, Daconti L, Villarreal T, Langsjoen J, Braude, D. Safety of bolus-dose phenylephrine for hypotensive emergency department patients. Am J Emerg Med 2018; 36(10): 1802-1806. https://doi.org/10.1016/j.ajem.2018.01.095
17. Ngan Kee, WD. Prevention of maternal hypo- tension after regional anaesthesia for caesarean section. Curr Opin Anaesthesiol 2010; 23(1): 304-309.
18. Magalhaes E, Goveia SC, De Araujo Ladeira CL, Nascimeno GB, Kluth Couski CS. Ephedrine vs phenylephrine; prevention of hypotension during spinal block for cesarean section and effects on fetus. Rev Bras Anasth 2009; 59(1): 1-10.
19. Lee A, Ngan Kee WD, Gin T. Prophylactic ephedrine prevents hypotension during spinal anesthesia for cesarean delivery but does not improve neonatal outcome: a quantitative systematic review. Candian J Anaes 2002; 49(6): 588-599.
20. Cooper DW, Carpenter M, Mowbray P, Desira WR, Ryall DM, Kokri MS. Fetal and maternal effects of phenylephrine and ephedrine during spinal anesthesia for cesarean delivery. Anesthesiology 2002; 97(6): 1582–1590. https://doi.org/10.1097/00000542-200212000-00034

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