

Phenylephrine Boluses Vs Noradrenaline Boluses for Hypotension after Spinal Anesthesia in LSCS

ADNAN IQBAL¹, HAFIZ MUHAMMAD JAVED², KHALEEL AHMAD³, MUHAMMAD ADEEL ASHFAQ⁴, MAHNOOR RAFIQUE BUTT⁵, MARRIUM KHALID⁶

¹*PGR Anesthesia, Aziz Bhatti Shaheed Teaching Hospital, UOG, Gujrat*

²*Assistant Professor Anesthesia, Head of Department, Supervisor, Aziz Bhatti Shaheed Teaching Hospital, UOG, Gujrat*

³*Associate Professor Anesthesia, Foundation University Medical College Islamabad*

^{4,5,6}*PGR Anesthesia, Aziz Bhatti Shaheed Teaching Hospital, UOG, Gujrat*

Correspondence to: Adnan Iqbal

ABSTRACT

Background: Hypotension is a frequent complication highly associated with spinal anesthesia during lower segment cesarean section that imposed adverse effects related to maternal as well as fetal.

Purpose: The purpose: of this study is to lighten the comparison of vasopressor (Phenylephrine boluses vs. noradrenaline boluses) use to treat hypotension after spinal anesthesia in LSC patients

Study design: randomized double-blind study design.

Method: This randomized double-blind study was performed at the department of anesthesia, critical care, and pain medicine at Aziz Bhatti Shaheed Teaching Hospital, Gujrat Pakistan, and was conducted from Jun 2020 to Jun 2021. The patients aged between 20 to 40 years who went through lower segment cesarean section were part of this study. A total of 60 patients were divided into two groups namely groups A and B. Group A contain 30 patients in the same way group occupied with 30 patients and by using a random allocation procedure or protocol, the randomized number was assigned to all patients via the computer-generated system. Group A received phenylephrine and Group B received noradrenaline.

Results: Statically analysis was performed using SPSS software. In the case of group A, the mean arterial pressure was measured at 115.03 ± 8.69 , heart rate, beats/min was measured at 65.72 ± 9.46 , and bradycardia was found in 14 (46.6%) patients out of 30 of group A with a mean value of beats 43.65 ± 3.23 , hypotension was found in 4.31 ± 2.11 cases and to treat its repeated episodes with phenylephrine boluses was used 4.21 ± 1.21 . In the case of group B, the mean arterial pressure was measured at 121 ± 9.86 , heart rate, beats/min was measured at 80.42 ± 8.01 , and bradycardia was found in 8 (26.6%) patients out of 30 of group B with a mean value of beats 45.23 ± 2.13 , hypotension was found in 2.21 ± 1.03 cases and to treat its repeated episodes with noradrenaline boluses was used 3.98 ± 1.32 and all the variables was found with significant results.

Conclusion: We conclude that noradrenaline shows ameliorated response to handle the hypotension situation after spinal anesthesia as compared to phenylephrine.

Keywords: Spinal anesthesia, phenylephrine bolus, noradrenaline bolus, lower segment cesarean section (LSCS)

INTRODUCTION

During the cesarean section, hypotension is a common physiological response with spinal anesthesia that have significant adverse maternal outcomes including nausea, vomiting, and dizziness with a 70% incidence rate.¹ Hypotension can be harmful to both the fetus as well as mother, like reductions in placental blood flow and fetal acidosis may occur as a result of prolonged hypotension. Effective caution and treatment for spinal hypotension have great clinical importance. Therefore, its common management recommends the use of vasopressors such as ephedrine, phenylephrine, and norepinephrine.² Study on these vasopressors provides a better response in lowering the incidence of fetal acidosis, vomiting, and nausea. On the other hand, phenylephrine considered a first-line agent assists in the reduction of cardiac output.³⁻⁴ From the previous few years, noradrenaline is getting attention as a substitute for phenylephrine in case of obstetric anesthesia to avoid hypotension.⁵ Usually, noradrenaline is considered a vasopressor in the critical care setting, mostly used to manage septic shock, it is an alpha-adrenergic agonist, and has little beta-adrenergic agonistic activity but doesn't cause adverse effects like bradycardia caused by using the phenylephrine.⁶

More, promising results have been obtained with norepinephrine infusion for prophylaxis to treat maternal hypotension. Thus, in the case of cesarean delivery, norepinephrine infusion is recognized as the best alternative to phenylephrine infusion.⁷ While the use of noradrenaline (NA) bolus to treat and manage maternal hypotension has not been properly studied.⁸ Limited numbers of studies have demonstrated the NA bolus to maintain blood pressure during cesarean delivery.⁹

¹⁰ Although clinical trials and research about the prevention of spinal hypotension have recommended prophylactic infusion use of intravenous bolus is still deemed a common medication preferred by anesthesiologists in China.¹¹ In this study, we aimed

to compare both phenylephrine bolus and noradrenaline bolus effectiveness to treat hypotension after spinal anesthesia during the lower segment cesarean section (LSCS).

METHODOLOGY

This randomized double-blind study was performed at the department of anesthesia, critical care, and pain medicine at Aziz Bhatti Shaheed Teaching Hospital, Gujrat Pakistan, and was conducted from Jun 2020 to Jun 2021. We obtained approval from the Ethical Committee of the Hospital and written consent was signed by all participants which contain all the information necessary to acknowledge the participant.

Inclusion criteria: The patients aged between 20 to 40 years who went through lower segment cesarean section were part of this study. A total 60 number of patients were divided into two groups namely groups A and B. Group A contain 30 patients in the same way group occupied with 30 patients and by using a random allocation procedure or protocol, the randomized number was assigned to all patients via the computer-generated system.

Exclusion criteria: The patients who come under the category of hypersensitivity to phenylephrine or norepinephrine, hypertensive disorder of pregnancy, diabetes, use of vasoactive medication, cardiovascular, cerebrovascular disease, concurrent with pre-hypertension, fetal abnormalities, fetal distress, twin gestation, diagnosed with anxiety or depression during pregnancy were excluded from the study. More patients younger than 20 and older than 40 years of age were also removed from our study.

Procedure: Group A received phenylephrine and Group B received noradrenaline. All the essential protocols were performed required for the LSCS. After dilution of both drugs phenylephrine and noradrenaline was loaded in a coded 10-mL syringe, 50 µg/mL phenylephrine dose and 5 µg/mL noradrenaline doses were used to treat the hypotension, and then data were collected for further analysis. The patients of both groups received the drug doses

through an intravenous bolus route. Blood pressure and heart rate were consistently monitored every 3 minutes till the end of the surgery. In case of dropped systolic blood pressure under baseline, patients are given a defined dose of drugs as per their group division. 0.7mg intravenous atropine was used to treat the bradycardia. In the case of bradycardia heart rate was less than 50 beats/min (bpm), and hypertension was associated with an increase in systolic blood pressure (120%). Data of all the patients was collected for comparison of phenylephrine and noradrenaline to further perform the static calculation.

Statically Analysis: The static analysis was conducted in SPSS software version 20.0. The final data for continuous variables were presented in mean and standard deviation. The association between the variables was determined using Pearson's Chi-square test. T-test was applied to compare the mean of continuous parameters between two groups and a p-value less than 0.05 was shows significant results.

RESULTS

General characteristics of participants are presented in the table.1. Out of 60 patients, 30 patients of group A had a mean age of 26 ± 9.56 years with a p-value of 0.23, and mean weight (kg) \pm SD was measured at 55.13 ± 7.20 with a p-value 0.52, mean height \pm SD (cm) was measured 158.43 ± 5.21 with p- value 0.46, mean BMI \pm SD kgm^{-2} was 25.33 ± 2.01 along p- value 0.52, and Gestation weeks was noted 39.2 ± 1.2 along p-value 0.62.

Group B also contained 30 patients with a mean age of 27 ± 8.39 , a p-value of 0.23, measured data of mean weight \pm SD (kg) was 59.47 ± 6.42 , measured mean height \pm SD (cm) of this group was 156.56 ± 6.13 , mean BMI \pm SD kgm^{-2} of patients was 25.54 ± 2.05 along p-value 0.52 and Gestation weeks was 39.5 ± 1.4 with p-value 0.62.

The variables were measured after spinal anesthesia of LSCS, their results were represented in table.2 with mean and

standard deviation. In the case of group A, the mean arterial pressure was measured at 115.03 ± 8.69 , heart rate, beats/min was measured at 65.72 ± 9.46 showing the lower heart rate in group patients with slightly unstable arterial blood pressure, bradycardia was found in 14 (46.6%) patients out of 30 of group A with a mean value of beats 43.65 ± 3.23 , hypotension was found in 4.31 ± 2.11 cases and to treat its repeated episodes with phenylephrine boluses was used 4.21 ± 1.21 and all the variables was found with significant results.

In the case of group B, the mean arterial pressure was measured at 121 ± 9.86 , heart rate, beats/min was measured at 80.42 ± 8.01 , which shows a slight variation in heart rate in group b patients with stable arterial blood pressure, bradycardia was found in 8 (26.6%) patients out of 30 of group B with the mean value of beats 45.23 ± 2.13 , hypotension was found in 2.21 ± 1.03 cases and to treat its repeated episodes with noradrenaline boluses was used 3.98 ± 1.32 and all the variables was found with significant results.

So, an overall comparison of both drugs shows that better results to control the hypotension were observed in group B patients who were treated with noradrenaline bolus while the response of phenylephrine bolus was not effectively measured in our study.

Table 1: Characteristics of 60 patients of current study

Characteristics	Group A, N=30	Group-B, N=30	P-value
Mean Age \pm SD(years)	26 ± 9.56	27 ± 8.39	0.23
Mean weight \pm SD (kg)	55.13 ± 7.20	59.47 ± 6.42	0.52
Mean height \pm SD (cm)	158.43 ± 5.21	156.56 ± 6.13	0.46
Mean BMI \pm SD kgm^{-2}	25.33 ± 2.01	25.54 ± 2.05	0.52
Gestation, weeks	39.2 ± 1.2	39.5 ± 1.4	0.62

Group A= Patients received phenylephrine bolus, Group B = Patients received noradrenaline bolus SD= Standard Deviation

Table 2: Comparison of women undergo through LSCS, receiving the phenylephrine and noradrenaline boluses after spinal anesthesia

Variables	Group A, n=30		Group B, n=30		F-value	P-value
	Mean	SD	Mean	SD		
Systolic arterial blood pressure (mmHg)	115.03	8.69	121	9.86	4.56	0.012
Heart rate, beats/min	65.72	9.46	80.42	8.01	3.32	0.022
Bradycardia beats less than 50/min	43.65	3.23	45.23	2.13	2.65	0.032
	14(46.6%)		8(26.6%)			
Hypotension cases	4.31	2.11	2.21	1.03	2.84	0.036
Vasopressor boluses needed to treat repeated hypotensive episodes	4.21	1.21	3.98	1.32	2.59	0.029

DISCUSSION

For years, the selection of vasopressor is a long-lasting debate to treat the hypotension of anesthesia¹² while potentially deleterious effects of alpha-agonist phenylephrine that reduced the uterine blood flow with an increase of peripheral vascular resistance.¹³ Although the researcher has applied invasive techniques to pregnant women to define the hemodynamic profile of vasoactive agents. Hypotension could be developed as a result of the reduction in peripheral vascular resistance that ultimately enhances the stroke volume, and heart rate and leads to induced cardiac output.¹⁴⁻¹⁵ In a study of randomized trial phenylephrine administration outcomes were the fastest and most effective means to restore arterial pressure.¹⁴ on the other hand, we had not observed sufficient effective response of phenylephrine to control arterial pressure as compared to noradrenaline. In the current study, the best response was observed with the use of noradrenaline. Noradrenaline was reported with high cardiac output as compared to phenylephrine during spinal anesthesia of LSCS.¹⁶

In one more attempted randomized control trial about the elective cesarean section by treating hypotension with phenylephrine and noradrenaline demonstrated that both vasopressors had reversed the post spinal hypotension without adverse effects like bradycardia.¹⁷ In our study we found less

number of patients with bradycardia by using noradrenaline in group B people. In a comparative study of both vasopressors but as prophylactic bolus demonstrated the specific response on different doses such as $10\mu\text{g}$ noradrenaline shows significantly lower bradycardia than $50\mu\text{g}$ of phenylephrine.¹⁸ Present research demonstrated that fewer hypotension episodes were observed in the 2nd group with lesser cases of bradycardia and significant stable arterial blood pressure was found in this literature study.

CONCLUSION

Eventually, we found that noradrenaline is more effective in comparison to phenylephrine bolus to prevent spinal hypotension with lesser adverse effects. But still, more research is required to confirm the safety of obstetric patients while using both drugs for LSCS.

REFERENCES

- 1- F. J. Mercier, M. Auge, C. Hofmann, C. Fischer, and A. Le ` Gouez, "Maternal hypotension during spinal anesthesia for caesarean delivery," *Minerva Anestesiologica*, vol. 79, no. 1, pp. 62-73, 2013.
- 2- Chen, D., Qi, X., Huang, X., Xu, Y., Qiu, F., Yan, Y., & Li, Y. (2018). Efficacy and safety of different norepinephrine regimens for prevention of spinal hypotension in cesarean section: a randomized trial. *BioMed research international*, 2018.

- 3- Kinsella, S. M., Carvalho, B., Dyer, R. A., Fernando, R., McDonnell, N., Mercier, F. J., ... & Consensus Statement Collaborators. (2018). International consensus statement on the management of hypotension with vasopressors during caesarean section under spinal anaesthesia. *Obstetric Anesthesia Digest*, 38(4), 171-172.
- 4- Ngan Kee, W. D., Lee, S. W., Ng, F. F., Tan, P. E., & Khaw, K. S. (2015). Randomized double-blinded comparison of norepinephrine and phenylephrine for maintenance of blood pressure during spinal anesthesia for cesarean delivery. *Anesthesiology*, 122(4), 736-745.
- 5- B. Carvalho and R. A. Dyer, "Norepinephrine for spinal hypotension during cesarean delivery: Another paradigm shift?" *Anesthesiology*, vol. 122, no. 4, pp. 728–730, 2015.
- 6- Lim, G., Facco, F. L., Nathan, N., Waters, J. H., Wong, C. A., & Eltzschig, H. K. (2018). A review of the impact of obstetric anesthesia on maternal and neonatal outcomes. *Anesthesiology*, 129(1), 192-215.
- 7- Hasanin A, Amin S, Refaat S, Habib S, Zayed M, Abdelwahab Y, et al. Norepinephrine versus phenylephrine infusion for prophylaxis against postspinal anaesthesia hypotension during elective caesarean delivery: a randomised controlled trial. *Anaesth Crit Care Pain Med*. 2019;38:601–7.
- 8- Xu S, Shen X, Liu S, Yang J, Wang X. Efficacy and safety of norepinephrine versus phenylephrine for the management of maternal hypotension during cesarean delivery with spinal anesthesia: a systematic review and meta-analysis. *Medicine* 2019;98: e14331.
- 9- Wang X, Shen X, Liu S, Yang J, Xu S. The efficacy and safety of norepinephrine and its feasibility as a replacement for phenylephrine to manage maternal hypotension during elective cesarean delivery under spinal anesthesia. *BioMed Res Int* 2018;2018:1869189.
- 10- Kinsella SM, Carvalho B, Dyer RA, Fernando R, McDonnell N, Mercier FJ, et al. International consensus statement on the management of hypotension with vasopressors during caesarean section under spinal anaesthesia. *Anaesthesia* 2018;73:71–92.
- 11- Allen TK, Muir HA, George RB, Habib AS. A survey of the management of spinal-induced hypotension for scheduled cesarean delivery. *Int J Obstet Anesth* 2009;18:356–361.
- 12- Langesaeter, E., L. A. Rosseland, and A. Stubhaug. "Continuous Invasive Blood Pressure and Cardiac Output Monitoring During Cesarean Delivery: A Randomized, Double-Blind Comparison of Low-dose versus High-Dose Spinal Anesthesia With Intravenous Phenylephrine or Placebo Infusion." *Obstetric Anesthesia Digest* 29.2 (2009): 94-95.
- 13- Vallejo, M. C., & Ramanathan, S. (2003). Should α -agonists be used as first line management of spinal hypotension?. *International Journal of Obstetric Anesthesia*, 12(4), 243-245.
- 14- Langeseter E, Rosseland LA, Stubhaug A. Continuous invasive blood pressure and cardiac output monitoring during cesarean delivery: a randomized, double-blind comparison of low-dose versus high-dose spinal anesthesia with intravenous phenylephrine or placebo infusion. *Anesthesiology* 2008; 109: 856–63.
- 15- Dyer RA, Reed AR, Van Dyk D, Arcache MJ, Hodges O, Lombard CJ, Greenwood J, James MF. Hemodynamic effects of ephedrine, phenylephrine, and the coadministration of phenylephrine with oxytocin during spinal anesthesia for elective cesarean delivery. *Anesthesiology* 2009; 111: 753–65
- 16- W. D. Ngan Kee, S. W. Y. Lee, F. F. Ng, P. E. Tan, and K. S. Khaw, "Randomized double-blinded comparison of norepinephrine and phenylephrine for maintenance of blood pressure during spinal anesthesia for cesarean delivery," *Anesthesiology*, vol. 122, no. 4, pp. 736–745, 2015.
- 17- Mohta, M., Garg, A., Chilkoti, G. T., & Malhotra, R. K. (2019). A randomised controlled trial of phenylephrine and noradrenaline boluses for treatment of postspinal hypotension during elective caesarean section. *Anaesthesia*, 74(7), 850-855.
- 18- Dong, L., Dong, Q., Song, X., Liu, Y., & Wang, Y. (2017). Comparison of prophylactic bolus norepinephrine and phenylephrine on hypotension during spinal anesthesia for cesarean section. *Int J Clin Exp Med*, 10(8), 12315-12321.