EFFICACY OF INTRAMUSCULAR PHENYLEPHRINE FOR MAINTENANCE OF MATERNAL HEMODYNAMICS IN CAESAREAN SECTION UNDER SPINAL ANESTHESIA

Muhammad Saeed, Muhammad Musa, Muhammad Mubashir Khan, Sajjad Qureshi, Muhammad Hassan, Fayyaz Ahmad Orfi

Combined Military Hospital, Sialkot Pakistan

ABSTRACT

Objective: To determine the efficacy of intramuscular phenylephrine for maintenance of maternal hemodynamics in caesarean section under spinal anesthesia.

Study Design: Case series.

Place and Duration of Study: Department of Anesthesia, Combined Military Hospital Sialkot, from Nov 2017 to May 2018.

Methodology: Sixty women having C-section under spinal anesthesia were included after informed written consent. These patients received phenylephrine 5mg intramuscularly just after institution of spinal anesthesia. Outcome variable was change in mean heart rate and mean arterial pressure for 30 minutes following spinal anesthesia and frequency of spinal anesthesia induced hypotension. A predesigned proforma was used to record patient's demographic details along with other study variables.

Results: The age of the patients ranged from 20 to 37 years with a mean of 28.3 ± 4.4 years. Immediately after the spinal anesthesia, the mean heart rate and mean of mean arterial pressure were 80.73 ± 5.082 beats per minute and 82.30 ± 4.820 mmHg respectively. There after there were only insignificant changes in the mean heart rate and mean of mean arterial pressure from baseline as shown by paired sample t-test (p-value>0.05). Only one patient developed hypotension after 4 minutes of spinal anesthesia and was successfully managed and her mean arterial pressure remained fairly stable thereafter.

Conclusion: Intramuscular phenylephrine (5 mg) given prophylactically was found to be effective in reducing the incidence of hypotension related to spinal anesthesia in patients undergoing lower segment caesarean section which along with fetomaternal safety profile recommends its use in future practice.

Keywords: Hypotension, Intramuscular phenylepherine, Spinal.

INTRODUCTION

Among the gynecological procedures, cesarean section is becoming exceedingly common and popular in developing countries. According to a study conducted in local population in 2015, the rate of cesarean section was found to be 21.7 per 100 deliveries[1]. Spinal anesthesia is preferred anesthetic practice for women undergoing cesarean section owing to its simplicity, rapidity, associated maternal awareness and wide spread availability of anesthetic agents[2]. However, the sympathectomy owing to neuraxial blockade from spinal anesthesia is amplified by the physiological hemodynamic changes of gestation, resulting in post-spinal hypotension (PSH) in as high as 60-80% of the mothers getting spinal anesthesia for cesarean delivery[3]. Different mechanisms accused for the hypotension are gravid uterus compressing over the vena cava and hampering the venous return and subarachnoid block leading to venous pooling of blood in the lower legs and reduced cardiac output[3,4].

Hypotension is thus a common complication of spinal anesthesia and is frequent in patients with hypertension or taking antihypertensive medications[3]. Administration of intravenous fluids to optimize the blood volume or use of vasopressor drugs are commonly used techniques to prevent hypotension induced by

Correspondence: Dr Muhammad Saeed, Classified Anaesthesia, CMH, Sialkot Pakistan (*Email: mughalms@yahoo.com)*

Received: 15 Feb 2019; revised received: 14 Apr 2019; accepted: 07 Oct 2019

spinal anesthesia[3-5]. While left uterine displacement and fluid pre-load are routinely engaged in an effort to avoid this problem, a vasopressor is almost often unavoidable[6]. Phenylephrine is a potent vasoconstrictor that is short acting and causes an increase in mean arterial pressure due to its alpha-1 agonist action[7]. At clinically appropriate doses, phenylephrine is a selective α1 receptor agonist. Only much higher doses lead to β agonist action[8]. It is commonly used in obstetric anesthesia to stabilize the hypotension after spinal anesthesia due to its α1 agonist action leading to marked arterial vasoconstriction[7,8]. Phenylephrine (PE) is desired vasopressor in the prevention and management of post-spinal hypotension because of faster onset of action, less placental passage, less incidence of fetal acidosis and less maternal nausea and vomiting[9].

A much feared complication of phenylephrine is hypertension after its IV infusion. Few recent studies claimed pre-emptive intramuscular dose to be equally effective yet safer in terms of incident hypertension[12-14]. The evidence was however limited while there limited published material in local population which compelled the present study.

METHODOLOGY

This was a case series carried at the department of Anesthesia, Combined Military Hospital Sialkot, from Nov 2017 to May 2018. Sample size of 60 cases was calculated with 95% significance level, 5% margin of error and anticipated frequency of PSH to be 4.0% with phenylephrine[15]. Non-probability, consecutive sampling was done and 60 pregnant women at term undergoing cesarean delivery on elective lists of Combined Military Hospital Sialkot were included into this study and informed written consent was taken from every patient. We only involved patients at term (gestational age ≥37 weeks) having singleton pregnancy (as per dating scan) falling under ASA (American Society of Anesthesiologists) Class-II. Pregnant women with placenta accretea and placenta previa and those with diabetes mellitus, pregnancy induced hyper-tension, cardiovascular or pulmonary disease were excluded. We also excluded patients with previous spinal surgery, spinal cord abnormalities and those with coagulopathy and allergy to anesthetic medicine. The study participants received 5 mg of phenylephrine intramuscularly just after administration of spinal anesthesia. Regular monitoring of all patients was done which included a pulse oximeter and non-invasive blood pressure (NIBP) and ECG. Preloading with 500ml ringer lactate (R/L) solution was done. One reading of heart rate and blood pressure was taken at baseline before giving spinal anesthesia which was delivered in sitting position with 25G needle with 15mg hyperbaric bupivacaine. Following this, all the patients were positioned supine with 15 degree of lateral tilt to avoid aortocaval compression. Post-spinal hypotension (systolic blood pressure ≤90 mmHg) was noted and was treated with 2.5mg bolus of phenylephrine and 200ml of intravenous R/L solution. Heart rate and mean arterial pressure (systolic and diastolic blood pressure) were measured every two minutes for 30 minutes. Outcome variable was change in mean heart rate and mean arterial pressure for 30 minutes following spinal anesthesia and frequency of spinal anes-thesia induced hypotension which was recorded in a predesigned proforma. All the patients' observation and spinal anesthetic injections were done by a single consultant anesthetist to eliminate bias.

RESULTS

The mean age of the patients was 28.3 ± 4.4 years (range: 20 to 37 years). The mean heart rate and mean of mean arterial pressure were 79.28 ± 5.98 beats per minute (BPM) and 80.78 ± 5.59 mmHg pre-operatively.

Immediately after the spinal anesthesia, the mean heart rate and mean of mean arterial pressure were 80.73 ± 5.082 BPM and 82.30 ± 4.820 mmHg respectively. There after there were only insignificant changes in the mean heart rate and mean of mean arterial pressure from baseline as shown by paired sample t-test in table-I & II. The heart rate and mean arterial pressure of the

patients remained fairly stable till 30 minutes following anesthesia. Only one patient developed hypotension after 4 minutes of spinal anesthesia and was successfully managed and her mean arterial pressure (MAP) remained fairly stable thereafter

Table-I: Changes in the mean Heart Rate from pre-operative value to 30 minutes after anesthesia.

Time Stamp	Heart Rate (bpm) (mean ± SD)	*p*-value
Pre-operatively	79.28 ± 5.98	-
Immediate after Spinal Anesthesia	80.73 ± 5.08	0.110
2 minutes	78.62 ± 5.17	0.470
4 minutes	78.73 ± 5.44	0.550
6 minutes	78.47 ± 5.93	0.388
8 minutes	78.17 ± 6.25	0.252
10 minutes	78.45 ± 5.79	0.369
12 minutes	78.70 ± 6.06	0.537
14 minutes	78.70 ± 6.14	0.539
16 minutes	78.23 ± 4.87	0.230
18 minutes	78.00 ± 3.97	0.141
20 minutes	78.40 ± 3.49	0.286
22 minutes	78.78 ± 3.59	0.537
24 minutes	78.90 ± 4.81	0.671
26 minutes	77.82 ± 4.41	0.110
28 minutes	78.20 ± 4.13	0.205
30 minutes	77.98 ± 4.39	0.164

Paired sample t-test comparing reading from pre-operative status, Observed difference was statistically insignificant.

DISCUSSION

Hypotension is a very common sequeal of the sympathetic vasomotor blockade due to spinal anesthesia in pregnant women undergoing caesarean section. Maternal complications such as dyspnea and nausea and vomiting frequently accompany severe spinal hypotension, and adverse effects on the neonate, including umbilical acidosis and decreased Apgar scores have been correlated with duration and severity of hypotension, decreased arterial blood pressure and heart rate[16]. Phenylephrine is an alpha-1 receptors agonist that is used when peripheral vasoconstriction is needed. When used IV, it is a drug with rapid onset and short duration of action (5-10 min) and may cause hypertension[17]. Therefore, there has been interest in efficacy of prophylactic intramuscular dose of phenylephrine.

In the present study, the mean age of the patients was 28.3 ± 4.4 years. A similar mean age of 28.4 ± 4.7 years has been reported by Khan *et al*[18] among women undergoing C-section at Aga Khan University Hospital, Karachi. Raees *et al*[19] (2012) reported similar mean age of 30.8 ± 5.1 years among pregnant women undergoing elective cesarean section at Lady Reading Hospital Peshawar while Eusaph *et al*[20] (2011) reported it to be 31.9 ± 2.3 years at Lady Willington Hospital, Lahore. Similar mean age of 30.4 ± 4.9 years has been reported by Akinola *et al*[21] (2010) in Nigerian such women [96]. Zhao *et al*[22] (2016) and Chen *et al*[23] (2016) reported it to be 29.85 ± 2.62 years and 31.6 ± 3.0 years respectively in Chinese women undergoing cesarean section.

Table-II: Changes in the mean arterial pressure from pre-operative value to 30 minutes after anesthesia.

Time Stamp	Mean Arterial Pressure (mmHg) (mean ± SD)	*p*-value
Pre-operatively	80.78 ± 5.59	-
Immediate after Spinal Anesthesia	82.30 ± 4.82	0.084
2 minutes	80.98 ± 6.37	0.844
4 minutes	82.38 ± 7.01	0.120
6 minutes	82.03 ± 7.01	0.242
8 minutes	81.85 ± 7.49	0.313
10 minutes	80.12 ± 6.67	0.517
12 minutes	82.55 ± 6.20	0.054
14 minutes	81.77 ± 7.39	0.341
16 minutes	82.08 ± 4.92	0.129
18 minutes	81.02 ± 5.38	0.794
20 minutes	80.88 ± 5.28	0.908
22 minutes	81.50 ± 4.77	0.408
24 minutes	81.68 ± 4.48	0.283
26 minutes	80.88 ± 5.50	0.911
28 minutes	82.23 ± 5.45	0.162
30 minutes	81.63 ± 5.47	0.410

Paired sample t-test comparing reading from pre-operative status, Observed difference was statistically insignificant.

We observed that the prophylactic intramuscular dose of phenylephrine attenuated the

hemodynamic response after spinal anesthesia in pregnant women undergoing C-section evident from a stable heart rate and mean arterial pressure up to 30 minutes following anesthesia. The frequency of hypotension in our study was 1.7%. Bhargav *et al*[12] (2018) reported similar trend in the mean heart rate and mean of mean arterial pressure in pregnant women undergoing C-section with prophylactic intramuscular dose of phenylephrine. They too observed very low frequency of hypotension among such women and reported it to be 6.7%. Similar conclusion was drawn by Singh *et al*[13] (2015) who observed similar stable heart rate and mean arterial pressure following prophylactic intramuscular phenylephrine. Though the vasopressor effect of phenylephrine was comparable to those of ephedrine yet the frequency of various side effects like hypotension, nausea and vomiting was lower in the phenylephrine group establishing its safety over ephedrine. In another study, Das *et al*[14] (2017) reported that the mean arterial pressure dropped significantly after spinal anesthesia in patients receiving prophylactic intramuscular phenylephrine and 10.0% patients developed hypotension. However, they concluded that the vasopressor effect of phenylephrine was better than ephedrine and was safer in terms of side effects like bradycardia, nausea and vomiting.

RECOMMENDATIONS

The present study was the first of its kind in local population and adds to the limited international research evidence on the topic. In the present study, we found pre-emptive intramuscular phenylephrine to be helpful in attenuating the hemodynamic response of spinal anesthesia without any substantial incidence of hypotension and bradycardia which establish its safety and recommends its use in future practice.

LIMITATION OF STUDY

A very important limitation to the present study was that we didn't consider the fetal outcome in terms of 5 and 7 minutes APGAR score which is an important concern and should be addressed before adopting it in routine practice. Such a study is highly recommended in future research.

CONCLUSION

Intramuscular phenylephrine 5 mg given prophylactically was found to be effective in reducing the incidence of hypotension related to spinal anesthesia in patients undergoing lower segment caesarean section which along with fetomaternal safety profile recommends its use in future practice.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Naeem M, Khan MZI, Abbas SH, Khan A, Adil M, Khan MU. Rate and indications of elective and emergency caesarean section; a study in tertiary care hospital of Peshawar. J Ayub Med Coll 2015; 27(1): 151-4.
2. Shin YD, Park SH, Kim HT, Park CJ, Lee JH, Choi YJ. The effect of anaesthesia technique on caesarean section. Pak J Med Sci 2016; 32(1): 147-50.
3. Fakherpour A, Ghaem H, Fattahi Z, Zaree S. Maternal and anaesthesia-related risk factors and incidence of spinal anaesthesia-induced hypotension in elective caesarean section: A multinomial logistic regression. Indian J Anaesth 2018; 62(1): 36-46.
4. Nag DS, Samaddar DP, Chatterjee A, Kumar H, Dembla A. Vasopressors in obstetric anesthesia: a current perspective. World J Clin Cases 2015; 3(1): 58-64.
5. Johnson E. Advances in understanding and management in obstetric anaesthesia: The great myth of our times. Indian J Anaesth 2017; 61(4): 285-8.
6. Bajwa SJS, Kulshrestha A, Jindal R. Co-loading or pre-loading for prevention of hypotension after spinal anaesthesia! a therapeutic dilemma. Anesth Essays Res 2013; 7(2): 155-9.
7. Heesen M, Kölhr S, Rossaint R, Straube S. Prophylactic phenylephrine for caesarean section under spinal anaesthesia: systematic review and meta-analysis. Anaesthesia 2014; 69(2): 143-65.
8. Stewart A, Fernando R, McDonald S, Hignett R, Jones T, Columb M. The dose-dependent effects of phenylephrine for elective cesarean delivery under spinal anesthesia. Anesth Analg 2010; 111(5): 1230-37.
9. Hasanin A, Mokhtar AM, Badawy AA, Fouad R. Post-spinal anesthesia hypotension during cesarean delivery, a review article. Egypt Anaesth 2017; 33(2): 189-93.
10. Naghibi K, Rahimi M, Mashayekhi Z. A comparison of intravenous ephedrine or phenylephrine, for prevention of postspinal hypotension during elective lower abdominal surgery: a randomized, double-blind case-control study. Adv Biomed Res 2017; 6(1): 60-66.
11. Moslemi F, Rasooli S. Comparison of prophylactic infusion of phenylephrine with ephedrine for prevention of hypotension in elective cesarean section under spinal anesthesia: a randomized clinical trial. Iran J Med Sci 2015; 40(1): 19-26.

12. Bhargav S, Nandwani H, Bhure A, Kulkarni S, Jain A, Tiwari Y. Comparison of hemodynamic changes amongst subjects using prophylactic ephedrine v/s phenylephrine intramuscularly for prevention of hypotension in elective caesarean section under subarachnoid block. Int J Med Res Prof 2018; 4(3): 29-32.
13. Singh J, Singh P, Agarwal A. To compare the efficacy of intra-muscular phenylephrine and ephedrine in LSCS to avoid post spinal hypotension. J Evo Med Dental Sci 2015; 4(19): 3247-53.
14. Das S. A comparative study of pre-emptive intra muscular phenylephrine and ephedrine to prevent hypotension during spinal anaesthesia in caesarean section. IOSR J Dent Med Sci 2017; 16(10): 41-4.
15. Ngan Kee WD, Lee A, Khaw KS, Ng FF, Karmakar MK, Gin T. A randomized double-blinded comparison of phenylephrine and ephedrine infusion combinations to maintain blood pressure during spinal anesthesia for cesarean delivery: the effects on fetal acid-base status and hemodynamic control. Anesth Analg 2008; 107(4): 1295-302.
16. 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(1): 71-92.
17. Abbasivash R, Sane S, Golmohammadi M, Shokuhi S, Toosi FD. Comparing prophylactic effect of phenylephrine and ephedrine on hypotension during spinal anesthesia for hip fracture surgery. Adv Biomed Res 2016; 5(1): 167-73.
18. Khan FA, Khan M, Ali A, Chohan U. Estimation of blood loss during Caesarean section: an audit. J Pak Med Assoc 2006; 56(12): 572-5.
19. Raees M, Yasmeen S, Jabeen S, Utman N, Karim R. Maternal morbidity associated with emergency versus elective caesarean section. J Postgrad Med Inst 2012; 27(1): 55-62.
20. Eusaph AZ, Iqbal S, Rana T, Asghar F. Evaluation of practices of blood transfusion in various indication of caesarean section. Ann KEMU 2011; 17(2): 183-6.
21. Akinola OI, Fabamwo AO, Tayo AO, Rabiu KA, Oshodi YA, Onyekwere CA. Evaluation of blood reservation and use for caesarean sections in a tertiary maternity unit in south western Nigeria. BMC Pregnancy Childbirth 2010; 10(1): 57-61.
22. Zhao L, Zhao XL, Cheng YM, Xu YY. Effects of different types of placenta previa on pregnancy outcome. Maternal Child Health China 2016; 31(6): 1163-5.
23. Chen CY, Su YN, Lin TH, Chang Y, Horng HC, Wang PH, et al. Carbetocin in prevention of postpartum hemorrhage: Experience in a tertiary medical center of Taiwan. Taiwan J Obstet Gynecol 2016; 55(6): 804-9.