ORIGINAL ARTICLE

Comparison of two different infusion rates of Phenylephrine as a Prophylaxis against Spinal Anaesthesia induced Hypotension in Elective Caesarian Sections

IRFAN ALI, FARRUKH AFZAL, MADIHA ZAFAR, *KHAWAR ALI*

ABSTRACT

Background. Spinal anaesthesia is the most commonly used technique for patients undergoing elective caesarean section. It is associated with hypotension which may lead to drop in cardiac output, decrease in placental blood flow and foetal hypoxia. Phenylephrine is commonly used to elevate arterial blood pressure by increasing systemic vascular resistance. The recommended infusion dose of phenylephrine ranges from 30 to 180µg/min.

Aim: To compare the effect of two different infusion rates of phenylephrine as a prophylaxis against S/A induced hypotension and bradycardia in obstetric patients undergoing elective C- Section.

Methodology: This randomized controlled was carried out in the operation theatres of KEMU affiliated Lady Aitchison Hospital Lahore , over a period of six months. After approval of institutional review board and informed consent ,220 women aged 18-40 years, planned to receive spinal anesthesia for elective caesarean section were recruited and randomly allocated into two groups. The average of the 3 readings of systolic blood pressure and heart rate was used as a baseline. Group-I received prophylactic phenylephrine infusion at 50µg/minute while Group-II received infusion at 100µg/minutes at a rate of 1ml/min immediately after spinal anaesthesia using 2ml of 0.75% Bupivacine for first 3 minutes. Infusion continued at same rate if systolic blood pressure remained between 80-100% of baseline until delivery. It was halved if systolic pressure increased > 110% of the baseline. Rescue boluses of Phenylephrine and Atropine were given if systolic pressure fell below 80% of the baseline and heart rate of < 50 beats/min respectively.

Results: No significant difference was found in the frequency of hypotension in both groups (p=0.072) whereas frequency of bradycardia was significantly lower in Group I as compared to Group II (p=0.000)

Conclusion: Prophylactic Phenylephrine infusion of 50µg/minute is better for prevention of Spinal Anaesthesia induced hypotension in patients undergoing elective caesarian section as it causes significantly less bradycardia as compared to 100ug/min infusion.

Key words: Phenylephrine Infusion, Spinal Anesthesia, Bradycardia, Hypotension

INTRODUCTION

Spinal anaesthesia is the most commonly used technique for patients undergoing elective Caesarean section. It is preferred over general anaesthesia due lack of airway complications, early mother baby bonding and early mobilization[1]. However spinal anaesthesia is associated with its own complications of which most common is hypotension the incidence of which is very high[2,7].

Hypotension in obstetric patients may lead to drop in cardiac output, decrease in placental blood flow and foetal hypoxia[3,4]. A variety of methods have been used to prevent spinal hypotension. These include physical maneuvers (compression stockings, left uterine displacement), intravenous fluid expansion, and prophylactic use of sympathomimetic drugs[5].

Department of Anaesthesiology , King Edward Medical University Lahore.

Correspondence to Dr. Farrukh Afzal Email: farukhafzaldr@gmail.com Cell: 0333-4444282

Current evidence suggests that infusions of vasopressors are best titrated to maintain blood pressure to near baseline levels[8]. Recent studies favor the use of phenylephrine in management of spinal induced hypotension[6]. Phenylephrine is an α-1 agonist which elevates arterial blood pressure by increasing systemic vascular resistance secondary to vasoconstriction. It has less adverse effects on foetal blood pH and maternal heart rate[7].

Tarek Ansari et al. noted that rapid colloid co-loading (simultaneous fluid infusion to prevent hypotension) along with phenylephrine infusion of 50µg/min has an incidence of hypotension 14.8% whereas with 100µg/min infusion at same rate the incidence was 4.7% with a p value 0.12.And the incidence of bradycardia with 50ug/min infusion is 1.8% while with 100ug/min incidence of bradycardia is 17.4% with p value of 0.005. Thus stating that with fluid co-loading incidence of hypotension with 50µg/min phenylephrine infusion is insignificantly little more than with 100µg/min (P value of 0.12) however

50ug/min of phenylephrine has significantly less incidence of maternal bradycardia than 100ug/min (P value 0.005).[7]

The recommended infusion dose of phenylephrine ranges from 30 to 180 µg/min. This wide dose range may precipitate high plasma concentrations that might precipitate hypertension and bradycardia so a user-friendly infusion regimen is needed. So we designed a study to compare the efficacy of two doses of phenylephrine in maintaining maternal blood pressure and heart rate without rapid co-loading (to prevent maternal excessive fluid overload).This study has never been conducted in our population before more over there is no trend of using phenylephrine infusion instead of which boluses of phenylephrine are used as needed. (The incidence of hypotension with this technique is 62.2% with a p value <0.001 as noted by Sen et al)[9].

The objective of this study was to compare the effect of two different infusion rates of phenylephrine in terms of frequency of spinal anaesthesia induced hypotension and bradycardia in obstetric patients undergoing elective Caesarean section..

MATERIALS AND METHODS

This was a randomized Controlled Trial conducted in Operation Theatres of Lady Aitchison Hospital, Department of Anaesthesiology King Edward Medical University Lahore over a period of six months.

After IRB and departmental approval, a sample of 220 patients (ages 18-40 years) planned to receive spinal anaesthesia for elective caesarean section was obtained through Non-Probability, Consecutive Sampling. using 95% confidence level, 80% power of test and taking expected frequency of hypotension to be 14.8% with phenylephrine 50µg/min and 4.7% with phenylephrine infusion of 100µg/min[7].

Patients with history of preeclampsia or multiple gestations on history and antenatal record, With more than 2 previous Caesarean sections, known hypertensive, Documented foetal abnormality (on ultrasound)and those with Allergy to local anaesthetic agent on history and medical record were excluded from the study.

Data collection procedure: Informed consent was taken from each patient. Patients were randomly divided in two groups by lottery method. Group I received prophylactic phenylephrine infusion of 50µg/min. Group II received phenylephrine infusion of 100µg/min. Relevant demographic data like name, age and data of study variables was recorded.

Standard monitoring was attached to the patient. Two wide bore cannulae were maintained in peripheral veins. Three measurements of non-invasive blood pressure at one minute interval were taken after the mothers were allowed a 5 minute rest period in the supine position with left lateral tilt. The average of the 3 readings of systolic blood pressure and heart rate was used as a baseline.

Patients were placed in lateral decubitus position. After infiltration with 2% lidocaine, 27G Quincke Spinal needle was used to perform spinal tap. Inj. hyperbaric bupivacaine 2ml of 0.75% (15 mg) was injected intrathecally. Immediately after spinal anaesthesia phenylephrine infusion was started at 1ml/min with designated concentration (50 or 100µg/ml) for first 3minutes. Infusion was continued at same rate if systolic blood pressure remained between 80-100% of baseline until delivery. It was halved if systolic pressure increased > 110% of the baseline. Rescue boluses of phenylephrine and atropine were given if systolic pressure and heart rate fell below 80% of the baseline.

Study variables, heart rate and systolic blood pressure were noted from the monitor every 5 minutes from 5-20 minutes of infusion. Rate of phenylephrine infusion, presence of hypotension and bradycardia was noted.

Data analysis: Collected data was entered into SPSS version 18. Quantitative variables such as age, blood pressure and heart rate have been presented by mean±SD. Categorical variable i-e hypotension and bradycardia have been presented by frequency and percentage. Chi-square test has been applied to compare frequency of hypotension and bradycardia between the groups taking p value ≤ 0.05 as significant.

Data has been stratified for age, parity, baseline systolic blood pressure (>120 and ≤120mmHg) and baseline heart rate (>70/min or ≤ 70/min) to address effect modifiers. Post-stratification Chi-square test has been applied taking p value ≤ 0.05 as significant.

RESULTS

The age of the patients ranged from 22 years to 38 years with a mean of 29.46±3.81 years According to parity, 87 (39.5%) patients were para 2, followed by para 3(38.6%) and para 1(21.9%) . Baseline heart rate of the patients ranged from 57 bpm to 110 bpm with a mean of 83.10±9.68 bpm. Baseline systolic blood pressure of the patients ranged from 100 mmHg to 150 mmHg with a mean of 125.23±13.96 mmHg.

Both groups were comparable in terms of mean age (p=0.986), parity (p=0.603), mean baseline heart rate (p=0.603) and mean systolic blood pressure (p=0.210)

Twenty two (10%) patients developed hypotension. The frequency of hypotension was

insignificantly higher in Group-I (13.6% vs. 6.4%; p= 0.072) as compared to Group-II as shown in Table 1.
When stratified, the frequency of hypotension was insignificantly higher in Group-I as compared to Group-II across

- various age groups; 22-27 years (10.0% vs. 7.7%; p=.718), 28-33 years (15.2% vs. 4.2%; p=.060), 34-38 years (16.7% vs. 9.5%; p=.482),
- Parity groups; primigravidas (11.5% vs. 9.1%; p=.782), para 2 (15.6% vs. 7.1%; p=.219), para 3 (12.8% vs. 4.3%; p=.157)
- Baseline heart rate groups; ≤70 bpm (12.5% vs. 6.7%; p=.636), >70 bpm (13.7% vs. 6.3%; p=.085) and
- Baseline systolic blood pressure groups; ≤120 mmHg (21.7% vs. 10.7%; p=.128) and >120 mmHg (7.8% vs. 1.9%; p=.142)

25 (11.4%) patients developed bradycardia. The frequency of bradycardia was significantly lower in Group-I (3.6% vs. 19.1%; p=.000) as compared to Group-II as shown in Table 2.
When stratified, the frequency of bradycardia was significantly lower in Group-I as compared to Group-II across

- Various age groups; 22-27 years (2.5% vs. 17.9%; p=.023), 28-33 years (4.3% vs. 20.0%; p=.021), 34-38 years (4.2% vs. 19.0%; p=.047),
- Parity groups; primiparas (3.8% vs. 22.7%; p=.039), para 2 (4.4% vs. 19.0%; p=.033), para 3 (2.6% vs. 17.4%; p=.027),
- Baseline heart rate groups; ≤70 bpm (25% vs. 53.3%; p=.037), >70 bpm (2.0% vs. 13.7%; p=.002) and
- Baseline systolic blood pressure groups; ≤120 mmHg (4.3% vs. 21.4%; p=.013) and >120 mmHg (3.1% vs. 16.7%; p=.012)

Table 1: Comparison of frequency of hypotension in both groups

Hypotension		Study Groups		Total	P value
		Group-I	Group-II		
Yes	Count	15	7	22	.072
	% within Study Groups	13.6%	6.4%	10.0%	
No	Count	95	103	198	
	% within Study Groups	86.4%	93.6%	90.0%	
Total	Count	110	110	220	
	% within Study Groups	100.0%	100.0%	100.0%	

Table 2: Comparison of frequency of Bradycardia between the Study Groups

Hypotension		Study Groups		Total	P value
		Group-I	Group-II		
Yes	Count	4	21	25	.000
	% within Study Groups	3.6%	19.1%	11.4%	
No	Count	106	89	195	
	% within Study Groups	96.4%	80.9%	88.6%	
Total	Count	110	110	220	
	% within Study Groups	100.0%	100.0%	100.0%	

DISCUSSION

Spinal Anaesthesia is one of the most commonly employed techniques for caesarian section. It is preferred over general anaesthesia by anaesthetists, obstetricians and most importantly patients themselves. This is because of numerous advantages it offers over general Anaesthesia such as avoidance of handling of a potentially difficult airway, an awake patient and early mother-child bonding, less fetal depression and early mobilization of the patient. However hypotension is a frequent complication , which if not anticipated , recognized or treated in time can have serious consequences[1,2,7].

In a recent retrospective study 46% of cesarean section patients who received regional anesthesia had a decrease in blood pressure (BP) of 30% or more.[10]Risk factors associated with an increased risk of spinal anaesthesia induced hypotension include Increasing age, Spinal anesthetic factors, e.g. Dose of local anesthetic, height of resultant block, Pre-existing hypertension, Higher infant birth weight, and Obesity.[11] The seriousness of both maternal and fetal side effects of sustained hypotension is established. Various methods used to prevent or treat spinal anaesthesia induced hypotension in obstetric population include

- Tilting the patient by means of a wedge to limit aortocaval compression by the gravid uterus is standard practice - though if fully effective would negate the need for this chapter. A recent study found that placing the wedge under the right lumbar area as opposed to under the right hip

resulted in a lesser incidence of maternal hypotension[12].

- The use of a lower dose of local anesthetic such as bupivacaine with the resultant lesser extent of sympathetic block will result in less hypotension - but at the potential cost of reduced block duration and increased maternal discomfort during cesarean section.
- Wrapping of the legs (to decrease bood pooling in the legs and increase venous return) is as effective as phenylephrine in maintaining blood pressure after epidural anesthesia for cesarean section[13] but is not widely practiced.
- Fluid therapy either pre-loading or co-loading
- Use of vasopressors such as phenylephrine and ephedrine
- Other methods such as Transcutaneous electrical nerve stimulation (TENS) which has been shown to be effective in maintaining blood pressure in patients undergoing cesarean section under spinal anesthesia and reduces the requirement for ephedrine[14].

A recent meta-analysis found no significant difference in the incidence of hypotension between pre-loading and co-loading and concluded that there was no They noted that, with either fluid strategy, the incidence of hypotension was high resulting in significant need for vasopressor therapy[15].

Use of vasopressors has been found to be the most effective method to combat hypotension.

The data for optimal bolus dosing of phenylephrine is unclear. One study found the 90% effective dose (ED90) of phenylephrine to be 147 µg IV (95% CI 98 to 222 µg) by using up-down sequential allocation for the treatment of spinal anesthesia-induced hypotension[16]. However, another study found that the 95% effective dose (ED95) of phenylephrine was 135 µg IV (95% CI 106 to 257 µg) to prevent spinal-induced hypotension alone and 159 µg IV by using up-down sequential allocation for the prevention of hypotension and nausea[17].

The most recent study of phenylephrine infusions[18] compared placebo or prophylactic phenylephrine infusions at 25, 50, 75, or 100 µg/min plus 2 L crystalloid co-load after spinal anesthesia. They found more hypotension in the control group compared with all phenylephrine groups but phenylephrine 75 and 100 µg/min groups were associated with more hypertension compared with control groups.

Our study was a randomized controlled trial conducted at Department of Anaesthesiology at KEMU affiliated Operation Theatres of Lady Aitchison Hospital, Lahore 6 months after the approval of synopsis from 05/12/2014 to 04/06/2015. This study involved 220 women aged between 18-40 years undergoing spinal anesthesia for caesarean section randomly allocated into two groups. Group-I received prophylactic phenylephrine infusion at 50µg/minute while Group-II received infusion at 100µg/minute.

The age of the patients ranged from 22 years to 38 years with a mean of 29.46±3.81 years. Neves et al. (2010) observed a similar mean age of 29.8±6.07 years among pregnant women undergoing spinal anesthesia for C-section in Brazil[19]. Imran et al. (2007) in Pakistan[20] and Ansari et al. (2011)[7] in UAE observed it to be 32.7±4.6 years and 32.39±8.15 years respectively. 39.5% patients were para 2, followed by para 3 (38.6%) and para 1 (21.9%). Baseline hear rate of the patients ranged from 57 bpm to 110 bpm with a mean of 83.10±9.68 bpm. Neves et al. (2010) and Imran et al. (2007) also observed a similar mean baseline heart rate of 84.33±11.41 and 83.36±12.97 bpm respectively. Baseline systolic blood pressure of the patients ranged from 100 mmHg to 150 mmHg with a mean of 125.23±13.96 mmHg. Our observation matches to that of Neves et al. (2010)and Imran et al. (2007) who observed mean baseline systolic blood pressure of 123.33±9.77 mmHg and 125.0±15.71 mmHg respectively among pregnant women undergoing spinal anesthesia for C-section.

Both the groups were comparable in terms of mean age (p=.986), parity (p=.603), mean baseline heart rate (p=.603) and mean systolic blood pressure (p=.210). Thus the randomization was effective and there was no inherent heterogeneity in the study groups.

The frequency of hypotension was insignificantly higher in Group-I (13.6% vs. 6.4%; p=.072) as compared to Group-II. A similar insignificant difference has already been reported by Ansari et al. in 2011 (14.8% vs. 4.7%; p=.12)[7].

When stratified, the frequency of hypotension was insignificantly higher in Group-I as compared to Group-II across various age groups; 22-27 years (10.0% vs. 7.7%; p=.718), 28-33 years (15.2% vs. 4.2%; p=.060), 34-38 years (16.7% vs. 9.5%; p=.482), parity groups; primiparas (11.5% vs. 9.1%; p=.782), para 2 (15.6% vs. 7.1%; p=.219), para 3 (12.8% vs. 4.3%; p=.157), baseline heart rate groups; ≤70 bpm (12.5% vs. 6.7%; p=.636), >70 bpm (13.7% vs. 6.3%; p=.085) and baseline systolic blood pressure groups; ≤120 mmHg (21.7% vs. 10.7%; p=.128) and >120 mmHg (7.8% vs. 1.9%; p=.142). Thus 50µg/minute phenylephrine infusion was as safe as 100µg/minute infusion in terms of occurrence of hypotension across all age and parity groups and irrespective of patient's baseline heart rate and systolic blood pressure.

The frequency of bradycardia was significantly lower in Group-I (3.6% vs. 19.1%; p=.000) as compared to Group-II. Ansari et al. in 2011 also observed 50µg/minute phenylephrine infusion to be better than 100µg/minute infusion in terms of lower frequency of bradycardia (1.8% vs. 17.4%; p=.005)[7].

When stratified, the frequency of bradycardia was significantly lower in Group-I as compared to Group-II across various age groups; 22-27 years (2.5% vs. 17.9%; p=.023), 28-33 years (4.3% vs. 20.0%; p=.021), 34-38 years (4.2% vs. 19.0%; p=.047), parity groups; primiparas (3.8% vs. 22.7%; p=.039), para 2 (4.4% vs. 19.0%; p=.033), para 3 (2.6% vs. 17.4%; p=.027), baseline heart rate groups; ≤70 bpm (25% vs. 53.3%; p=.037), >70 bpm (2.0% vs. 13.7%; p=.002) and baseline systolic blood pressure groups; ≤120 mmHg (4.3% vs. 21.4%; p=.013) and >120 mmHg (3.1% vs. 16.7%; p=.012). Thus 50µg/minute phenylephrine infusion was better than 100µg/minute infusion in terms of occurrence of bradycardia across all age and parity groups and irrespective of patient's baseline heart rate and systolic blood pressure.

Thus prophylactic phenylephrine infusion of 50µg/minute was associated with significantly lower frequency of bradycardia (3.6% vs. 19.1%; p=.000) with only insignificant increase in frequency of hypotension (13.6% vs. 6.4%; p=.072) as compared to 100µg/minute infusion.

CONCLUSION

On the basis of our study it can be advocated that in future practice, female patients undergoing spinal anesthesia for cesarean section should receive prophylactic phenylephrine infusion of 50µg/minute to reduce the risk of hypotension and bradycardia and thus decreasing maternal and fetal morbidity associated with spinal hypotension.

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