

COMPARISON OF VARIABLE RATE PHENYLEPHRINE INFUSION WITH RESCUE PHENYLEPHRINE BOLUSES VERSUS RESCUE BOLUSES ALONE FOR PREVENTION OF HYPOTENSION DURING SPINAL ANESTHESIA FOR ELECTIVE CESAREAN DELIVERY

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ABSTRACT

Objective: To compare effectiveness of infusion with phenylephrine plus rescue boluses and rescue boluses in preventing frequency of maternal hypotension in patients undergoing cesarean section under spinal anesthesia.

Study Design: Quasi experimental study.

Place and Duration of Study: Anesthesia Department, Holy Family Hospital Rawalpindi, from Nov 2015 to May 2016.

Methodology: A total of 80 patients were randomly divided using lottery method in group A and B. Spinal anesthesia was given with co-loading as 15 ml/kg of ringer lactate, with 12mg of hyperbaric bupivacaine (0.75%). No pre-medication was used. Patients received variable amount phenylephrine infusion starting at 0.75µg/kg/min (group A) or variable rate prophylactic saline infusion at 0.0075ml/kg/min (group B) (control group). Maternal hypotension was treated with rescue boluses of phenylephrine (50-100µg).

Results: Mean age was 30 ± 2.23years' vs. 31± 2.81 years (group A Vs group B) ($p=0.0818$). The two groups did not differ in American society of Anaesthesiologists ASA status. Mean BMI in group A and group B was 24 ± 2.813 vs. 25 ± 3.114 ($p=0.1358$). Mean NIBP in group A and group B was 110/70mm Hg ± 8.62 vs. 111/80mm Hg ± 10.224 ($p=0.6376$). Phenylephrine infusion with rescue boluses was operational in 32 (80%) subjects (there was less incidence of maternal hypotension) compared to boluses only was efficacious in 14 (35%) of all patients $p<0.001$.

Conclusion: Our study concluded that phenylephrine infusion with rescue boluses provided better control of blood pressure than rescue boluses alone during cesarean section under spinal anesthesia.

Keywords: Boluses, Cesarean section, Hypotension, Phenylephrine infusion, Spinal anesthesia.

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INTRODUCTION

The type of anesthesia, whether general or regional depends upon the indication of cesarean, its urgency, physical condition of patient and also the choice of patient and surgeon. Spinal anesthesia is preferred for cesarean sections over general anesthesia for its obvious benefits like avoidance of airway instrumentation, less risk of aspiration, awake mother, extension of analgesia to postoperative period and prevention of depressant effects of anesthetic drugs on fetus¹⁻³.

A frequent problem following spinal anesthesia is hypotension. Its incidence is 50-90% if no prophylactic measures are taken¹. Hypoten-

sion ensues due to vasodilation by sympathetic blockade and is provoked by diminished venous return due to aorto-caval compression^{1,2}. It adversely affects both mother and fetus. It can cause nausea, vomiting, dizziness, headache, impaired utero placental circulation and organ hypo perfusion in mother while in fetus it may lead to fetal acidosis^{1,4}. To counter hypotension, several methods can be adopted including fluids and different vasopressors but to date, no method has been established with complete success. At present, different fluid regimes and vasopressors are used including physical maneuvers (left uterine displacement & compression stockings), intravenous fluid expansion with crystalloids and colloids and prophylactic use of vasopressors^{3,5}. The vasopressors include ephedrine, phenylephrine, methoxamine, dopamine and mephenter-

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mine but out of these phenylephrine is most preferred for optimal control of blood pressure and reduced incidence of fetal acidosis¹⁻³. Phenylephrine is a selective alpha-1 agonist and has both direct & indirect sympathomimetic effects. Direct effects are mediated by alpha-1 receptors and indirect effects result from norepinephrine release from nerve terminals⁵. It is currently drug of choice for maternal hypotension as it is associated with less fetal acidosis, contrary to old belief, according to which ephedrine was considered gold standard^{2,5}. It is more desirable for hypotension with bradycardia. Different infusion rates of phenylephrine show dose related reduction in cardiac rate^{2,5,6}.

Optimal dosing regimen for phenylephrine administration is not well established. Although prophylactic infusion avoids hypotension but also leads to reactive hypertension and bradycardia, on contrary bolus administration is easier but more hypotension and bradycardia are associated. In a study conducted by Siddik-Sayyid *et al*, incidence of hypotension in infusion group was only 20% compared to 90% in rescue boluses alone⁵. So variable rate infusion can be started at 50µg/min with greater hemodynamic stability and can be increased up to 75-100µg/min and for bolus dose ranges from 40-100µg⁷⁻⁹.

Rationale of this study was to develop an effective strategy to counter maternal hypotension as little previous data is available in Pakistan on variable rate infusion of phenylephrine. Formulation of a regimen which provides better and tighter controls of maternal BP will not only help in standardizing the dosages but also reducing cost and patient discomfort.

METHODOLOGY

This quasi-experimental study was done in Department of anesthesia, Holy Family Hospital, Rawalpindi. A total of 80 patients sample size was calculated with help of WHO sample size calculator, with following parameters: level of significance: 5%, power of test: 90%, anticipated population proportion in group A: 20%, anticipated population proportion in group B is 90%.

Inclusion criteria: patients of ASA 1 & 2, age 20-40 years, singleton pregnancy, elective caesarian section under spinal anesthesia were included. Exclusion criteria: patients of American Society of Anaesthesiologists (ASA) 3 & 4, contraindications to spinal block, unwilling for spinal and BMI>35 were excluded. Patients were selected by consecutive non probability technique and divided randomly by a random number table generated by computer in groups A and B. Group were allocated by sealed opaque envelopes. Anaesthesia personnel not involved in anesthetic management prepared either a phenylephrine infusion or saline in 50 ml syringe according to instructions contained within each sealed envelope and gave it to attending anesthesiologist. Intravascular access had been established with two 18 G cannula. Baseline vitality has been assumed. Control group was the one receiving saline infusion (group B). In the sitting position, neuraxial anesthesia was induced with 25 G, Quincke needle at level L2-L3. Under aseptic measures 2ml of 0.75% hyperbaric bupivacaine was given intrathecal after observing clear CSF flow. Patient was placed supine with 10-degree head down and wedge was sited below right hip to avert aortocaval compromise.

Block was assessed every 2 minutes with iced saline for 10 minutes. All patients were given oxygen by mask at a rate of 5L/min. Each group were co-loaded with 15ml/kg lactated Ringer's solution. Patients were randomized to obtain a prophylactic variable infusion of phenylephrine first at 0.75µg/kg/min (group A) or 0.0075ml/kg/min (group B) prophylactic variable infusion of saline. Blood pressure, heart rate and oxygen saturation were monitored at an interval of 3 minutes up to 15 minutes, hypotension-free efficacy was measured.

Maternal hypotension was treated with rescue boluses of phenylephrine (50-100µg). Cardiac rates below 50 beats/min were treated with 0.5 mg of Atropine accompanied by hypotension. Procedure began as soon as the desired block level was reached. General endotracheal anesthesia was dealt for inadequate

or failed block and patients were omitted out of study.

Data collection was done on a well-formed proforma and SPSS 15 version was utilized to analyze it. Frequency was calculated for effectiveness of prevention of maternal hypotension. Means \pm Standard Deviations was calculated for age, heart rate, baseline NIBP, systolic BP and BMI. Effect modifiers like age, ASA & BMI was controlled by stratification. Post stratification chi square test was used to match the usefulness in two groups. The *p*-value at a level of ≤ 0.05 had been considered statistically significant.

RESULTS

Eighty patients were recruited to compare efficacy of phenylephrine infusion plus rescue boluses (group A) and rescue boluses only (group B).

Table-I: Demographic of study population (n=40).

	Group A	Group B	<i>p</i> -value
	Mean \pm SD	Mean \pm SD	
Age (years)	30 \pm 2.223	31 \pm 2.81	0.0818
Body Mass Index	24 \pm 2.813	25 \pm 3.114	0.1358

Table-II: Group wise physiologic variables (n=40).

	Group A	Group B	<i>p</i> -value
	Mean \pm SD	Mean \pm SD	
Heart Rate (bpm)	82 \pm 18.772	85 \pm 20.347	0.4951
Baseline NIBP (mm Hg)	110 \pm 8.621	111 \pm 10.224	0.6376

Table-III: Efficacy status.

	Group A	Group B	<i>p</i> -value
Effective	32 (80%)	14 (35%)	<0.001
Not effective	8 (20%)	26 (65%)	

B) and the outcomes were scrutinized in terms of less incidence of maternal hypotension between the two groups: The mean age of study sample was 30.78 ± 6.81 years. Demographic profile is tabulated as table-I.

T-test was used to calculate the *p*-value in table-I & II.

In group A systolic BP of 32 (80%) patients were ranging 100 to 110 mm Hg vs 8 (20%) 111 to 120 mm Hg. Whereas in group B 33 (83%) patients had systolic BP range 100 to 110 mm Hg vs 7 (17%) 111 to 120 mm Hg. Mean systolic BP of group A and group B was 110 ± 8.621 mm Hg vs 111 ± 10.224 mm Hg.

The cardiac rate and mean NIBP were analyzed and are tabulated as table-II.

Both groups were examined for effectiveness and effectivity was noted as group A and group B as 32 (80%) vs 14 (35%) ($p < 0.001$). Chi square test was applied and *p*-value was found to be < 0.01 which is statistically significant as shown in table-III.

DISCUSSION

Phenylephrine is a selective alpha-1 agonist and has both direct & indirect sympathomimetic effects. It is currently drug of choice for maternal hypotension.

Our study shows that the mean age in group A and group B was 30 ± 2.23 years' vs 31 ± 2.81 years ($p = 0.0818$). The two groups did not differ in ASA status. Mean BMI in group A and group B

was 24 ± 2.813 vs 25 ± 3.114 ($p = 0.1358$). All the patients in both groups had ASA Grade II. Phenylephrine infusion with rescue boluses was effective in preventing maternal hypotension in 32 (80%) patients while boluses only was efficacious in 14 (35%) patients.

Similar findings were detected in another study by Siddik-Sayyid *et al*, incidence of hypotension in infusion group was only 20% compared to 90% in rescue boluses alone⁵. So variable rate infusion can be started at $50 \mu\text{g}/\text{min}$ with greater hemodynamic stability and can be increased up to $75-100 \mu\text{g}/\text{min}$ and for bolus dose ranges from $40-100 \mu\text{g}$ ¹⁰.

Wang *et al*¹¹ in their meta-analysis have found norepinephrine as superior substitute to phenylephrine. It prevents maternal hypotension to the same extent and gives additional benefit of prevention of bradycardia and intraoperative nausea and vomiting.

In another study conducted by Ngan *et al*¹² in which the prophylactic infusion of IV phenylephrine for the avoidance of hypotension through spinal anesthesia for cesarean delivery was investigated in a randomized, double-blind, controlled trial. Phenylephrine was instilled at 100 µg/min (n=26) for 3 min closely after intrathecal injection. Phenylephrine was infused at 100 µg/min from the time of delivery whenever systolic blood pressure (SAP) (which was noted every minute) was lower than the baseline¹³⁻¹⁶. After each measurement of SAP <80% of the starting point, a control group (n=24) expected IV bolus phenylephrine 100 µg. Phenylephrine infusion decreased incidence 6 (23%) from 26 to 21 (88%) from 24; $p < 0.0001$ of hypotension compared to control. In the infusion group, the heart rate was significantly slower compared to the control group ($p < 0.0001$) over time^{17,18}. Even though the infusion group received a large total dose of phenylephrine compared to the control group, umbilical cord blood gas and APGAR scores were comparable. Infusion of prophylactic phenylephrine is a modest, innocuous and effective technique of preserving blood pressure in the delivery of cesarean spinal anesthesia.

CONCLUSION

Our study concluded that phenylephrine infusion with rescue boluses provides better control of blood pressure than rescue boluses alone during cesarean section under spinal anesthesia.

CONFLICT OF INTEREST

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

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