ORIGINAL ARTICLE

ROLE OF EPHEDRINE INFUSION IN SPINAL ANAESTHESIA INDUCED HYPOTENSION

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Background: Spinal anaesthesia is commonly used during caesarean deliveries. In most of the cases hypotension is a common clinical problem after spinal anaesthesia for caesarean delivery. Severe hypotension can lead to maternal and/or foetal morbidity. This study aimed to see the effect of ephedrine infusion in spinal anaesthesia induced hypotension. **Methods:** A randomized controlled trial was conducted at Maternal and child health centre (MCH), Department of Anaesthesia, PIMS, Islamabad for 6 months. One hundred admitted or referred women who were undergoing caesarean section were included in the study. The patients were randomized to receive either preload crystalloids or co-load plus ephedrine infusion during spinal anaesthesia. The study outcome was judged as frequency of hypotension in the two groups. **Results:** The mean age of patients in group I (colloid crystalloid ± ephedrine infusion) was 29.4±3.7 years whereas in group II (preload crystalloids) it was 28.9±3.6 years. The frequency of hypotension was significantly higher (56%) in group II as compared to group I (16%) (p<0.001). Hypotension was significantly associated with group II (p<0.001). Additional ephedrine bolus was given to more patients (54%) in group II compared to group I (8%). **Conclusion:** Crystalloid co-load plus ephedrine results in less frequencies of hypotension than preload crystalloids.

Keywords: Spinal anaesthesia, colloid crystalloids, ephedrine, preload crystalloids, hypotension

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INTRODUCTION

In obstetrics, regional anaesthesia is the most common method of anaesthesia in caesarean delivery because it allows mother to immediately interact with baby and remain awake. In the United States regional anaesthesia is used for 95% of planned caesarean deliveries.[1] Extensive sympathetic blockade by spinal anaesthesia causes arteriolar dilatation, vasodilatation and suppression of chronotropy and inotropy of the heart. Aortocaval compression in combination of these effects leads rapidly to hypotension, bradycardia and low cardiac output.[2]

Hypotension is a common clinical problem after spinal anaesthesia for caesarean delivery, if it is severe it can lead to maternal and/or foetal morbidity.[3] Other associated complications include nausea, vomiting and pulmonary aspiration in mothers, foetal bradycardia and foetal acidosis. Prevention of spinal hypotension decreases the foetal risks and maternal adverse symptoms. It is better to prevent than to treat established hypotension.

There are numerous methods which are used clinically to prevent maternal hypotension. These include, proper positioning of mother by left uterine displacement to prevent decrease in venous return to the heart, and fall in blood pressure due to vasodilatation can be prevented by either fluid administration to compensate for upcoming intravascular fluid deficit or vasoconstrictors are used to reduce the capacitance of vessels. Ephedrine, Phenylephrine or Metaraminol are used as vasoconstrictors. Leg compression stockings minimize venous pooling in legs. All these methods are used to increase venous return to heart and maintain blood pressure.[4]

Widely recommended technique to prevent maternal hypotension during spinal anaesthesia is preload with crystalloid or colloid fluids.[5] Another approach, known as co-load, is to administer fluid bolus started at the time of identification of cerebrospinal fluid during spinal anaesthesia. When local anaesthetic block starts to take effect intravascular compartment expands due to vasodilatation from sympathetic blockade, fluid given at this time as co-load fills up compartment and fluid redistribution and excretion is limited.[6]

Best prophylaxis of maternal hypotension during caesarean section is still controversial.[7] The combination of simultaneous rapid crystalloid infusion with vasopressor has also been suggested without harming mother and baby (as observed with Apgar Score).[2,5,7] To control hypotension during spinal anaesthesia ephedrine has been the vasopressor of choice for many years, but there are still controversies about the best regimen of its use, whether to use it in infusion or in intermittent boluses, whether to use it for control of hypotension once it appears or to use it prophylactically.[8]

A study done on comparison of fluid preload (crystalloid or colloid) with crystalloid co-load plus ephedrine infusion showed that incidence of hypotension is low (10%) with crystalloid co-load plus ephedrine group compared to crystalloid preload group

(51%).[5] There has been minimum local evidence regarding this important intervention. In our institution prevention of hypotension is done by preloading the patient with 15 to 20 ml/Kg of crystalloid fluid before spinal anaesthesia and ephedrine is given as IV boluses for treatment of hypotension after spinal anaesthesia.

The aim of this study was to compare the effects of crystalloid preloading with crystalloid co-loading plus simultaneous ephedrine infusion for prophylaxis of hypotension during caesarean section in spinal anaesthesia.

METHODOLOGY

After approval from Hospital Ethical Committee, a written informed consent was taken from all the parturients who completely fulfilled the inclusion criteria, i.e., patients falling in classification of American Society of Anaesthesiologists as Class-I and II, who had elective caesarean section, gestational age was between 38–42 weeks, BMI <35, age 18–35 years, and had normal singleton pregnancy. Patients who had any contraindication to spinal anaesthesia (patient refusal, coagulopathy), pregnancy-induced hypertension (PIH), eclampsia, essential hypertension (diagnosed on history, BP records and lab findings on antenatal visits), any cardiovascular disease (valvular heart disease, cardiomyopathies), multiple gestation, placenta previa (on ultrasonography), known sensitivity to bupivacain, crystalloids, and patients who had emergency procedure (cord presentation, antepartum haemorrhage, foetal distress) were excluded from the study.

A pre-anaesthesia assessment of patients was documented a day before surgery. Patients were randomly divided into group I (co-load plus ephedrine infusion) and group II (preload) by computer generated table of random numbers. Monitoring included heart rate, ECG, pulse oximeter, and non-invasive blood pressure measurement. In operating theatre intravascular access with two large bore IV cannula (18G, 16G) was established.

Baseline vitals were taken. Mean of three readings of systolic blood pressure was taken as baseline measurement. Patients in group I received rapid intravenous crystalloid fluid (ringer lactate) bolus 15 ml/Kg started at time of identification of cerebrospinal fluid during spinal anaesthesia and infusion through infusion pump was started at 2 ml/min containing 30 mg of ephedrine in 50 ml of normal saline (1.2 mg/min) for group I and placebo in 50 ml of normal saline for group II. Rest of fluid was given according to maintenance requirement. Patients in group II received 15 ml/Kg crystalloid solution (Ringer lactate) 15–20 minutes prior to induction of spinal anaesthesia.

Spinal anaesthesia was performed under full aseptic measures using inter space L1, L2, or L3, L4 while patient in sitting position. A 25G Quincke spinal needle was used for injecting 2 ml of injection Bupivacain 0.75% hyperbaric in 30 Sec intra-thecally after observing clear CSF. Patients were positioned supine with 10 degree head clown and wedge placed under right hip to prevent aortocaval compression. Block was accessed every two minutes with spirit swab for cold sensation till 10 minutes. Oxygen via face mask at 5 L/min was given. Systolic blood pressure was monitored at 2, 4, 6, 8, 10, 15 and 20 minutes and recorded. Any episode of hypotension was treated with ephedrine 5 mg repeated at 2 min interval if hypotension persisted. Infusion was stopped if BP was more than 20% of baseline systolic BP. Bradycardia (pulse rate less than 50 per min) was corrected with atropine 0.5 mg IV. Inadequate or failed block for planned procedure was dealt with general endotracheal anaesthesia and those patients were excluded from study. Data was analysed using SPSS-10.

RESULTS

A total of 100 cases undergoing elective caesarean section were randomly equally assigned to receive either preload crystalloid or co-load crystalloids with ephedrine infusion. The average age of patients in group I (co-load crystalloid ± ephedrine infusion) was 29.4±3.7 years whereas in group II (preload crystalloids), it was 28.9±3.6 years.

In group I the mean weight of patients was 67.4±10.7 Kg compared to 71.1±9.4 Kg in group-II. Similarly, the average height of patients in group I was 151.6±20.6 Cm compared to 154.8±5.8 Cm in group II. The average BMI was 26.8±3.5 in group I and 29.5±3.9 in group-II.

The indications of surgery were previous caesarean section in most of the patients whereas breech presentation and oligohydramnios were other frequent causes. In group I out of the 50 cases, 11 (22.0%) had one previous C-section, 13 (26.0%) had two previous C-sections and 2 (4.0%) had three previous C-sections. Eight (16.0%) cases had breech presentation and 2 (4.0%) each had cephalo-pelvic disproportion (CPD) and precious pregnancy, while 1 (2.0%) had decreased foetal movement as an indication of surgery. Similarly, in group II, 18 (36.0%) had one previous Caesarean section, 10 (20.0%) had two previous C-sections, and 2 (4.0%) had three previous C-sections, 7 (14.0%) were found to have breech presentation of baby, 5 (10.0%) patients each had oligohydramnios and precious pregnancy, and 3 (6.0%) had cephalo-pelvic disproportion as the main indication of surgery. The surgical indications were not statistically different among the two study groups.

The baseline systolic BP was equal among study groups, i.e., 122.38±9.79 mmHg in group I and 121.32±11.43 mmHg in group II. After 15 minutes in group I the systolic BP was 111.26±13.64 mmHg and in

group II, the average systolic BP was noted to be 106.6±11.5 mmHg. After 20 minutes the average systolic BP was 120.36±10.68 mmHg in group I and 109.32±12.26 mmHg in group II (Table-1).

The baseline diastolic BP was 79.3±8.99 mmHg in group I compared to 79.24±7.99 mmHg in group II. After 15 minutes the diastolic BP was noted at 74.36±7.62 mmHg in group I whereas it was 67.62±10.19 mmHg in group II. After 20 minutes of intervention the mean diastolic BP was 75.96±8.50 mmHg in group I and 69.26±12.10 mmHg in group II (Table-2).

The baseline average heart rate was 94.70±13.86 per minute in group I compared to 94.82±12.15 per minute in group II. After 10 minutes of intervention in group I, the heart rate significantly dropped to 87.30±14.39 per minute whereas it was 96.04±15.23 per minute in group II. At 15 minutes the heart rate was found to be 85.74±13.20 per minute in group I whereas it was 93.4±15.5 per minute in group II. After 20 minutes of intervention the mean heart rate was 85.84±13.92 per minute in group I and 94.64±14.25 per minute in group II (Table-3).

The frequency of hypotension was significantly higher (56%) in group II as compared to group I (16%). It was found that hypotension was significantly associated with group II (p<0.001). Similarly, the additional ephedrine bolus was given to more patients (54%) in group II as compared to group I (8%) (Table-4).

Table-1: Systolic BP of two study groups

	Baseline	2 min	4 min	6 min	8 min	10 min	15 min	20 min
Group I	122.38±9.79	116.3±13.25	111.26±13.64	109.68±14.46	113.08±14.30	114.08±13.17	117.78±10.06	120.36±10.68
Group II	121.32±11.43	112.86±16.86	108.02±12.84	102.86±11.90	101.66±11.95	104.00±11.24	106.72±11.68	109.32±12.26
***p*-value**	0.6195	0.2595	0.2243	0.0039	0.0000	0.0000	0.0000	0.0000

Table-2: Diastolic BP of two study groups

	Baseline	2 min	4 min	6 min	8 min	10 min	15 min	20 min
Group I	79.3±8.99	76.2±10.83	70.9±12.05	69.82±12.11	72.36±10.59	71.38±9.59	74.36±7.62	75.96±8.50
Group II	79.24±7.99	72.26±13.07	68.32±9.79	63.86±9.39	63.14±12.14	65.46±11.27	67.62±10.19	69.26±12.10
***p*-value**	0.9719	0.1040	0.2429	0.0071	0.0001	0.0057	0.0003	0.0018

Table-3: Heart Rate of two study groups

	Baseline	2 min	4 min	6 min	8 min	10 min	15 min	20 min
Group I	94.70±13.86	93.26±17.69	92.18±18.77	91.60±17.48	91.38±17.15	87.30±14.39	85.74±13.20	85.84±13.92
Group II	94.82±12.15	98.52±16.28	118.42±18.44	99.28±17.37	98.04±17.49	96.04±15.22	93.22±15.54	94.64±14.25
***p*-value**	0.9634	0.1251	0.1872	0.0299	0.0574	0.0040	0.0110	0.0024

Table-4: Hypotension and additional ephedrine boluses in study groups [n (%)]

	Group 1	Group 2	*p*
Hypotension			
Yes	8 (16)	28 (56)	<0.001
No	42 (84)	22 (44)	
Additional ephedrine boluses			
Yes	4 (8)	27 (54)	<0.001
No	46 (92)	23 (46)	

DISCUSSION

Regional anaesthesia is the most common methods used in caesarean deliveries.[9] Hypotension is a common clinical problem faced by patients on spinal anaesthesia and if severe it can lead to both maternal and foetal morbidity. Other problems are also common these include nausea, vomiting, pulmonary aspiration in mothers and bradycardia and acidosis in the foetus. Spinal anaesthesia is frequently given to patients undergoing caesarean section because of its simple technique which produces fast and highly effective anaesthesia whilst avoiding morbidity and mortality associated with other modes of anaesthesia. The incidence of hypotension after spinal anaesthesia is common. The preventive measures like crystalloid given preload or co-load have been used to avoid hypotension.[4,6]

The mean systolic blood pressure was significantly low in the preload crystalloid group compared to co-load crystalloid plus ephedrine infusion group. In the current study the frequency of hypotension was high in preload crystalloids and was significantly less in the co-load and ephedrine group. Khan *et al*[10], reported crystalloid co-load as a better option than preload crystalloids for prevention of hypotension in patients undergoing elective caesarean section. The results of current study validate the findings of previous studies on concern topic. Khosheideh *et al*[7], demonstrated a higher incidence of hypotension in the crystalloid group compared to the crystalloid and ephedrine group (55.6% vs 25%). Gunusen I *et al*[5] reported that moderate to severe hypotension was lower in the ephedrine and co-load crystalloid group when compared with preload crystalloid alone (10% vs 51%).

Khan *et al*[10], demonstrated that incidence of hypotension was significantly greater in the preload crystalloid group when compared with co-load crystalloid group (70% vs 44%). Chan *et al*[11] reported that patients in the pre-hydration group exhibited a

hypotension incidence rate of 65% versus ephedrine group in which an incidence of 35% was observed.

Many other investigators have also witnessed a similar trend. Hexa-ethyl starch co-loading or crystalloid co-loading is the best method of preventing maternal hypotension after the initiation of spinal anaesthesia.[12,13] Khan *et al*[10] concluded that a significantly lower incidence of post spinal hypotension was found in co-load group than preload group and patients in co-load group required less vasopressor doses than those in preload group.

It was also noted that none of patients in the co-load plus ephedrine group developed bradycardia. This finding was found comparable to Khooshideh *et al*[7] and Jabalameli *et al*[14]. The combination of co-load crystalloid and ephedrine infusion in our study reduced the requirement of bolus infusions significantly when compared with pre load crystalloid group.

Theoretical foundation of different studies indicates that the concerned topic has limited scope so the current study explores the anaesthesiologist and health worker issues. The study on women undergoing caesarean section will enhance programmatic and scientific implications as the maternal mortality rate in Pakistan is amongst the highest in the world.

CONCLUSION

Crystalloid co-load plus ephedrine is associated with less incidence of hypotension than preload crystalloids. There are very few homodynamic effects of the combination intervention and thus, fewer requirements of bolus infusion doses. For reduction of hypotension in spinal anaesthesia the combination intervention of co-load crystalloids plus ephedrine infusion can be used.

LIMITATIONS

The aim was specifically targeting frequency of hypotension after the study interventions. However, a more detailed approach of data collection would have shown other information such like side-effects of the interventions and any adverse effects during drug administration. Larger scale study would have given comprehensive results. The neonatal outcome was not shown in this study which would have given more reliable information regarding short term and long term effects of the drug.

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