ORIGINAL ARTICLE

HEMODYNAMIC EFFECTS OF SIMULTANEOUS ADMINISTRATION OF INTRAVENOUS EPHEDRINE AND SPINAL ANESTHESIA FOR CESAREAN DELIVERY

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ABSTRACT

Background: In the anesthesia practice prevention and management of hypotension related to spinal anesthesia remains a difficult problem and there was no consensus on its optimal management. The incidence of hypotension during spinal anesthesia for cesarean section is reported to be as high as 80%, despite fluid preload and lateral uterine displacement. Ephedrine, an indirectly acting sympathomimetic amine is probably the vasopressor of choice in obstetric anesthesia. Although ephedrine has mixed α and β adrenoreceptor activity it maintains arterial pressure mainly by increase in cardiac output and heart rate as a result of its predominant activity on β-1 adrenoreceptor. It may cause maternal tachycardia. It has less effect on uteroplacental blood flow as compared to other vasopressors.[3]

Objectives: This study was conducted to observe hemodynamic effects of ephedrine in spinal anesthesia during cesarean delivery on mother and to study the incidence of hypotension in the compared groups.

Methods: A prospective randomized double blind study. 100 ASA (American society of Anesthesiology) physical status I and II women undergoing elective cesarean delivery divided into study and control groups. Study group was received IV dose of 20 mg (2 ml) ephedrine over 60 seconds simultaneously with intrathecal dose of 2 ml 0.5% heavy bupivacaine. Control group was received IV 2 ml saline simultaneously with intrathecal dose of 2 ml 0.5% heavy bupivacaine.

Results: After 5 minutes mean pulse rate in group B is significantly lower than those of group A ($p<0.05$). Fall in blood pressure in group B is significantly more as compared to group A ($p<0.05$). First rescue ephedrine time in group A is significantly more than group B ($p<0.05$). No difference in apgar score at 1minute and at 5 minute between the study groups. Incidence of hypotension, bradycardia, nausea and vomiting are significantly higher in group B as compared to group A.

Conclusion: Prophylactic bolus dose of 20 mg intravenous ephedrine given at the time of intrathecal block and after 10 ml/kg intravenous crystalloids preload reduce the incidence and severity of hypotension.

Keywords: Intravenous ephedrine, Spinal anesthesia, Cesarean delivery

INTRODUCTION

Spinal anesthesia was introduced into clinical practice by German Surgeon Karl August Bier in 1898. It is one of the most popular techniques for lower limb and lower abdominal procedures, including caesarean section. Anesthesia to a parturient is unique because it requires highest degree of care and anesthesiologist has to look after two individuals, the mother and fetus. In elective cesarean section under spinal anesthesia hypotension has been reported in as high as 80% of patients.[1] Hypotension may be detrimental to the mother and fetus. The resulting hypoperfusion of placenta may lead to fetal acidosis and bradycardia. A number of strategies for preventing hypotension have been investigated. The use of lateral uterine displacement is routine. Other strategies have included the use of IV fluid preload. Gravity (Tredelenberg or leg rising), compression devices on the legs and prophylactic vasopressors, of available vasopressors, ephedrine is most commonly used. The goal of this study is to observe homodynamic effects of intravenous ephedrine in spinal anesthesia during cesarean delivery on mother and fetus and to determine the efficacy and safety of 20 mg intravenous ephedrine

for the prevention of hypotension during spinal anesthesia for cesarean delivery.

MATERIALS AND METHODS

This study was conducted at civil hospital, B. J. Medical College, Ahmedabad; approval of the college ethics committee and written informed consent from all the patients were obtained. It was a prospective randomized double blind study. There were 100 ASA physical status I and II women undergoing elective cesarean. Delivery of term, uncomplicated and having singleton pregnancies were selected and randomly divided into two groups. Group A Receive IV dose of 20 mg (2 ml) ephedrine over 60 seconds simultaneously with intrathecal dose of 2 ml 0.5% heavy bupivacaine. Group B receive IV 2 ml saline simultaneously with intrathecal dose of 2 ml 0.5% heavy bupivacaine. Patients satisfying the inclusion criteria were randomly divided into groups of 50 each. Randomization was performed by the drawing of coded, opaque, shuffled envelops and the study dose was prepared by an anesthesiologist not involved in patient assessment

Inclusion Criteria:

- ASA physical status I and II
- Women undergoing elective cesarean delivery of term.
- Singleton pregnancy.

Exclusion Criteria:

- Patients with pre existing hypertension.
- Patients with pregnancy induced hypertension.
- Patients with known cardio vascular or cerebrovascular disease.
- Patients having contra indication to spinal anesthesia.
- Hb< 8gm/dl
- Pt. with psychiatric illness.
- Pt. having clinical evidence of dehydration.

Routine investigations in the form of Hb, RBS, RFT, LFT, X-ray, ECG, serum electrolytes were carried out.

On arrival to operation theatre patients were placed in modified supine position with 15 of left uterine tilt. Patients were premedicated with ranitidine 15 mg intravenously and with ondansetrone 4 mg intravenously on arrival to the operation theatre. Standard monitoring included non-invasive arterial blood pressure electrocardiogram and pulse oximetry and visual examination of respiration. Baseline arterial pressure and heart rate were recorded. A large bore IV catheter was then inserted into forearm vein and IV preloading of 10 ml / kg lactated Ringer's solution was given over 15 minutes after which the intravenous infusion was slowed at minimum rate required to maintain vein patency. Spinal anesthesia was administered with the patient in right lateral position. After skin infiltration with2% 2 cc lidocaine with the help of 26G needle. A 23 G spinal needle was inserted at the $L_2 – L_3$ or L_3- L_4 space and hyperbaric 0.5% bupivacaine (2 ml) was injected into subarachnoid space simultaneously along with intravenous dose of 2 ml (20 mg) ephedrine or 2 ml of saline. The patient was then immediately turned supine with left lateral tilt. Oxygen was given at 4 L/min by clear face mask until delivery.One minute after the spinal injection, the onset of spinal anesthesia was confirmed by asking the patient to subjectively verify numbness of the legs and sensory level of T4 – T6 was achieved. The syringe was prepared by one researcher and administered by a second who remained blinded to its contents. Patient assessment and care were conducted and study data were recorded by another researcher.

Arterial pressure and heart rate were recorded at 1 minute intervals up to 20 minutes or until delivery and every 5 minutes thereafter up to 60 minutes or up to the end of surgery. Hypotension defined as a decrease in systolic arterial pressure more than 20% below baseline or to below 100 mmHg, was treated by using IV boluses of ephedrine 5 mg every minute as required. Reactive hypertension was defined as an increase in SAP of more than 20% above baseline. Bradycardia was defined as maternal heart rate <60/min. Tachycardia was defined as heart rate >100/min. The supplementary and total doses of ephedrine required before delivery and any instances of nausea, vomiting, bradycardia, hypertension and tachycardia were recorded. Times from skin incision to delivery and from uterine incision to delivery were recorded. After delivery, apgar scores were assessed at 1 min. and 5 min by attending pediatrician. All patients received oxytocin 20units/L in 500 ml of crystalloid after delivery. Post operative examination of the patient was carried out and level of spinal anesthesia was recorded. The parameters were assessed and compared for main outcome and measurements are demographic parameters, delivery time, first rescue ephedrine time, changes over time in systolic arterial blood pressure and heart rate between the study groups, Apgar scores at 1 min and 5 min interval in the study groups and incidence of complications such as hypotension, hypertension, tachycardia, bradycardia, nausea and vomiting.

RESULTS

The observations made were analyzed using appropriate statistical tools. The patients in both the groups were comparable with respect to their age, height, weight and delivery time. This study shows that majority of patients of both the groups were of ASA (American society of Anesthesiology) grade I.

The table 1 shows that after giving spinal anaesthesia in group A pulse rate decrease for first 3 minutes and thereafter start rising. In group B there is fall in the pulse rate from giving spinal anaesthesia to the end of surgery. After 5 minutes the mean pulse rate in group B is significantly lower than those of group A ($p<0.05$).

Table 1: Mean pulse at different time intervals

Time(min)	Group A (n = 50)	Group B (n = 50)	P value (t test)
Base line	80.16	82.36	0.048*
1	76.92	82.24	0.000*
2	72.30	80.76	0.000*
3	72.08	79.32	0.000*
4	74.84	77.64	0.024*
5	76	76.84	0.503
5 to 10	76.88	74.08	0.033*
10 to 15	77.12	73.04	0.002*
15 to 20	77.96	72.92	0.000*
20 to 25	79.26	72.88	0.000*
25 to 30	80.04	72.12	0.000*
30 to 35	80.60	71.64	0.000*
35 to 40	81	71.40	0.000*
40 to 50	81.24	71.24	0.000*
50 to 60	83.48	71.16	0.000*
>60	83	71	0.014*

*Statistically Significant

Table 2 Comparison of Systolic Arterial Blood Pressure

Time(min)	Group A (n=50)	Group B (n=50)	P value (t test)
Base line	119.68	121	0.004*
1	118.64	120.60	0.000*
2	116.60	119.32	0.000*
3	114.84	117.08	0.000*
4	113.32	114.72	0.245
5	114.86	112.28	0.054
5 to 10	115.60	108.28	0.000*
10 to 15	116.44	106.44	0.000*
15 to 20	117.44	108.64	0.000*
20 to 25	118.72	108.68	0.000*
25 to 30	119.12	108.80	0.000*
30 to 35	119.48	108.84	0.000*
35 to 40	120.32	108.68	0.000*
40 to 50	120.76	108.76	0.000*
50 to 60	120.60	108.84	0.000*
>60	120	113	0.048*

*Statistically Significant

The table 2 shows systolic BP at different time intervals, with maximum fall occurring at 4 min in group A and at 10to15 minutes in group B. Fall in blood pressure in group B is significantly more as compared to group A ($p<0.05$).

Table 3 Comparison of 1st rescue ephedrine (5mg) time

	1st Rescue Ephedrine Time (min)
Group A(n=50)	16
GroupB(n=50)	9.5
P value(t test)	0.002

*Statistically Significant

Table 4: Comparison of Apgar score in Newborns

Apgar Score	Group A (n=50)		Group B (n=50)	
	At 1 min	At 5 min	At 1 min	At 5 min
0-3	-	-	-	-
4-6	-	-	-	-
7	2	1	2	-
8	39	6	38	6
9-10	9	43	10	44

The table 3 shows that first rescue ephedrine time in group A is significantly more than group B.($p<0.05$) The table 4 shows that there is no difference in apgar score at 1minute and at 5 minute between the study groups.No Apgar scores are below 7 at 1 or 5 minute in both groups.

Table 5: Incidence of intra-operative complications

Complications	Group A (n=50)	Group B (n=50)	p value
Hypotension	4(8%)	18(36%)	0.001*
Bradycardia	0	3(6%)	0.079
Nausea & vomiting	2(4%)	5(10%)	0.240
Hypertension	1(2%)	0	0.315
Tachycardia	0	0	-

*Statistically Significant

The table 5 shows that incidence of hypotension is significantly higher in group B as compared to group A. The incidence of bradycardia is higher in group B. The incidence of nausea and vomiting is also higher in group B. The incidence of hypertension in group A is 2%. No patients in group A or B develop tachycardia.

DISCUSSION

The recommended level of anesthesia for cesarean section is T4-T6.The standard recommended dose for this is 0.5% hyperbaric bupivacaine 2cc that is 10 mg. In our study we have used the same standard dose of bupivacaine. The standard dose for intravenous ephedrine is 5-25 mg. In our study we have used 20 mg intravenous bolus dose prophylactically for group A and 5 mg intravenous ephedrine as rescue bolus dose if systolic arterial blood pressure is below 100 mmHg or if fall in systolic arterial blood pressure is more than 20% below baseline in either group. In our study we have compared the hemodynamic parameters-blood pressure and heart rate changes as well as first rescue ephedrine time, neonatal Apgar score and intraoperative complications of spinal anesthesia and use of ephedrine between the study groups.

In 1994, P. A. Hall et al [4] conducted a study of comparison of infusion of phenylephrine and ephedrine in spinal anesthesia for cesarean section. They conclude, an infusion of phenylephrine 10microg/min with bolus 20 microgm was shown to be significantly less effective in maintaining systolic

arterial pressure within 20% limits of baseline compared with an infusion of ephedrine 1 or 2 mg/ min with bolus doses of 6 mg.

In May 2001, Lionel Simon et al [5] do a study to compare the incidence of maternal hypotension associated with spinal anesthesia for cesarean section when 10 mg, 15 mg, 20 mg prophylactic bolus dose of intravenous ephedrine used. They found that incidence of hypotension was significantly higher in those receiving a 10 mg prophylactic dose of ephedrine than in those receiving either a 15 mg or 20 mg prophylactic dose of ephedrine.

In 2000, Warwick D.Ngan Kee et al [6] performed a dose response study of prophylactic intravenous ephedrine 10 mg, 20 mg, 30 mg for the prevention of the hypotension during spinal anesthesia for cesarean delivery. In conclusion they have found that in patient having spinal anaesthesia for cesarean delivery after IV crystalloid preload, the minimum effective dose of IV ephedrine given one minute after the spinal anesthesia to reduce the incidence of hypotension was 30 mg. However, this dose did not completely eliminate hypotension, nausea and vomiting or fetal acidosis and it caused reactive hypertension in some patients.

In 2004, Dr. Hemant Bhagat et al [7] conducted a study on evaluation of preloading and ephedrine as a combined prophylaxis for hypotension during subarachnoid anesthesia. They concluded that combination therapy with preloading & ephedrine is an effective prophylaxis against spinal hypotension and provides better hemodynamic stability when compared to the use of preloading or ephedrine alone.

In March 2009, Kol IO et al [8] conducted a study on the effects of IV ephedrine 0.5 mg/kg during spinal anesthesia for cesarean delivery. The findings suggest that prophylactic bolus dose of IV ephedrine 0.5 mg/ kg given at time of intrathecal block after crystalloid fluid preload 15 ml/kg Ringer lactate solution, plus rescue boluses 5mg ephedrine reduce the incidence of maternal hypotension, nausea and vomiting. It has not any adverse effect on neonatal outcome.

In our study we found that after giving spinal anesthesia in group A pulse rate decrease for first 3 minutes and thereafter start rising. The fall in pulse rate for first 3 minutes may be due to onset of sympathetic block after spinal anesthesia and time of onset of ephedrine effect which is 4-5 minutes after intravenous dose. In group B there is fall in pulse rate from giving spinal anesthesia to the end of surgery. This is due to sympathetic block produced by spinal anesthesia. After 5 minutes the mean pulse rate in group B was significantly lower than those of group A. This finding is similar to the finding of the study performed by Kol IO et al. [8]who concluded that mean pulse rate in ephedrine group was higher than those of control group.

In our study we have found that after giving spinal anaesthesia maximum fall in BP occurring at 4 minute in group A and at 10 to 15 minutes in group B. The fall in BP for first 4 minutes in group A is due to onset of sympathetic block after spinal anaesthesia and time of onset of ephedrine effect which is 4-5 minutes after intravenous dose. The fall in blood pressure in group B is significantly more as compared to group A. This finding is similar to the finding of the study performed by Kol IO et al[8] who concluded that fall in BP in control group is more as compared to ephedrine group.

In our study first rescue ephedrine time was significantly more in group A than group B. This finding is similar to the finding of the study performed by Kol IO et al [8]

In our study we found no significant difference in Apgar score between the study groups despite the significant difference in the incidence of hypotension which may be due to early recognition and restoration of blood pressure with rescue ephedrine. this findings is supported by the study done by Warwick D et al [6]who performed a dose response study of prophylactic intravenous ephedrine 10 mg, 20 mg, 30 mg for the prevention of the hypotension during spinal anesthesia for cesarean delivery. This finding is similar to the finding of the study performed by Kol IO et al[8] who concluded that neonatal outcome were similar between the study groups.

Hypotension was found in 4 patients in group A and 18 patients in group B. Out of 18 patients in group B 5 patients required two doses of 5 mg rescue ephedrine. Thus the incidence of hypotension in group B (36%) significantly more than that of group A (8%).This finding was similar to the finding observed by Lionel Simon et al [5] who performed a study to compare the incidence of maternal hypotension associated with spinal anesthesia for cesarean section when 10 mg, 15 mg, 20 mg prophylactic bolus dose of intravenous ephedrine used. They found that incidence of hypotension was significantly higher in those receiving a 10 mg prophylactic dose of ephedrine than in those receiving either a 15 mg or 20 mg prophylactic dose of ephedrine. This finding was also similar to the finding of the study performed by Kol IO et al [8] who concluded that there were significant lower incidence of hypotension in the ephedrine group compare with the control group.

There were 6% patients in group B developed bradycardia as compared to 0% patients in group A. This is due to effect of ephedrine on β-1 adrenergic receptor on the heart. Stimulation of these receptors by ephedrine leads to increase in pulse rate in group A. This finding was similar to the finding of the study performed by Kol IO et al[8] who concluded that ratio of bradycardia in the control group was significantly higher than that of ephedrine group.

There was lower incidence of the nausea and vomiting in group A as compared to group B. This finding was similar to the finding of the study performed by Kol IO et al[8] who concluded lower incidence of nausea and vomiting in ephedrine group as compared to control

group. The incidence of hypertension in group A was 2% and in group B was 0%. In the study done by Warwick D et al [6] the incidence of hypertension was 45%.But duration of ephedrine administration in their study was 30 seconds while this in our study was 60 seconds. This may explain lower incidence of hypertension in our study.

There was no difference in the incidence of tachycardia between the study groups (0% in both groups). This finding was similar to the finding of the study performed by Kol IO et al[8] who concluded no difference in the ratio of tachycardia between the study groups which could be explained by both the effect of rescue ephedrine and baroreceptor mediated increase in heart rate who became hypotensive.

CONCLUSION

Maintenance of the body physiology as near normal as possible during anesthesia is one of the primary goals of the anesthesiologist. As we know, marked hemodynamic changes are often seen following subarachnoid block in pregnant patients.. Therefore our study conclude that simultaneous administration of prophylactic bolus dose of 20 mg intravenous ephedrine given at the time of intrathecal block and after 10 ml/kg intravenous crystalloids preload reduce the incidence and severity of hypotension.

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