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Original Article

Comparative Evaluation of Pre-operative Intramuscular Ephedrine Hydrochloride and Mephentermine Sulfate for Reduction of Spinal Anesthesia-induced Hypotension during Cesarean Section - A Clinical Study

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Abstract

Background: Ephedrine has potent alpha and weak beta stimulatory effects. Due to its alpha receptor affect, it increases heart rate (HR) and cardiac output.

Aims and Objectives: To evaluate and compare the effects of intramuscular (IM) ephedrine hydrochloride and mephentermine sulfate for reduction of spinal anesthesia-induced hypotension in lower segment cesarean section (LSCS).

Materials and Methods: After taking informed consent, 90 healthy full-term pregnant female patients of age 20-35 years of American Society of Anesthesiologists Grade I and II, posted for elective LSCS under spinal anesthesia were included in the study. They were randomly divided into 3 groups of 30 patients each. Patients of Group I - receiving 1 ml injection normal saline intramuscularly 5 min before giving spinal anesthesia; patients of Group II receiving 30 mg injection mephentermine sulfate intramuscularly 5 min before giving spinal anesthesia; patients of Group III - receiving 30 mg injection ephedrine hydrochloride intramuscularly 5 min before giving spinal anesthesia. After giving spinal anesthesia, observation was made for HR, systolic blood pressor, diastolic blood pressor, and SPO_2 at every 2 min interval for first 20 min and then every 5 min up to 1 h. Apgar score was recorded at 1 min and 5 min after delivery.

Results: We found that both ephedrine hydrochloride and mephentermine sulfate given intramuscularly before spinal anesthesia decreases the incidence of spinal anesthesia-induced hypotension. Apgar score was lower in mephentermine sulfate group.

Conclusion: Ephedrine hydrochloride 30 mg IM 5 min before spinal anesthesia can be recommended for reduction of spinal anesthesia-induced hypotension in elective LSCS.

Key words: Apgar score, Ephedrine hydrochloride, Hypotension, Lower segment cesarean section, Mephentermine sulfate

INTRODUCTION

Spinal anesthesia causes blockade of sympathetic vasoconstrictor fibers resulting in venous dilation and pooling of blood in lower extremity causes hypotension which is more aggravated in pregnant patients due to aortocaval compression by the gravid uterus. Hypotension is especially deleterious in obstetrics patients where it affects both mother as well as fetus. Effects of hypotension on fetus are due to decrease uteroplacental blood flow causes fetal bradycardia, depression, and decreased Apgar score.[1-6]

Numerous agents have been used in an effort to minimize the incidence of hypotension, i.e., fluid preloading either crystalloids or colloids, specific positioning, i.e., leg raising,

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inflatable splints, using tourniquet, graded stockings up to mid-thigh, judicial use of Esmarch's bandage, and judicious use of vasopressors such as methergine, paredrine, metaraminol, dopamine, dobutamine, and mephentermine.[7-11]

Ephedrine has potent alpha and weak beta stimulatory effects. Due to its alpha receptor effect, it increases heart rate (HR) and cardiac output and has less effect on the peripheral vasculature. Ephedrine is most commonly used vasopressors to treat hypotension in obstetric patients.

Mephentermine increases blood pressure and cardiac output by catecholamine secretion which causes profound vasoconstriction and decreases uteroplacental blood flow.

Considering these facts present study was carried to evaluate and compare the effects of intramuscular (IM) ephedrine hydrochloride and mephentermine sulfate for reduction of spinal anesthesia-induced hypotension in lower segment cesarean section (LSCS), to compare the neonatal Apgar score and to compare other side effects.[12-16]

MATERIALS AND METHODS

The present study was carried out at the S.S. Medical College and associated Sanjay Gandhi Memorial Hospital, Rewa, Madhya Pradesh, from August 2014 to July 2015.

After approval from the Institutional Ethical Committee, the study was carried out on 90 healthy full-term pregnant female patients of age 20-35 years of American Society of Anesthesiologists Grade I and II, posted for elective LSCS under spinal anesthesia.

Patients, with known hypersensitivity to injection bupivacaine, having antepartum hemorrhage, pregnancy-induced hypertension, twin pregnancy, placenta previa, cord prolapsed, cardiac disease (ischemic heart diseases, valvular heart diseases, left ventricular failure, atrioventricular conduction block, and uncontrolled hypertension), renal dysfunction, deranged liver function test, and endocrinal or neurological disorders were excluded from the study. Procedure was explained and written informed consent was obtained from the patients.

Around 90 patients who fulfill all selection criteria were randomly divided into three groups of 30 patients each.

1. Group I - receiving 1 ml injection normal saline intramuscularly 5 min before giving spinal anesthesia
2. Group II - receiving 30 mg injection mephentermine sulfate intramuscularly 5 min before giving spinal anesthesia
3. Group III - receiving 30 mg injection ephedrine hydrochloride intramuscularly 5 min before giving spinal anesthesia.

All patients were kept nil orally for at least 6 h before surgery. After shifting the patients to operating table, monitors for non-invasive blood pressure, electrocardiogram, and pulse oximeter were attached. Two intravenous (IV) lines were secured. All the patients were preloaded with 10 ml/kg body weight Ringer lactate solution. After preloading baseline parameters, HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), and SPO_2 were recorded.

All the patients were uniformly premeditated with injection glycopyrrolate 0.2 mg IV, injection ranitidine 50 mg IV, and injection ondansetron 4 mg IV. The study drug was provided as coded identical syringes, as per randomization protocol and was injected intramuscularly 5 min before giving spinal anesthesia.

Patients were reassured and explained about the procedure and lumber puncture was performed in L4-L5 interspace with 25-gauge standard wire gauge needle in left lateral position after confirming free flow of cerebrospinal fluid subarachnoid block (SAB) was given with injection 0.5% heavy bupivacaine 2.2 ml; then, patients were made supine, wedge was applied under right buttock, and observation was made for HR, SBP, DBP, and SPO_2 at every 2 min interval for first 20 min and then every 5 min up to 1 h.

After confirmation of sensory block by pinprick method with 26-gauge needle up to T5-T6 level, surgery was started. After cord clamp of fetus injection oxytocin 10 IU IV was given in infusion and injection ergometrine 0.25 mg IV was given. Apgar score was also noted at 1 min and 5 min after delivery.

SBP <90 mm Hg or more than 20% fall below baseline was considered as hypotension and was treated by IV fluids and injection ephedrine 6 mg IV.

HR <60 bpm or more than 20% decrease from baseline was considered bradycardia and treated with injection atropine 0.6 mg intravenously.

Simultaneously, any other side effects such as nausea, vomiting, pain, discomfort, and chills and rigors were noted and managed accordingly.

At the end of the study, the observations were decoded, tabulated, and statistically analyzed using mean, standard deviation, *P* value, and Student's *t*-test. For comparison, $P < 0.05$ was taken to be statistically significant and <0.0001 was taken to be highly significant.

RESULTS AND DISCUSSION

Spinal anesthesia is a popular technique for LSCS. It has several advantages over general anesthesia such as less stress, effective motor and sensory block, fewer chances of aspiration pneumonitis, difficult or failed intubation. Apart from these advantages, it has got some complications. Out of them, hypotension is the most common and immediate complication. This is due to the sympathetic blockade which causes decreased arteriolar and venous tone and decreased venous return. Vasopressors are the mainstay for prevention and treatment of hypotension following spinal anesthesia. Ephedrine is the most commonly recommended vasopressors to treat hypotension in obstetric patients. Vasopressors can be given by IM or IV routes.

In our study, all the patients in all the three groups were comparable to each other with respect to age, weight, height, time interval SAB-delivery, and duration of surgery as shown in Table 1.

Baseline SBP was 116.9 ± 7.99, 118 ± 7.91, and 120.6 ± 8.29 in Groups I, II, and III, respectively, which was comparable in all groups. After injecting the study drug, there was increase in SBP in Groups II and III, but there was no increase SBP in patients of Group I. Maximum fall in SBP was recorded from 2 to 10 min after giving spinal anesthesia, and it was 98.0 ± 7.1, 109.5 ± 12.32, and 107.6 ± 6.33 in Groups I, II, and III, respectively. Fall in SBP was significantly lower and earlier in Group I (2-5 min after spinal) as compared to Groups II and III (3-8 min after spinal). Fall in SBP was comparable in Groups II and III. At the end of surgery, SBP was comparable in all groups. This delay of fall in blood pressor and less number of patients in Groups II and III is due to drug-induced stimulation of alpha and beta receptors and increase in cardiac output which overcomes the effects of spinal anesthesia. Recovery in SBP starts after 10-20 min due to delivery of fetus and vasoconstrictor effect of ergometrine (Table 2).

Baseline DBP was 74 ±7.3, 76 ± 8.5, and 77.47 ± 5.9 in Groups I, II, and III, respectively, which is comparable in all groups. After injecting the study drug, increase in DBP in Groups II and III was not significant. After SAB, there was a significant decrease in DBP in Group I as compared to Groups II and III. It was 60.4 ± 10.5, 69.4 ± 12.4, and 68.4 ± 8.8 in Groups I, II, and III, respectively. At the end of surgery, DBP was comparable in all groups (Table 3).

In our study, incidence of hypotension was 60% (18 patients), 23.33% (7 patients), and 26.66% (8 patients) in Groups I, II, and III, respectively. There was significantly higher incidence of hypotension in Group I as compared to Groups II and III. This can adversely affect mother as well fetus. Hypotension was treated with IV ephedrine. Rescue dose of ephedrine requirement was 6 mg in 15 patients in Group I as compared to 7 patients in Group II and 8 patients in Group III. Dose of ephedrine 9 mg was required in 3 patients in Group I, and in Groups II and III, any patient did not require this dose so less amount of rescue drug is require in Groups II and III (Table 4).

Similar results were found in a study of Grubb *et al.* 2004.[3] They studied IM ephedrine 50 mg for reduction of spinal anesthesia-induced hypotension in LSCS and observed hypotension in 70% patients in the control group and 25% in ephedrine group.

Loughrey *et al.,* 2002[9] studied ephedrine in dose of 6 mg and 12 mg IV with control and observed hypotension in 27% in E 12 group as compared to 60% in control group.

Cucchiara and Restall, 1973[5] studied the effects of IM mephentermine 30 mg after spinal anesthesia in elderly

Table 1: Patients characteristics

Patients characteristics	Group I	Group II	Group III	*P* value
Age (years)	24.7±4.75	25±4.57	24.3±4.36	>0.05
Weight (kgs)	54.5±6.1	53.8±6.2	53.3±5.3	>0.05
Height (cms)	153±6.47	154±6.3	153±6.3	>0.05
Duration of Surgery (min)	42.1±5.58	42.33±4.31	43.0±5.51	>0.05
Time interval SAB-delivery	8.53±1.13	7.73±0.69	8.63.0±1.03	>0.05

SAB: Subarachnoid block

Table 2: SBP

Time interval of SBP	Group I	Group II	Group III	*P* value		
				Group I versus Group II	Group II versus Group III	Group I versus Group III
Baseline	116.9±7.99	118±7.91	120.6±8.29	>0.05	>0.05	>0.05
0 min	117.9±7.37	121±7.3	122.2±7.35	>0.05	>0.05	>0.05
5 min	98.73±10.47	109.5±12.32	108.73±6.09	<0.05	>0.05	<0.05
10 min	98.0±7.1	109.8±5.36	107.6±6.33	<0.05	>0.05	<0.05
20 min	109.4±4.84	113.7±10.26	115.9±9.4	<0.05	>0.05	<0.05
30 min	109.1±9.4	118.8±9.5	115.0±7.09	<0.05	>0.05	<0.05
End of surgery	112±13.2	114±10	111.6±9.07	>0.05	>0.05	>0.05

SBP: Systolic blood pressure

patients undergoing transurethral resection of prostate and observed hypotension in 24% patients of mephentermine group.

Vercauteren *et al.*, 2000[14] studied the effects of IV ephedrine 5 mg after low-dose spinal anesthesia and observed hypotension in 25% patients of ephedrine group as compared to 55% patients in control group.

Similar results were not found in studies of Ayorinde *et al.*, 2001.[1] They compare the ephedrine 45 mg IM after spinal anesthesia in LSCS with phenylephrine 4 mg and control group and observed hypotension in 70% patients in control compared to 45% patients in ephedrine group.

Webb and Shipton, 1998[15] observed the incidence of hypotension after spinal anesthesia in 50% of patients of 37.5 mg ephedrine IM as compared to 80% of patients in control group.

Baseline HR was comparable in all groups. After injecting the drug, HR was comparable in all groups. After SAB, there was an increase in HR in all groups but, in Group I, it was significantly higher as compared to Groups II and III (Table 5). As HR was increased when blood pressure tends to fall. Similar results were found Ayorinde *et al.*, 2001,[1] Sahu *et al.*, 2003,[13] and Nagan Kee *et al.*, 2001 observed a similar increase in HR.

Hypotension causes reduction in uteroplacental blood flow. Even short duration of hypotension causes fetal hypoxia and bradycardia. Apgar score was > or = to 7 in all patients at 1 min and 5 min, but on statistical analysis, it was significantly lower in Group II as compared to Groups I and III (Table 6). The incidence of low Apgar score in Group II was not found in literature but may be due to decrease uteroplacental blood flow. Ayorinde *et al.*, 2001[1] observed similar results with ephedrine. They did not

Table 3: DBP

Time interval of DBP	Group I	Group II	Group III	*P* value		
				Group I versus Group II	Group I versus Group III	Group II versus Group III
Baseline	74±7.3	76±8.5	77.47±5.9	>0.05	>0.05	>0.05
0 min	74.3±7.9	79±8	78.2±5.4	>0.05	>0.05	>0.05
5 min	60.4±10.5	69.4±12.4	68.4±8.8	<0.05	>0.05	<0.05
10 min	60.6±10.5	72.27.0±7.4	69.06±6.8	<0.05	>0.05	<0.05
20 min	65.7±11	73.7±10	69.7±9.5	<0.05	>0.05	<0.05
30 min	65.1±9.18	70.6±8.93	70.7±9.6	<0.05	>0.05	<0.05
End of surgery	65.5±13.6	68±11.4	68.1±9.94	>0.05	>0.05	>0.05

DBP: Diastolic blood pressure

Table 4: Incidence of hypotension

Hypotension	Group I	Group II	Group III
Number of patients	18	7	8

Table 5 HR

Time interval of HR	Group I	Group II	Group III	*P* value		
				Group I versus Group II	Group I versus Group III	Group II versus Group III
Baseline	102.5±10.2	87.4±12.38	85.93±11.14	0.936	0.665	0.631
0 min	103.9±8.6	86±10.85	84.87±9.63	0.108	0.026	0.671
5 min	116.2±5.68	85.53±10.01	83.6±9.6	0.022	0.002	0.449
10 min	116.2±5.83	84.5±8.62	82.43±8.84	0.0016	<0.0001	0.362
20 min	91.4±4.93	83.23±8.87	82.2±9.28	<0.0001	<0.0001	0.662
30 min	93.73±4.10	83.2±9.42	81.87±9.55	<0.0001	<0.0001	0.589
End of surgery	94.9±7.64	82.57±9.27	81±10.41	<0.0001	<0.0001	0.54

HR: Heart rate

Table 6: Apgar score at 1 min and 5 min

Apgar score	Group I	Group II	Group III	*P* value		
				Group I versus Group II	Group II versus Group III	Group I versus Group III
At 1 min	8.5±0.53	7.7±0.69	8.7±0.47	<0.05	<0.05	>0.05
At 5 min	9.5±0.5	9.26±0.69	9.7±0.5	<0.05	<0.05	>0.05

Table 7: Incidence of complications

Complication	Group I	Group II	Group III
	N (%)	*N* (%)	*N* (%)
Bradycardia	00 (00)	00 (00)	00 (00)
Nausea and vomiting	12 (40)	05 (16.66)	05 (16.66)
Pain	09 (30)	10 (33.33)	10 (33.33)
Chills and rigor	02 (6.66)	02 (6.66)	03 (10)
Allergic reaction	00 (00)	00 (00)	00 (00)

find any difference in Apgar score as compared to control group. Sahu *et al.*, 2003[13] observed Apgar score >7 or = in all patients of ephedrine, mephentermine, and control groups. Apgar score is better in patients operated under regional anesthesia than general anesthesia. It was observed by Marx *et al.*, 1969[10] and James *et al.*,1977.[6] They observed Apgar score at 1 min was lowest with general anesthesia.

Bradycardia was not found in any of the patients in our study may be due to the level of spinal is T5-T6 and inotropic effect of ephedrine hydrochloride or injection mephentermine sulfate (Table 7).

Complained of nausea and vomiting were seen in 12 patients of Group I as compared to 5 patients in Group II and 5 patients in Group III. Higher incidence of nausea and vomiting in Group I patients is due to higher incidence of hypotension (Table 7).

Pain (retrosternal) was found in 9 patients of group and 10 patients each in Groups II and III (Table 7).

Chills and rigors were found in 2 patients each in Groups I and II and 3 patients in Group III. This was comparable in all groups (Table 7).

All complications are managed accordingly.

CONCLUSION

From the present study, the following conclusions can be drawn:

- Mephentermine sulfate is equally efficacious than ephedrine hydrochloride for prevention of spinal anesthesia-induced hypotension in pregnant patients undergoing LSCS
- Apgar score was lower in patients receiving mephentermine sulfate as compared to ephedrine hydrochloride, but it was never below 7 in all patients of all groups
- Neonatal outcome was good in all patients of all groups
- Both mephentermine sulfate and ephedrine hydrochloride have similar side effects.

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