Efficacy of Phenylephrine and Ephedrine in maintaining maternal blood pressure intra operatively during spinal anesthesia for caesarean section

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Abstract

Introduction: Spinal anaesthesia has become a popular technique for caesarean section. It however has the potential to cause rapid onset of maternal hypotension which may have detrimental maternal and neonatal effects. Thus, a number of strategies for treating hypotension have been investigated. Careful positioning and volume preloading with crystalloid or colloids have been used to prevent it, but these are not complete measures and vasopressor is required to correct hypotension quickly.

Methodology: After approval from our institutional ethics committee, 100 parturients ASA I and II scheduled for elective as well as emergency Caesarean section under sub arachnoid block (SAB) were studied. All parturients were at term, had uncomplicated singleton pregnancy with cephalic presentation.

Results: Phenylephrine and Ephedrine are effective given prophylactically IV bolus followed by infusion in maintenance of arterial pressure within 15% limit of baseline. Phenylephrine has quicker and shorter duration of action effect in comparison to Ephedrine.

Conclusion: Vasopressor drugs Phenylephreine and Ephedrine, effectively maintained arterial blood pressure during spinal anaesthesia for caesarean section

Key words: Phenylephrine, Ephedrine, Caesarean section

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Introduction

The delivery of the infant into the arms of a conscious and pain free mother is one of the most exciting and rewarding moments in medicine. With the increasing in the incidence of Caesarean section[1], the anaesthesiologist is trapped in a delicate web of decision making over the type of anaesthetic technique to be employed which guarantees the safety of both the mother and fetus.

In the recent decades there has been a worldwide shift in obstetric anaesthesia practice in favour of regional anaesthesia with spinal anaesthesia being the most popular among them.[2] Spinal anaesthesia was introduced into clinical practice by German Surgeon Karl August Bier in 1898[3]. More than a century has passed and today it is one of the most popular techniques for lower limb and lower abdominal procedures including caesarean section. Its popularity is due to the advantages it confers – relative simplicity, rapidity, certainty, duration, low failure rates, minimal side effects, an awake mother, least exposure of mother and fetus to anaesthetic drug and circumvention of life threatening complications like aspiration, failed intubations and depressed neonate. But, like any other anaesthetic technique, it is not devoid of complications, the most common being hypotension which may adversely affect both mother and fetus.

In caesarean section under spinal anaesthesia hypotension has been reported in as many as 85% of the patients.[4] Maternal hypotension is associated with distressing symptoms like dizziness, nausea, vomiting and may also interfere with surgical procedure and also can cause fetal bradycardia[5] and acidosis.[6] Careful positioning and volume preloading with crystalloid or colloids have been used to prevent it, but these are not complete measures[7,8] and vasopressor is required to correct hypotension quickly.[9] Infusion of large volume of crystalloids over a short period of time carries a risk of pulmonary oedema and postoperative urinary retention.

Most of the studies are centred around the effects of preloading[10,11,12] or vasopressors.[13,14,15] Phenylephrine, an alpha-1 adrenergic agonist whose action would be expected to counteract decrease in systemic vascular resistance induced by spinal anaesthesia has been found to be safe and effective when given IV bolus doses to patients undergoing caesarean section. Ephedrine has mixed alpha and beta adrenoreceptor activity. It maintains the arterial blood pressure mainly by increasing cardiac output and heart rate.

The usual approach to use vasopressors in this clinical setting is reactive rather than proactive, spinal anaesthesia induced maternal hypotension is allowed to

develop and then treated accordingly. We have, instead, studied prophylactic bolus followed by infusion doses of Phenylephrine and Ephedrine for maintenance of maternal arterial pressure during spinal anaesthesia in Caesarean section.

Methodology

Comparative study was done on parturient coming for elective as well as emergency Caesarean section conducted under spinal aesthesia. After approval from our institutional ethics committee, 100 parturient ASA I and II scheduled for elective as well as emergency Caesarean section under sub arachnoid block (SAB) were studied. All parturient were at term, had uncomplicated singleton pregnancy with cephalic presentation.

The protocol was explained to all patients in detail in their own language and informed written consent was taken.

Following criteria's were adopted for selecting parturients.

Inclusion Criteria:

- Patients scheduled for elective as well as emergency lower segment Caesarean section.
- Aged between 18-35 years.
- Patients with ASA Class I and II

Exclusion Criteria:

a) Patient refusal for the procedure
b) Patients with significant coagulopathies and other contra-indications for spinal anaesthesia.
c) Patient with pregnancy induced hypertension
d) Patients with history of significant systemic disorders (cardiovascular, respiratory or central nervous system)
e) Patients On Vasoactive drugs

Patient's height and weight were measured during the pre-anaesthetic visit. Baseline values for maternal systolic blood pressure, diastolic blood pressure and heart rate were recorded. Inj. Ranitidine 50 mg and ondensetran 4 mg were given intravenously 30 mins before surgery.

Patients were transported to the operating theatre in left lateral position with an 18G intravenous cannula in a peripheral vein. Parturients were preloaded with 15ml/kg of ringer lactate. Basal parameters that is pulse rate, systolic and diastolic arterial pressure, oxygen saturation, ECG were recorded thrice and mean value was taken as a base line values. Preanaesthetic drill and emergency intubation are kept ready. Partureints were alloted into two groups of 50 each by computerized selection.

Group P: Inj.Phenylephrine 20µg as IV bolus, immediately after SAB, followed by infusion 10µg/min. Group E: Inj. Ephedrine 6 mg as IV bolus, immediately after SAB, followed by 0.1 mg/min infusion.

Lumbar puncture was performed under strict aseptic precautions in left lateral position by a midline approach using 23 G Quincke spinal needle inserted at L_{2-3} or L_{3-4} vertebral interspace. 9mg(1.8ml) of inj bupivacaine heavy of 0.5% was given intrathecally. The patient was then immediately turned supine with constant maintenance of left uterine displacement. Oxygen was administered at 4 lts / min by a HUDSON'S face mask.

Pulse rate, systolic and diastolic arterial pressure, oxygen saturation, ECG were recorded after subarachnoid block, then at every 1 min for 20 min and thereafter every 5 min till the end of surgery. Whenever hypotension (defined as fall in systolic pressure >15% from the baseline value) occurred, only bolus dose of study drug was given IV.

The bradycardia i.e. a pulse rate of 60 min^{-1} or less, for more than 30 secs was treated with increments of atropine 0.3 mg I.V, upto maximum of 2.4mg. Fall in saturation <95 %, treated by 100% O2 supplementation through Magill's circuit.

Sensory level was checked using spirit swab, surgery was allowed to do after attaining T8 levels. Uterine incision and delivery time were noted down. Injection Oxytocin was infused IV at 10 units/ hr for 1st hour and 5 units per hour for next hr of study. Neonatal condition was assessed by APGAR score at 1 and 5 minutes after delivery. Arterial blood gas values by fetal scalp vein or umbilical vein sampling was not done. Infusion of the study drug was stopped at skin suturing.

Post operatively patient was monitored for SBP, DBP, MAP, HR at 1st,5th, 10th followed by every 10 min upto 60mins(based on the pharmacodynamics of the drugs used) and any possible side effects.

Statistical Methods: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Power of study being 80%.

Results

In our study of comparing efficacy of prophylactic bolus followed by infusion of phenlyepherine and ephedrine in maintaining arterial blood pressure, 100 partureints were grouped into Group P consisted of 50 patients who received inj. Phenylephrine 20 µg IV bolus, followed by infusion of 10 µg/min and Group E consisted of 50 patients who received Inj. Ephedrine 6

mg IV bolus, followed infusion of 0.1mg/min immediately after spinal anaesthesia.

Table 1: Age, height and Weight distribution of subjects studied

Basic variables	Group E	Group P	P value
Age in years	26.04±4.34	26.06±4.34	0.982
Height in cm	157.08±3.45	157.06±5.67	0.983
Weight in kg	72.72±6.84	72.84±7.62	0.934

The age of the patients ranged from 18-35 years. The mean age in Group E was 26.04 with a standard deviation of 4.34. Mean age in group E was 26.04 with a standard deviation of 4.34. Weight of the patients ranged from 42-75 kilograms. The mean values for weight in group Ewere 72.72±6.84 kilograms. The mean values for weight in Group P were 72.84 ± 7.62 kilograms.

Patients' height ranged from 142-160 centimeters. The mean values for height with standard deviations were 153.20 ± 4.26, 151.83 ± 4.66 and 151.43 ± 4.33 centimeters for Group Pand Group E.

Hence age, height and weight were comparable in all 2 groups and were found to be statistically not significant.

Table 2: Comparsion of systolic blood pressure between the two groups

SBP (mm Hg)	Group E (n=50)	Group P (n=50)	P value
0 minute	129.44±9.71	125.02±12.46	0.051
1 minute	125.08±8.66	123.10±14.83	0.417
2 minute	124.56±11.04	130.56±22.04	0.088
3 minute	127.72±14.93	128.56±21.10	0.819
4 minute	126.34±12.22	129.96±18.86	0.257
5 minute	122.62±11.73	132.36±17.65	0.002**
7 minute	127.86±8.68	127.66±20.83	0.950
10 minute	129.92±9.10	125.14±18.54	0.105
12 minute	124.96±6.29	122.14±15.61	0.239
15 minute	123.88±6.07	120.32±15.84	0.141
17 minute	123.26±7.80	120.76±13.71	0.265
20 minute	122.24±7.02	117.94±11.92	0.030*
25 minute	131.86±10.59	122.30±10.82	<0.001**
30 minute	134.58±12.29	120.90±13.75	<0.001**
35 minute	135.27±9.68	120.66±13.81	<0.001**
40 minute	128.63±6.96	121.19±11.88	0.004**
45 minute	131.52±4.28	124.95±13.73	0.019*
50 minute	132.8±7.47	120.78±7.12	<0.001**
55 minute	131±14.14	116.00±0.00	0.272
60 minute	-	-	-

SBP well maintained in both the groups till 20th min, subsequently group P stabilized towards the basal & group E slightly higher than the basal

Table 3.Comparison of diastolic blood pressure

DBP (mm Hg)	Group E (n=50)	Group P (n=50)	P value
0 minute	82.62±5.78	76.78±14.16	0.008**
1 minute	75.00±7.79	73.00±14.62	0.396
2 minute	75.82±9.44	74.74±17.25	0.699
3 minute	74.10±14.55	77.48±18.77	0.317
4 minute	71.62±11.36	78.86±13.92	0.005**
5 minute	73.98±13.49	77.24±15.45	0.264
7 minute	71.02±12.13	76.50±20.13	0.102
10 minute	74.10±9.77	72.78±17.28	0.639
12 minute	71.28±9.34	70.74±16.02	0.837
15 minute	68.50±8.37	68.92±15.57	0.867
17 minute	69.60±8.82	69.92±16.12	0.902
20 minute	75.42±16.83	68.42±16.59	0.039*
25 minute	70.44±11.03	71.90±17.62	0.620
30 minute	75.72±7.26	70.66±18.77	0.078+
35 minute	78.13±9.94	74.42±16.31	0.263
40 minute	78.13±7.39	75.97±11.48	0.378
45 minute	72.34±6.63	79.50±8.80	0.002*
50 minute	74.10±5.00	73.22±6.53	0.694
55 minute	74.33±4.00	68.00±0.00	0.060+
60 minute	-	-	

Persistent fall in DBP in both the groups, DBP in Phenylepherine group stayed slightly higher compared to ephedrine group.

Table 4: Comparsion of Mean blood pressure between the two groups

MAP (mm Hg)	Group E (n=50)	Group P (n=50)	P value
0 minute	98.26±5.73	92.80±13.09	0.008**
1 minute	91.74±7.93	89.82±13.47	0.387
2 minute	92.15±9.69	93.36±17.93	0.675
3 minute	91.94±13.95	94.46±18.22	0.439
4 minute	89.84±11.26	95.80±15.38	0.029*
5 minute	90.24±11.53	95.52±15.77	0.059+
7 minute	89.88±8.84	93.60±19.87	0.229
10 minute	92.70±8.83	90.20±16.93	0.357
12 minute	89.30±6.85	87.96±14.57	0.558
15 minute	86.92±7.11	85.98±14.81	0.687
17 minute	87.52±7.98	86.80±14.25	0.756
20 minute	90.94±12.64	84.90±13.71	0.024*
25 minute	90.74±7.91	88.74±14.28	0.389
30 minute	95.40±7.77	87.20±16.33	0.002**
35 minute	97.03±9.07	89.90±13.94	0.014*
40 minute	94.77±6.22	91.25±11.11	0.129
45 minute	92.14±5.30	94.70±9.26	0.225
50 minute	93.70±5.37	89.11±6.55	0.057+
55 minute	59.56±17.29	84.00±0.00	0.087+
60 minute	-	-	-

There was fall in MAP in both the groups and was not statistically significant. UI and delivery time was average of 60±5 secs in ephedrine group and 61±7 secs in phenyl ephedrine group. It was not stastically significant.

Table 5: Comparison of Fetal APGAR scoring between two groups.

Groups	Group E	Group P	P valve	Inference
Apgar 1	8.06	8.89	0.41	NS
Apgar 5	8.67	8.78	0.41	NS

APGAR score did not reveal any untoward effect on fetal status, since all new born of two groups had APGAR score greater than 7. Ephedrine group had no hypotension, no bradycardia, no vomiting but 6% patients had nausea. Phenylephrine group had no hypotension, 12 patients had bradycardia requiring treatment, no nausea and no vomiting

Discussion

Although, Caesarean section is one of the oldest operations in recorded history, anaesthesia for Caesarean section is just a century old and is not bereft of controversies. On one hand, anaesthetic techniques like local anaesthesia have been scoffed at, by both anaesthesiologists and obstetricians. While, on the other hand, the obstetric airway with its ensuing complications have instilled fear into the anaesthesia-logists. Thus general anaesthesia for parturients was approached with great degree of caution and decision making.

Amidst this chaos, regional anaesthesia especially spinal anaesthesia proved to be the most preferred technique for Caesarean section. The reason being, the unique potential of spinal technique to provide anaesthesia with a blend of low degree of physiologic trespass and with profound degrees of sensory denervation and muscle relaxation. Thus, the safety of spinal anaesthesia is of dual nature; pharmacological as well as physiologic. The only flaw with this technique is the risk of hypotension especially in gravid parturients.

Dinesh Sahu and colleagues[16] found that maternal hypotension during spinal anaesthesia for Caesarean delivery was a persistent problem in approximately 85% of cases. Other studies quote an incidence of 50-80%. Differing definitions of "significant" hypotension are partly responsible for the wide variation in incidence of hypotension reported in literature.

Careful positioning and volume preloading with intravenous crystalloid solution or colloid solution have been standard practice for prevention of hypotension, but these are not complete measures [16].

Systolic blood pressure: In this study both the vasopressor effectively maintained arterial pressure within 15% limit of baseline value though phenylephrine maintained better in first 5 minutes of bolus dose as compared to ephedrine. which may be due to, phenylephrine having peak effect within one minute, whereas ephedrine has 2-5 mins.[16] The result is similar to study done by Dinesh sahu comparing the bolus dose of 20µg phenylephrine and ephedrine 6 mg. Thomas and Colleagues[17] reported that bolus phenylephrine 100 µg is as effective as ephedrine 5 mg in restoring maternal arterial pressure above 100 mmHg. Moran and Colleageus[18] gave ephedrine 10 mg or phenylephrine 80µg IV bolus to maintain systolic arterial pressure above 100 mmHg.

In this study fall in SBP after stopping of infusion of study drugs was acute in phenlepherine compared to gradual fall in ephedrine. This accounts for the longer action of ephedrine than phenylephrine.

In this study even though there was a gradual fall in DBP in both the drugs, the values of DBP were higher due to alpha action of Phenylephrine compared to Ephedrine.

Heart rate: In this study there was a significant fall in heart rate (24% of study group) with phenyl ephrine requiring treating with atropine. Heart rate increased more than pre operative valves with ephedrine which may be due to beta agonistic action of ephedrine. Result correlates with the study by Dinesh Sahu[16].

P.A.Hall and colleages[19] studied prophylactic bolus followed by infusion of ephedrine(6mg iv bolus followed by 1mg/min infusion) and phenylephrine (20µg iv bolus followed by 10 µg infusion), showed 20% incidence of bradycardia requiring treatment with atropine .This result correlate with our study.

Thomas D.G. et al[17] showed 58% incidence of bradycardia (heart rate less than 60 beats /min) when phenylephrine was given as IV bolus after induction of spinal anaesthesia, but in our study the incidence was 24%(12 pateints). This is unlike in a study by Taylor JC[32(23)] et al who reported two cases of overdose resulting in extreme hypertension and headache.

Ramanathan and colleages[20] studied 5mg ephedrine and phenyephrine 100µg iv bolus, they concluded that transient maternal hypotension does not affect neonatal acid – base status, both ephedrine and phenylephrine do not cause fetal acidosis, when used for treating maternal hypotension.

On Neonatal Outcome: In the study neonatal assessment which done by APGAR scoring at 1st and 5th min was more than 8 in both the study groups, fetal scalp vein or umbilical blood gas analysis was not done. This result correlated well with study done by Alahuhta and colleages[21] with ephedrine 5mg or phenylephrine 100µg followed by 50mg/hr ephedrine and 1000 µg/hr phenylepherine, showed no change in APGAR scoring, fetal heart rate and umbilical artery pH.

La Porta and colleages[22] compared phenylephrine and ephedrine in treating maternal hypotension due to spinal anaesthesia for cessarean delivery. Treated with ephedrine 5mg iv bolus, phenylephrine 40 µg iv bolus injections. Showed no significant differences APGAR scoring, acid base levels.

Thomas and Colleagues[17], Moran and Colleageus[18] concluded that phenylephrine is as effective as ephedrine and when used in small incremental bolus injections, it appears to have no adverse neonatal effects in healthy, non laboring parturients.

Adverse Effect: In the present study under taken there was 6% incidence of nausea in ephedrine group compared to phenyl ephedrine group. Nausea was not associated with hypotension. The incidence is less compared to incidence of nausea occurring in parturients undergoing cesearean section under spinal anaesthesia (23-68%). None of the patients had vomiting in both the groups. The incidence of complications were less when compared to study done by P.A.Hall and colleages[19], showed nausea was 30% in ephedrine group and 40% in phenyl ephrine group.

Dinesh sahu and colleages[16] study with bouls iv ephedrine and phenylephrine showed 10% incidence of nausea in both ephedrine and phenyl ephedrine group. This severity is considerably more compared to present study. In conclusion, we have found that prophylactic IV bolus followed by infusion of phenylephrine and ephedrine are effective in maintenance of arterial pressure within 15% limit of baseline, though phenylephrine has quicker peak effect in comparison to ephedrine and it causes reduction in heart rate, which may be advantageous in cardiac patients and patients in whom tachycardia is undesirable.

Conclusion

Thus it can be concluded that prophylactic IV bolus followed by infusion Phenylephrine, Ephedrine can be safely used during spinal anaesthesia for caesarean section for treatment of hypotension. Phenyl ephrine would better preferred in a patient like PIH, Mitral stenosis and other cardiac disorders, where strict and titrable control of haemodynamics is required

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