JMSCR Volume||2||Issue||5||Pages 1084-1091||May 2014 2014

www.jmscr.igmpublication.org Impact Factor-1.1147
ISSN (e)-2347-176x

Journal Of Medical Science And Clinical Research
IGM Publication An Official Publication Of IGM Publication

Phenylephrine Infusion vs. Ephedrine Infusion: Effect on Fetal Acidosis

Authors

Urvashi Yadav[1], Dheer Singh[2], Kunwar Bharat[3], Reena Verma[4]

[1]Department of Anaesthesiology, Rural Institute of Medical Sciences and Research Saifai, Etawah, Uttar Pradesh, India
[2]Department of Anaesthesiology, Rural Institute of Medical Sciences and Research Saifai, Etawah, Uttar Pradesh, India
[3]Department of Pediatrics, Rural Institute of Medical Sciences and Research Saifai, Etawah, Uttar Pradesh, India
[4]Department of Obs and Gynae, Rural Institute of Medical Sciences and Research Saifai, Etawah, Uttar Pradesh, India

Corresponding Author
Dheer Singh
E-03, New Type-3, Rural Institute of Medical Sciences and Research,
Saifai, Etawah, Uttar Pradesh, India
E mail: *aujash@yahoo.com*

Abstract
This randomized double blind study was started with an objective of comparing the fetal effects of two commonly used vasopressors – ephedrine and phenylephrine in elective caesarean section.
Methods: One hundred patients were randomized into two groups to receive either 100 µg/ml phenylephrine (group-P, n=50) or 5mg/ml ephedrine (group-E, n=50). Immediately after spinal injection the study solution was started prophylactically in every patient at the rate of 60ml/hr. A predefined algorithm was used to adjust the infusion rate according to the systolic blood pressure (SBP). After delivery, arterial and venous blood samples were taken from a double-clamped segment of umbilical cord for immediate blood gas analysis with a blood gas analyser
Keywords: prophylactic, infusion, vasopressors, elective caesarean section, fetal acidosis.

INTRODUCTION

Spinal anaesthesia (SA) is nowadays considered the standard anaesthetic technique for elective caesarean section[1]. However, the chance of hypotension is a major limitation of this technique. The incidence of hypotension is more than 80% without any prophylactic measures[2,3]. This hypotension with or without bradycardia has detrimental effects on both mother and fetus[4,5] .The incidence of hypotension can be lowered by several ways but till date, no single method completely prevents hypotension[4,5]. Contemporary articles emphasize on the arterial rather than venous

circulation and project the reduced systemic vascular resistance as the primary factor for the genesis of maternal hypotension[6-8]. Over the last few years, there is a trend to rely more on vasopressors than either crystalloid or colloid alone[4,6,7].

Different vasopressors are commonly used at present with varying degrees of success [6]. Despite the use of prophylactic intravenous (i.v.) infusion[6] or bolus[7] ephedrine for the last three decades, a good number of failures have also been reported[9] and a rescue phenylephrine bolus dose appears effective when ephedrine alone fails to correct hypotension[3]. Prophylactic phenylephrine infusion significantly lowers the incidence of spinal anaesthesia-induced maternal hypotension[6,7,10] despite its limitations like bradycardia, hypertension and reduced cardiac output at higher dose[3,8]. Advantage of phenylephrine include high efficacy, ease of titration, ability to use liberal doses to maintain maternal blood pressure near normal and prevent nausea and vomiting without causing fetal acidosis.

Considering all above aspects, it is planned to carry out a study comparing the effects of phenylephrine infusion and ephedrine infusion on fetal acidosis during spinal anaesthesia in elective cesarean section.

MATERIAL AND METHODS

After obtaining institutional ethics committee's approval, 100 nonlaboring women older than 18 years, American Society of Anaesthesiologists (ASA) physical status I or II, weighing more than 50 kg and less than 90 kg, height 145–165 cm, having uncomplicated singleton pregnancy beyond 36 weeks, scheduled to have elective caesarean section under spinal anaesthesia were decided for this study. Fetal malpresentation, pregnancy-induced hypertension (PIH), hypertension, cardiac disease, renal disease, fetal anomaly, diabetes mellitus and patients on chronic medication were excluded from the study. Written informed consent was obtained and patients were advised overnight fasting.

Patients received antacid premedication and standard noninvasive monitoring was applied. Baseline. IV infusion of lactated Ringer's solution was started at 5 ml/min. Patients were randomly assigned into two groups to receive phenylephrine 100mcg/ml (group-P) or ephedrine 5 mg/ml (group-E). Two identical 20ml syringes (containing 12ml vasopressor) were prepared containing either phenylephrine 100µg/ml or ephedrine 5mg/ml.

Spinal anesthesia was induced with a 25-gauge Whitacre needle at L2-3 or L3-4 vertebral interspaces, and hyperbaric 0.5% bupivacaine 2.5 ml was injected intrathecally.. At intrathecal injection ,We started rapid iv fluid infusion (20ml/kg) and commenced the vasopressor at 60ml/hr. Hemodynamic data were downloaded.

Infusions were administered with a syringe pump that was connected to the i.v line and were continued for a minimum of 2 min, after which the infusion was given according to a predefined protocol based on the SAP measurement each minute. After each 1-min measurement of SAP, the

infusion was stopped if the SAP was more than baseline, and it was continued or restarted if the SAP was less than or equal to baseline.Here, we defined hypotension as a decrease in SAP to<80% of baseline and hypertension as an increase in SAP to >120% of baseline.. The dosing regimens for phenylephrine were selected on the basis of recent studies.

The times of skin incision, uterine incision, and delivery were recorded. The infusion and bolus protocol was continued to replace surgical losses and maintain SAP. The total volumes of study solutions given by bolus and by infusions were recorded.

After delivery, oxytocin 10 IU was given by slow IV injection, arterial and venous blood samples were taken from a double-clamped segment of umbilical cord for immediate blood gas analysis with a blood gas analyzer by the attending pediatrician who was unaware of study group. Cases having technical difficulty in performing blood gas analysis were excluded from the study. Apgar scores were assessed 1 and 5 min after delivery by the attending pediatrician. Presuming the effectiveness of vasopressors over i.v fluid as 30% and the difference between PE over E as 30% to be clinically relevant, with a power of 80% (β=0.2) at 0.05 level of significance (α=0.05), the sample size was calculated as 44 in each group (*n*=44). We assessed 100 patients for study eligibility keeping the chance of possible dropouts. All the data was tabulated &analyzed with Microsoft Excel 2007. Statistical analysis of data was done using Arithmetic mean & standard deviation. Parametric data among two groups was compared using "unpaired t" test and comparison of non-parametric data was done using chi-square(χ^2) test through Minitab software. "P" value <0.05 was considered statistically significant.

RESULTS

All patients completed the study. Both groups were comparable with regard to demographic profile, pre-operative vital parameters, block height, induction to delivery time and incision to delivery time [TABLE-1].

We found that ephedrine causes more acidosis in the fetus [Umbilical Arterial pH (Mean ± S.D.) in group-E is (7.20 ± 0.037) compared to (7.29±0.008) in group-P (p- value <0.001)][TABLE-2].

TABLE -1

DEMOGRAPHIC PROFILE, PRE-OP VITAL PARAMETERS

Comparison	Group (P)	Group (E)	T test (p value)
Age (Mean±SD) (Yrs);Range	27.16±5.13(20 – 35)	28.27±4.39(20 –38)	1.17(0.12)
Weight (Mean±SD) (Kg);Range	56.62±4.56(50 – 65)	56.17±2.98(50-60)	0.58(0.28)
Height (Mean±SD) (cm)	155.5±4.19	156.17±2.98	0.59(0.556)
Baseline Heart Rate(Mean ± SD)(bpm)	72.23±6	74±5.4	1.54(0.126)
Baseline Systolic BP (Mean ± SD) (mm Hg)	122.98±6.03	120.23±7.6	1.87(0.064)
Induction to delivery time (Mean ± S.D.)(Min)	27.45± 2.30	26.5 ± 2.35	1.92(0.058)
Incision to delivery time (Mean ± S.D.) (Min)	10.98 ± 1.38	10.23 ± 2.57	1.82(0.072)
Requirement of Vasopressor (Mean± S.D.) (ml)	8.52± 1.68	6.7±1.53	t=35.77 p<0.001

TABLE- 2

FETAL PARAMETERS

Comparison	Group-P	Group-E	t-test/ χ^2	p-value
Umbilical Arterial pH(Mean ± S.D.)	7.29±0.008	7.20±0.037	t= 15.69	<0.001
Umbilical Arterial pH<7.2	2%	28%	χ^2 =15	<0.001
Umbilical Arterial $pC0_2$ (Mean ± S.D.)mm Hg	53.12 ±2.05	62.84± 6.18	t=10.66	<0.001
Umbilical Arterial pO_2 (Mean ± S.D.)mm Hg	16.59 ± 1.83	14.6 ± 1.23	t=6.40	<0.001
Umbilical Arterial Oxygen Content (Mean ± S.D.)ml/dl	7.23 ± 1.05	4.66 ± 1.04	t=12.39	<0.001
Umbilical Venous pH (Mean ± S.D.)	7.34 ± 0.007	7.30± 0.022	t=12.8	<0.001
Umbilical Venous pCO_2 (Mean ± S.D.)mm Hg	45.78± 2.52	45.17± 2.65	t=1.20	0.233
Umbilical Venous pO_2 (Mean ± S.D.)mm Hg	27± 2.24	31.53± 1.50	t=11.99	<0.001
Umbilical Venous Oxygen Content (Mean ± S.D.)mm Hg	14± 0.56	14.12± 0.58	t=0.77	0.446
Apgar Score At 5 Minutes (Mean ± S.D.)	9.90±0.49	9.78±0.29	t=1.49	0.14

DISCUSSION

Incidence of hypotension was comparatively lower with phenylephrine infusion and minimum recorded B.P occurred later compared to ephedrine infusion. Appreciating that the mean arterial pressure is a better indicator of tissue perfusion, we have used SBP as a clinically useful endpoint on which our therapy was based and most of the earlier studies have used SBP as primary outcome[2,6,7,9-12,14,15].Our findings are consistent with recent published data on management of maternal hypotension during spinal anesthesia[16-17]. Mercier FJ et al., 2007[16] analyses the different preventive and curative strategies for management of hypotension during spinal anaesthesia for cesarean section. Prophylactic phenylephrine, with or without ephedrine according to maternal heart rate, is at least as effective as ephedrine, with less adverse effects. We used large total dose of phenylephrine,

this may cause concern about potential adverse effects on uteroplacental blood flow. However, the high values for UA and venous pH in our study were indirect evidence that there was no significant adverse effect. It should also be noted that we studied only healthy patients undergoing elective cesarean deliveries. It may not be valid to extrapolate our findings to patients with non-reassuring fetal heart rate patterns or impaired uteroplacental blood flow, to preeclamptic patients, or to patients with prolonged induction to delivery times.

Fetal parameters

Umbilical arterial (UA) *pH*, pO_2 and O_2 content was lower where as UA pCO_2 was higher with ephedrine group [Table2]. . Umbilical venous (UV) pH was lower in group E where as UV pCO_2 and venous oxygen content was similar in both groups (Table 2). It was consistent with previous studies[4,11,12]. Ngan Kee WD et al 2008[11] found that UA *pH* and base excess was lower with ephedrine compared with phenylephrine. Depression of fetal *pH* and base excess with ephedrine has been postulated to be related to ephedrine induced stimulation of fetal metabolism. Their results showed that as proportion of ephedrine increased UA pCO_2 was increased and UA oxygen content was decreased without changes in UV values, suggesting an increase in fetal CO_2 excretion and oxygen extraction. Conversely UV pO_2 was decreased as proportion of phenylephrine was increased. This could reflect phenylephrine having a greater vasoconstrictive effect on uteroplacental circulation, since reduction in uteroplacental blood flow has been shown to correlate directly with decrease in fetal pO_2.

There was no difference among groups in UV oxygen content, O_2 delivery to fetus is unlikely to be much affected. Although not all studies comparing phenylephrine and ephedrine had shown differences in UA and UV pO_2, this could reflect the comparatively large doses of phenylephrine used in this study. Overall when considering the effects of vasopressor on the fetus, effect on both oxygen demand and oxygen supply should be considered. The balance between these should be reflected by fetal acid –base status which in this study was better with phenylephrine than ephedrine. Their results were similar with our study. The Apgar score, assessed at 1 minute and 5 minutes, were comparable in both groups.

CONCLUSION

We have found that, when titrated by infusion to maintain arterial pressure during spinal anesthesia for cesarean section, phenylephrine was associated with less fetal acidosis.

REFERENCES

1. Riley ET, Cohen SE, Macario A, Desai JB, Ratner EF. Spinal versus epidural anesthesia for cesarean section: A comparison of time efficiency, costs, charges, and complications. Anesth Analg. 1995;80:709–12.
2. Saravanan S, Kocarev M, Wilson RC, Watkins E, Columb MO, Lyons G. Equivalent dose of ephedrine and

phenylephrine in the prevention of post-spinal hypotension in caesarean section. Br J Anaesth.2006;96:95–9.

3. Stewart A, Fernando R, McDonald S, Hignett R, Jones T, Columb M. The dose-dependent effects of phenylephrine for elective cesarean delivery under spinal anesthesia. Anesth Analg. 2010;111:1230–7.
4. Lee A, NganKee WD, Gin T. A quantitative, systematic review of randomized controlled trials of ephedrine versus phenylephrine for the management of hypotension during spinal anesthesia for cesarean delivery. Anesth Analg. 2002;94:920–6.
5. Cyna AM, Andrew M, Emmett RS, Middleton P, Simmons SW. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. Cochrane Database Syst Rev.2006;4:CD002251.
6. NganKee WD, Khaw KS, Ng FF, Lee BB. Prophylactic phenylephrine infusion for preventing hypotension during spinal anesthesia for cesarean delivery. Anesth Analg. 2004;98:815–21.
7. NganKee WD, Khaw KS, Ng FF. Prevention of hypotension during spinal anesthesia for cesarean delivery: An effective technique using combination phenylephrine infusion and crystalloid cohydration.Anesthesiology. 2006;104(6):13 48–9.
8. Dyer RA, Reed AR. Spinal hypotension during elective cesarean delivery: Closer to a solution. Anesth Analg. 2010;111:1093–5.
9. Mercier FJ, Riley ET, Frederickson WL, Roger-Christoph S, Benhamou D, Cohen SE. Phenylephrine added to prophylactic ephedrine infusion during spinal anesthesia for elective cesarean section.Anesthesiology. 2001;95:668–74.
10. Cooper DW, Carpenter M, Mowbray P, Desira WR, Ryall DM, Kokri MS. Fetal and maternal effects of phenylephrine and ephedrine during spinal anesthesia for cesarean

delivery. Anesthesiology.2002;97:1582–90.
11. NganKee WD, Lee A, Khaw KS, Ng FF, Karmakar MK, Gin T. A randomized double-blinded comparison of phenylephrine and ephedrine infusion combinations to maintain blood pressure during spinal anesthesia for cesarean delivery: The effects on fetal acid-base status and hemodynamic control.Anesth Analg. 2008;107:1295–302.
12. Cooper DW, Gibb SC, Meek T, Owen S, Kokri MS, Malik AT, et al. Effect of intravenous vasopressor on spread of spinal anaesthesia and fetal acid-base equilibrium. Br J Anaesth. 2007;98:649–56.
13. Cooper DW, Jeyaraj L, Hynd R, Thompson R, Meek T, Ryall DM, et al. Evidence that intravenous vasopressors can affect rostral spread of spinal anesthesia in

pregnancy. Anesthesiology. 2004;101:28–33.

14. Allen TK, George RB, White WD, Muir HA, Habib AS. A double-blind, placebo-controlled trial of four fixed rate infusion regimens of phenylephrine for hemodynamic support during spinal anesthesia for cesarean delivery. Anesth Analg. 2010;111:1221–9.
15. NganKee WD, Khaw KS, Ng FF. Comparison of phenylephrine infusion regimens for maintaining maternal blood pressure during spinal anaesthesia for caesarean section. Br J Anaesth. 2004;92:469–74.
16. Mercier FJ, Bonnet MP De la Dorie A, Moufouki M, Banu F, Hanaf A, Edouard D, Roger-Christoph S. Spinal Anaesthesia for caesarian section: Fluid loading, vasopressor and hypotension. Ann Fr Anesth Reanim. 2007 Jul-Aug; 26(7-8):988-93.
17. Cooper DW, Carpenter M, Mowbray P, Desira WR, Ryall DM, Kokri MS. Fetal and maternal effects of phenylephrine and ephedrine during spinal anesthesia for cesarean delivery. *Anesthesiology* 2002; 97: 1582–90.