

# The Effect of Ephedrine on Fetal Outcome in Treatment of Maternal Hypotension Caused by Spinal Anesthesia During Cesarean Section

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## Abstract

**Objective:** Spinal anesthesia causes hypotension which is a physiologic component during cesarean section. Ephedrine is used for prevention and treatment of maternal hypotension during spinal anesthesia. The aim of this study is to evaluate the effect of transient hypotension which is normalized with ephedrine on fetal outcome.

**Materials and methods:** Eighty women with singleton pregnancies scheduled for elective cesarean section under spinal anesthesia were divided to two groups. The control group was women with normal BP, and case group were women with hypotension who received ephedrine. Two groups were compared for these variables: maternal BP and HR, nausea and vomiting, neonate Apgar and fetal cord blood gases.

**Results:** No difference was found between two groups for variables of age, BMI, weight, height, mean BP, mean HR, serum volume, fetal Apgar in 1 and 5 min and fetal cord fetal blood gases. Dosage of oxytocin used was significantly different between two groups ( $P$ -value = 0.003).

**Conclusion:** Transient hypotension which is treated by ephedrine does not have any effect on acid base situation of baby and treatment of hypotension with ephedrine in pregnant women is a safe procedure.

**Keywords:** Cesarean section, Spinal anesthesia, Ephedrine, Neonatal morbidity

## Introduction

Ephedrine is one of the vasopressor drugs that reduce maternal hypotension. However, it can increase fetal

acidosis (1). Some studies show that the rate of acidosis is related to ephedrine dosage and were showed 5–10 mg ephedrine is choice (2, 3). Ephedrine has indirect alpha and beta agonist effects. It can increase heart rate and cardiac output with restored systolic BP, but the risk of fetal acidosis can increase (1, 3, 4). Other studies do not support higher umbilical acidosis in patients who received ephedrine (6, 7).

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Hypotension is a side effect of spinal anesthesia. Some risk factors of it are: peak sensory block height at or above T5, age more than 40 years old and systolic blood pressure base line less than 120 mmHg (4). However, this complication is severe and more common in pregnancy because IVC compression with pregnant uterus and higher sensory block level causes high intra abdominal pressure (5).

In this study, we compared patients who were hypotensive and received ephedrine with normal BP patients regarding the effects on fetal acid–base status.

## Materials and Methods

Our clinical trial was conducted in Tehran University of Medical Sciences, Mirza Koochak Khan Women's teaching hospital, Tehran, Iran. All patients signed consent before being included in the study. Inclusion criteria were: women with term singlet pregnancy selected for elective cesarean section under spinal anesthesia with 1 and 2 ASA (American Society of Anesthesiologists) risk class. The exclusion criteria were: blood pressure more than 140/90 mmHg or systolic blood pressure less than 85 mmHg, women with cardiovascular, cerebrovascular, renal and liver disease, psychological instability or agitation, autoimmune disease, diabetic mellitus, acute infection disease and other contraindications for spinal anesthesia.

All patients were monitored with electrocardiogram, pulse oximetry and "Non-Invasive Blood Pressure" (NIBP) system, and all of them received 2–3 liter/min O<sub>2</sub> via nasal canola. Then we inserted IV line in to the forearm vein with a 16–gauge IV canola. Before spinal anesthesia, all patients received 400–600 ml ringer serum and proper dose of H<sub>2</sub> blocker. When they had supine position (with 10–15 degree left ward tilt in operation table) for at least 2 minutes we measured patient's blood pressure (BP) and heart rate (HR) from right arm with automated intermittent oscillatory NIBP monitoring system two times, before performing spinal anesthesia as the baseline measurement and every 1minut for the first 10 minutes and then every 3 minutes. Then mean baseline of BP and HR for two measurements were calculated.

Spinal anesthesia was performed in aseptic condition with a 25 gauge Quincke needle in sitting position, using 12–15 mg of hyperbaric Bupivacaine 0.5% in ambient temperature injected by a midline approach in the intrathecal space (L3–L4 or L4–L5). Then patient positioned supine with 10–15 degree left ward tilt in operation table immediately.

If in supine position systolic BP had fallen to less than 80% of baseline, 5–10 mg ephedrine was injected, and if HR was less than 60/min with hypotension or nausea and vomiting with HR less than 80/min and normal BP, 0.6 mg of Atropine was injected.

Frequency of nausea and vomiting and time duration from spinal anesthesia to delivery (min) were detected. Apgar scores with their details were detected 1 and 5 minutes after delivery. For assessment of umbilical cord blood gasses, we clamped two segments of cord and took a blood sample for blood gas analysis preferably from umbilical vein. Then pH, pCO<sub>2</sub>, pO<sub>2</sub> and Base Excess were assessed with AVL Compact 3, gasometry instrument and isomeric method.

## Statistical Analysis

The collected data from data sheets were organized by SPSS software – 16.0. Data statistical analysis were performed by an expert consultant using descriptive, independent samples *t* – test, Crosstabs, Chi–square, Fisher's Exact Test and Pearson correlation test. P–value <0.05 was considered significant.

## Results

Totally 89 patients were screened for study, and 80 of them were selected. Eight patients were excluded because of incomplete report of umbilical blood gases and one because of overt not diagnosed fetal anomaly. Forty patients were hypotensive and received ephedrine (Group 1) and another group of 40 patients were pregnant women with normal BP after spinal anesthesia (Group 2).

Patient characteristics and hemodynamic changes are shown in table 1 and time between spinal anesthesia to umbilical cord clamp, total ringer lactate volume (ml), total Oxytocin dosage, 1 and 5 minutes Apgar scores and details of umbilical cord blood gasses are shown in table 2.

This tables show that there was no significant difference between groups 1 and 2 in all variables except for total Oxytocin dosage, so that the oxytocin dosage in 1 group was significantly higher than 2 group (*p*=0.003).

All Apgar scores were more than 8 at 1 minute after delivery and more than 9 at 5 minute. Frequency and percent of neonate Apgar in 1 and 5 minute are shown in figure 1.

About each of 5 Apgar components (heart rate, respiration, activity, grimace, appearance of neonate), the best result was related to neonatal heart rate and all neonates had HR>100/min at 1 and 5 minutes.

**Table 1: Patients' Characteristics and Hemodynamic Changes**

Variable	Group	Min	Max	Mean ( $\pm$ sd)*	P-Value
Age	1	19.00	40.00	29.50 ( $\pm$ 4.45)	.932
	2	19.00	44.00	29.40 ( $\pm$ 5.85)	
BMI	1	20.52	39.52	30.19 ( $\pm$ 4.65)	.642
	2	22.58	39.25	30.67 ( $\pm$ 4.43)	
Weight	1	57.00	110.00	80.35 ( $\pm$ 13.72)	.631
	2	60.00	118.00	81.83 ( $\pm$ 13.63)	
Height	1	150.00	174.00	163.07 ( $\pm$ 6.83)	.929
	2	150.00	174.00	163.20 ( $\pm$ 5.59)	
Mean systolic BP	1	103.50	137.00	119.43 ( $\pm$ 8.57)	.855
	2	91.00	138.50	119.81 ( $\pm$ 9.71)	
Mean diastolic BP	1	56.50	93.00	76.3 ( $\pm$ 8.53)	.864
	2	45.00	100.00	76.7 ( $\pm$ 12.04)	
Mean HR	1	74.00	119.50	99 ( $\pm$ 12.54)	.373
	2	74.00	124.50	96 ( $\pm$ 12.43)	

\* Mean  $\pm$  Standard deviation

There was no significant relation between 1 and 5 minute Apgar scores with age, weight, height, BMI, BP (mean, systolic and diastolic), time between spinal anesthesia to umbilical cord clamp, total ringer lactate volume (ml) and total Oxytocin dosage (all *P*-values <0.05).

There was no significant relation between pH, pO<sub>2</sub>, pCO<sub>2</sub>, and base excess of umbilical cord blood gasses with age, weight, height, "BMI" (Body Mass Index), mean maternal BP and HR and Oxytocin dosage. But

only was a coordinate trend between better results of umbilical cord blood gasses and reduce of serum volume, but there was a significant relation only with pH increase (*p*=0.021). This better trend exist between reduce of the time between spinal anesthesia and umbilical cord clamp with umbilical cord blood gasses results, but only was significant in increase of pO<sub>2</sub> (*p*=0.004).

Higher 1 minute Apgar score was caused to better result of umbilical cord blood gasses, but was signifi-

**Table 2: Characteristics of Anesthesia procedure and fetal outcome**

Variable	Group	Min	Max	Mean ( $\pm$ sd)*	P-Value**
Anesthesia to cord clamp time	1	10.30	16.00	1 ( $\pm$ 2.88)	.351
	2	9.70	16.00	4 ( $\pm$ 2.83)	
Serum volume	1	1200.00	2500.00	1842 ( $\pm$ 275.39)	.063
	2	1300.00	2200.00	1742 ( $\pm$ 189.31)	
Oxytocin dosage	1	35.00	100.00	65.38 ( $\pm$ 19.78)	.003
	2	30.00	80.00	53.75 ( $\pm$ 14.04)	
Apgar score 1 min	1	7.00	10.00	8.57 ( $\pm$ 0.84)	.472
	2	5.00	10.00	8.40 ( $\pm$ 1.27)	
Apgar score 5 min	1	8.00	10.00	9.50 ( $\pm$ 0.55)	.165
	2	6.00	10.00	9.25 ( $\pm$ 0.98)	
pH	1	7.03	7.40	7.29 ( $\pm$ 0.07)	.858
	2	7.00	7.40	7.30 ( $\pm$ 0.06)	
Base excess	1	-8.50	4.70	-3.04 ( $\pm$ 3.11)	.188
	2	-16.20	0.80	-4.04 ( $\pm$ 3.40)	

\* Mean  $\pm$  Standard deviation

\*\* *P*-value < 0.05 was considered significant.

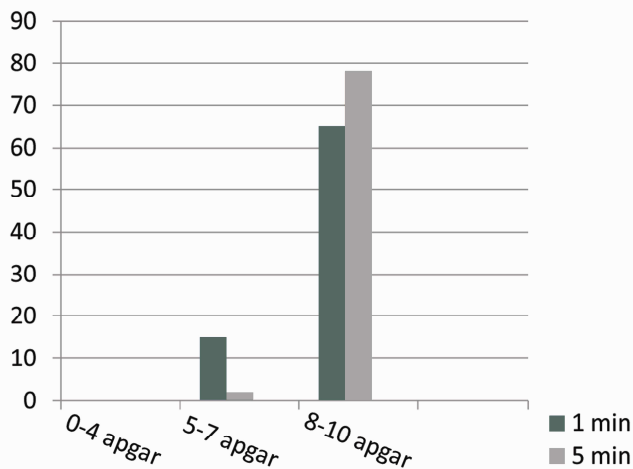


Figure 1. Frequency of neonate Apgar in 1 and 5 minute.

cant in increase of pH ( $p=0.002$ ) and positively base excess ( $p=0.004$ )

Twenty one of eighty patients have nausea and vomiting. Ninety of them were in 1 group. There was significant relation between nausea and vomiting with hypotension ( $p=0.000$ ).

So there was significant relation among nausea and vomiting with serum volume ( $p=0.002$ ) and Oxytocin dosage ( $p=0.027$ ), (Figures 2 and 3).

## Discussion

In our study, mean of characteristics variables did not have significant difference among tow groups and total patients. It can be show distribution of these variables is randomly and equally.

Transient hypotension that treats with ephedrine doesn't have any effect on acid base situation and treatment of hypotension with ephedrine in pregnant women. Also there are reports which reports fetal acidosis after ephedrine use (1, 3, 4), our finding will supports previous reports which found ephedrine is safe for neonate by assessing Apgar and Umbilical arterial pH (6, 7). It can be discussed by short duration of low perfusion state that is not enough to cause acidosis. But because of transient hypotension and resultant decrease in uterine perfusion, can be a discussing the cause of higher dose of oxytocin in this group. Another cause can be hypotension because of hormonal level changes.

Apgar scores is a good index of immediate survival of neonatal outcome and fetal blood gases analysis is a sensitive indicator of adequate placental perfusion

(1). But Apgar score is a pregnancy predictor better than umbilical cord blood pH (3).

As compression, our Apgar scores are higher than some studies and equal with another but in our study as these studies exist no significant relation between Apgar scores and poor early neonatal outcome (1, 8).

HR is less sensitive as compare with other Apgar details. In neonate cardiac arrest, neonate HR is the first sign that change and to be normal too. Cyanosis is second change, then hypotonia and apnea to be normal (9). Our finding also proof this reports.

Unstable hemodynamic situation can be the cause need to increase in serum volume and then decreased umbilical cord blood PH indirectly.

Our finding shows significant frequency of nausea and vomiting that have that shows the same results like others (10). It can be the result of higher level of anesthesia due to increase of vagal tone (11).

Because of significant relation between high dose of oxytocin and nausea–vomiting in one way and with event of nausea–vomiting and hypotension in another way, the cause and effect between oxytocin and nausea–vomiting that exist in texts can be the side effect of hypotension.

The limitation of study: we should be select elective cesarean section and disperse with emergency cases and for significant results, we had expanded exclusion criteria. Also if phenylephrine available in Iran, we can use it in our study as another group.

In summary: transient hypotension which is treated with ephedrine doesn't have any effect on acid base situation and treatment of hypotension with ephedrine in pregnant women is safe and inexpensive and has no side effects on neonate.

## References

1. Desala I, Kushimo OT. Is ephedrine infusion more effective at preventing hypotension than traditional prehydration during spinal anesthesia for cesarean section in African parturient? *International journal of obstetric anesthesia* 2005; 14:294–9.
2. Tsen LC, Boosalis P, Segal S, Datta S, Bader AM. Hemodynamic effects of simultaneous administration of intravenous ephedrine and spinal anesthesia for cesarean delivery. *J Clin Anesth* 2000; 12: 378–82.
3. 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.

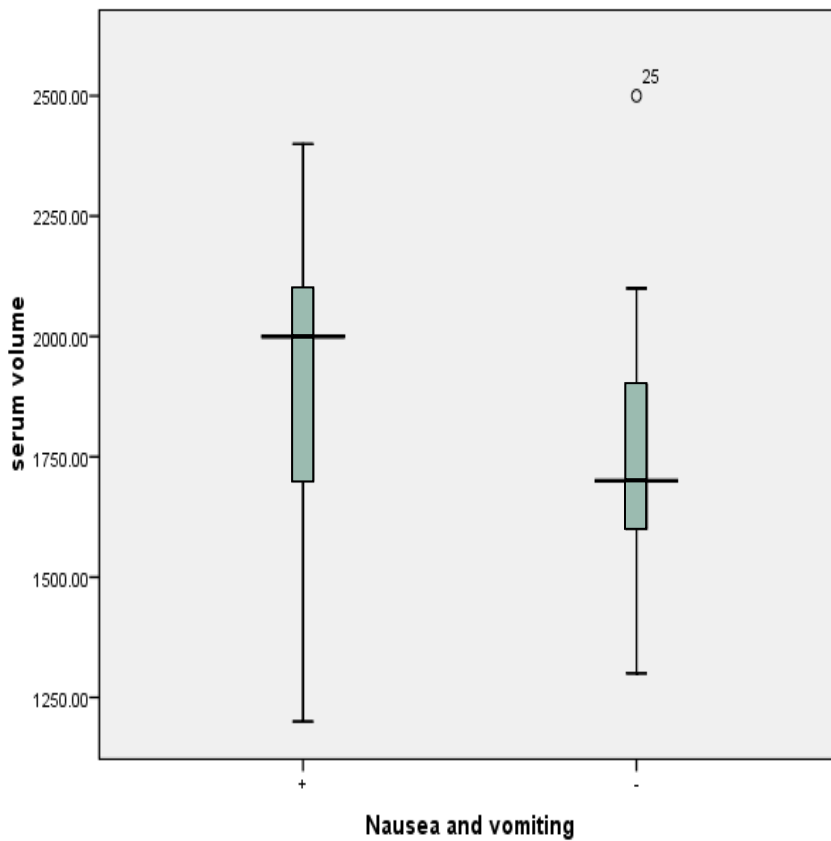


Figure 2. Boxplot show higher mean of serum volume in patients with nausea and vomiting.

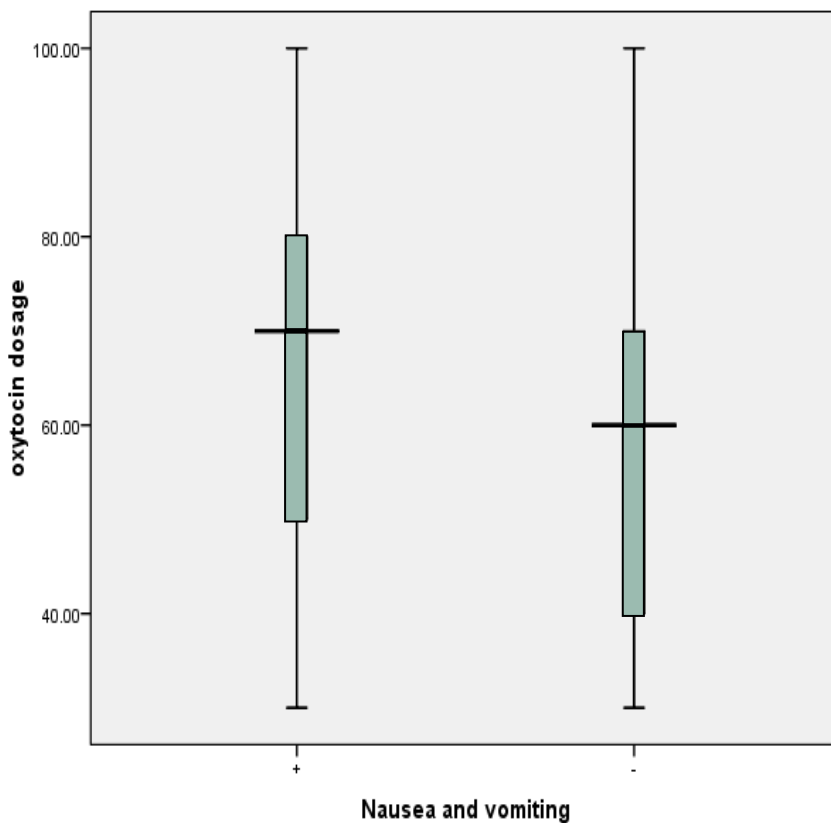


Figure 3. Boxplot show higher mean of oxytocin dosage in patients with nausea and vomiting.

4. Joseph M, Neal MD. Hypotension & Bradycardia During Spinal Anesthesia: Significance, Prevention, and treatment. *Techniques in Regional Anesthesia and Pain Management* 2000; 4: 148–54.
5. Hartley H, Seed PT, Ashworth H, Kubli M, O’Sullivan G, and Reynolds F. Effect of lateral versus supine wedged position on development of spinal blockade and hypotension. *International Journal of Obstetric Anesthesia* 2001; 10: 182–8.
6. Kol IO, Kaygusuz K, GURSOY S, Cetin A, Kahramanoglu Z, Ozkan F, et al. The effects of intravenous ephedrine during spinal anesthesia for cesarean delivery: A randomized controlled trial. *J Korean Med Sci* 2009; 24: 883–8.
7. Lee A, Ngan Kee WD, Gin T. Prophylactic ephedrine prevents hypotension during spinal anesthesia for Cesarean delivery but does not improve neonatal outcome: A quantitative systematic review. *Can J Anaesth* 2002; 49: 588–99.
8. Ngan Kee WD, Lee A, Khaw KS, Ng FF, Karmakar MK, Gin T. A Randomized Double-Blinded Comparison of Phenylephrine and Ephedrine Infusion Combinations to Maintain Delivery: The Effects on Fetal Acid–base Status and Hemodynamic Control. *Anesth Analg* 2008; 107: 1295–302.
9. Robeil M, Kliegman MD, Richard E, Behrman MD, Hal B, Jenson MD, Bonita F, Stanton MD; Nelson Text book of pediatrics; 18 Editions; 2008; 703.
10. Prakash S, Pramanik V, Chellani H, Salhan S, Gogia AR. Maternal and neonatal effects of bolus administration of ephedrine and phenylephrine during spinal anaesthesia for caesarean delivery: a randomised study. *Int J Obstet Anesth* 2010; 19: 24–30.
11. Lee A, Ngan Kee 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.