Comparison of the Effect of Combined Infusion of Ephdrine and Phenylephrine, Ephdrine, or Phenylephrine in Prevention of Post Spinal Hypotension in Cesarean Section

Ali Hadi Muslih Al-ma'ini, Bushra Noori Jama'an***

ABSTRACT:

BACKGROUND:

Hypotension is the most common complication after spinal anesthesia for patients undergoing cesarean section. Prevention and treatment of post-spinal hypotension has been frequently investigated.

AIM OF STUDY:

Our study aimed to compare the effect of prophylactic infusion of combined ephedrine and phenylephrine, ephedrine, or phenylephrine alone in prevention of maternal hypotension after cesarean section.

PATIENTS AND METHODS:

90 pregnant women that underwent elective cesarean delivery under spinal anesthesia were included and divided into: group A received an infusion of combined ephedrine and phenylephrine; group B received ephedrine infusion, and group **C** received phenylephrine infusion. Maternal parameters were recorded.

RESULTS:

There was an insignificant difference in demographic data among the groups. The maternal MAP shows no statistically significant difference, but the combined group shows less hypotensive episodes and less maternal side effects.

CONCLUSION:

Prophylactic infusion of ephedrine and phenylephrine combination can effectively decrease spinal anaesthesia related hypotension without any significant side effect.

KEYWORDS: spinal anaesthesia, Cesarean section, hypotension, ephedrine, Phenylephrine.

INTRODUCTION:

Cesarean section is a surgical procedure in which one or more incisions are made through the mother's abdomen and uterus to deliver one or more babies. [1,2,3]

Choice of anaesthesia is determined by multiple factors, including the indication for operative delivery, its urgency, patient and obstetrician preferences, and the skills of the anesthetist. [4]

Regional anaesthesia has become the preferred technique because general anesthesia has been associated with a greater risk of maternal morbidity and mortality. Other advantages include (1) less neonatal exposure to potentially depressant drugs, (2) a decreased risk of maternal pulmonary aspiration, (3) an awake mother at the birth of her child, and (4) the option of using spinal opioids for postoperative pain relief. [4]

Hypotension is usually defined as a 25% decrease in systolic or mean arterial pressure or an absolute decrease of 40 mmHg [5]. Rapidly developing hypotension after spinal anaesthesia may cause unpleasant dizziness and nausea in about 50% patients [5]. In pregnant women, greater sensitivity to local anaesthetics results in higher blocks, and compounded by the effects of aortocaval compression, hypotension occurs with greater frequency and severity. [5]There is also an increase in sympathetic versus parasympathetic activity which predisposes to a greater degree of peripheral vasodilation. Epidural blockade produces a similar extent of sympathectomy, but there is a lower incidence and severity of hypotension since the rate of onset of sympathectomy is slower, allowing more time for cardiovascular compensation.[6]

Many strategies have been described to prevent and treat hypotension in obstetric patients.

*Al-Fallujah Teaching Hospital for Pediatrics and Maternity, Anbar, Iraq

**College of Medicine/ Al-Mustansyria University, Baghdad, Iraq

Nonpharmacological techniques include use of lateral uterine displacement, intravenous prehydration (preload) and lower limb wrapping. Unfortunately, these are not very effective and it is usually necessary to use a vasopressor [7].

Ephedrine has been used as the agent of choice in the prevention and treatment of hypotension following spinal anesthesia in pregnant women. It is a mixed action adrenergic agent that not only release stored norepinephrine from nerve endings but also directly stimulate α and β receptors. It raises the systolic and diastolic blood pressures by vasoconstriction and cardiac stimulation. [8]

Phenylephrine is a direct-acting, synthetic adrenergic drug that binds primarily to α_1 receptors. Phenylephrine is a vasoconstrictor that raises the systolic and diastolic blood pressures. It has no effect on the heart itself but, rather, induces reflex bradycardia when given parenterally, so it is used in hospitalized and surgical patients for treatment of hypotension. [8]

AIM OF THE STYUDY:

By using combined infusion of ephedrine and phenylephrine, our aim is to compare its effectiveness in prevention of post spinal hypotension in cesarean sections, with the use of ephedrine or phenylephrine alone.

PATIENTS AND METHODS:

A prospective, randomized, double blinded study was carried out in Gynecology & Obstetric operation theaters of Al-Yarmook teaching Hospital, Baghdad, Iraq, during the period from February 1st, 2018 to October 1st, 2018. The approval of the project of the study was obtained from the Iraqi Board for medical specialties, written informed consent from each participant in the study and permission from the hospital were obtained. 90 full-terms pregnant women were included in this study; divided blindly into three groups: group A, B and C (n=30 each).

The inclusion criteria: Full-terms pregnant women, 18-40 years of age, scheduled for elective cesarean section under spinal anaesthesia, BMI 18.5_35 and height 150- 170 cm.

The exclusion criteria: Patient refusal, any contraindication to spinal anesthesia , pre-existing or pregnancy-induced hypertension, systemic or psychological diseases, known fetal congenital anomalies, emergency cesarean section., anaemia (Hb < 10 mg/dl) and allergy to the drugs used in the study.

Data was collected, a detailed history was obtained, a general examination was done and investigations were evaluated.

All patients were monitored for basal vital signs (ECG, HR, NIBP, and Spo2). Two 18-gauge intravenous cannulas were placed, one for fluid infusion, and the other for infusion of prophylactic study drugs.

Under complete aseptic technique, spinal anaesthesia was conducted using a 22-25gauge sprotte needle with 12.5 mg hyperbaric bupivacaine 0.5% (2.5mL) in the L 3-4 interspaces in the midline, after confirming the free flow of the CSF.

Immediately after induction of spinal anaesthesia, vasopressor infusion was given as follow: Group A received 20 ml NaCl 0.9% infusion containing 6 mg of ephedrine + 100 µg phenylephrine for 20 minutes, Group B received 20 ml NaCl 0.9% infusion containing 12 mg ephedrine for 20 minutes and Group C received 20 ml NaCl 0.9% infusion containing 200 µg phenylephrine for 20 minutes. All infusion solutions were prepared previously and labeled with numerical code.. Blood pressure was measured every 3 minutes and recorded at baseline, 5, 10, 15, 20, 30, and 40 minutes. Moreover, HR and SpO_2 were controlled throughout anesthesia.

RESULTS:

The total number of women who recruited in this study was 90. Spinal anesthesia for C/S was done for all of them. They were divided into three groups: Group A included 30 pregnant women who was given prophylactic infusion of combined vasopressors (ephedrine and phenylephrine) immediately after spinal anesthesia. Each of Group B and Group C were included 30 pregnant women, ephedrine and phenylephrine have been administered to the patients in group B and group C respectively.

Comparison in patients' demographic data between study groups

There was no statistically significant difference between study groups regarding age (P= 0.633), BMI level (P= 0.068), and gravidity (P= 0.627).

Comparison in means of maternal baseline parameters between study groups

We found that, maternal baseline mean arterial pressure (MAP), SPO2, and HR values were not significantly different between the three groups (P=0.192, P=0.93, and P= 0.279 respectively).

Hypotension during Spinal Anesthesia:

Incidence: The patients in group A show less hypotensive attacks, 86.7% of the patients in this had no hypotensive attacks during spinal anesthesia compared to 70% of the patients in group B and 76.7% of those in group C.

Comparison in means of maternal parameters between combined group and ephedrine group

The comparison in means of MAP level between combined group and ephedrine group is shown in table (1). It was obvious that there was no significant difference (P > 0.05) in means of MAP level between combined group and ephedrine group.

Table 1: Comparison in means of maternal MAP level between group A and group B.

Variable	MAP		P – Value
	Combined Group Mean ± SD	Ephedrine Group Mean ± SD	
5 Min	100.32 ± 5.68	98.38 ± 5.95	0.202
10 Min	94.84 ± 10.49	92.90 ± 13.75	0.542
15 Min	89.25 ± 13.04	84.53 ± 15.57	0.208
20 Min	85.38 ± 16.03	81.43 ± 19.20	0.391
30 Min	92.33 ± 8.82	94.42 ± 5.44	0.257
40 Min	81.3 ± 4.5	82.4 ± 5.4	0.271

Concerning the comparison in means of heart rate between these two groups, heart rate was significantly increased in the patients of group B compared to that of group A at 5, 10, 15, 20, 30 and 40 minutes of surgery As shown in table (2).

Table 2: Comparison in means of maternal heart rate between group A and group B.

Variable	Heart Rate		P – Value
	Combined Group Mean ± SD	Ephedrine Group Mean ± SD	
5 Min	85.73 ± 8.69	95 ± 13.15	0.021
10 Min	82.86 ± 8.71	97.53 ± 16.29	0.001
15 Min	79.43 ± 7.56	93.50 ± 15.15	0.001
20 Min	79 ± 7.37	90.26 ± 13.94	0.001
30 Min	80.33 ± 7.17	86 ± 9.02	0.009
40 Min	81.30 ± 7.2	87 ± 9.31	0.009

Comparison in means of maternal parameters between combined group and phenylephrine group

Regarding the comparison in means of MAP level, insignificant difference (P > 0.05) was seen between combined group and phenylephrine group in means of MAP level. Table (3) shows this comparison in mean of MAP level between the two groups.

Table 3: Comparison in means of maternal MAP level between group A and C

Variable	MAP		P – Value
	Combined Group Mean ± SD	Phenylephrine Group Mean ± SD	
5 Min	100.32 ± 5.68	101.32 ± 5.40	0.486
10 Min	94.84 ± 10.49	96.10 ± 9.83	0.634
15 Min	89.25 ± 13.04	89.85 ± 13.31	0.861
20 Min	85.38 ± 16.03	85.14 ± 17.85	0.956
30 Min	92.33 ± 8.82	94.78 ± 6.22	0.219
40 Min	85.38 ± 16.03	81.43 ± 19.20	0.391

Concerning the comparison in means of heart rate between these two groups we found that there was no significant difference (P > 0.05) between group A and group C at 5, 15, 20, 30 and 40 minutes . While mean of heart rate after 10 minutes from induction was significantly decreased (P= 0.031) in group C compared to that in group A (82.86 versus 77.80) as shown in table (4).

Table 4: Comparison in means of maternal heart rate between group A and group C.

Variable	HR		P – Value
	Combined Group Mean ± SD	Phenylephrine Group Mean ± SD	
5 Min	85.73 ± 8.69	83.16 ± 14.48	0.409
10 Min	82.86 ± 8.71	77.80 ± 9.01	0.031
15 Min	79.43 ± 7.56	73.53 ± 19.50	0.128
20 Min	79 ± 7.37	71.70 ± 18.62	0.051
30 Min	80.33 ± 7.17	80.46 ± 10.78	0.955
40 Min	82.85 ± 8.73	80.16 ± 13.45	0.406

Comparison in means of maternal parameters between Ephedrine group and Phenylephrine group

Regarding the comparison in means of MAP level, insignificant difference (P > 0.05) was seen between ephedrine group and phenylephrine group in means of MAP level. Table (5) shows this comparison in mean of MAP level between the two groups

Table 5: Comparison in means of maternal MAP level between group B and group C.

Variable	MAP		P – Value
	Ephedrine Group Mean ± SD	Phenylephrine Group Mean ± SD	
5 Min	98.38 ± 5.95	101.32 ± 5.40	0.696
10 Min	92.90 ± 13.75	96.10 ± 9.83	0.494
15 Min	84.53 ± 15.57	89.85 ± 13.31	0.912
20 Min	81.43 ± 19.20	85.14 ± 17.85	0.433
30 Min	94.42 ± 5.44	94.78 ± 6.22	0.975
40 Min	82.4 ± 5.4	81.43 ± 19.20	0.776

Concerning the comparison in means of heart rate between these two groups, heart rate was significantly increased (P < 0.05) in patients of group B to that in group C as shown in table (6).

Table 6: Comparison in means of maternal heart rate between group B and group C.

Variable	HR		P – Value
	Ephedrine Group Mean ± SD	Phenylephrine Group Mean ± SD	
5 Min	95 ± 13.15	83.16 ± 14.48	0.013
10 Min	97.53 ± 16.29	77.80 ± 9.01	0.001
15 Min	93.50 ± 15.15	73.53 ± 19.50	0.001
20 Min	90.26 ± 13.94	71.70 ± 18.62	0.021
30 Min	86 ± 9.02	80.46 ± 10.78	0.009
40 Min	87 ± 9.31	80.16 ± 13.45	0.009

DISCUSSION:

The prevention and treatment of maternal hypotension associated with spinal anaesthesia for lower segment Caesarean section still remain as a challenge to all anaesthetists [9]. Moving the uterus to the left and pre-loading with intravenous fluid s have been used to reduce the severity of hypotension, but with limited efficacy, as recent studies have demonstrated the inefficiency of prior hydration due to fast redistribution [10]. . Our results supported by the study published by Simin Atashkhoie[11] et al that indicated that the prophylactic infusion of low doses of ephedrine and phenylephrine in spinal anesthesia for cesarean section might result in a significant decrease in the frequency and severity of maternal hypotension. Ritu Singh et al [12] also proved that the combination of both phenylephrine and ephedrine is efficacious for spinal-induced hypotension. While a study published by Sabyasachi Das[13],, proved that prophylactic phenylephrine infusion is superior to ephedrine infusion or combination of phenylephrine and ephedrine in the management of maternal hypotension during spinal anaesthesia for caesarean delivery. Warwick D. Ngan Kee, et al [14], used varying combinations of ephedrine and phenylephrine and found that the combination appear to have no advantage compared with phenylephrine alone when administered by infusion for the prevention of hypotension associated with spinal anesthesia for cesarean delivery.. Sun Woo Jung et al [15] also concluded that the incidence of hypotension was higher in ephedrine group, but the heart rate was lower in phenylephrine group than other groups. Mercier, V. et al also concluded that combination reduces the total amount of vasopressors needed and seems to be more effective to treat hypotension after spinal anaesthesia for Cesarean section [16].

CONCLUSION: Our study showed that the use of combined ephedrine and phenylephrine was not associated with significant decrease in maternal blood pressure and heart rate after spinal anaesthesia.

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