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COMPARATIVE STUDY BETWEEN NOREPINEPHRINE BOLUS AND NOREPINEPHRINE INFUSION IN PREVENTION OF POST-SPINAL HYPOTENSION IN CESAREAN SECTION

By

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ABSTRACT

Background: Post-spinal hypotension in patients of cesarean section (CS) remains a common scenario in our practice with an incidence of hypotension is up to 71%. Norepinephrine is potent α adrenergic receptor and a weak β adrenergic agonist. It is suitable for maintaining blood pressure as phenylephrine and ephedrine in cesarean section.

Objectives: The aim of this work was to evaluate and compare the effects of prophylactic bolus norepinephrine and norepinephrine infusion on blood pressure during spinal anesthesia for cesarean section.

Patients and Methods: Eighty patients of American Society of Anesthesiology (ASA) physical status (I-II), aged (20-40) years old and undergoing to elective cesarean section who randomly classified into 2 equal groups: Group (I) received prophylactic bolus norepinephrine (10 ?g) and Group (II) received prophylactic norepinephrine infusion (0.05 ?g/kg/min). Fixed rate infusion and bolus dose of norepinephrine started immediately after spinal anesthesia.

Results: There were significant differences between group I and group II as regards maternal hemodynamic variables which was needed multiple doses of noradrenalin in group II. There were no significant differences in the intraoperative nausea and vomiting between groups. There were no significant differences between group I and group II as regards the fetal outcome.

Conclusion: Prophylactic bolus of norepinephrine and prophylactic norepinephrine infusion were effective for maintaining blood pressure of spinal anesthesia in cesarean section, and safe on maternal and fetal status. Norepinephrine infusion was superior to the intermittent boluses.

Key words: Spinal anesthesia; norepinephrine; hypotension; cesarean section.

INTRODUCTION

Hypotension is a common side effect of spinal anesthesia for cesarean section. The incidence of post spinal hypotension in the cesarean section is up to 71% *(Klohr et al., 2010)*. Hypotension is the physiological consequence of spinal block and can have a potentially deleterious maternal and fetal impact *(De Giorgio et al., 2012)*. When post spinal anesthesia hypotension for cesarean section is severe and sustained, it may lead to serious complications as well as nausea and vomiting, impairment of the uterine blood

flow with fetal hypoxia, acidosis and cardiovascular collapse *(Cyna et al., 2006)*. Preventive measures of hypotension after spinal anesthesia included fluid loading, co-loading, leg wrapping, left lateral position, and vasopressors as phenylephrine and ephedrine *(Loubert, 2012)*.

Norepinephrine has α-adrenergic properties that can be used to prevention and treatment of spinal anesthesia induced vasodilation. Norepinephrine has mild and doses dependent β-adrenergic effects that might be beneficial to counteract pure vasoconstriction and a more effective vasopressor for maintaining blood pressure during spinal block *(Hiltebrand et al., 2011)*.

The aim of this work was to evaluate and compare the effects of prophylactic bolus norepinephrine and norepinephrine infusion on blood pressure during spinal anesthesia for cesarean section.

PATIENTS AND METHODS

This is a prospective, single blinded, randomized and parallel study. The study was carried out in Al-Azhar University Hospitals from November 2017 to September 2018. After obtaining the Research and Ethics Committee approval in Al-Azhar University and written informed consents, eighty patients of (ASA) physical status (I-II), aged (20-40) years old and undergoing to elective cesarean section were included in this study. They were randomly classified into 2 equal groups:

Group I: Received prophylactic bolus norepinephrine (10 ?g/ml).

Group II: Received prophylactic norepinephrine infusion (0.05 ?g/kg/min).

The primary outcomes were incidence of hypotension episodes (SBP < 20% from baseline), hypertension episodes (SBP > 20% from baseline) and number of boluses of vasopressors used.

The secondary outcomes were nausea, vomiting, neonatal birth weight and neonatal outcome (measured Apgar scores at 1,5,10 minutes and umbilical cord blood pH) to evaluate the effect of noradrenalin bolus and noradrenalin infusion on neonatal outcome.

Inclusion criteria:

Patients of ASA grade I or II, single fetus and full term pregnancy undergoing elective cesarean section.

Exclusion criteria:

No single fetus, age less than 18 year, height less than 130 cm or more than 180 cm, weight less than 50 kg or more than 100 kg, contraindications to spinal anesthesia, allergy to drugs used in the study, placenta previa, diabetes mellitus, hypertension, contraindication of spinal anesthesia, allergy to local anesthesia, cardiovascular diseases, cerebrovasacular diseases, and chronic hypertension or pregnancy induced hypertension.

Routine preoperative evaluation to patient's criteria was assessed for the study by details history taking, physical examination and the patient’s investigations in the anesthesia clinic before surgery by an anesthesiologist.

Patients were fasted for 8 hours and had no premedication. Patients have two 18 gauge intravenous cannula. The baseline hemodynamic measurements

(heart rate, oxygen saturation, electrocardiography and non-invasive arterial blood pressure) were recorded using monitoring system. External cardiotocography was used to monitor the fetal heart rate (HR). The skin was infiltrated with 2 ml lidocaine (1%). A 25 gauge spinal needle was inserted at L4–5 vertebral interspace. A mixture of 10 mg of hyperbaric bupivacaine (0.5%) and 25 ?g fentanyl was injected at the subarachnoid space. At the start of intrathecal injection, intravenous (i.v.) fluid was started through a large bore i.v. cannula. There was other a large bore intravenous cannula for norepinephrine infusion.

Statistical analysis:

The statistical analysis was done by using Statistical Package for Social Science evaluation (SPSS) version 22.0 and Excel 2010. Comparison between groups by Student's t test for parametric data and Mann–Whitney test for non-parametric data. Data was presented as median, numbers, proportions and means ± standard deviation. Comparison of proportions was performed using Chi square test. P value ≤ 0.05 was considered statistically significant and P value > 0.05 was considered statistically non-significant.

RESULTS

Eighty patients undergoing to elective cesarean section who randomly classified into 2 equal groups: Group I received prophylactic bolus norepinephrine (10 ?g) and Group II received prophylactic norepinephrine infusion (0.05 ?g/kg/min).

There were no statistically significant differences between two groups as regards demographic data (age (years), weight (kg), height (cm), ASA classification (I-II), duration of surgery, and indications of cesarean section (breech presentation, cephalopelvic disproportion, and previous cesarean section (Table 1).

Table (1): Demographic data between groups

Groups / Parameters	Group I (n=40)	Group II (n=40)	P- value
Age (years)	27.76± 5.4	29.52± 4.3	> 0.05
Weight (Kg)	78.2± 8.4	75±8.6	> 0.05
Height (Cm)	165 ±5.1	162±4.7	> 0.05
ASA (I/II)	23/17	25/15	> 0.05
Duration of surgery	83.5±8.3	88.5±5.5	> 0.05
Indications: - Breech presentation - Cephalopelvic disproportion - Previous C. S.	 12 7 21	 10 6 24	> 0.05

- Data represented in means ± standard deviation (M ± SD) and numbers. P values > 0.05 are considered non-significant.

There were significant differences between group I and group II which increase number of hypotension episodes, number of hypertension episodes, frequency of bradycardia, and number of boluses of vasopressors used in group I (Fig. 1).

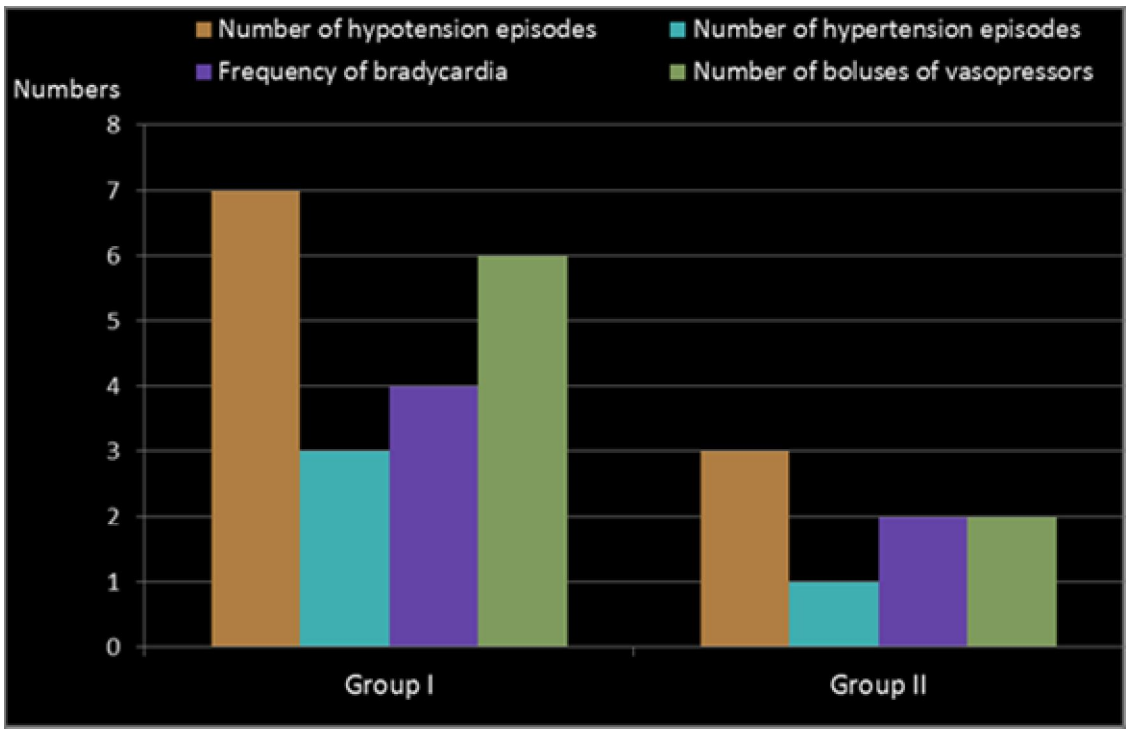

Figure (1): Maternal hemodynamic variables (number of hypotension episodes, number of hypertension episodes and number of boluses of vasopressors used)

There were non-significant differences between group I and group II as regards incidence of intraoperative nausea and vomiting (Table 2).

Table (2): Incidence of intraoperative nausea and vomiting

Groups / Parameters	Group I (n=40)	Group II (n=40)	P- value
Number of patients showing nausea	8	6	> 0.05
Number of patients showing vomiting	5	4	> 0.05

-Data are expressed as numbers.

There were non-significant differences between group I and group II as regards the fetal outcome: baseline fetal heart rate, birth weight, Apgar score, umbilical arterial blood gas and umbilical venous blood gas (Table 3).

Table (3): Fetal variables: The fetal outcome (baseline fetal heart rate, birth weight, Apgar score, umbilical arterial blood gas, and umbilical venous blood gas)

Groups / Parameters	Group I (n=40)	Group II (n=40)	P- value
Baseline fetal heart rate (beats/min)	146.7±13.5	141±16.1	> 0.05
Birth weight (kg)	3.29±0.2	3.23±0.3	> 0.05
Apgar <7 at 1 min	6	5	> 0.05
Apgar <7 at 5 min.	5	4	> 0.05
Apgar <7 at 10 min.	2	1	> 0.05
Umbilical arterial blood gas:			
pH	7.31	7.29	>0.05
PO_2 (kPa)	15	16	> 0.05
PCO_2 (kPa)	50	49	> 0.05
Base excess (mmol/l)	-1.9	-2.2	> 0.05
Lactate (mmol/l)	2.4	2.3	> 0.05
Umbilical arterial blood gas:			
pH	7.34	7.29	> 0.05
PO_2 (kPa)	30	26	> 0.05
PCO_2 (kPa)	42	44	> 0.05
Base excess (mmol/l)	-1.2	-1.1	> 0.05
Lactate (mmol/l)	2.2	2.1	> 0.05

- Data represented in means ± standard deviation (M ± SD) and numbers. P values > 0.05 are considered non-significant.

DISCUSSION

In this study, the effects of prophylactic bolus norepinephrine and norepinephrine infusion were assessed on blood pressure during spinal anesthesia for cesarean section. The ideal vasopressor used in post-spinal hypotension has inexpensive, reliable, quick in onset, easily available, favorably affecting maternal heart rate (HR) and minimizing detrimental effects upon the fetus and placental perfusion *(Nag et al., 2015)*.

The present study showed that non statistically significant difference between two groups as regards age, weight, height, ASA classification (I/II), duration of surgery, and indications of cesarean section (breech presentation, cephalopelvic disproportion, and previous cesarean section.

In our study, there were significant differences between groups as regards maternal hemodynamic variables (number of hypotension episodes, number of hypertension episodes, and number of boluses of vasopressors used).

(Elnabtity and Selim, 2018) compared norepinephrine with ephedrine for spinal hypotension who found that

norepinephrine was effective for maintain blood pressure in obstetric patients.

(Ngan Kee et al., 2015) compared norepinephrine to phenylephrine in patients undergoing cesarean delivery under spinal anesthesia to maintain systolic blood pressure (SBP). They found that maternal cardiac output and heart rate (HR) were greater in women treated with norepinephrine compared with that treated with phenylephrine.

Nausea and vomiting are common symptom of hypotension in the spinal anesthesia. There was non-significant difference between two groups as regards incidence of intraoperative nausea and vomiting were in agreement with *(Elnabtity and Selim, 2018)* who found that the incidence of maternal complications (nausea, vomiting, pruritus, headache, restlessness, and shivering) during the operation was comparable, and no statistically significant differences were detected between norepinephrine with ephedrine groups.

In our study, there were no significant differences between group I and group II as regards the fetal outcome (baseline fetal heart rate, birth weight, Apgar score, umbilical arterial blood gas, and umbilical venous blood gas). This was in agreement with *(Ngan Kee et al., 2015)* compared the prophylactic continuous norepinephrine infusion (2.5 ?g/min) with a bolus norepinephrine (5 ?g/ml) in patients having spinal anesthesia for elective cesarean delivery.

(Vallejo et al., 2017) study compared phenylephrine (0.1 ?g/kg/min) with norepinephrine (0.05 ?g/kg/min) using a fixed rate of infusion on parturient having cesarean delivery under spinal anesthesia who found that norepinephrine fixed rate of infusion has efficacy for preventing maternal hypotension.

(El Shafei et al., 2015) compared norepinephrine with ephedrine to prevent of post spinal hypotension in coronary artery disease for knee arthroscopy. They found that norepinephrine is more effective than ephedrine in the maintenance of systolic blood pressure.

CONCLUSION

Prophylactic bolus of norepinephrine and prophylactic norepinephrine infusion were effective for hypotension of spinal anesthesia in cesarean section and safe on maternal and fetal status. Norepinephrine infusion was superior to the intermittent boluses.

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دراسة مقارنة بين الحقن المباشر والحقن الكهربائى لعقار نورأدرينالين فى منع إنخفاض الضغط بعد التخدير النصفى للعمليات القيصرية

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خلفية البحث : يعد إنخفاض ضغط الدم بعد التخدير النصفى للعمليات القيصرية مشكلة كبيرة فى المجال الطبى والذى يحدث بمعدل يصل إلى ٧١ % ، ويعد عقار نورأدرينالين له تأثير قوى على المستقبلات ألفا وله تأثير ضعيف على المستقبلات بيتا لذلك فهو مناسب فى المحافظه على ضغط الدم أثناء العمليات القيصرية مثل عقارالفنيل إفرين وعقارالإفدرين.

الهدف من البحث: إجراء دراسة مقارنة بين الحقن المباشر والحقن الكهربائى لعقار نورأدرينالين فى منع إنخفاض ضغط الدم بعد التخدير النصفى للعمليات القيصرية.

المرضي وطرق البحث: أجريت هذه الدراسة علي ثمانين سيدة خضعن لإجراء ولادات قيصرية بمستشفيات جامعة الأزهر ذوى الفئة الصحية ١ أو٢ (حسب تصنيف الجمعية الأمريكية لأطباء التخدير) ، وتتراوح أعمارهن بين ٢٠ و٤٠ سنة ، وقد تم تقسيم السيدات بطريقة عشوائية إلى مجموعتين ، المجموعة الأولى : تم حقن عقار نورأدرينالين مباشرة بمعدل (١٠ميكروجرام) بعد التخدير النصفى ، والمجموعة الثانية: تم حقن عقار نورأدرينالين بالمحقن الكهربائى بمعدل ٠,٠٥ ميكروجرام/كجم/ دقيقة.

النتائج: أظهرت النتائج إلى وجود فروق فى الدلالات الإحصائية بين المجموعتين من حيث وجود ثبات فى ضغط الدم فى المجموعة الثانية ، أما المجموعة الأولى فقد إحتاجت إلى حقن متكرر من عقار نورأدرينالين ، كما أظهرت النتائج عدم وجود فروق فى الدلالات الإحصائية بين المجموعتين من حيث الغثيان والقئ وعدم وجود مضاعفات ظاهرة على المواليد.

الاستنتاج: عقار نورأدرينالين له تأثير فعال على المحافظة على ضغط الدم بعد التخدير النصفى وآمن للنساء اللاتى تجرى لهن عمليات قيصرية ، كما أنه آمن على أطفالهن . كما أثبتت الدراسة أن حقن عقار نورأدرينالين بالمحقن الكهربائى أفضل من الحقن المباشر.