ANESTHESIOLOGY

Norepinephrine Infusion for Preventing Postspinal Anesthesia Hypotension during Cesarean Delivery

A Randomized Dose-finding Trial

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ABSTRACT

Background: Norepinephrine has been recently introduced for prophylaxis against postspinal hypotension during cesarean delivery; however, no data are available regarding its optimum dose. The objective of this study is to compare three infusion rates of norepinephrine for prophylaxis against postspinal hypotension during cesarean delivery.

Methods: The authors conducted a double-blinded, randomized, controlled study including full-term pregnant women scheduled for cesarean delivery. Norepinephrine infusion was commenced after subarachnoid block. Patients were randomized into three groups, which received norepinephrine with starting infusion rates of 0.025 μg · kg^{-1} · min^{-1}, 0.050 μg · kg^{-1} · min^{-1}, and 0.075 μg · kg^{-1} · min^{-1}. Infusion was stopped when intraoperative hypertension occurred. The primary outcome was the frequency of postspinal hypotension (defined as decreased systolic blood pressure less than 80% of the baseline reading). The three groups were compared according to the following: systolic blood pressure, heart rate, frequency of intraoperative hypertension, frequency of bradycardia, and neonatal outcomes.

Results: Two hundred eighty-four mothers were included in the analysis. The frequency of postspinal hypotension was lower for both the 0.050-μg · kg^{-1} · min^{-1} dose group (23/93 [24.7%], odds ratio: 0.45 [95% CI: 0.24 to 0.82], $P = 0.014$) and the 0.075-μg · kg^{-1} · min^{-1} dose group (25/96 [26.0%], odds ratio: 0.48 [95% CI:0.26 to 0.89], $P = 0.022$) compared with the 0.025-μg · kg^{-1} · min^{-1} dose group (40/95 [42.1%]). The two higher-dose groups (the 0.050-μg · kg^{-1} · min^{-1} group and the 0.075-μg · kg^{-1} · min^{-1} group) had higher systolic blood pressure and lower heart rate compared with the 0.025 μg · kg^{-1} · min^{-1} group. The three groups were comparable in the frequency of intraoperative hypertension, incidence of bradycardia, and neonatal outcomes.

Conclusions: Both the 0.050-μg · kg^{-1} · min^{-1} and 0.075-μg · kg^{-1} · min^{-1} norepinephrine infusion rates effectively reduced postspinal hypotension during cesarean delivery compared with the 0.025-μg · kg^{-1} · min^{-1} infusion rate.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Hypotension after spinal anesthesia for cesarean delivery is common, usually treated with phenylephrine or ephedrine
- Norepinephrine was recently introduced in obstetric anesthesia but the optimal dose is unknown

What This Article Tells Us That Is New

- This randomized, double-blinded trial compared prophylactic norepinephrine infusions of 0.025, 0.050, or 0.075 μg · kg^{-1} · min^{-1}, started after bupivacaine spinal anesthesia, in full-term parturients having elective cesarean delivery
- The primary outcome, maternal hypotension (systolic blood pressure less than 80% of baseline), occurred less frequently after both 0.050 and 0.075 μg · kg^{-1} · min^{-1} compared 0.025 μg · kg^{-1} · min^{-1} norepinephrine

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Postspinal hypotension is a frequent maternal complication during cesarean delivery.[1] Without prophylactic vasopressors, postspinal hypotension affects nearly 60% of women during cesarean delivery[2,3]; thus, using vasopressors has been highly recommended for routine prevention of postspinal hypotension during cesarean delivery.[4]

The commonly used vasopressors during cesarean delivery are phenylephrine and ephedrine. Phenylephrine is sometimes associated with maternal cardiac depression; this limits its use in mothers with cardiac comorbidities.[5] Ephedrine use is commonly associated with maternal tachycardia as well as decreased fetal *p*H.[5]

Norepinephrine is another vasopressor that was recently introduced in obstetric anesthesia.[6] Norepinephrine is characterized by α-adrenergic agonistic activity in addition to a weak β-adrenergic agonistic activity; thus, norepinephrine is considered a vasopressor with minimal cardiac depressant effect[6]; these pharmacologic properties would make norepinephrine an attractive alternative to phenylephrine and ephedrine in obstetric anesthesia. Although the use of norepinephrine for prophylaxis against postspinal hypotension has shown promising results,[6–8] evidence is lacking on the optimum dose for norepinephrine infusion during cesarean delivery. The aim of this study was to compare three norepinephrine infusion rates (0.025, 0.050, and 0.075 μg · kg^{-1} · min^{-1})

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after an initial bolus of 5 μg for prophylaxis against postspinal hypotension during cesarean delivery.

Materials and Methods

A randomized, controlled, double-blinded trial was conducted in Cairo University Hospital, Cairo, Egypt, after approval of the research ethics committee (N-49–2017[b]). The study was registered prior to patient enrollment at clinicaltrials.gov registry system (NCT03182088; principal investigator: Ahmed Hasanin, M.D., Assistant Professor of Anesthesia and Critical Care Medicine, Cairo University, Cairo, Egypt; date of registration: June 9, 2017). The study was conducted from August 2017 through December 2017. Written informed consent was obtained from the recruited mothers. Randomization was achieved by a statistician using an online random number generator. Patient codes were placed into sequentially numbered sealed opaque envelopes by a research assistant who was not involved in the study. An anesthesia resident not involved in patient management was responsible for opening the envelope. The anesthesia resident prepared the study drug according to the instructions contained within each envelope and gave it to the anesthesiologist.

Full-term, singleton, pregnant women, scheduled for elective cesarean delivery, aged between 18 and 35 yr, were included in the study. Patients with cardiac morbidities, hypertensive disorders of pregnancy, peripartum bleeding, body mass index above 40 kg/m^2, and baseline systolic blood pressure (SBP) less than 100 mmHg were excluded from the study.

Upon admission to the operating room, monitors were applied (electrocardiography, pulse oximetry, noninvasive blood pressure monitor). Arterial blood pressure was measured using a General Electric Solar 8000i monitor (General Electric, USA). Baseline SBP was obtained in the supine position as the mean of three consecutive readings at 2-min intervals with a difference of less than 10%. After insertion of two peripheral 18-gauge lines (one for fluids and the other for vasopressor infusion), patients were premedicated with metoclopramide (10 mg intravenous) and ranitidine (50 mg intravenous). Patients received subarachnoid block with rapid crystalloid coload. Ten milligrams of hyperbaric bupivacaine in addition to 20 μg fentanyl were injected in the L3–L4 or L4–L5 interspace using a 25-gauge spinal needle in the sitting position.

After subarachnoid block, patients were divided into one of three groups:

1. 0.025 $\mu g \cdot kg^{-1} \cdot min^{-1}$ group (n = 95): received 5 μg norepinephrine bolus followed by norepinephrine infusion in a starting dose of 0.025 $\mu g \cdot kg^{-1} \cdot min^{-1}$
2. 0.050 $\mu g \cdot kg^{-1} \cdot min^{-1}$ group (n = 93): received 5 μg norepinephrine bolus followed by norepinephrine infusion in a starting dose of 0.050 $\mu g \cdot kg^{-1} \cdot min^{-1}$
3. 0.075 $\mu g \cdot kg^{-1} \cdot min^{-1}$ group (n = 96): received 5 μg norepinephrine bolus followed by norepinephrine infusion in a starting dose of 0.075 $\mu g \cdot kg^{-1} \cdot min^{-1}$

Norepinephrine was prepared as 8 μg/ml and was delivered using a syringe pump. To achieve blinding, the infusion rate was adjusted by a research assistant who was not involved in patient management. The syringe pump was placed so that the anesthetist could not observe the infusion rate. If the infusion was to be stopped or resumed, the anesthetist was responsible for giving the order, and the research assistant stopped (or resumed) the infusion. Norepinephrine bolus was given at the same time cerebrospinal fluid was obtained. Norepinephrine infusion continued until 5 min after delivery of the fetus.

Intraoperative hypertension (defined as SBP greater than 120% of the baseline reading) was managed by stopping norepinephrine infusion. The infusion was resumed when blood pressure returned to its normal value. Postspinal hypotension (defined as decreased SBP less than 80% of the baseline reading during the period from intrathecal injection to delivery of the fetus) was managed by IV ephedrine 9 mg. Severe postspinal hypotension (defined as decreased SBP less than 60% of the baseline reading) was managed by IV ephedrine 15 mg. Additional vasopressor bolus was given if SBP did not respond to the first dose within 2 min. Intraoperative bradycardia (defined as heart rate less than 55 beats per minute without hypotension during the period from intrathecal injection to delivery of the fetus) was managed by stopping the vasopressor infusion. If bradycardia was associated with hypotension, the patient was managed by IV ephedrine 9 mg. If bradycardia persisted after the previous measures, an IV atropine bolus (0.5 mg) was given.

After subarachnoid block, patients were positioned in the supine position with left uterine displacement. Block success was assessed using pinprick, and patients with failed block (defined as sensory level below T4) were excluded from the study. Maternal heart rate was continuously monitored during the operation, and blood pressure was measured starting from the baseline preinjection reading at 1-min intervals for six readings after intrathecal injection, followed by 2-min intervals for six readings, and finally at 5-min intervals until the end of the operation. Intermittent auscultation of fetal heart rate was achieved using handheld sonicaid before starting the operation. Cohydration was continued up to a maximum of 1.5 l. After delivery of the fetus, oxytocin was given as an initial bolus of 0.5 U over 5 s followed by 40 mU/min infusion.

Our primary outcome was the frequency of postspinal hypotension. Secondary outcomes included hemodynamic data (SBP and heart rate at the baseline reading and the

subsequent 15 readings), the frequency of severe postspinal hypotension, frequency of postdelivery hypotension (defined as decreased SBP less than 80% of the baseline reading after delivery of the fetus and starting oxytocin infusion), frequency of intraoperative nausea and vomiting, frequency of intraoperative hypertension, intraoperative requirements of ephedrine and atropine, surgical data (time between skin incision and delivery of the fetus), umbilical blood gases, and Apgar score for the fetus at 1 and 10 min postdelivery.

Statistical Analysis and Sample Size Calculation

The sample size was calculated using MedCalc Software version 14 (MedCalc Software bvba, Belgium). Our primary outcome is the frequency of postspinal hypotension. A previous study[7] reported the incidence of 49% for postspinal hypotension in parturients receiving norepinephrine infusion of 0.050 $\mu g \cdot kg^{-1} \cdot min^{-1}$. At alpha error of 0.05, we calculated that 204 patients (68 patients per group) would give 80% power to detect 20% absolute reduction in the frequency of postspinal hypotension in the treatment group. However, to allow the comparisons between the control group and each treatment group, an adjusted *P* (Bonferroni correction) of 0.025 was considered significant for the primary outcome, and the required sample size increased to 244 patients (82 patients per group). The number was increased to 279 patients (93 patients per group) to compensate for possible dropouts.

Statistical Package for Social Science software, version 15 for Microsoft Windows (SPSS Inc., USA), was used for data analysis. Categorical data were expressed as frequency (%). Continuous data were tested for normality using the Shapiro–Wilk test and presented as either mean (SD) or median (quartiles) as appropriate. The primary outcome (frequency of postspinal hypotension) was analyzed using the chi-square test. Secondary outcomes (frequency of bradycardia, reactive hypertension, nausea, and vomiting) were analyzed using the chi-square test or Fisher's exact test as deemed appropriate. Continuous data were analyzed using one-way ANOVA with *post hoc* Tukey modification (for normally distributed data) and using the Kruskal–Wallis test on ranks (for skewed data). For repeated measures, a two-way repeated-measures ANOVA was used to evaluate dose (between-groups factor) and time (repeated measures). *Post hoc* pairwise comparison was performed using Bonferroni test. A *P* value of less than or equal to 0.05 was considered statistically significant.

Results

Three hundred eight patients were screened for eligibility. Eighteen patients were excluded, 290 patients underwent randomization, 4 patients did not receive the intervention because of failed subarachnoid block, 2 patients in the 0.075-$\mu g \cdot kg^{-1} \cdot min^{-1}$ group did not complete the intervention because of interrupted infusion, and 284 patients were available for final analysis (fig. 1). Demographic data and baseline characteristics were comparable in both study groups (table 1). The frequency of postspinal hypotension was lower in the 0.050-$\mu g \cdot kg^{-1} \cdot min^{-1}$ group and the 0.075-$\mu g \cdot kg^{-1} \cdot min^{-1}$ group compared with the 0.025-$\mu g \cdot kg^{-1} \cdot min^{-1}$ group (24.7%, 26.0%, and 42.1%; *P* values, 0.014 and 0.022, respectively) without significant difference between the two former groups ($P = 0.868$; table 2).

The two higher-dose groups (0.050-$\mu g \cdot kg^{-1} \cdot min^{-1}$ group and 0.075-$\mu g \cdot kg^{-1} \cdot min^{-1}$ group) had higher SBP and lower heart rate compared with the 0.025-$\mu g \cdot kg^{-1} \cdot min^{-1}$ group in most readings (figs. 2 and 3). However, the frequency of bradycardia requiring atropine administration was comparable between the three study groups (table 2; *P* value equals 0.402).

The frequency of severe postspinal hypotension, nausea, vomiting, intraoperative hypertension, and postdelivery hypotension was comparable between the three groups (*P* values: 0.537, 0.809, 0.932, 0.835, and 0.924, respectively). Neonatal outcomes were also comparable in the three groups (tables 2 and 3).

Discussion

We compared three doses for norepinephrine infusion during cesarean delivery. The two higher doses (0.050 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and 0.075 $\mu g \cdot kg^{-1} \cdot min^{-1}$) were equally effective in decreasing the frequency of postspinal hypotension compared with the lower dose (0.025 $\mu g \cdot kg^{-1} \cdot min^{-1}$). Although the SBP was higher in the 0.075-$\mu g \cdot kg^{-1} \cdot min^{-1}$ group compared with the 0.050-$\mu g \cdot kg^{-1} \cdot min^{-1}$ group in some readings, this difference was mostly less than 5 mmHg. No further advantage was found for delivering the higher-dose infusion of 0.075 $\mu g \cdot kg^{-1} \cdot min^{-1}$ compared with the 0.050 $\mu g \cdot kg^{-1} \cdot min^{-1}$ infusion. Thus, we suggest that 0.050 $\mu g \cdot kg^{-1} \cdot min^{-1}$ is the best dose for norepinephrine during cesarean delivery.

Norepinephrine had been recently introduced in obstetric anesthesia by Ngan Kee *et al.*[6] using a computer-controlled infusion system. Cesarean delivery is a very common procedure performed daily in nearly every hospital; thus, reaching a simple, feasible approach for prevention of postspinal hypotension during cesarean delivery would be a priority in addition to protocol efficiency. More recently, Ngan Kee *et al.*[8] used a manually adjusted norepinephrine infusion that ranged between 1.25 μg/min and 5 μg/min. They reported a lower incidence of postspinal hypotension in the norepinephrine group compared with the control group. However, the latter study is

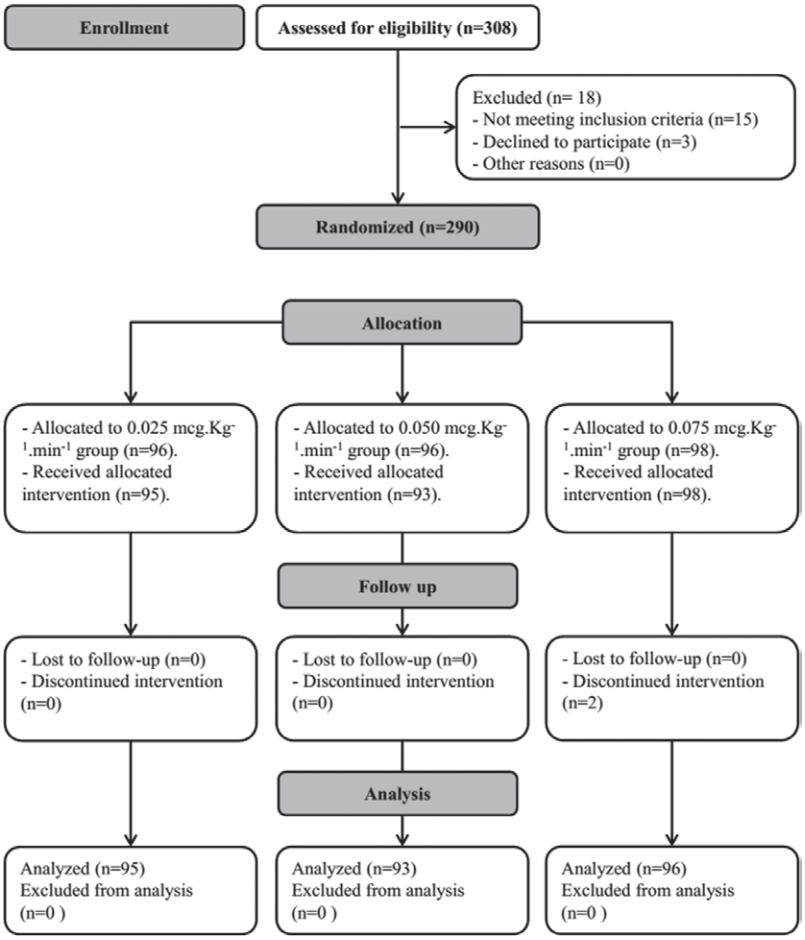

Fig. 1. Consolidated Standards of Reporting Trials (CONSORT) chart showing patient recruitment.

Table 1. Demographic Data, Operative Data, and Baseline Characteristics

	0.025-μg · kg^{-1} · min^{-1} Group (n = 95)	0.050-μg · kg^{-1} · min^{-1} Group (n = 93)	0.075-μg · kg^{-1} · min^{-1} Group (n = 96)
Age, yr	29 (24, 32)	28 (24, 32)	27 (24, 31)
Body mass index, kg/m^2	29 (28, 31)	29 (26, 31)	29 (28, 32)
Time from subarachnoid block to delivery of the fetus (minutes)	19 ± 5	18 ± 5	18 ± 5
Baseline vital signs			
Systolic blood pressure, mmHg	124 ± 13	123 ± 12	124 ± 11
Heart rate, beats per minute	96 ± 19	92 ± 14	95 ± 17

Data are presented as mean ± SD and median (quartiles).

limited by the absence of any vasopressor in the control group.

In an open-label study, Vallejo *et al.*[7] compared norepinephrine and phenylephrine fixed-rate infusions (0.050 μg · kg^{-1} · min^{-1} and 0.1 μg · kg^{-1} · min^{-1}). They reported that both infusions were comparable; however, the frequency of postspinal hypotension in both groups was still high (49% and 66%, respectively); thus, we used the same dose reported by Vallejo *et al.*[7] (0.050 μg · kg^{-1} · min^{-1}) as the middle dose in our study.

Table 2. Maternal Outcomes

	0.025-μg · kg^{-1} · min^{-1} Group (n = 95)	0.050-μg · kg^{-1} · min^{-1} Group (n = 93)	0.075-μg · kg^{-1} · min^{-1} Group (n = 96)	OR or *Mean Difference* between 0.050-μg and 0.025-μg Groups (95% CI)	OR or *Mean Difference* between 0.075-μg and 0.025-μg Groups (95% CI)
Postspinal hypotension	40 (42.1)	23 (24.7)*	25 (26.0)†	0.45 (0.24 to 0.82)	0.48 (0.26 to 0.89)
Severe postspinal hypotension	7 (7.4)	4 (4.3)	4 (4.2)	0.57 (0.16 to 2)	0.55 (0.16 to 1.93)
Postdelivery hypotension	5 (5.3)	6 (6.3)	6 (6.3)	1.27 (0.37 to 4.32)	1.2 (0.35 to 4.07)
Bradycardia	4 (4.3)	3 (3.2)	7 (7.3)	0.76 (0.17 to 3.49)	1.79 (0.51 to 6.32)
Intraoperative hypertension	6 (6.3)	8 (8.6)	7 (7.3)	1.34 (0.47 to 4.19)	1.17 (0.38 to 3.61)
Nausea	8 (8.4)	10 (10.8)	8 (8.3)	1.31 (0.49 to 3.48)	0.99 (0.36 to 2.75)
Vomiting	7 (7.4)	7 (7.5)	6 (6.3)	1.02 (0.34 to 3.04)	0.84 (0.27 to 2.59)
Ephedrine requirements, mg	7 ± 10	5 ± 9*	5 ± 9†	*2.38 (–0.29 to 5.04)*	*2.49 (–0.14 to 5.11)*
Atropine requirements, mg	0.04 ± 0.15	0.02 ± 0.09	0.04 ± 0.13	*0.19 (–0.18 to 0.06)*	*0.001 (–0.039 to 0.042)*

Data are presented as mean ± SD, frequency (%), odds ratio (OR; 95% CI: lower limit to upper limit), and *mean difference (95% CI: lower limit to upper limit)*.
*Denotes statistical significance between the 0.025-μg · kg^{-1} · min^{-1} group and the 0.050-μg · kg^{-1} · min^{-1} group. †Denotes statistical significance between the 0.025-μg · kg^{-1} · min^{-1} group and the 0.075-μg · kg^{-1} · min^{-1} group.

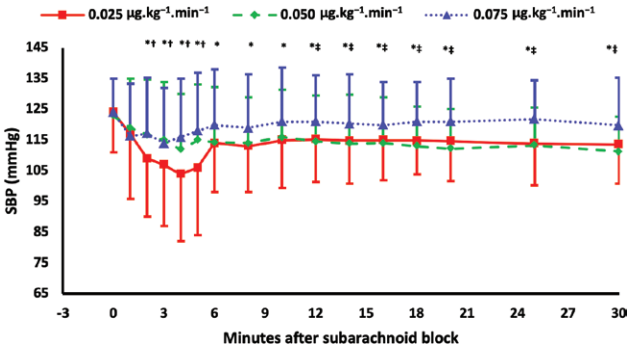

Fig. 2. Systolic blood pressure (SBP). Markers are means, and error bars are SDs. *Statistical significance between the 0.025-μg · kg^{-1} · min^{-1} group and the 0.075-μg · kg^{-1} · min^{-1} group. †Statistical significance between the 0.025-μg · kg^{-1} · min^{-1} group and the 0.050-μg · kg^{-1} · min^{-1} group. ‡Statistical significance between the 0.050-μg · kg^{-1} · min^{-1} group and the 0.075-μg · kg^{-1} · min^{-1} group. *Post hoc* Bonferroni correction was performed for within- *versus* between-subject comparisons.

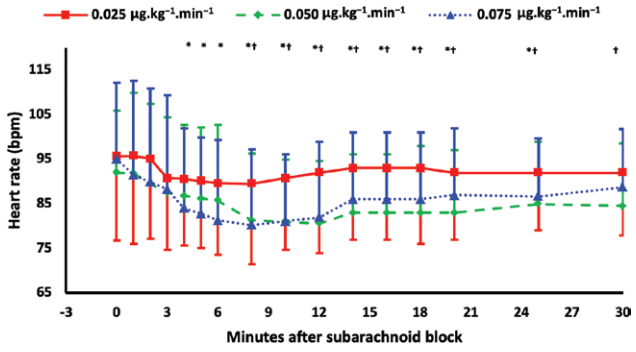

Fig. 3. Heart rate. Markers are means, and error bars are SDs. *Statistical significance between the 0.025-μg · kg^{-1} · min^{-1} group and the 0.075-μg · kg^{-1} · min^{-1} group. †Statistical significance between the 0.025-μg · kg^{-1} · min^{-1} group and the 0.050-μg · kg^{-1} · min^{-1} group. *Post hoc* Bonferroni correction was performed for within- *versus* between-subject comparisons. bpm, beats per minute.

Table 3. Neonatal Outcomes

	0.025-μg · kg^{-1} · min^{-1} Group (n = 95)	0.050-μg · kg^{-1} · min^{-1} Group (n = 93)	0.075-μg · kg^{-1} · min^{-1} Group (n = 96)
Umbilical artery *p*H	7.31 (7.26, 7.34)	7.32 (7.27, 7.34)	7.33 (7.27, 7.35)
Umbilical artery Pco_2, mmHg	45 (43, 55)	46 (42, 55)	45 (42, 53)
Umbilical artery Po_2, mmHg	27 (21, 31)	27 (20, 33)	28 (21, 33)
Umbilical artery HCO_3, mEq/dl	24 (22, 25)	24 (23, 25)	24 (22, 25)
Apgar score at 1 min	9 (8, 9)	9 (8, 9)	9 (8, 9)
Apgar score < 7 at 1 min	3 (3.2)	3 (3.2)	4 (4.2)
Apgar score at 10 min	10 (10, 10)	10 (10, 10)	10 (10, 10)

Data are presented as median (quartiles) and frequency (%).

Although there was a significant reduction in heart rate in all groups compared with the baseline reading, especially in the higher doses, few cases experienced marked bradycardia requiring atropine (four [4.3%] cases in the 0.025-μg · kg^{-1} · min^{-1} group, three [3.2%] cases in the 0.050-μg · kg^{-1} · min^{-1} group, and seven [7.3%] cases in the 0.075-μg · kg^{-1} · min^{-1} group); thus, we assume that norepinephrine could be the appropriate vasopressor in mothers with low baseline heart rate and in mothers with compromised cardiac function. We did not measure maternal cardiac output; however, it has been recently suggested that monitoring of maternal heart rate could be used as a surrogate for cardiac output.[4] Few cases of intraoperative hypertension were observed in the three study groups; however, these events were transient and resolved with stoppage of the infusion. However, we declare that our study was not high-powered enough to evaluate this side effect.

Our primary outcome was the frequency of postspinal hypotension defined as decreased SBP by 20% or more compared with the baseline reading. This definition is the most commonly used definition in similar studies.[6–10] The latest international consensus statement on the management of hypotension using vasopressors during cesarean delivery[4] had recommended to avoid SBP less than 80% of the baseline measurement. According to this international consensus statement, duration of hypotension could be more critical than severity.[4] We measured the SBP at 1-min intervals for 6 min followed by 2-min intervals until delivery of the fetus. Corke *et al.*[11] had reported that hypotension of duration less than 2 min did not affect neonatal outcomes.

Although norepinephrine is usually administered through central veins, peripheral administration of norepinephrine was also reported to be feasible and safe.[12] In obstetric anesthesia, norepinephrine was safely administered through peripheral veins provided that it was diluted and given through a large-bore catheter.[8,13] In our study, we used norepinephrine with a concentration of 8 μg/ml; this concentration was very near to previous studies in obstetric anesthesia.[8,13] Cardenas-Garcia *et al.*[12] used norepinephrine concentrations up to 32 μg/ml in peripheral veins with local tissue complications less than 2%.

We used a prophylactic bolus of norepinephrine before starting the infusion. Our hypothesis was based on a previous study, which reported that the use of a prophylactic bolus of phenylephrine before starting infusion was beneficial[14]; however, we had no data about the proper prophylactic norepinephrine bolus, and we therefore used a dose of 5 μg as an exploratory dose that could be adjusted in future studies. This dose was previously used by Ngan Kee *et al.*[8] for management of hypotension during cesarean delivery under prophylactic norepinephrine infusion.

The choice of a fixed, on-and-off rate *versus* a titrated rate for vasopressor infusion during cesarean delivery is still debatable. Titrated infusion rates might decrease the frequency of intraoperative hypertension; however, it might also increase the number of physician interventions. No studies, to the best of our knowledge, have yet compared titrated and fixed rates for vasopressor infusions during cesarean delivery. Because this is the first dose-finding study for norepinephrine in cesarean delivery, we preferred using fixed rate on-and-off infusion regimen to facilitate the comparison of different doses. We are already running a new study (clinicaltrials.gov, NCT0332853) that compares the variable infusion rate of norepinephrine and phenylephrine using the best dose reported in this study as a starting dose in the norepinephrine group (0.050 μg · kg^{-1} · min^{-1}).

According to the recent consensus statement for management of postspinal hypotension,[4] ephedrine is the preferred second-line drug for management postspinal hypotension in patients receiving α-agonists as the first-line prophylactic drug. We did not use phenylephrine because there are limited data for the possible cardiac depressant effect of combining two potent α-receptor

agonists. Norepinephrine bolus protocols were recently reported in obstetric anesthesia[13,15]; however, these data were published after we started recruiting our patients.

Prophylactic vasopressors are used in nearly every cesarean delivery[5,16]; however, the ideal vasopressor protocol for this purpose had not been established yet.[5] The most commonly used vasopressors during cesarean delivery are ephedrine and phenylephrine.[5] Phenylephrine is more preferable because it does not cause fetal acidosis; however, phenylephrine is characterized by reflex bradycardia and decreased cardiac output.[5] Norepinephrine is a vasopressor that has potent α-adrenergic agonistic activity in addition to some β-adrenergic agonistic activity; thus, it has been suggested as an alternative to phenylephrine that would not compromise cardiac function.[6] This makes norepinephrine a possible choice in mothers with relative contraindications of phenylephrine, such as low baseline heart rate or poor cardiac function.

Our study has the advantage of being a randomized, double-blinded study. However, we had some limitations. We did not use advanced hemodynamic monitors for cardiac output measurement, and we did not include parturients with cardiac morbidities. All our patients were scheduled for elective and not emergency caesarean sections. In conclusion, both 0.050-μg · kg^{-1} · min^{-1} and 0.075-μg · kg^{-1} · min^{-1} norepinephrine infusion rates effectively reduced postspinal hypotension during cesarean delivery compared with the 0.025-μg · kg^{-1} · min^{-1} infusion rate. A dose of 0.050 μg · kg^{-1} · min^{-1} seems to be a reasonable starting dose after subarachnoid block. More studies are warranted for refining and improving our infusion protocol and for exploring the incidence of possible side effects.

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Competing Interests

The authors declare no competing interests.

Reproducible Science

Full protocol available at: ahmedmohamedhasanin@gmail.com. Raw data available at: ahmedmohamedhasanin@gmail.com.

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