ORIGINAL RESEARCH ARTICLE

Diponegoro International Medical Journal 2025 July, Vol 6, No.1: 41-45
e-ISSN: 2745-5815

Comparison of Intravenous Ephedrine Administration of 5 mg and 10 mg Doses on Post Spinal Anesthesia Hypotension in Caesarean Section at Dr. Kariadi General Hospital Semarang

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Keywords:

Spinal Anesthesia
Ephedrine
SC
Hypotension

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Article history:

Received 03-05-2025
Accepted 26-05-2025
Availableonline 30-07-2025

ABSTRACT

Background: Hypotension after spinal anesthesia or combined epidural anesthesia in caesarean section (CS) causes adverse effects on the mother and fetus/neonatal. Hypotension often occurs therefore vasopressors could be used routinely and should be used as prophylaxis.
Methods: : Simple randomized controlled trial study of 52 patients undergoing CS at RSUP dr. Kariadi Semarang. Subjects revealed two groups, namely intravenous ephedrine at a dose of 5 mg and a dose of 10 mg. Hemodynamic variables were measured every 3 minutes until the operation was completed.
Results: In the comparison of mean arterial pressure (MAP) between the ephedrine 5 mg and ephedrine 10 mg groups, a statistically significant difference was obtained at 30 minutes ($P < 0.05$) while in the measurement of heart rate (HR) between the ephedrine 5 group mg and ephedrine 10 mg, a statistically significant difference was obtained from 3 to 15 minutes. Hypotension was obtained in 1 patient in the ephedrine 10 mg group and 3 patients in the ephedrine 5 mg group.
Conclusion: 10 mg intravenous ephedrine as a prophylactic agent after spinal anesthesia for patients undergoing CS was associated with a lower incidence of hypotension, suggesting a potential for improved hemodynamic stability.

DIMJ, 2025, 6(1), 41-45 DOI: https://doi.org/10.14710/dimj.v6i1.26813

1. Introduction

Spinal anesthesia for cesarean section (CS) has become widely preferred due to its better maternal safety and neonatal outcomes compared to general anesthesia. However, spinal anesthesia for CS is not without side effects. Hypotension, defined as a drop in systolic blood pressure (SBP) below 80% of the baseline, is the most common complication, with an incidence ranging from 7.4% to 74.4%. The dominant mechanism underlying spinal anesthesia-induced hypotension is vasodilation, which outweighs vasoconstriction. This vasodilation occurs due to the blockade of sympathetic nerve fibers at the preganglionic level.[1] If left untreated, hypotension can lead to complications for both the mother and fetus. For pregnant women, hypotension may cause nausea and vomiting, and in severe cases, it can result in loss of consciousness, pulmonary aspiration, respiratory depression, or even cardiac arrest. The associated nausea, vomiting, and lightheadedness are attributed to decreased cerebral blood flow, leading to maternal morbidity.[2,3]

The use of ephedrine as a preventive agent for hypotension in CS patients undergoing spinal anesthesia typically ranges from 5 to 30 mg as an IV bolus.[4–9] A 10 mg bolus dose is commonly used and has been identified in a recent meta-analysis as the optimal dose.[10] The international consensus recommends a initial dose 10 mg IV bolus ephedrine. The effect of IV ephedrine bolus on arterial pressure is temporary, with an onset of 3–5 minutes and a duration of 10–15 minutes. However, higher doses of ephedrine have been associated with maternal hypertension and fetal acidosis, raising concerns about its side effects.[11,12] Considering the risks, an optimal dose of 10 mg, as supported by prior research, is often recommended. Nonetheless, previous evidence has shown that a prophylactic 5 mg dose of ephedrine can significantly reduce the incidence and severity of hypotension compared to placebo.[9] Nevertheless, a comparison of lower doses, such as 5 mg and 10 mg, has not yet been conducted. This study aims to analyze

the comparison between administering 5 mg and 10 mg intravenous ephedrine on the incidence of post-spinal anesthesia hypotension in CS patients at Dr. Kariadi General Hospital, Semarang.

2. Methods

This study employed a simple randomized controlled trial design to compare the effects of 5 mg and 10 mg intravenous ephedrine on hypotension following spinal anesthesia in CS patients. Pregnant women at term, aged 20–35 years, scheduled for CS under spinal anesthesia, and classified as ASA (American Society of Anesthesiologists) physical status I–II were included in the study. Patients were excluded if they were shorter than 145 cm, had high-risk pregnancies, carried more than one fetus, or experienced complications during pregnancy. Additional exclusion criteria included a history of pregnancy-induced hypertension, baseline SBP below 90 mmHg, contraindications to spinal anesthesia, allergies to local anesthetics or ephedrine, and conversion from regional to general anesthesia. A sample size calculation determined that 26 participants were needed in each group, resulting in two study groups: one receiving 5 mg and the other 10 mg of intravenous ephedrine.

Participants who met the inclusion criteria and were scheduled for CS at Dr. Kariadi General Hospital, Semarang, were invited to participate. The study's background and objectives were explained to patients and their families, and written informed consent was obtained. Patients were then randomized into two groups. Group I received 5 mg intravenous ephedrine, and Group II received 10 mg intravenous ephedrine. Ephedrine was administered immediately after the spinal anesthetic procedure was initiated. Preoperative data, including systolic and diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR), were recorded. Preloading was performed using Ringer's lactate at a dosage of 15 mL/kg body weight over 15 minutes.

Spinal anesthesia was administered using 2.5 mL of 0.5% heavy bupivacaine combined with 25 mcg fentanyl. The sensory and motor blockade was assessed following the administration of anesthesia. Hemodynamic parameters were measured every three minutes after spinal anesthesia was administered. Throughout the surgical procedure, hypotension, bradycardia, nausea, vomiting, shivering, and other side effects were monitored and recorded. Hypotension was managed with a 5 mg bolus of intravenous ephedrine, while bradycardia was treated with 0.5 mg intravenous atropine. The total volume of fluids, ephedrine, and atropine administered during the procedure was documented. After the delivery of the baby, oxytocin (20 IU) diluted in 500 mL of Ringer's lactate was administered at a rate of 10–15 drops per minute.

Postoperative outcomes were assessed, including the occurrence of hypotension, bradycardia, nausea, vomiting, and shivering, for up to two hours in the recovery room. Nausea and vomiting were evaluated using the postoperative nausea and vomiting (PONV) score. Data analysis was performed using SPSS version 25 for Windows (IBM SPSS Inc., USA). An independent t-test was used to compare normally distributed pre-test and post-test data, while the Mann-Whitney test was applied for non-normally distributed data. Categorical data were analyzed using the chi-square test. A significance level of $p < 0.05$ was considered statistically significant. Ethical clearance was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Diponegoro University (Ethical Approval No. 1609/EC/KEPK-RSDK/2023).

3. Result

This study included 52 patients who were analyzed for outcomes. These patients were evenly divided into two groups of 26 participants each, meeting the study's inclusion criteria. No subjects were excluded or dropped out during the study. Demographic and preoperative data for both groups are summarized in Table 1. Among the variables, only height showed a statistically significant difference between the two groups, while BMI differences were not significant. Overall, the homogeneity of baseline data reduced the likelihood of bias in this study.

Table 1. Demographic and Preoperative Profiles

Variables	Group [Mean ± SD / n (%)]		P Value
	Ephedrine 5mg	Ephedrine 10mg	
Maternal Age	30.15 ± 2.82	27.92 ± 5.48	0.071[a]
Gestational Age	36.37 ± 3.73	36.82 ± 2.86	0.971[b]
Obstetric History			[b]
Gravida	2.42 ± 1.36	1.96 ± 1.14	0.232[b]
Para	1 ± 1.09	0.65 ± 0.79	0.279[b]
Abortus	0.42 ± 0.64	0.3 ± 0.73	0.268[b]
Previous Medical History			[b]
Asthma	2 (7.6)	1 (3.8)	0.552[c]
Surgical History	16 (61.5)	17 (65.3)	0.773[c]
Body Height	158.53 ± 4.99	157.07 ± 4.84	0.028[a*]
Body Weight	72.11 ± 11.48	69.86 ± 11.43	0.159[a]
BMI	28.65 ± 4.16	28.32 ± 4.48	0.596[a]
TDS	115.92 ± 7.52	115.94 ± 7.34	0.876[b]
TDD	76.5 ± 9.33	76.34 ± 8.25	0.895[a]
MAP	89.64 ± 7.96	89.54 ± 7.26	0.627[b]
HR	83.69 ± 11.28	84.65 ± 10.09	0.647[b]
ASA			
I	6 (23.1)	5 (19.2)	0.817[cb]
II	20 (76.9)	21 (80.8)	

[a]*Independet sample t-test*
[b]*Mann-Whitney test*
[c]*Chi-Square test*
[*]P value < 0.05

Intraoperative hemodynamic variables were assessed every three minutes until the surgery concluded, resulting in ten times intervals for analysis. A statistically significant difference in SBP was observed between the 5 mg and 10 mg ephedrine groups at 21 and 42 minutes ($P < 0.05$). The highest mean SBP in the 5 mg group was 119 mmHg (110–125.25) at six minutes, while the 10 mg group recorded 126 mmHg (118–128) at three minutes. Conversely, the lowest mean SBP in the 5 mg group was 105.19 ± 6.16 mmHg at 42 minutes, and in the 10 mg group, it was 105.92 ± 6.97 mmHg at 21 minutes. Detailed comparisons are presented in Figure 1.

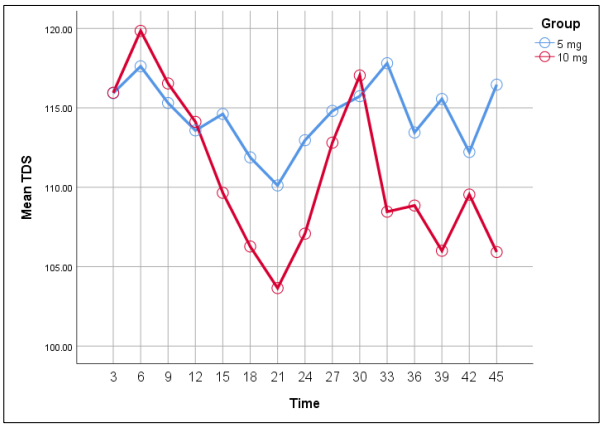

Figure 1. Systolic Blood Pressure Comparison

For DBP, a significant difference was found only at 30 minutes ($P < 0.05$). The highest mean DBP in the 5 mg group was 77.3 ± 11.87 mmHg at six minutes, compared to 88.05 ± 6.23 mmHg in the 10 mg group at 21 minutes. The lowest mean DBP in the 5 mg group was 69 ± 8.03 mmHg at 21 minutes, while the 10 mg group had a mean of 70.38 ± 6.06 mmHg at six minutes. Results are shown in Figure 2. Similarly, a significant difference in MAP occurred at 30 minutes ($P < 0.05$). The highest MAP in the 5 mg group was 94.23 ± 6.67 mmHg at 21 minutes, while the 10 mg group reached 96.58 ± 5.27 mmHg at the same time. The lowest MAP in the 5 mg group was 81.62 ± 3.35 mmHg at 45 minutes, compared to 83.83 mmHg (82.75–86.58) in the 10 mg group at 39 minutes. These findings are detailed in Figure 3.

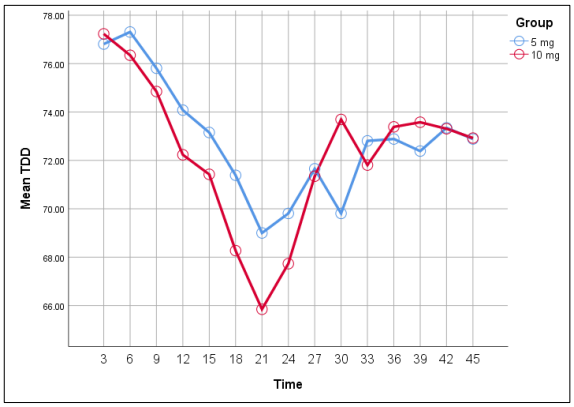

Figure 2. Diastolic Blood Pressure Comparison

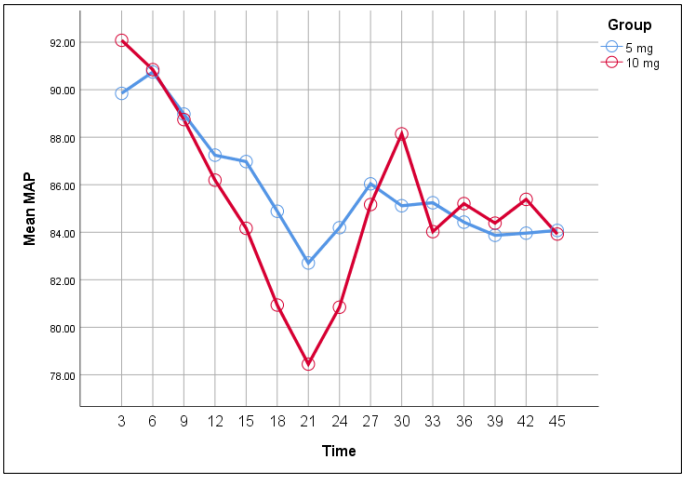

Figure 3. Mean Arterial Pressure Comparison

HR comparisons revealed statistically significant differences between the two groups from three to 15 minutes post-administration ($P < 0.05$). The highest mean HR in the 5 mg group was 85.65 ± 11.28 beats per minute (bpm) at three minutes, while the 10 mg group recorded 94.23 ± 11.97 bpm at the same time. The lowest mean HR in the 5 mg group was 77.00 ± 11.4 bpm at 15 minutes, compared to 82 bpm (75.75–87.25) in the 10 mg group at 39 minutes. These comparisons are displayed in Figure 4.

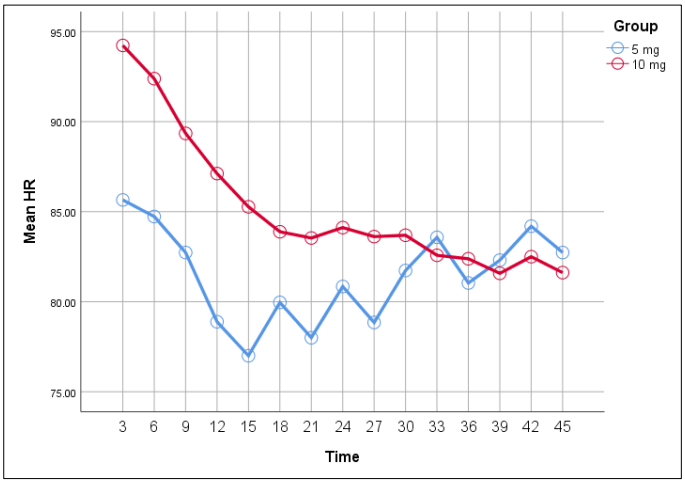

Figure 4. Heart Rate Comparison

Intraoperative fluid administration did not show a statistically significant difference between the two groups ($P > 0.05$), with averages of 743.46 mL in the 5 mg group and 736.54 mL in the 10 mg group. Additional intraoperative ephedrine was required in only two patients from the 5 mg group, but this difference was not statistically significant. No atropine supplementation was required in either group. Postoperative complications, including hypotension, shivering, and PONV, were absent in both groups. A comprehensive comparison is provided in Table 2.

Table 2. Other Variables Comparison

Variables	Group (Mean ± SD)		P value
	Ephedrin 5 mg	Ephedrin 10 mg	
Intraoperative Fluid	743.46 ± 81.09	736.54 ± 77.19	0.832[a]
Additional Intraoperative Ephedrine	2 (7.6)	0	0.74[b]
Intraoperative Hypotension	3 (11.5)	1 (3.8)	0.391[b]
Additional Intraoperative Atropine Sulfate	0	0	-
Postoperative Complications			
Hypotension	0	0	-
Shivering	0	0	-
PONV	0	0	-

[a]*Mann-Whitney test*
[b]*Chi-Square test*

4. Discussion

This study represents the first comparison of 5 mg and 10 mg intravenous ephedrine doses. Recent systematic reviews and meta-analyses highlight that 5–10 mg intravenous ephedrine is the optimal prophylactic dose for preventing hypotension during spinal anesthesia in CS. However, these meta-analyses primarily compared ephedrine with other vasopressor agents, such as phenylephrine, rather than directly comparing 5 mg and 10 mg doses of ephedrine.[10]

In this study, the ability of ephedrine to prevent hypotension was assessed by analyzing various hemodynamic parameters, including SBP, DBP, MAP, and HR across multiple time intervals during CS procedures. Statistically significant differences in hemodynamic variables were observed at several time points. Previous studies have demonstrated significant increases in blood pressure with varying prophylactic doses of intravenous ephedrine, ranging from 5 mg to 30 mg. Higher doses were associated with increased instances of intraoperative hypertension, with a positive correlation between higher ephedrine doses and the number of hypertensive patients.

A comparative study evaluating three intravenous ephedrine doses, including a 30 mg dose, found that the highest dose caused reactive hypertension and tachycardia within 12 minutes post-administration. In the group receiving 10 mg of ephedrine, there were 17 cases of hypotension, one case of hypertension, a maximum SBP of 111 mmHg, a minimum SBP of 69 mmHg, and nine patients reported nausea and vomiting.[4] Another study on 10 mg intravenous ephedrine reported an SBP range of 110–130 mmHg and HR between 90 and 110 beats per minute.[7] These findings indicated an increase in SBP and HR compared to the control group, with a lower incidence of hypotension and nausea/vomiting.[5] Additionally, a quasi-experimental study reported significantly fewer cases of hypotension and nausea/vomiting in the 10 mg ephedrine group compared to controls, with 12 hypotensive cases and six cases of nausea/vomiting.[13]

In studies evaluating 5 mg ephedrine, the highest recorded SBP was 122 mmHg, while the lowest was 110.4 mmHg, with 15 patients experiencing hypotension. No cases of hypertension or nausea/vomiting were reported.[8] In a study using 0.5 mg/kg of intravenous ephedrine, significant differences were observed compared to the control group in SBP, HR, and the number of hypotensive and nauseous/vomiting patients.[6] In the current study, three patients in the 5 mg group and one patient in the 10 mg group experienced hypotension, with no hypertension or other postoperative complications reported in either group. The hemodynamic outcomes of this study are consistent with previous findings for each dose, demonstrating that 10 mg has advantages, such as fewer hypotensive episodes, reduced need for additional ephedrine, and better-controlled intraoperative hemodynamics. Furthermore, prior studies have generally favored the 10 mg dose over 5 mg.

Significant hemodynamic changes at the 21-minute mark are attributable to the surgical process, including asepsis, antisepsis, and draping, which typically take around 10 minutes, followed by CS procedures such as incision and delivery by the 20th minute. Hemodynamic alterations, such as blood pressure drops and HR increases, often occur after the delivery of the baby during CS.[14] According to the National Health Service (NHS), the decision-to-delivery interval should be under 30 minutes for category 1 CS and 75 minutes for category 2. However, rapid deliveries carry risks, including transfusion, broad ligament hematomas, and uterine artery ligation, when incision-to-delivery takes less than two minutes. Despite these recommendations, there is insufficient evidence to establish optimal decision-to-incision or decision-to-delivery intervals for emergency or urgent CS.[15]

The consensus on managing hypotension during CS after spinal anesthesia designates ephedrine as a second-line prophylactic agent and a first-line treatment for hypotension and bradycardia. Intravenous ephedrine is recommended at doses starting at 5 mg and not exceeding 15 mg to prevent fetal acidosis.[11,12] By comparing 5 mg and 10 mg doses, this study provides new insights into more precise dosing of ephedrine as a prophylactic agent against hypotension during CS under spinal anesthesia.

This study has several limitations. First, the single-center nature of the study and the minimal sample size limit the generalizability and comprehensive interpretation of the comparative effects of 5 mg and 10 mg intravenous ephedrine in CS patients. Second, the study only evaluated maternal hemodynamic variables, which do not provide a

complete picture of fetal conditions following the CS procedure.

5. Conclusion

This study found significant differences in the occurrence of hypotension, blood pressure (SBP, DBP and MAP), HR, and total ephedrine requirements between 5 mg and 10 mg intravenous ephedrine doses following spinal anesthesia in CS at RSUP Dr. Kariadi Semarang, with the 10 mg dose was associated with a lower incidence of hypotension. Future research is recommended to include fetal variables (e.g., fetal heart rate, umbilical arterial blood gas, and APGAR scores), compare the effectiveness of ephedrine with other vasopressor agents, and employ larger-scale or multicenter designs for broader applicability.

Ethical Approval
None

Conflicts of Interest
None

Funding
None

Author Contributions
None

Acknowledgments
None

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