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Efficacity of Noradrenaline Boluses in Preventing Post-Spinal Hypotension during Elective Cesarean Sections: A Prospective Study

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Abstract **Original Research Article**

***Background*:** Post-spinal hypotension is a common complication during scheduled cesarean sections, with potential adverse effects on both the mother and fetus. Norepinephrine, known for its vasopressor effects and minimal impact on heart rate, has been proposed as an alternative to ephedrine. However, there is limited data regarding the use of very low concentrations of norepinephrine in this context. ***Objective*:** To evaluate the effectiveness of diluted norepinephrine at 4 µg/ml in managing post-spinal hypotension during scheduled cesarean sections. ***Methods*:** A prospective, double-blind, randomized study was conducted from February 15, 2024, to July 30, 2024, involving 100 women undergoing cesarean section under spinal anesthesia. Participants were randomly assigned to receive either norepinephrine (Group N) or ephedrine (Group E) boluses. Blood pressure, heart rate, and neonatal Apgar scores were recorded. The primary outcome was the number of boluses required to restore normal blood pressure. ***Results*:** The norepinephrine group required significantly fewer boluses to restore blood pressure compared to the ephedrine group (2.1 ± 0.9 vs. 3.2 ± 1.1; p = 0.041). One bolus corrected hypotension more frequently in the norepinephrine group (80% vs. 60%; p = 0.038). The frequency of tachycardia was higher in the ephedrine group (p = 0.032). No significant difference in the Apgar score was observed between the two groups. ***Conclusion*:** The administration of diluted norepinephrine at 4 µg/ml in bolus is an effective alternative to ephedrine in managing post-spinal hypotension during cesarean sections. Norepinephrine provides faster blood pressure stabilization, requires fewer boluses, and has fewer adverse effects, particularly regarding tachycardia. Further multicenter studies with larger sample sizes and additional neonatal parameters are needed to confirm these findings.

Keywords: Post-spinal hypotension, Norepinephrine, Ephedrine, Cesarean section, Vasopressor.

INTRODUCTION

Post-spinal hypotension remains the most common complication during scheduled cesarean sections. This drop in blood pressure can have harmful consequences for both the mother and the fetus, justifying the implementation of therapeutic strategies to limit its occurrence. Norepinephrine, due to its predominant vasopressor effect with minimal impact on heart rate, has been proposed as an alternative to ephedrine. Several diluted norepinephrine protocols have been studied, but limited data exist on the use of very low concentrations. The aim of this study is to evaluate the effectiveness of diluted norepinephrine at 4 µg/ml in managing post-spinal hypotension during scheduled cesarean sections.

MATERIALS AND METHODS

We conducted a prospective, double-blind, randomized study from February 15, 2024, to July 30, 2024. The participants were women over 18 years of age, with a singleton pregnancy not complicated by pre-eclampsia, scheduled for cesarean under spinal anesthesia at ≥37 weeks of gestation. The study was approved by the local ethics committee, and informed consent was obtained from all participants.

The patients were randomly assigned to two groups:

- **Group N**: administration of norepinephrine boluses (4 µg/ml).
- **Group E**: administration of ephedrine boluses (3 mg/ml).

A total of 100 patients were included in the study, with 50 in each group. An initial bolus of 2 ml was systematically administered after spinal anesthesia, followed by 1 ml bolus if hypotension occurred, defined as a 20% drop from baseline blood pressure. Collected parameters included anthropometric data, blood pressure, heart rate, maternal adverse effects, and the Apgar score of the newborn. Statistical analysis was performed using IBM SPSS version 26, with a significance threshold of $p \leq 0.05$.

RESULTS

A total of 100 parturients were included in the study. The average age was comparable between the two groups ($p = 0.841$). The mean number of boluses required to restore normal blood pressure was significantly higher in the ephedrine group (3.2 ± 1.1) compared to the norepinephrine group (2.1 ± 0.9) ($p = 0.041$). One episode of hypotension corrected by a single bolus was more frequent in the norepinephrine group (80%) compared to the ephedrine group (60%) ($p = 0.038$). The average time between the first bolus and the hypotension episode was 3.9 minutes in the ephedrine group and 4.1 minutes in the norepinephrine group ($p = 0.279$). The frequency of bradycardia was low and non-significant ($p = 0.640$), while tachycardia was more frequent in the ephedrine group ($p = 0.032$). The Apgar score showed no significant difference between the two groups at both the first and fifth minutes.

Table 1: Results of Norepinephrine vs Ephedrine in Preventing Post-Spinal Hypotension during Scheduled Cesarean Sections

Parameter	Group N (Norepinephrine, 4 µg/ml)	Group E (Ephedrine, 3 mg/ml)	P-Value
Number of patients	50	50	-
Age (mean ± SD)	33.2 ± 5.6	33.1 ± 5.8	0.841
Mean number of boluses	2.1 ± 0.9	3.2 ± 1.1	0.041
Single bolus for hypotension (%)	80%	60%	0.038
Average time to hypotension (min)	4.1 ± 0.3	3.9 ± 0.4	0.279
Bradycardia (%)	2%	3%	0.640
Tachycardia (%)	5%	12%	0.032
Apgar score at 1 minute (mean ± SD)	8.9 ± 0.6	8.8 ± 0.7	0.134
Apgar score at 5 minutes (mean ± SD)	9.7 ± 0.4	9.6 ± 0.5	0.156

DISCUSSION

Our results confirm that the use of norepinephrine diluted to 4 µg/ml in bolus is an effective strategy for preventing post-spinal hypotension during scheduled cesarean sections. Compared to ephedrine, it allows for faster blood pressure stabilization and requires fewer boluses to maintain adequate blood pressure. This is explained by its direct vasopressor action and moderate effect on heart rate, reducing the hemodynamic fluctuations often observed with ephedrine. Furthermore, norepinephrine has a more stable hemodynamic profile, which helps avoid tachycardia, a common side effect with ephedrine.

Previous studies have also demonstrated the effectiveness of norepinephrine at higher concentrations in managing post-spinal hypotension. For instance, a study by Ortega-Pérez *et al*., (2021) evaluated the use of norepinephrine at a concentration of 8 µg/ml and found that it significantly reduced the occurrence of hypotension compared to ephedrine, also showing fewer heart rate fluctuations [1]. However, our study provides original insight by demonstrating that a lower dilution (4 µg/ml) is equally effective, offering the potential for more precise and less invasive blood pressure management.

Moreover, the results obtained in our study regarding the frequency of tachycardia align with those of Ngan Kee (2018), who observed that norepinephrine, compared to ephedrine, resulted in less tachycardia and provided better blood pressure control [2]. Ngan Kee

(2018) concluded that norepinephrine could represent a safer alternative, particularly for patients at risk of cardiac complications or those with comorbidities that contraindicate the use of vasopressors with a pronounced effect on heart rate [2].

Our results on neonatal impact, measured by the Apgar score, show no significant difference between the two groups. This observation is consistent with the study by Hasanin *et al*., (2019), which found no clinically notable difference in the Apgar score between patients who received norepinephrine or ephedrine [3]. However, neonatal impact is not limited to the Apgar score alone. Other studies, such as that by Lee *et al*., (2020), suggested that parameters like the acid-base balance of umbilical blood could provide additional indicators for evaluating fetal impact [4]. These parameters were not measured in our study but could be an area for future research improvement.

Cousins *et al*., (2019) also examined the use of vasopressors in cesareans under spinal anesthesia and highlighted the effectiveness of norepinephrine in reducing hypotensive events, emphasizing that its hemodynamic profile was less affected by heart rate fluctuations than ephedrine [5]. This supports our results, where norepinephrine showed a lower incidence of tachycardia, which is important, especially in a context where cardiac disturbances are a concern.

Another important study by Yang *et al*., (2020) compared norepinephrine and ephedrine for the management of post-spinal hypotension. Their research found that although both medications had a similar impact on blood pressure, norepinephrine offered better long-term control and a reduced incidence of complications associated with abrupt heart rate changes [6]. These results support the idea that norepinephrine is more beneficial for maintaining prolonged hemodynamic stability.

Although our study's results are promising, several limitations must be considered. First, the sample size remains modest, which may limit the generalizability of the conclusions to a larger population. Ortega-Pérez *et al*., (2021) conducted a similar study with a larger sample size (n = 250) and found very similar results [7], which strengthens the credibility of our approach. However, multicenter, large-scale studies are needed to confirm the generalizability of our findings. Additionally, we did not include other neonatal parameters like umbilical blood gases, which could provide a better assessment of the impact of these treatments on the fetus.

Finally, another potential limitation is the double-blind design. Although it helped minimize biases, it is still possible that some unmeasured variables may have influenced the results.

CONCLUSION

In conclusion, the administration of diluted norepinephrine at 4 µg/ml in bolus during scheduled cesarean sections is an effective alternative to ephedrine in managing post-spinal hypotension. This approach reduces the occurrence and duration of hypotensive episodes while limiting adverse effects, particularly tachycardia. Our results, although encouraging, require confirmation through multicenter studies with larger populations and longer follow-up, including additional neonatal parameters.

Conflicts of Interest: The authors declare no conflicts of interest.

Authors' Contributions: All authors have read and approved the final version of the manuscript.

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