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Management of low blood pressure during spinal anaesthesia for caesarean section: Comparison between ephedrine and low-dilute norepinephrine

SUMMARY:

This prospective study, conducted over six months at the Ibn Rochd University Hospital in Casablanca, compared the efficacy of weakly diluted norepinephrine and ephedrine for the management of hypotension induced by spinal anesthesia during caesarean sections. Among 120 patients (mean age: 25.5 ± 5.5 years), norepinephrine was distinguished by improved hemodynamic stability, ensuring more precise heart rate control (maximum of 97.47 bpm vs. 133.7 bpm) and higher systolic blood pressure (126.19 mmHg vs. 80.84 mmHg), while optimally preserving the pH of umbilical cord blood (7.25 versus 7.21). Despite comparable gasometric parameters and Apgar scores between groups, a dose of 16 mcg norepinephrine demonstrated slightly better hemodynamic control than that of 8 mcg. These results suggest that weakly diluted norepinephrine represents a safer and more effective therapeutic alternative to ephedrine in this clinical setting, thus ensuring better maternal and fetal safety.

INTRODUCTION :

General anesthesia in pregnant women is considered high-risk due to the altered physiology of pregnancy, including the increased risk of inhalation and difficult intubation. In addition, it delays mother-child contact. Thus, spinal anesthesia (RA) is preferred over caesarean section, offering a simple, reliable and effective technique while avoiding the risks of general anesthesia.

However, AR is not without complications, including low blood pressure due to compression of the inferior vena cava and sympathetic blockade, which can impair maternal and fetal perfusion. This hypotension can have serious consequences, requiring preventive and therapeutic management. Vasopressors, including ephedrine, are commonly used. However, its effects on maternal and fetal hemodynamics raise questions. This study therefore aims to compare ephedrine to weakly diluted norepinephrine to evaluate their respective efficacy in the management of caesarean section-induced AR-induced hypotension.

PATIENTS AND METHODS:

Goal of the study

The study aims to compare the effectiveness of norepinephrine and ephedrine in the treatment of hypotension induced by spinal anesthesia in caesarean section in the intensive care unit of the maternity unit of the Ibn Rochd University Hospital.

Study type

This is a descriptive and analytical prospective study, which was conducted over six months (January to June 2024) in the intensive care unit of the maternity unit of the Ibn Rochd University Hospital in Casablanca. It included all patients eligible for caesarean section according to pre-established inclusion criteria.

Inclusion criteria

All patients who underwent caesarean section under spinal anaesthesia during our study period were included in our study.

Exclusion criteria

All patients who underwent caesarean section under another anaesthesia technique (general anaesthesia, epidural anaesthesia or combined perispinal anaesthesia, conversions to general anaesthesia after failure of spinal anaesthesia) were excluded from this study.

Perioperative period

SBP, DBP and MAP, as well as HR were collected just before AR (t0), then spinal anesthesia (t1), then fetal extraction (t2) and finally skin closure (t3). Hypotension was defined in our study as systolic figures below 90mmHg or if there is a drop of more than 30% in preanesthetic blood pressure figures; considered as reference figures.

As soon as this arterial hypotension appeared, a group of patients were injected with boluses of 6 mg of ephedrine every 2 min until blood pressure normalized with a total dose of 30 mg. The other group benefited from a weakly diluted administration of norepinephrine boluses. In this same group (Group II), boluses of 8 and 16 mcg were administered. Boluses (ephedrine or norepinephrine weakly diluted) were considered effective when they allowed a SBP value greater than 80% of the reference SBP value to be restored, from spinal anesthesia to delivery.

Preparation of ephedrine boluses

One ampoule of ephedrine (30mg/1ml) is diluted in 10 ml of saline (NaCl 0.9%), obtaining a final concentration of 3 mg/ml. This solution is administered by direct intravenous injection as a bolus, with a common dose of 3 to 6 mg (i.e. 0.5 to 1 ml of the prepared solution).

Preparation of norepinephrine boluses

One ampoule of norepinephrine (8 mg/4 ml) is diluted in 500 ml of 5% glucose serum, resulting in a concentration of 16 µg/ml. For bolus administration, a 10 mL syringe is used.

Protocol of spinal anaesthesia

After obtaining verbal informed consent, each parturient was placed in a half-seated position, legs extended along the table, back rounded, and head bent. The puncture levels were the L2 – L3, L3 – L4 or L4 – L5 intervertebral spaces depending on the achievement of cerebrospinal fluid return. AR was achieved by administering 10-12.5 mg bupivacaine 0.5% (= 2 ml) + 25 ug fentanyl (= 0.5 ml) by means of a pencil-tip needle, with a slow injection over 30 seconds. Gentle tilting of the patient into a slight DLG and then back into the supine position. The installation of the sensitive and motor block is evaluated by the hot/cold test and the modified Bromage score. Maintaining contact with the patient throughout the caesarean section. All parturients received 10 IU of oxytocin after fetal extraction.

Criteria for discharge from the post-operative monitoring room

All patients had the following criteria before discharge from the ICU: disappearance of motor block, deep ventilation and effective cough, a change in systolic blood pressure (BP) of ± 20% compared to pre-anesthetic BP, normal consciousness, normal mucocutaneous staining, O2 saturation (SpO2) > 92% in room air.

Data collection

Data collection was done prospectively on the basis of a pre-established exploitation sheet which contained the following data: age, gestational age, parity, indication for caesarean section, level of puncture, anaesthetics used, level of the block, heart rate, SBP, MAP, pH metry, etc

Statistical study

Our study has 2 parts:

► A descriptive part is epidemiological, clinical, anesthetic and evolutionary data.

► An analytical part where we divided our population into 2 subgroups, a group I with patients who received ephedrine and a group 2 including patients who received weakly diluted norepinephrine as a treatment method for low blood pressure during spinal anesthesia.

The statistical analysis was carried out using the SPSS software. A p-value <0.05 was considered significant. The literature search was carried out on the basis of articles extracted from the databases Pub Med, Google Scholar, Cochrane and other specialized journals.

RESULTS:

Epidemiological, clinical and anesthetic drug use were similar in the two groups

Analysis of haemodynamic data from parturients:

At t0, there were no significant differences between the 2 groups. On the other hand, at t1, t2, t3, ephedrine showed a significant increase in heart rate compared to norepinephrine which led to only a moderate increase followed by a slight decrease.

Ephedrine then causes a significant and sustained increase in HR at all times while norepinephrine has a less pronounced effect on HR, maintaining values closer to the Baseline, with an average HR in group II at 93.47 ± 7.4 bpm at t0, 87.47± 4.7 bpm at t1, 97.47 ± bpm at t2, 80.47± 6 bpm at t3 versus 97.7 ± 4.1 bpm at t0, 133.7 ± 6.3 bpm at t1, 126.7 ± 3.8 bpm at t2, 97.7 ± 6.81 bpm at t3 in group I (FIGURE 1). The mean SBP in group I patients was 120.75 ± 2.57 mmHg at t0, 89.42 ± 2.3 mmHg at t1, 80.84 ± 3.77 mmHg at t2, 121.31 ± 3.25 mmHg at t3, while in group II was 128.97 ± 1.46 mmHg at t0, 100.28 ± 2.22mmHg at t1, 126.19 ± 1.30mmHg at t2, 125.10 ± 6.24mmHg at t3 (FIGURE 2), By analyzing these data, we can say that at T0 and T1 there is no significant difference between the groups. At t2, ephedrine showed a decrease in SBP while norepinephrine maintained higher values. At t3, no significant difference but ephedrine shows an upward.

Norepinephrine then seems to be more effective in maintaining SBP after its initial decline.

The evolution of MAP between the two groups showed that it is more stable in group II of parturients (81.66 ± 2.49mmHg at t0, 62.76 ± 1.74mmHg at t1, 77.43 ± 2.43 mmHg at t2, 85.03 ± 2 mmHg at t3) compared to group I (80.28 ± 2.50 mmHg at t0, 42.48 ± 1.71 mmHg at t1, 54.95 ± 2.30 mmHg at t2, 83.80 ± 2.41 mmHg at t3), t0 and t1, there was no significant difference between the 2 groups. But at t2 and t3, norepinephrine maintains a slightly higher MAP.

FIGURE 1: Combined box diagram comparing the evolution of the heart rate between the 2 groups

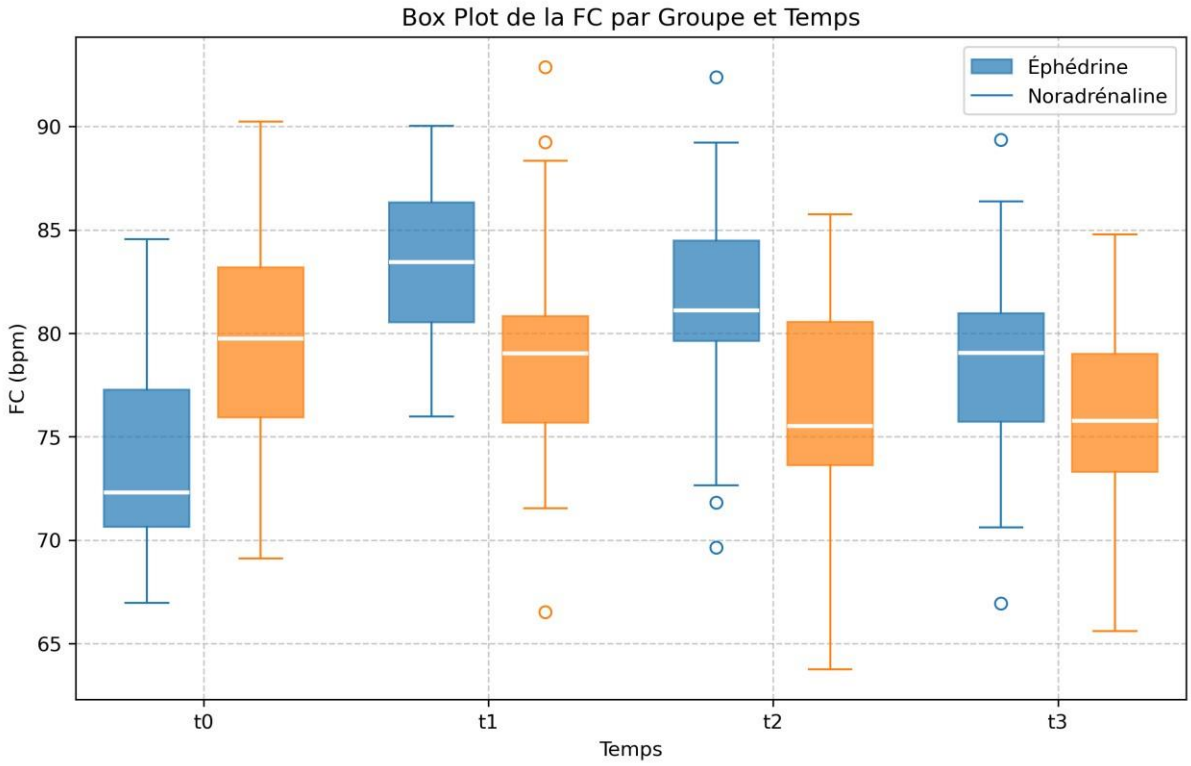
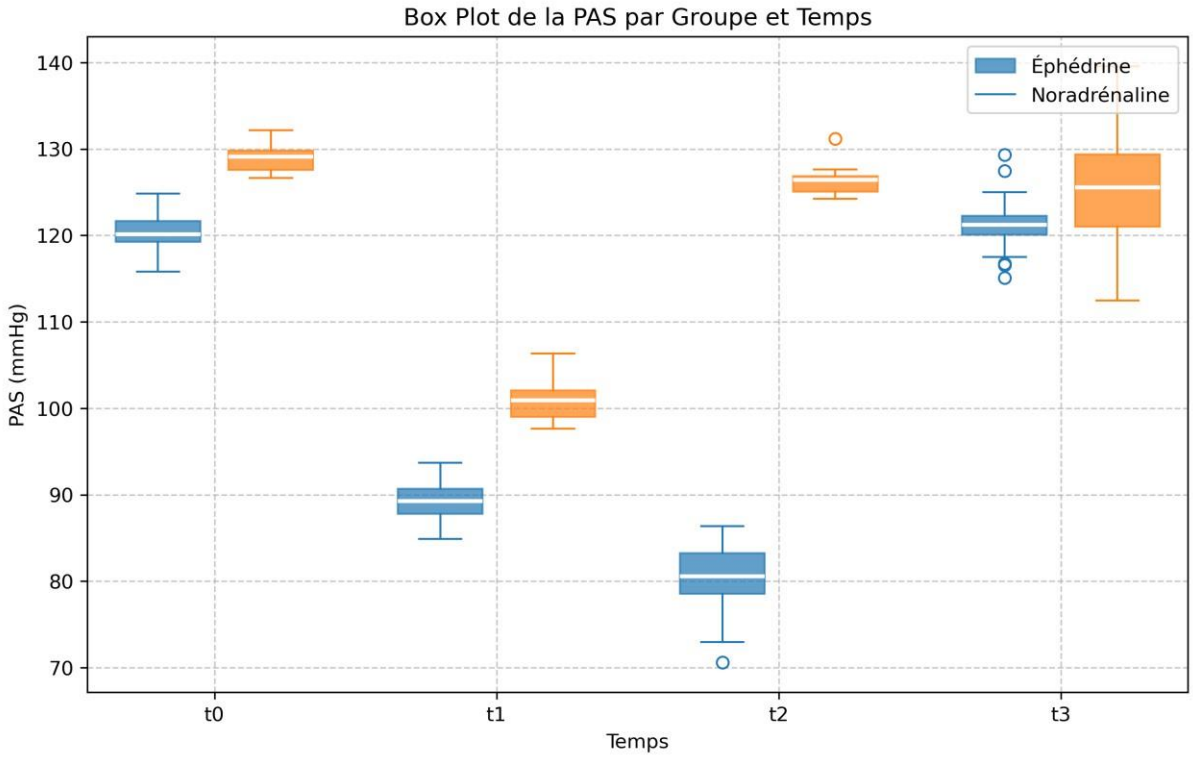


FIGURE 2: Combined c-box diagram comparing the evolution of SBP between the 2 groups.



Analysis of basic neonatal features:

The average Apgar score in Group I at the first minute was 8.2 ± 1 and 9 ± 0.4 at the fifth minute. In group II the average was 7.96 ± 0.5 at the first minute and 10 at the 5th minute. In the 2 groups at the 10th minute, all the newborns had an Apgar score equal to 10, so we can conclude that there is no significant difference in the Apgar score at the first, 5th, 10th minutes between the 2 groups. Norepinephrine shows superiority in maintaining blood pH at the umbilical cord. But there was no significant difference in PaO2, PaCO2, HCO3- between the 2 groups. With an average pH metrical in group I that was 7.21 ± 0.04, compared to 7.25 ± 0.03 in group II.
In the group of patients who received norepinephrine (group II), several low-dose dosages were tested. This analysis compares the effects of 8 mcg and 16 mcg doses of norepinephrine on SBP and HR. The 16 mcg dose shows a slightly lower heart rate than the 8 mcg dose (FIGURE 3), and a slightly higher SBP than the 8 mcg dose (FIGURE 4).

FIGURE 3: Combined box diagram comparing the means of HR within the 2 norepinephrine groups (8 mcg and 16 mcg)

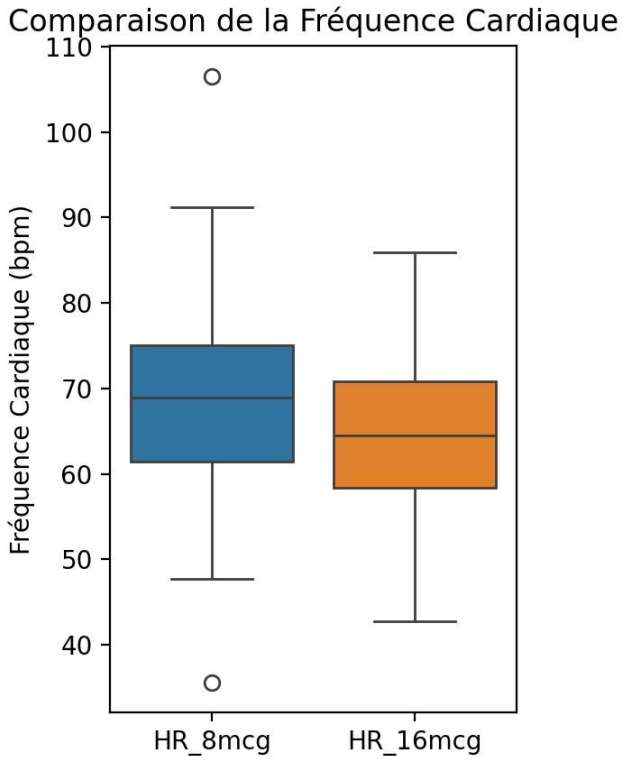
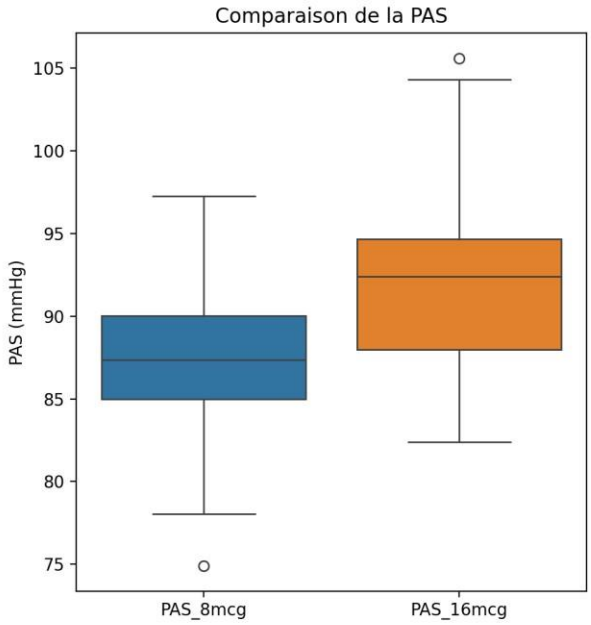


FIGURE 4: Combined box diagram comparing the means of SBP within the 2 norepinephrine groups (8 mcg and 16 mcg)



DISCUSSION :

A/Anesthetic Data

Anesthetics used

The dose of bupivacaine appears to be statistically significant in several studies, some authors have even focused exclusively on this variable, such as Qiu et al.(81) in 2012 who found a lower incidence of hypotension after a lower dose of spinal anesthesia associated with morphine.

Roofthooft et al.(82) in 2008 also proposed the possibility of performing spinal anesthesia with less local anesthetics (5 to 7 mg bupivacaine), with sufficient analgesia and less hypotension.

According to Leroy et al.(83), given the bivariate association between bupivacaine dose and hypotension, it may seem legitimate to propose a reduction in the doses of local anesthetics, particularly in the presence of other associated risk factors for hypotension.

However, because of the risk of insufficient metameric extension, it could be proposed to use combined perispinal anaesthesia more regularly in this context.

The average dose of bupivacaine administered in our population was 10.8 ± 0.8 mg with extremes ranging from 10 to 12.5 mg. These results are similar to those found in other series (78,79,80,83).

Block Level

Several studies in the literature find a significantly increased risk of hypotension depending on the metameric level of anesthesia.

This level is identified at T6 for the study by Brenck et al. (84), T5 for the study by Ohpasanon et al. (85), and T4 for the study by Fakherpour et al. (77).

Pathophysiologically, an extensive metameric level is associated with a greater sympathetic block with a possible impact on the occurrence of low blood pressure.

B/Evolving Data

There is a statistically significant relationship between heart rate variation and vasopressor use.

Our results are comparable to those of Lucie L.(86) in France and Tchaou et al.(87) in Benin, who found that ephedrine caused more tachycardia than weakly diluted norepinephrine.

In addition, the use of large doses of ephedrine can have harmful maternal consequences such as the occurrence of supraventricular tachycardia or arrhythmias such as extrasystoles (88).
However, recent literature has found a more stable heart rate compared to ephedrine in patients receiving norepinephrine (89,90,91). This is in line with studies by Ngan Kee WD, Lee A, Khaw KS (99) and Mohta M, Janani SS, Sethi AK (100) showing the benefits of norepinephrine in maintaining better hemodynamic stability with less tachycardic effect and less side effect on heart rate compared to ephedrine. In addition, we also observed a superiority of weakly diluted norepinephrine in the management of low blood pressure in our study compared to ephedrine, which maintained a more stable and higher blood pressure than ephedrine after the initial decline. Our results are in line with those of Onwochei DN, Ngan Kee WD, Fung L (101) and Ngan Kee (102, 103, 104), demonstrating the usefulness of norepinephrine in maintaining better maternal cardiac output.
Also with regard to neonatal adaptation to ectopic life, weakly diluted norepinephrine has shown an advantage in maintaining blood pH at the umbilical cord compared to the use of ephedrine. However, there was no difference for Apgar scores at 1 and 5 minutes.
Many authors have reported low values of umbilical pH after ephedrine administration (91,92,93). These alterations in pH (higher lactates, high catecholamine dosages) were particularly marked when high doses of ephedrine were used (50 mg intramuscular or 3 to 4 mg/min intravenous) (91,94,103,104). A more recent meta-analysis finds this tendency to develop fetal acidosis as soon as the total dose of ephedrine is greater than 15–20 mg (95). Thus, the prophylactic administration of ephedrine does not effectively control hypotension during caesarean sections under spinal anaesthesia. In addition, it can have deleterious maternal and neonatal consequences.
Meta-analyses by Veeser et al and Xu et al showed that neonatal acidosis occurred more frequently with ephedrine than with weakly diluted norepinephrine (96,97). In addition, the ranking established by the meta-analysis of Singh et al suggested that ephedrine was the worst vasopressor in terms of neonatal cord base excess (98).
In 2015, Ngan Kee demonstrated that using norepinephrine results in better neonatal pH, lower catecholamine levels in umbilical vessels and a similar APGAR score (105). These results are supported by other publications by the same author (106,107).

C/Comparison between 8 mcg and 16 mcg of low-dilute norepinephrine

Our study found that the 16mcg dose showed a higher SBP but a lower heart rate than the 8mcg dose. This suggests that the 16 mcg dose may be more effective in maintaining SBP, but with an increased risk of bradycardia. The 8 mcg dose therefore appears to offer a better balance between efficacy on SBP and minimizing the risk of bradycardia.
Our results are in line with those of Vallejo MC, Attaallah AF, Elzamzami Y (102), exploring the optimal dosage of norepinephrine to prevent hypotension under spinal anesthesia, and she shows that low doses are sufficient to effectively stabilize blood pressure.

CONCLUSION :

Our study not only underlines the effectiveness of norepinephrine in terms of maternal hemodynamics but also demonstrates its safety of use by a non-inferiority in terms of neonatal pH.
Many still use ephedrine in doses exceeding the recommended doses, with deleterious effects on the newborn, although several studies now demonstrate the superiority of slightly diluted norepinephrine.

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