

Management of Arterial Hypotension Induced by Spinal Anesthesia during Cesarean Section at the Parakou University Hospital in Benin in 2020: Ephedrine versus Noradrenaline

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How to cite this paper: Tchaou, B.A., Massaoulé, S.B., Oriane, D.B.M. and Yapo, B. (2022) Management of Arterial Hypotension Induced by Spinal Anesthesia during Cesarean Section at the Parakou University Hospital in Benin in 2020: Ephedrine versus Noradrenaline. *Open Journal of Anesthesiology*, 12, 351-367.
<https://doi.org/10.4236/ojanes.2022.1212031>

Received: October 16, 2022

Accepted: December 18, 2022

Published: December 21, 2022

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Abstract

Background: Spinal anesthesia (SA) is a preferred anesthetic technique for childbirth through caesarean section. It causes a sympathetic block responsible for low blood pressure which can be prevented or treated with vasopressors. **Aim:** This research aims to compare the effect of Noradrenaline with that of Ephedrine in the management of arterial hypotension caused by SA during Caesarean act. **Study method:** It was a cross-sectional study with two comparative settings which took place at the Teaching hospital of Parakou from April 15th to August 15th 2020. It included all parturients who underwent a caesarian act and received spinal anesthesia. To prevent hypotension two groups were formed. The first group parturient received Noradrenaline (10 μ) as prophylactic and the second group received Ephedrine (10 mg) before anesthesia. The main evaluation criteria were the time before the hypotension occurs and, the secondary endpoint was the number of hypotension episode. The two groups were compared using the usual statistical tests. The study received the approval of the Local Ethical committee of University of Parakou. **Results:** Two hundred and four parturients were compiled with 102 in each group. The mean age was 28.37 ± 6.15 years with extremes of 16 and 45 years. The main indications for Caesarean section were respectively iterative Caesarean section (46.57%) for scheduled Caesarean section and acute fetal distress (15.69%) for emergency Caesarean section. The incidence of hypotension was 38.24%. The mean delay of occurrence of hypotension was sig-

nificantly longer in adrenaline group (19.90 min) than ephedrine group (12.53 min) with $P = 0.001$. According to the secondary endpoint the number of episodes of hypotension, number of tachycardia, and the total doses of each vasopressor were significantly lower in adrenaline group than in the ephedrine group. **Conclusion:** The use of Noradrenaline according to the established protocol demonstrated its efficiency compared with Ephedrine in the management of hypotension after spinal anesthesia.

Keywords

Spinal Anesthesia, Caesarean Section, Hypotension, Ephedrine, Noradrenaline

1. Introduction

Childbirth is the physical and psychological culmination of pregnancy. This is a way through which it leads to the reality of the childbirth and which is usually done via the downer route that is vaginal. However, in thousands of cases, and for multiple reasons related to either the mother or the newborn, the outcome is via the upper route: it is the caesarean act [1]. Thus, several anesthetic techniques are used to perform the cesarean act safely. Spinal anesthesia (SA) is the technique of choice for Caesarean delivery of parturient classified as ASA 1 and 2. It is an anesthetic technique that exposes the pregnant woman to fewer complications compared with general anesthesia (GA) [1]. By 2014, SA accounted for 60% of anesthetic techniques used for caesarean sections according to the French Society of Anesthesia and Intensive Care (SFAR) [2]. This anesthetic technique has three main effects: sympathetic block, sensory block and motor block. The sympathetic block is the major element that conditions hemodynamic stability and is responsible for low blood pressure, which secondarily leads to a decrease in uteroplacental flow [3]. This finding was made by Cowper *et al.* who reported that SA leads to maternal hypotension in 50% - 80% of cases [3]. Similarly, other authors have shown that SA-induced hypotension is thought to result from pre-ganglionic sympathetic block and therefore vasodilation [4] [5].

Numerous preventive and curative measures have been developed [6] [7], including the use of vasoconstrictors [1] [8]. Two sympathomimetic agents have been widely studied in different protocols. Ephedrine was the first vasopressor used in the management of post SA-induced hypotension, but it is not without consequences and is thought to be responsible for neonatal acidosis [4] [8].

Phenylephrine is currently the recommended first-line vasopressor with fewer side effects [9] [10] [11]. In obstetrics, there are other molecules in common practice that act on cardiac output and blood pressure, the principal one being Noradrenaline (NA). In 2015, Ngan Kee *et al.*, as well as other authors have reported using preventive norepinephrine versus phenylephrine similar effects of the two products [12] [13] [14] [15]. In Benin, it was assumed that Norepinephrine and Phenylephrine had similar effects and that Phenylephrine was more difficult to

access because of its high cost: 3500 FCFA (6.35 US dollars) by ampoule compared to 1200 FCFA (2.18 US dollars) by ampoule for Noradrenaline, it seems appropriate to initiate this study whose aim is to compare the effect of Noradrenaline to that of Ephedrine in the management of SA-induced hypotension during caesarean section.

2. Patients and Method

2.1. Study Framework

The operating rooms of the Gynecology-Obstetrics Department of the University Hospital of Parakou in Benin were used as a study setting. Six (6) obstetrician-gynecologists, 3 anesthesiologists and 18 nurse anesthetists are involved in this sector.

2.2. Study Method

Type and period of study: This was a non-randomized semi-experimental study comparing two intervention strategies with data collection carried out over a period of 5 months from April 15 to August 15, 2020. The protocol was submitted to the Ethics Committee of the Faculty of Medicine and approved according to the number (REF 0318/CLERB-UP/P/SP/R/SA).

Study population: It was made up of parturient who had undergone caesarean section under spinal anesthesia in the operating bloc of the Gynecology-Obstetrics Department of the Parakou University Hospital during the period of the study.

Inclusion criteria: Parturient classified as ASA 1 and 2 who underwent caesarean section under spinal anesthesia during the period of the study and who gave their informed consent or that of a close relative to participate in the study were included.

Exclusion Criteria: Patients who underwent caesarean section under spinal anesthesia and did not receive either of the two vasopressors used in the study were excluded.

Criteria for non-inclusion: Patients with high blood pressure (pre-existing or gestational), pre-eclampsia (regardless of severity) and who had a caesarean section were not included. The variables studied were of two orders.

The dependent variable: the occurrence of hypotension after administration of the local anesthetic (Bupivacaine).

The independent variables: grouped into sociodemographic data, clinical data, data related to the caesarean section, data related to the anesthesia and evolutionary data under vasopressors.

- Sociodemographic data: age, socio-professional category and marital status.
- Clinical data: patient history, temperature, blood pressure (BP), heart rate (HR), pulsed oxygen saturation (SpO₂), respiratory rate (RR), weight, height, body mass index (BMI) and ASA classification.
- Data related to Caesarean section: indication for Caesarean section, type of Caesarean section, time between induction and incision, time between inci-

sion and extraction, and duration of the procedure.

- Data related to anesthesia: pre-anesthetic consultation, qualification of the anesthetist, local anesthetic and adjuvants used, site of injection of the local anesthetic, plasma volume expanders and their doses, vasopressors (Ephedrine or Noradrenaline) and the doses used.
- Evolutionary data: vital constants (temperature, BP, RR, SpO₂, and HR), time to onset of hypotension after spinal anesthesia and number of hypotension episodes, number of boluses of the vasopressor and total dose used, and side effects observed.

2.3. Method of Data Collection

Collection tools: we used the patients' medical records, a pre-established survey form and the multipara meter monitor for intraoperative monitoring.

Collection technique: The data of each patient were collected by direct observation using a questionnaire that we filled in after consulting the medical records in preoperative care and follow-up in the operating theatre in intraoperative care.

Sampling procedure: A systematic recruitment of all patients who had a scheduled or emergency caesarean section during the study period and who met our inclusion criteria was carried out.

Collection procedure: On arrival in the operating room, the patients were positioned on the operating table in a lying position with left lateral inclination and the monitoring begun. Basic hemodynamic measurements: TA, HR, SpO₂, RR, ETCO₂, electrocardiography (ECG) were recorded using a multi parameter monitor. After measurement of the basic hemodynamic variables and complete disinfection of the puncture site, a 25 Gauge (25 G) lumbar puncture needle was inserted via a needle introducer in the interspinous space between L3 - L4 or L4 - L5 and exceptionally between L2 - L2 in the sitting position. After confirmation of the free flow of cerebrospinal fluid, a mixture of 7.5 - 10 mg of 0.5% hyperbaric Bupivacaine and 200 μ g of morphine was injected intrathecally, and the patient was returned to a supine position. The quality of the spinal anesthesia was evaluated by three criteria: sympathetic block, level of sensory block, and motor block. The sensory block was sought by the "hot-cold" test, while the motor block was assessed by the BROMAGE score. At the beginning of the intrathecal injection, rapid intravenous therapy with lactated ringer's solution or saline solution 0.9% was carried out using a large diameter catheter (G18 or G20 catheter). The choice of vasopressor to be administered to each patient and the blood pressure management protocol was recorded on the survey form and made available to the anesthetist. Thus, two groups with equal numbers of parturients were obtained, depending on the type of vasopressor used. The presentation of the two vasopressors and the administration protocol were as follows:

- **Noradrenaline tartrate 2 mg/mL** (Levophied®, Hospira, Inc., Lake Forest, IL, USA) 1 mg/0.5mL diluted in 10 mL syringes of SS 0.9% to give 10 gamma per mL.

- **Ephedrine Sulphate 30 mg/mL** (Ephedrine Sulphate®, Akorn, Inc., India), diluted in 10 mL syringes of SS 0.9% to give 3mg/mL Ephedrine.
 - Each patient in the NA group (Noradrenaline group) had received an intravenous prophylactic bolus of Noradrenaline 10 μ g at during the intrathecal injection of the local anesthetic, plus rescue boluses of Noradrenaline 10 μ g whenever maternal systolic blood pressure was less than or equal to 90 mm Hg.
 - Each patient in group E (Ephedrine group) received a prophylactic bolus of 10 mg of Ephedrine during the intrathecal injection of the local anesthetic, plus rescue boluses of 10 mg of Ephedrine whenever maternal systolic blood pressure was less than or equal to 90 mm Hg.

The number of boluses of vasopressors used apart from the prophylactic doses was recorded and considered to be the main outcome of the study. Heart Rate (beats/min) and Blood Pressure (mm Hg) were recorded every 2 min after intrathecal injection until delivery of the baby and then every 5 min until the end of the surgery.

Endpoint

The primary endpoint was the delay since vasopressor injection and the hypotension occurrence. Secondary we record the number of hypotension episodes, the tachycardia episodes, the need of vasopressor rescue, and the total doses of the vasopressor.

The side effects as hypertension, bradycardia, nausea, vomiting, headache, vertigo and other were recorded.

2.4. Data Processing and Analysis

All the data were entered twice in the EPI data 3.1 software and the data analyses using the Epi Info v7.2 software from the Center of Disease Control (CDC). Text entry and the creation of tables and graphs were done using Microsoft Office® 2013. The qualitative variables were expressed in terms of frequency, percentage with a 95% confidence interval. The quantitative variables were expressed in terms of mean and standard deviation in the case of normal distribution and in terms of median with interquartile range in the opposite case. The Chi-square test or the Fisher exact test was used to compare the percentages. The Student's t-test was used to compare averages. For these comparisons the significance threshold will be set at 0.05% or 5%.

3. Results

Sociodemographic data

During the period of study, 1025 parturients consulted the Gynecology-Obstetrics Department of the University Hospital of Parakou and among them 797 gave birth (77.76%). Three hundred and fourteen deliveries were performed by caesarean section, representing 39.40% of deliveries. According to our inclusion criteria we collected 204 patients (25.60%), divided into 2 groups of 102 patients

for Noradrenaline and Ephedrine respectively.

The average age of the study population was 28.37 ± 6.15 years with extremes of 16 and 45 years. The most represented age group was between 26 and 35 years old. Married or cohabiting women accounted for 94.60% of the study population ($n = 193$). Housewives numbered 90% or 44.17% of the sample. The data on other specific variables were described in the second column in **Table 1**.

Of the 204 parturients operated on, 159 patients (77.94%) had an ASA 1 score and 45 of them (22.06%) had an ASA 2 score.

Duration of the different phases of the Caesarean section

The average duration of the induction-incision phase (minutes) was 12.58 ± 7.36 with extremes of 2 and 75 minutes. The average duration of the incision-extraction phase (minutes) was 4.44 ± 4.42 with extremes of 1 and 34 minutes. The mean duration of the caesarean section (minutes) was 38.34 ± 18.04 with extremes of 13 and 153 minutes.

Data related to anesthesia

- Pre-anesthetic consultation and qualification of the anesthetist

In our series, 110 parturients (53.92%) got a pre-anesthetic consultation before the caesarean section was performed. The consultation was performed in 99.02% ($n = 202$) by the anesthetist nurses under cover of the anesthetist and intensive care doctors. On the other hand, 94 (46.08%) got a pre-anesthetic visit before the procedure was carried out.

- Anesthetic drugs and adjuvants used

Table 1. Characteristics of parturient at baseline.

	Population	Noradrenaline	Ephedrine	<i>P</i>
Age (years)	28.37 ± 6.15	26.71 (18 - 36)	29.67 (20 - 41)	0.047
Weigth (Kg)	72.30 ± 11.70	70.24 (54 - 138)	76.19 (48 - 120)	0.121
Height (m)	1.62 ± 0.04	1.61 (1.56 - 1.66)	1.63 (1.52 - 1.75)	0.103
Body mass Index (BMI)	27.33 ± 3.86	27.06 (21.63 - 53.91)	28.44 (19.72 - 43.87)	0.285
Temperature	36.57 ± 0.53	36.56 (36 - 37.7)	36.69 (36 - 38)	0.366
Pulse	93.49 ± 16.95	94.86 (68 - 120)	96.77 (66 - 145)	0.691
Systolic Blood Pressure	127.17 ± 11.20	129.86 (102 - 141)	121.14 (92 - 143)	0.005
Diastolic blood pressure	76.20 ± 11.08	75.24 (60 - 90)	73.04 (36 - 94)	0.450
Breath frequency	18.20 ± 1.68	17.62 (14 - 22)	18.32 (16 - 22)	0.085
Oxygen Saturation	98.60 ± 1.12	98.76 (96 - 100)	98.60 (95 - 100)	0.573
Type of caesarian				0.071
Planned		8 (38.10%)	36 (63.16%)	
Emergency		13 (61.90%)	21 (36.84%)	
Caesarian duration (min)	$40.37 (18 - 102)$	$40.52 (18 - 78)$	$40.18 (20 - 102)$	0.938

The local anesthetic used in the series was 0.50% hyperbaric Bupivacaine. The average dose administered was 9.95 ± 0.31 milligrams, with extremes of 8 and 10 milligrams. The adjuvant used in our series was morphine at a dose of 200 micrograms.

- Plasma volume expanders

For vascular pre-filling, Ringer Lactate was used in 98.04% (n = 200) and SS 9% was used in 1.96% of cases (n = 4). On the other hand, during co-filling, Ringer lactate was used in 97.55% of cases (n = 199) and SS% was used in 2.45% of cases (n = 5).

- Vasopressor doses used

The two vasopressors used in our series were Ephedrine and Noradrenaline. The average dose of Ephedrine (mg) used was 18.73 ± 9.41 with extremes of 10 - 50 mg. The average dose of Noradrenaline (mcg) used was 12.48 ± 4.56 with extremes of 10 - 30 mcg.

Outcome data

Incidence of bradycardia, tachycardia, hypotension and increased blood pressure

Hypotension appeared in 38.24% of cases (n = 78) after the prophylactic doses of vasopressor with an average onset time of 14.62 ± 8.38 minutes and extremes 1 and 46 minutes.

In the series of the study, additional boluses were administered to 20 parturients (19.60%) in the Noradrenaline group and 59 parturients (57.84%) in the Ephedrine group.

When we consider the patients with hypotension (n = 78) the data of each group were compared in **Table 2**. The parturient in adrenaline group was significantly younger and had a high baseline systolic blood pressure.

The primary endpoint parturient in Noradrenaline group had significantly long delay of hypotension occurrence, low number of hypotension episodes. On the other hand, they had received low doses of vasopressors and less episodes of tachycardia. The side effects were the same in both groups. Those data were summarized in **Table 2** and **Table 3**.

- Hypotension and maternal parameters upon installation

Table 2. Comparison of two groups according to endpoint in patients with hypotension.

	Noradrenaline	Ephedrine	<i>P</i>
Delay for hypotension occurrence	19.90 (10 - 46)	12.53 (1 - 31)	<0.001
Number episodes of hypotension	1.05 (1 - 2)	1.61 (1 - 5)	0.004
Number of hypertension episodes	0.05 (0 - 1)	0.21 (0 - 2)	0.113
Number of bradycardia episodes	0.10 (0 - 1)	0.02 (0 - 1)	0.121
Number of tachycardia episodes	0.10 (0 - 1)	0.98 (0 - 5)	0.002
Number of vassopressor bolus	1.00 (0 - 2)	1.54 (1 - 4)	0.002
Total dose of each vasopressor	20.48 (20 - 30)	25.44 (20 - 50)	0.003

Table 3. Comparison of the side effects in two groups.

	Noradrenaline	Ephedrine	<i>P-value</i>
Side effects			0.510
Nausea	4 (57.14%)	9 (32.14%)	
Vomiting	0 (0.00%)	6 (21.43%)	
Frissons	2 (28.57%)	5 (17.86%)	
Headaches	1 (14.29%)	7 (25.00%)	
Vertigo	0 (0%)	1 (3.57%)	

Table 4. Relationship between hypotension and maternal parameters upon installation.

	N	Hypotension		RP	IC _{95%}	<i>P</i>
		n	%			
SBP						
>125	121	37	30.58	0.62	0.44 - 0.87	0.008
≤125	83	41	49.48	1		
Heart rate						
>80	155	59	38.06	0.98	0.65 - 1.47	0.929
≤80	49	19	38.78	1		
BMI						
Obesity (≥30)	35	20	57.14	1.30	0.81 - 2.08	0.017
Overweight (25 - 29.99)	135	43	31.85	0.72	0.46 - 1.13	
Normal (18.50 - 24.99)	34	15	44.12	1		

Table 4 presents the relationship between the occurrence of hypotension and maternal parameters at the time of installation.

- Hypotension and time interval during the operation

There was a link between the onset of hypotension and the delay between induction and incision. **Table 5** shows the relationship between hypotension and time interval during the operation.

4. Discussion

Sociodemographic data

- Frequency of caesarean section

During the study period, we recorded 797 deliveries, of which 314 were caesarean sections (39.39%). The rate of caesarean delivery in the study is identical to that reported by Mongbo *et al.* who in a study conducted in 2016 in Cotonou had reported 37.6% of caesarean cases [16]. On the other hand, Atadé *et al.* in a study carried out in the same hospital in 2004, reported a caesarean section rate of 24.51% [17]. The high rates of caesarean section observed in this study and in

Table 5. Relationship between hypotension and time interval during the operation.

	N	Hypotension		RP	IC _{95%}	P
		N	%			
Time between induction and incision						
>15	46	25	54.35	1.62	1.15 - 2.29	0.015
≤15	158	53	33.54	1		
Time between incision and extraction						
>5	44	21	47.73	1,34	0.92 - 1.95	0.163
≤5	160	57	35.63	1		
Duration of the intervention						
>35	89	36	40.45	1.11	0.78 - 1.57	0.663
≤35	115	42	36.52	1		

the Mongbo study compared to the Atadé study could be explained by the fact that free cesarean section has become a reality in Benin since 2006.

- Age

The average age in our study was 28.37 ± 6.15 years with extremes of 16 and 45 years, and the most represented age group was that of patients aged 26 to 35 years (49.51%). This age range corresponds to the optimal age of fertility and this result was similar to those reported by Ali Elnabtity *et al.* in Egypt 2018 and Dyer *et al.* in South Africa in 2010 which were 27.04 ± 4.5 years and 27.1 ± 3.7 years respectively [18] [19]. On the other hand, in Liege, Belgium, the study conducted by Lecoq *et al.* in 2010 found a mean age of 39 years justified by the high frequency of late pregnancies often at risk requiring cesarean section for delivery [20]. We did not note any significant differences in age between the parturients of the two groups.

Clinical data

- ASA score

In the present study, 77.94% of parturients (n = 159) had an ASA 1 score. The same finding was made by Dembélé *et al.* in Mali (53.3%) [21]. In contrast, in France in 2015, Bordes *et al.* had reported that more than half of their patients had an ASA class greater than or equal to 2 [22]. This difference could be explained by the youth of our study population and young subjects being a prior carrier of less comorbidities.

- Weight

The average weight of the parturients was 72.30 ± 11.70 kg. This finding was also made by Xian Wang *et al.* in 2018 in China who had reported in their study a mean weight of 76.5 ± 8.1 kg [23]. In contrast, Lecoq in Liege had reported a mean weight of 65 ± 10 kg [20]. This difference could be explained by the eating habits and lifestyle in each region. However, the excess weight noted in the different studies can easily be explained by hormonal impregnation responsible for

water retention and consequently weight gain. This excess weight is confirmed by the average BMI of the parturients in the series, which was 27.33 ± 3.86 kg/m², and that of Vallejo *et al.* in a study carried out in the United States (33.6 ± 6.6 kg/m²) [24].

Data related to cesarean section

- Phases of the cesarean section

The mean time from induction to incision was 12.58 ± 7.36 minutes. There was a significant difference ($P < 0.001$) between the two groups with 12.82 and 12.34 min for the NA group and the E group, respectively. This difference could be explained by the delay in the onset of sensory block, related to the number of protein receptors (binding to α -1-acid glycoprotein (AGA)) to which Bupivacaine binds for inhibition of nerve impulse transmission along the axonal lipid membrane, a factor that varies from one individual to another and independently of the administration of the vasopressor.

- Time between incision and extraction

The mean time from incision to extraction was 4.44 ± 4.42 minutes. There was a significant difference ($P < 0.001$) between the two groups with 4.95 and 3.93 for the NA and E groups respectively. This difference could be explained by the ability and experience of the obstetrician to quickly perform the fetal extraction, this being independent of the vasopressor used.

- Duration of the procedure

The average procedure time in the study was 38.34 ± 18.04 minutes. This result differs from that of Ali Elnabity *et al.* who reported a mean duration of 50.1 ± 6.25 minutes [19]. This difference could be explained by the fact that Ali Elnabity's study only involved scheduled cesarean sections that are performed outside the emergency context.

Data related to anesthesia

- Frequency of spinal anesthesia

Out of 314 cases of cesarean section, 280 were performed under spinal anesthesia, *i.e.* 89.17%. This high rate of cesarean section under spinal anesthesia is intended to avoid complications related to general anesthesia. Indeed, the pregnant woman in the third trimester being considered as a subject with a full stomach, whether in emergency surgery or in scheduled surgery, is prone to many complications when the technique proposed in case of general anesthesia. Thus, hormonal impregnation and the decrease in pulmonary compliance during pregnancy are responsible for edema and hyper vascularization of the upper aerodigestive tract with a consequent increased incidence of difficult intubation. In contrast to this technique, spinal anesthesia offers the advantage of preserving the freedom of the airways during delivery and also allows the woman to experience this delivery in the same way as a vaginal delivery.

- Frequency of low blood pressure

Like any anesthetic technique, spinal anesthesia is not without consequences. Indeed, it induces three types of blocks: the sympathetic block, the sensory block

and the motor block. The sympathetic block is responsible for a pharmacological arterial hypotension. Thus, in the present study, out of 204 patients, 78 showed arterial hypotension, *i.e.* a rate of 38.24%. Our result is far lower than those observed in the literature where the rate of arterial hypotension induced by spinal anaesthesia is estimated to be between 55% and 90% [25] [26]. The systematic use of a prophylactic dose of vasopressor in our methodology could be the basis of this result with a low rate of arterial hypotension. The anticipation of management by the anesthesiologists through prophylactic doses of vasopressors is an attitude to be promoted and generalized to all the centers in Benin in order to improve the hemodynamic state of the patients during spinal anesthesia.

Anesthetic drugs and injection site

Hyperbaric Bupivacaine 0.50% was used with every patient at a mean dose of 9.95 ± 0.31 milligrams. Bupivacaine is a local anesthetic that reversibly blocks nerve conduction; moreover, due to its physicochemical properties, it has a duration of action of 3h - 3h 30 minutes, which allows sufficient analgesia during cesarean section, which is generally a medium-length procedure (45 minutes to 1 hour). Also the smaller volume of CSF in pregnant women (<1000 mL) justifies these low doses administered intrathecally [17].

Time to onset of arterial hypotension

The mean time to onset of hypotension was 14.62 ± 8.38 minutes. We had no significant difference between the two groups ($P = 0.513$). However, the mean time to hypotension in the E group was higher (8.51 minutes) than in the NA group (4.10 minutes); this may be explained by differences in the pharmacokinetic properties of the 2 vasopressors (short onset and duration of action of norepinephrine compared to ephedrine) [11].

Filling fluids and quantities

LR was used in 98% of cases for vascular filling in our study. This could be explained not only by its power of volume expansion [27], but especially the absence of risk of occurrence of hyperchloremic acidosis observed in case of use of SS 0.9% or allergic reactions in case of use of macromolecules.

- Qualification of the anesthetist

In this study, the majority of anesthetic procedures (99.02%) were performed by certified nurse anesthetists (IADE) under the supervision of a MAR. This predominance was also reported by Bonkougou *et al.* in Burkina-Faso in 2017, Diango *et al.* in 2013 in Mali and Chobli *et al.* in Togo in 2012 with frequencies of 71.60%; 91.90% and 93.71% respectively [28] [29]. This situation could be explained by the low number of anesthesiologists in sub-Saharan Africa in general and in Benin in particular.

Evolutionary data

- Maternal data: Bradycardia, tachycardia, arterial hypotension and hypertension

In our series, bradycardia occurred in 2.94% of the cases and would be due either to AR or to a side effect of the vasopressors used. A significant difference

was found between the two groups with a P value < 0.001 . The mean number of bradycardia was 0.07 and 0.02 in the NA and E groups, respectively. El Shafei *et al.* in 2015 in a comparative study between Noradrenaline and Ephedrine in patients with coronary artery disease had found that Noradrenaline is more effective than Ephedrine in maintaining BP with reduction in HR, which is beneficial in patients with coronary artery disease. Thus, they found a mean number of 3 in the norepinephrine group versus 0 in the ephedrine group [30]. Ali Elnabtity *et al.* in 2018 reported a mean number of 1 in the norepinephrine group, with no incidence in the second group [19]. This bradycardia observed in these different studies could be explained on the one hand by the pharmacological effect of Bupivacaine on calcium and potassium channels with effects on contractility and cardiac arrhythmias, and on the other hand by the direct actions of β_1 -adrenergic stimulation of Noradrenaline that may increase the heart rate, but this is maintained due to an overall neutral state due to reflex bradycardia by α -adrenergic stimulation.

- Tachycardia

The frequency of tachycardia was 24.51%. A significant difference was found between the two groups with a P value < 0.001 . The mean number of tachycardia was 0.25 and 0.64 in the NA and E groups, respectively. This result was close to that of Ali Elnabtity *et al.*, who also reported low incidences of tachycardia. In the E group, the mean number was 1 versus 0 in the NA group [19]. Indeed, Ephedrine is a synthetic sympathicomimetic, acting as an indirect agonist of β_1 adrenergic receptors and to a much lesser degree of α -receptors; thus, it leads to the release of endogenous norepinephrine by the postganglionic nerve endings of the orthosympathetic system. This explains why it increases the heart rate [31].

- Arterial hypotension

The mean number of hypo BP episodes in this study was 0.22 and 0.92 for the NA and E groups respectively; there was a significant difference with a P value < 0.001 . El Shafei *et al.* reported a mean number of 10 in the ephedrine group versus 6 in the norepinephrine group [30], Ali Elnabtity *et al.* and Hassani *et al.* reported a mean of 3 and 1.25 respectively in the ephedrine group versus 1 in the norepinephrine group [19] [32]. This higher incidence in the E group is explained by the slow onset of action of ephedrine compared to norepinephrine, allowing hypotension to occur more frequently. This shows that NA is more effective. In contrast to our results and those of these authors, Erkinaro *et al.* did not report a significant difference between the two groups in the maintenance of blood pressure with 10% for the Ephedrine group and 9% for the Phenylephrine group [33].

- Arterial hypertension

The mean number of occurrences of hypertension found in our series was 0.05 in the NA group and 0.15 in the E group. Ali Elnabtity *et al.* had reported a mean of high blood pressure: 2 in the Ephedrine group versus 1 in the Noradrenaline group [19]. This increases in blood pressure in the E group can be attri-

buted to a side effect of Ephedrine still referred to as dose-dependent reactive hypertension, and this is when the dose of Ephedrine is greater than or equal to 30 mg [31]. This finding highlights the superiority of the quality of Noradrenaline over Ephedrine.

- Additional Bolus

Additional boli in the study were a function of the onset of arterial hypotension. They were 19.60% in the NA group versus 57.84% in the E group. Thus, we noted a significant difference between the two groups, explained by the α -adrenergic effect and the weak β -adrenergic effect of Noradrenaline to maintain BP. This, once again, demonstrates the superiority of Noradrenaline in terms of consumption. Ali Elnabtity *et al.* had made the same finding but with a lower frequency, 3.27% and 4.92% for the NA and E groups, respectively [19].

- Observed side effects

With regard to the side effects observed, nausea was more frequently observed in the NA group (53.57%) than in the E group (46.43%). This finding could be explained pharmacologically by the antiemetic effect of Ephedrine [34].

- Factors associated with arterial hypotension

- Arterial hypotension and systolic blood pressure before induction

In the present series of studies, pre-induction SBP was associated with the occurrence of arterial hypotension ($P = 0.008$). Indeed, those who had a PAS lower than 125 mm Hg before induction had more episodes of hypotension. This finding was also made by Fakherpour *et al.* in 2018 [35] and could be explained by the fact that sympatholysis related to spinal anaesthesia would occur in terrain where the capacity to activate a sympathetic system in a very rapid manner could be impaired. These patients would then be at greater risk of arterial hypotension.

- Arterial hypotension and body mass index

A BMI ≥ 30 kg/m² was a factor associated with the occurrence of arterial hypotension in this study ($P = 0.017$). This relationship is also found in the literature, but the threshold for which the risk exists varies between 25 kg/m² and 30 kg/m² [35] [36]. We can therefore suggest that there is a tendency for obese people to have low blood pressure. Some studies also reveal an association between weight gain during pregnancy and the occurrence of hypotension after spinal anaesthesia. This is the case of the 2018 study by Fakherpour *et al.*, which showed a statistical association for weight gain of 11 to 20 kg [26]. This result on obesity could be due to insufficient dosage of initial vasopressor amines. Indeed, these are not administered according to the patient's weight. The dosage of amines may be insufficient in obese patients because of a larger volume of distribution, which may increase the incidence of arterial hypotension.

- Arterial Hypotension and Induction-Incision Time

The time between induction of spinal anaesthesia and incision appears in the present study to be a factor associated with the occurrence of hypotension. Indeed, a delay of more than 15 minutes increases the risk of occurrence of arterial

hypotension (RP = 1.62 95% CI [1.15 - 2.29] ($P = 0.015$)). This makes perfect sense that the longer the delay between induction and incision, the higher the probability of occurrence of arterial hypotension would be. One hypothesis could be that the occurrence of arterial hypotension is frequently at the time of initiation of the sympathetic block, when the patient's compensatory mechanisms have not yet been brought into play. It would be interesting to promote an effort of rapidity of the intervening parties: obstetrician.

5. Limitations of the Study

Our study has some limitations. On the one hand, the small number of parturients does not allow establishing a good correlation between the results. On the other hand, the execution of the protocol was done by several rotating teams whose practices differ from one team to another, with the exception of the doses of ephedrine and noradrenaline which were imposed on each team.

6. Conclusion

Spinal anesthesia is an anesthetic technique which has established itself over time as the best anesthesiological management for Caesarean sections. The only disadvantage is the hypotension it induces due to its pharmacological effects. It appears from this study that Noradrenaline is more effective than Ephedrine in the prevention and treatment of spinal anesthesia-induced hypotension during caesarean section with a maintained heart rate. The adoption of this product and the protocol for the prevention and treatment of hypotension is necessary to reduce the serious complications that are often responsible for death.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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