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Comparison of Crystalloid Preloading and Coloading for Prevention of Spinal-induced Hypotension in Cesarean Delivery: A Randomized Controlled Trial at a Tertiary Facility in Ghana

Amanda Quarshie[1], Audrey Anno[1], Robert Djagbletey[2], Pokua Sarpong[1], Daniel Sottie[1], Brenda J. Phillips[2], Phyllis Demi Lassey[2], George Aryee[2], Raymond Essuman[2], Ebenezer Owusu Darkwa[2]*

[1]Department of Anesthesia, Korle-Bu Teaching Hospital, Accra, Ghana; [2]Department of Anaesthesia, University of Ghana Medical School, Accra, Ghana

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***Correspondence:** Ebenezer Owusu Darkwa, Department of Anaesthesia, University of Ghana Medical School, Accra, Ghana. E-mail: eoddarquah@yahoo.co.uk
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Abstract

BACKGROUND: Spinal anesthesia is the recommended technique for cesarean section. It is easy to perform and provides a reliable, safe, effective, and fast sensory and motor block of high quality. Hypotension, which can be deleterious to both mother and baby, is however a common side effect. Preloading has not been shown to consistently prevent spinal-induced hypotension.

AIM: The aim of this study was to compare coloading with preloading using crystalloids for preventing spinal anesthesia-induced hypotension in parturients undergoing scheduled cesarean delivery.

MATERIALS AND METHODS: A single-blinded, randomized, and controlled study was conducted on 88 patients at term scheduled for elective cesarean delivery under spinal anesthesia at the Korle-Bu Teaching Hospital. Parturients were randomly assigned to receive a preload of 12.5 mL/kg of Ringer's Lactate (Group P) before the spinal anesthetic or a coload of 12.5 mL/kg of Ringers Lactate (Group C) at the time of the spinal procedure. Blood pressure, heart rate, incidence and timing of nausea and vomiting, and amount and frequency of vasopressor used were recorded for the first 10 minutes post-spinal anesthesia. Neonatal Apgar scores were determined at 1 and 5 minutes after birth.

RESULTS: The two groups were comparable with respect to age, weight, height, gestational age, ASA classification, baseline hemodynamic measurements, time to onset of hypotension, and time to delivery of baby post-spinal anesthesia. Post-spinal anesthesia changes in the heart rate, systolic blood pressure and mean arterial blood pressure were also comparable between the two groups. None of the patients in both groups experienced nausea or vomiting without hypotension. Although the cumulative dose of ephedrine to treat hypotension in the preload group was higher compared to the coload group, the difference was not statistically significant (16.3 vs. 12.4; p-value = 0.110).

CONCLUSION: Preloading and coloading with 12.5 mL/kg of Ringer's Lactate are comparable but neither is effective alone for preventing spinal-induced hypotension in the obstetric population. A vasopressor regimen is required to improve efficacy of the fluid load for preventing spinal-induced hypotension.

Introduction

Regional anesthesia and in particular, spinal block is the recommended anesthetic technique for cesarean section delivery [1], [2], [3]. Approximately 4000 cesarean sections are performed in Korle-Bu Teaching Hospital (KBTH) annually. Most (95%) of these cesarean sections are performed under spinal anesthesia [4]. Post-spinal hypotension occurs very frequently and if not actively prevented may be associated with maternal and fetal morbidity [5], [6]. The reported incidence of spinal anesthesia-induced hypotension in obstetric patients worldwide varies widely, from 55% to 85% [7], [8]. One study in West Africa reported an incidence of 23% [9]. Spinal-induced hypotension in obstetric patients can be severe and may result in maternal morbidity such as nausea, vomiting, and dizziness secondary to cerebral hypoperfusion. Hypotension may be associated with bradycardia progressing to cardiac arrest if poorly managed [1], [8]. Reduction in placental perfusion as a result of maternal hypotension may cause neonatal acidosis and reduction in Apgar scores [2], [8].

Hypotension is very common following spinal anesthesia for cesarean section, and without intervention, up to 90% of parturients may experience it [2], [6]. There is no consensus on the definition of spinal hypotension. However, it is commonly defined as systolic blood pressure of <80% of baseline or <100 mm/Hg or both in some literature. Other definitions use a fixed systolic blood pressure like 100 mmHg or 90 mmHg, below which hypotension is said to have occurred [6], [10].

Hypotension in obstetrics is more severe than in the general population [11], [12]. Factors responsible for this include progesterone-mediated increase in sensitivity

to subarachnoid local anesthetics, decreased sensitivity to endogenous vasoconstrictors, increased synthesis of endothelium-derived vasodilator, aortocaval compression, and decreased cerebrospinal fluid volume [11], [12].

Various methods of maintaining maternal hemodynamic stability including uterine displacement with the left lateral tilt, and physical methods to improve venous return like leg wrapping have been tried without consistent success [11], [13]. At present, fluid loading techniques and vasopressors are being used for preventing as well as treating spinal hypotension [11], [14], [15], [16], [17], [18], [19], [20], [21].

The type, volume, and timing of fluid load have been the subject of debate and study over several decades by anesthetists worldwide [5], [14], [22], [23], [24], [25], [26], [27], [28], [29], [30]. Crystalloid preloading (infusing a bolus of fluid over 20–30 min before the induction of spinal anesthesia) has been the traditional method of fluid loading for most anesthetists in accordance with findings from earlier studies [31]. This is currently the standard practice at the Korle-Bu Teaching Hospital.

In contrast, some studies suggest crystalloid coloading (infusing a bolus of fluid, over 10 min immediately after injection of local anesthetic) as a strategy for reducing spinal-induced hypotension because the administration of the fluid coincides with the onset of spinal nerve blockade when hypotension mostly occurs [7], [32], [33], [34], [35]. However, other studies have reported contrary findings on the effectiveness of coloading in preventing spinal-induced hypotension [36], [37].

Materials and Methods

Study design

This was a prospective, randomized, controlled, and single-blinded study.

Study site

The study was conducted at the KBTH, a tertiary referral center in Ghana. The KBTH has a 2000-bed capacity with over 6000 members of staff and 23 theater suites. The study was conducted in the three obstetric theatre suites of the hospital. Cesarean sections are performed daily, round the clock, approximately 4000 cases annually in obstetric theatre suites.

Study population

Pregnant women aged between 20 and 40 years with singleton uncomplicated pregnancies at term scheduled for cesarean delivery under spinal anesthesia were included in the study.

Pregnant women with a history of chronic or pregnancy-induced hypertension (PIH), diabetes mellitus, cardiovascular disease, cerebrovascular disease, known fetal anomalies, coagulopathy, and hematocrit < 30% were excluded from the study.

Sample size

A total number of 88 consecutively recruited pregnant women were randomized into two groups of 44 each (Group P: preloading and Group C: coloading).

Procedures

All the patients who participated in the study were assessed preoperatively at the pre-anesthesia clinic. Pregnant women were educated on the recommended standard pre-operative fasting guidelines to ensure that they were appropriately fasted before surgery. These women were assigned randomly generated serial numbers. Those who had even numbers were assigned to group (P) while those with odd numbers were assigned to group (C).

In the theater suite, each patient had a 16-gauge intravenous cannula inserted in the non-dominant hand and positioned supine with a left lateral tilt of 15° to reduce aortocaval compression. Standard non-invasive monitoring, including electrocardiography, blood pressure, and pulse oximetry, using GE® Dash 4000 monitor was instituted. Baseline values of systolic, diastolic, mean blood pressures, oxygen saturation of hemoglobin, and heart rates were recorded. Baseline blood pressure was calculated as the mean of three consecutive readings 1 min apart.

All patients received maintenance fluid at a rate of 4 mL/kg/h. Group P patients received 12.5 mL/kg Ringer's Lactate over 20 min immediately before initiation of spinal anesthesia. Group C patients received a rapid infusion of 12.5 mL/kg Ringer's Lactate over 10 min, starting at the time of dural puncture. Hypotension was treated with administration of additional fluid and intravenous ephedrine in all patients.

Spinal anesthesia was induced in the sitting position under strict asepsis at L3/L4 or L4/L5 intervertebral space. Skin infiltration with 2 mLs of 2% lidocaine was administered at intended site dural puncture. Intrathecal administration of 0.5% heavy bupivacaine (10mg) and 25 μg of fentanyl given over 15 s using a 25-gauge pencil-point spinal needle.

After spinal injection, patients were immediately placed in a supine position with a left lateral tilt of 15°. The extent of sensory block was checked every minute, using ice till a sensory level of T5 was achieved, after which surgery commenced.

The following parameters were checked every minute after spinal injection for 10 min: systolic blood pressure, mean blood pressure, heart rate, and pulse oximetry.

Maternal hypotension in this study was defined as systolic blood pressure < 100 mmHg or < 80% of baseline. This definition was chosen because below 80% of baseline systolic blood pressure, symptoms of hypotension such as faintness, nausea, and vomiting become apparent in patients [10]. Hypotension was treated with 5–10 mg boluses of intravenous ephedrine, and 100 mL boluses of extra crystalloid given till blood pressure returned to at least 90% of baseline. Bradycardia (HR < 50 bpm) was treated with 0.3 mg boluses of atropine and repeated if necessary.

The timing, number of doses, and the total amount of ephedrine used to treat hypotension was noted. Patients were observed and actively questioned for nausea or vomiting, and their timing also noted. After delivery of the baby, the mothers were given 10 IU of oxytocin by intravenous injection. A midwife, blinded to patients group, assessed the Apgar scores of the babies at 1 and 5 min after delivery.

Data analysis

Data were entered using the Microsoft Access® database, cleaned with Microsoft Excel®, and analyzed using IBM SPSS® (version 20). Independent t-test was used to compare demographic and health characteristics such as age, weight, height, and gestational age. Repeated Measures ANOVA was used in analyzing heart rate (HR), systolic blood pressure (SBP), and mean arterial blood pressure. Chi-square/ Fishers exact test was used in analyzing the association between categorical variables. A statistically significant level was set at alpha 0.05.

Ethical considerations

Approval to conduct the study was sought from the Ethical and Protocol Review Committee of the University of Ghana Medical School (Protocol Identification Number: MS-Et/M.2-P3.2/2014-2015). Written informed consent was obtained from all the participants before recruitment into the study.

Results

Eighty-eight pregnant women took part in this study. Forty-four were enrolled in the preload group (P) and 44 in the coload (C) group. The two groups were comparable with respect to age, weight, height, gestational age, and ASA classification (Table 1).

Table 1: Background characteristics of participants

Variable	Group		p-value
	Preload	Coload	
Age (years); mean (± SD)	30.7 (± 4.5)	30.2 (± 4.2)	0.510
Weight (kg); mean (± SD)	80.0 (± 16.3)	79.5 (± 15.8)	0.770
Height (cm); mean (± SD)	162.2 (± 8.5)	159.7 (± 10.0)	0.510
Gestational age; mean (± SD)	38.0 (± 1.3)	38.0 (± 1.6)	0.230
ASA status; n (%)			
II	33 (75.0)	37 (84.0)	0.290
III	11 (25.0)	7 (16.0)	

The differences between the baseline hemodynamic measurements between the two study groups were not statistically significant (Table 2).

Table 2: Hemodynamic parameters

Variable	Group; mean (± SD)		p-value
	Preload	Coload	
HR (beats/mins)	102.0 (± 15.0)	98.0 (± 14.0)	0.220
SBP (mmHg)	129.0 (± 16.7)	128.0 (± 11.4)	0.740
MAP (mmHg)	94.0 (± 11.0)	93.0 (± 10.0)	0.850

The time to onset of hypotension and time to delivery of the baby post-spinal anesthesia was not statistically significant between the two groups (Table 3).

Table 3: Time to onset of hypotension and delivery of the baby

Variable	Group		p-value
	Preload	Coload	
Time of intrathecal injection to delivery of the baby (min); mean (± SD)	13.0 (± 1.2)	16.0 (± 1.5)	0.700
Time to onset of hypotension post-spinal block (min); mean (± SD)	6.0 (± 0.2)	4.7 (± 0.5)	0.850

SD: Standard deviation

The mean heart rate changes between the two groups were comparable with the highest recorded at the 3rd to the 4th min post-spinal block. Although the preload group had a non-significantly higher baseline heart rate (Table 2), the coload group maintained a non-significantly higher heart rate compared to the preload group post-spinal anesthesia (Figure 1).

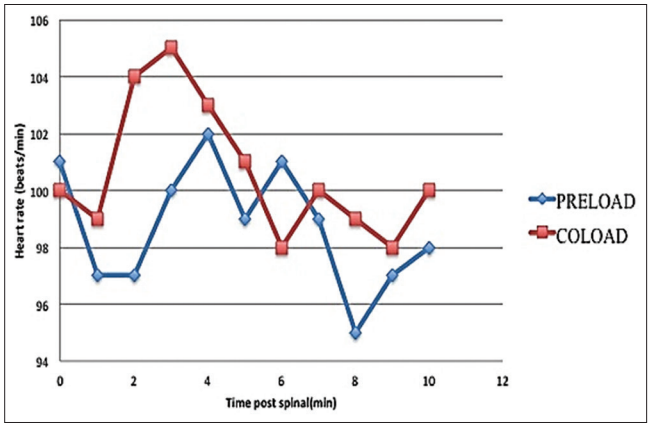

Figure 1: Changes in heart rate in the first 10 min post-spinal anesthesia

The mean systolic blood pressure changes between the two groups were not statistically significant ($p > 0.05$) with the lowest pressures recorded at the 3rd to the 4th min post-spinal block. The average drop in systolic blood pressure was comparable between the two groups (72% in the preload group and 75% in the coload group) (Figure 2).

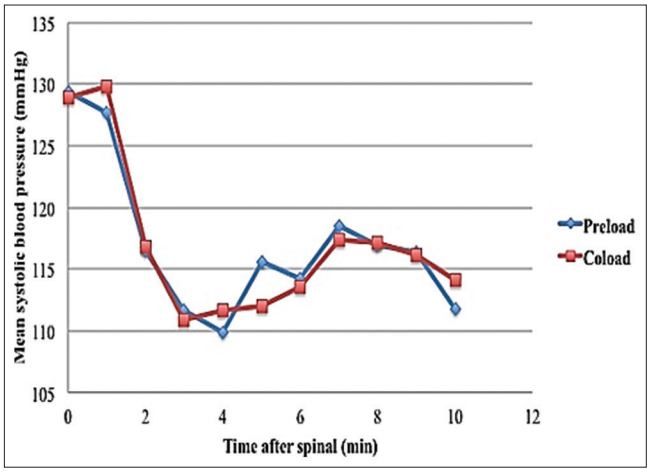

Figure 2: Changes in systolic blood pressure for the first 10 min post-spinal anesthesia

There was no significant difference in the variation of mean blood pressure between the two groups post-spinal anesthesia (Figure 3).

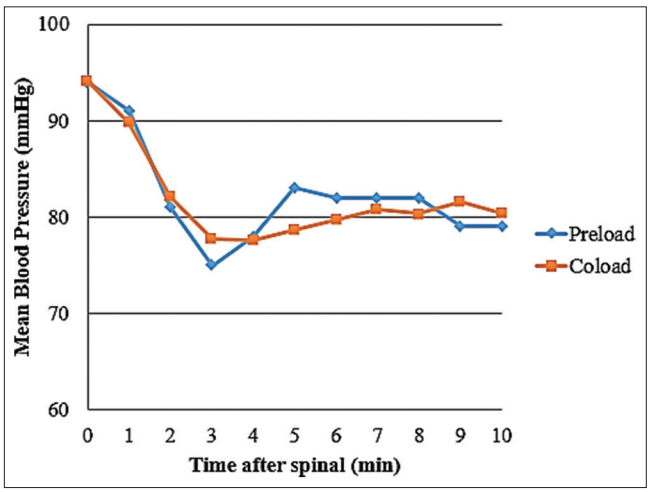

Figure 3: Changes in mean arterial blood pressure for the first 10 min post-spinal anesthesia

None of the patients in both groups experienced nausea or vomiting without hypotension. Of the patients who developed hypotension in the preload group, 19.4% experienced nausea. About 50% of those who experienced nausea in the preload group vomited (Table 4).

Table 4: Incidence of spinal hypotension, nausea, vomiting, vasopressor requirement, and neonatal APGAR scores

Variable	Preload	Coload	p-value
Hypotension			
Post-spinal hypotension, n (%)	31 (70.5)	23 (52.3)	0.080
Nausea and vomiting			
Nausea, n (%)	6 (13.6)	5 (11.4)	0.830
Vomiting, n (%)	3 (6.8)	5 (11.4)	0.220
Vasopressor requirements			
The average number of ephedrine boluses to treat hypotension	1.83	1.39	0.028*
Cumulative dose of ephedrine to treat hypotension	16.3	12.4	0.110
Neonatal APGAR Scores			
1 min	8.91	8.93	0.760
5 min	9.8	9.6	

*p<0.05: Statistically significant.

In the coload group, 21% of those who developed hypotension had nausea. All the patients (100%) who developed nausea in the coload group vomited (Table 4). Although the cumulative dose of ephedrine to treat hypotension in the preload group was higher compared to the coload group, the difference was not statistically significant (Table 4).

The oxygen saturation of hemoglobin remained normal for all patients who took part in the study, ranging between 97% and 100%.

Discussion

The two groups of patients studied were comparable in their demographic and health characteristics (Table 1).

Baseline systolic and mean arterial blood pressures were comparable between the two groups studied (Table 2). Hence, preloading with crystalloids did not result in a significant increase in blood pressure, as reported in other studies [28]. Baseline mean heart rates were high and normal in both groups reflecting the general hyperdynamic circulation state of pregnancy, but the difference between them was not significant.

Hypotension remains a major drawback of spinal anesthesia as the recommended anesthetic technique for cesarean section [1], [2], [3], [5], [6]. Studies comparing preloading and coloading in the obstetric population have reported widely varying incidence of hypotension.

Jacob *et al.* [30] and Banerjee *et al.* [14] in similar studies using crystalloid volumes of 15 mL/kg found non-significant differences in incidence of post-spinal hypotension between preloaded and coloaded patients. However, Oh *et al.* [35] using a similar volume of crystalloid and a smaller sample size found significant reduction in hypotension in coloaded patients.

Khan *et al.* [32] in a study comparing preloading versus coloading found the incidence of post-spinal hypotension to be 44% versus 70% which was statistically significant. Similarly, Dyer *et al.* [7] found an incidence of 60% post-spinal hypotension in the preload group and 36% in the coload group and was statistically significant. These studies administered crystalloid volume of 20 mL/kg. Bouchnak *et al.* [36] also using a crystalloid volume of 20 mL/kg in their study found a non-significant but high incidence of hypotension among preloaded (83.3%) and coloaded patients (96.7%).

In our study, the incidence of hypotension was lower in the coload group compared to the preload group: 52.3% versus 70.5%, respectively, though this difference was not statistically significant (p = 0.08). The differences in findings could be attributed to the differences in the definition of hypotension, volume of crystalloid administered, the timing and rate of

crystalloid infusion and sample size. The high incidence of hypotension in the preload group of this study supports previous evidence that preloading is generally ineffective at preventing or abolishing spinal-induced hypotension on its own [26]. A crystalloid preload redistributes quickly in the extravascular space. It increases blood volume and venous pressure transiently stimulating secretion of atrial natriuretic peptide, leading to peripheral vasodilation. This can cause preloaded fluid to be extravasated with increased excretion, so that at the time of onset of spinal mediated sympatholytic vasodilatation, only one-third of preloaded fluid remains intravascularly to boost the reduced venous return and prevent hypotension [14], [28].

Crystalloid coloading has been reported to decrease ephedrine requirement to maintain maternal blood pressure [7], [32], [35]. In this study, crystalloid coloading did not reduce ephedrine requirement of the patients. There was a significantly higher frequency of vasopressor use in the preload group most likely as a result of higher incidence of post-spinal hypotension observed in this group. However, the mean cumulative dose of ephedrine used to manage hypotension was not statistically significant between the two groups. This finding differs from that of previous studies where ephedrine requirements were significantly higher in the preload group compared to the coload group [7], [30], [32], [35]. The differences in findings could be attributed to the volume of crystalloid administered, the timing and rate of crystalloid infusion. Furthermore, the dose of ephedrine and frequency of dosing may have also contributed to the differences in cumulative dose of ephedrine required.

Maternal hypotension may be complicated by reduced uterine perfusion, feto-neonatal acidosis and low Apgar scores [38], [39], [40]. In this study, there was no significant difference in neonatal Apgar scores between the two groups. None of the newborns had an Apgar score below eight in either group at 1 and 5 min including those born to mothers who experienced hypotension. This observation is similar to findings in other studies [7], [14], [32] and supports the fact that transient spinal-induced hypotension which is treated promptly with vasopressor in healthy term pregnant women may not adversely affect neonatal outcome [7], [40].

Cerebral hypoperfusion secondary to hypotension underlies nausea and vomiting from spinal anesthesia. There was a relatively lower incidence of nausea and vomiting in this study in both preload and coload groups compared to other studies [7], [30], [32]. In this study, blood pressure was monitored at 1 min intervals for the first 10 min post-spinal and therefore, hypotension was promptly detected and managed with vasopressors thus preventing cerebral hypoperfusion that results in nausea and vomiting.

Nausea and vomiting were always associated with hypotension in this study, which supports the fact that these side effects are caused by decreased perfusion and hypoxemia of the chemoreceptor trigger zone in the brain as a consequence of reduced maternal blood pressure [38].

There was a wide variation in the weights of patients studied (48–98 Kg). Therefore, infusion of a fixed volume of crystalloid could have resulted in varying degrees of intravascular expansion for the patients studied. Infusion of crystalloids at a standardized volume of 12.5 mLs/kg resulted in a uniform expansion of the intravascular volume of the patients allowing for comparison between the study groups.

Hemodynamic measurements were done for the first 10 min post-spinal anesthesia. Occurrence of hypotension after this time was not recorded. However, the cumulative amount of ephedrine given for the entire duration of the surgery were recorded and analyzed.

Conclusion

Preloading and coloading with 12.5 mL/kg of Ringer's Lactate are comparable but neither is effective alone for preventing spinal-induced hypotension in the obstetric population. A vasopressor regimen is required to improve efficacy of the fluid load for preventing spinal-induced hypotension. Frequent monitoring (every minute) of hemodynamic variables after spinal anesthesia enables prompt recognition and treatment of hypotension with a vasopressor and ensures a good maternal and neonatal outcome.

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Authors' Contribution

Amanda Quarshie is a consultant Anesthetist of the Department of Anaesthesia, KBTH. The author designed the study. Robert Djagbletey is a Senior Lecturer and a consultant Anesthetist of the Department of Anaesthesia, University of Ghana Medical School, KBTH. He helped in preparing the manuscript. Ebenezer Owusu Darkwa is a Senior Lecturer and a consultant Anesthetist of the Department of Anaesthesia, University of Ghana Medical School, KBTH. He assisted in design of the study, analysis of the results and wrote the manuscript. Daniel AY

Sottie is a consultant Anesthetist of the Department of Anaesthesia, KBTH. He assisted in the design of the study. Brenda Phillips is a Consultant Anesthetist of the Department of Anaesthesia, University of Ghana Medical, KBTH. She assisted in the design, drafting of the study proposal and review of the manuscript. Phyllis Demi Lassey is a consultant Anesthetist of the Department of Anaesthesia, University of Ghana Medical School, Korle-Bu Teaching Hospital. He was involved in the study design and review of the manuscript. Audrey Anno is a consultant Anesthetist of the Department of Anaesthesia, Korle-Bu Teaching Hospital. She assisted with the data collection. Pokua Sarpong is a consultant Anesthetist of the Department of Anaesthesia, Korle-Bu Teaching Hospital. She assisted in the design of the study. Raymond Essuman is a research assistant of the Department of Anaesthesia, University of Ghana Medical School. He assisted in data collection, data entry and analysis of the study. George Aryee is a research assistant of the Department of Anaesthesia, University of Ghana Medical School. He assisted in data collection, data entry and analysis of the study. All authors read and approved the final manuscript.

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