



## **Effects of Delayed Spinal Anaesthesia Induction after Preloading on the Maternal Blood Pressure During Caesarean Deliveries.**

Afolayan Jide Michael,<sup>1</sup> Olaogun Oluwole Dominic<sup>2</sup>

<sup>1</sup>*Department Of Anaesthesia, Ekiti State University, Ado-Ekiti, Nigeria.*

<sup>2</sup>*Department Of Obstetrics And Gynaecology, Ekiti State University, Ado-Ekiti, Nigeria.*

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**Abstract: Background:** Unreported cases of severe hypotension and cardiac arrest had occurred in a few patients in our centre. This severe hypotension was traceable to delayed induction of spinal anaesthesia for more than one hour after crystalloid preloading has been administered.

**Objectives:** The study tested the hypothesis that hypotension during spinal anaesthesia becomes more severe when surgery and anaesthesia are delayed for an hour after initial administration of crystalloid preloading during spinal anaesthesia for caesarean section.

**Methods:** All the 100 parturients received 15ml/kg crystalloid preload within 15 minutes before induction of spinal anaesthesia, immediately parturients in group N (n=50) had spinal anaesthesia and 10 ml/kg normal saline infusion within 15 minutes following induction of subarachnoid block. Parturients in group D (n=50) had their induction of spinal anaesthesia deliberately delayed by one hour after crystalloid preloading had been administered, they also received 10 ml/kg normal saline infusion within 15 minutes following induction of subarachnoid block. Maternal haemodynamics, total rescue fluid and ephedrine used were documented.

**Results:** At 25<sup>th</sup> minute a significant amount of patients (45/90% versus 9/18%) in group D had hypotension compared to patients in group N, the difference was statistically significant ( $P < 0.001$ ). Total average rescue dose of fluid administered to manage hypotension was significantly higher in patients in group D than the one administered to patients in group N. The mean total dose of ephedrine that was consumed is significantly higher in parturients in group D ( $16.4 \pm 1.8$  mg) than in patients in group N ( $5.0 \pm 1.9$  mg).

**Conclusion:** This study showed that incidence of hypotension during spinal anaesthesia becomes more severe when surgery and anaesthesia are postponed for one hour after initial administration of crystalloid preloading during spinal anaesthesia for caesarean section.

**Keywords:** spinal anaesthesia, preload, coload, hypotension

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## I. INTRODUCTION

Crystalloid preloading is essential whenever spinal anaesthesia is about to be instituted.<sup>[1,2,3,4]</sup> Performance of a spinal block produces vasodilatation within the blocked area and a reflex vasoconstriction in unblocked areas of the body to maintain blood pressure.<sup>[1]</sup> Imbalance between vasodilatation and vasoconstriction is the most common mechanism underlying hypotension associated with spinal anaesthesia and occurs if the block is widespread or in the presence of hypovolemia, even with a limited block.<sup>[2,4,5]</sup>

Pathophysiologically, The mechanism for vasodilatation is blockade of the sympathetic nerve fibers at the preganglionic level by the local anaesthetic agent used.<sup>[6,7,8]</sup> It has been generally believed established that the sympathetic block extends one to two segments higher than the somatic level. However, recent results based on better methods for skin blood flow measurement using the laser Doppler technique have demonstrated that the extension of the sympathetic blockade correlates poorly with that of the somatic block.<sup>[3]</sup>

Patients with elective or emergency situation who has been worked up for caesarean delivery, who has been administered crystalloid preload, can have her caesarean section halted for more than one to two hours before her case could be revisited again. The reason for this temporary postponement may be is because of another patient requiring emergency surgery due to who may need very urgent care because of her critical and life threatening conditions. This patient, who has already been preloaded, will have to leave operating table and move to the waiting room. Based on our experience in our centre, patient may have to wait she can stay there for between 30 minutes and two hours before having the planned procedure done waiting for the caregiver to revisit her case. Although, it has not been not previously documented in the literature, delayed induction of spinal anaesthesia after crystalloid preloading during spinal anaesthesia for caesarean section can occur in obstetric practice, especially in resource poor countries with limited facilities and personnel. This can occur when obstetricians decide to abandon initial parturients scheduled for caesarean section and shift attention to another patient in more critical condition such as cord prolapsed, fetal distress, and obstetric haemorrhage. These obstetric emergencies can force any caregiver to shift attention from initial patient to the ones in critical conditions, which can also be life threatening. Delay in induction of anaesthesia can occur when progression to induction of spinal anaesthesia is halted for more than one hour after crystalloid preloading in parturients undergoing caesarean section. In some critical situations, patients in labour ward theatres who are scheduled for emergency or elective caesarean section and have had crystalloid preloading may have their anaesthesia and surgery delayed, for about 30 minutes to 2 hours, owing to the shift in attention of the care givers to another serious emergency condition in another parturients. This emergency obstetric condition in another patients may warrant the previous parturients, who had had preloading, to be abandoned for some time in the labour ward theatre. In this situations, the anaesthetists are seriously caught in the web of severe hypotension that may follow induction of anaesthesia in this group of patients with delayed induction of spinal anaesthesia following crystalloid preloading. Unreported cases of severe hypotension and cardiac arrest had occurred in some of these patients who had delayed induction of spinal anaesthesia after crystalloid preloading, despite the fact that a repeat preloading was administered to them before induction of spinal anaesthesia.

Based on our literature review, there were no research works on hypotension due to delayed induction of anaesthesia following preloading. There were no records of cases of severe hypotension and cardiac arrest after delayed spinal anaesthesia following administration of crystalloid preloading.

## II. MATERIALS AND METHOD

This was a prospective observational study. The study received Institutional Ethical Committee Research Review approval from Ekiti State University Teaching Hospital, Ado-Ekiti, Nigeria (protocol number: EKSUTH/A67/2024/05/007). The study was conducted in Ekiti State University Teaching Hospital, Ado-Ekiti, Nigeria between January, 2022 and December, 2023. Written informed consent was taken from each of the participants. This study was carried out on parturients planned for elective caesarean section under spinal anaesthesia. One hundred parturients of ASA physical status 1 or 2 scheduled for elective cesarean section under subarachnoid block were enrolled in the study. Exclusion criteria included age under 18 years, height

<150cm, weight <65kg, bleeding disorders, chronic hypertension, pregnancy induced hypertension, preeclampsia, eclampsia, known cardiovascular diseases, gestational age less than 36 weeks, packed cell volume of less than 30%, or any contraindication to spinal anaesthesia.

All patients were reviewed in the ward a day before surgery. Written informed consent was received directly from all patients who participated in the study. They were reliably informed that their procedure could be converted to general anesthesia if there was any failed or difficult spinal anesthesia.

One hundred women scheduled for elective caesarean section under subarachnoid block were recruited for the prospective observational study. The study population was randomized into two groups by picking opaque envelopes containing table of random numbers generated with a computer. A standard anaesthetic machine, multiparametre monitor, laryngoscopes and other resuscitating equipment and drugs were made available in the operating suite in case there was any urgent need to convert to general anaesthesia. All the parturients received 15ml/kg normal saline within 15 minutes before induction of spinal anaesthesia, immediately parturients in group N (n=50) had 10ml/kg normal saline infusion within 15 minutes following induction of subarachnoid block. Parturients in group D (n=50) had their induction of spinal anaesthesia and surgery deliberately delayed by one hour after crystalloid preloading, they also received 10ml/kg normal saline infusion within 15 minutes following induction of subarachnoid block. Maternal haemodynamics, total rescue fluid and ephedrine used were documented.

All patients received ranitidine 50mg and 10mg metoclopramide intravenously prior to surgery. For each of the patients, two 16G intravenous cannulae were put in place for the purpose of this study. Following the application of routine monitoring, non-invasive monitoring was commenced and documented including non-invasive blood pressure (NIBP), oxygen saturation ( $S_pO_2$ ), pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP). In each group each patient had a total fluid of 25ml/kg excluding rescue fluid. Induction of spinal anaesthesia was achieved with patients in sitting position. Their legs were hanging from the edge of the operating table with the support of a stool under their feet. They were asked to bend the neck forward and arch out their back maximally. Under aseptic condition, the spinal needle was introduced into the subarachnoid space. After withdrawing the stylet from the spinal needle, appearance of the free flow of cerebrospinal fluid in the hub of the needle indicated a successful placement. All patients received 2.5ml of 0.5% hyperbaric bupivacaine over 15s intrathecally in the L<sub>3-4</sub> or L<sub>2-3</sub> intervertebral space with a 25 G Quincke's spinal needle (Becton Dickson, Franch Lakes, NJ, USA). The patients were immediately put in supine position with a 15° left lateral tilt using wedge under the right hip. Sensory block height was assessed using loss of sensation to gentle pin prick test. A sensory block height of T6 was the minimum desired level of block for the commencement of the caesarean section. The following parameters: pulse rate, systolic blood pressure, diastolic blood pressure, and oxygen saturation were recorded every three minute for the first fifteen minutes, every 5 min for the next 15 minutes and every ten minutes thereafter till the end of surgery. Following the delivery of the baby, the mother was given 10 units of oxytocin intravenously, then she had infusion of 40 units of oxytocin in 500 mls normal saline to run for 4 hours.

Maternal hypotension was defined as a decrease in systolic blood pressure to less than 80% of the baseline systolic blood pressure or systolic blood pressure less than 90 mmHg. Hypotension was managed with intravenous fluid as first line of management as quick as possible whenever it was detected in the patients. However, some patients who had hypotension earlier might still have hypotension later intraoperatively despite intervention by the anaesthetists. Hence, the need to continuously monitor the blood pressure, up till 25<sup>th</sup> minute. Ephedrine in aliquots of 3 or 6mg, was administered whenever there were two consecutive readings of hypotension or hypotension was unresponsive to rapid fluid management. Total amount of rescue ephedrine and fluid administered were documented. Management of hypotension continued until systolic blood pressure recovered to the baseline reading.

Primary outcome measure was the incidence of maternal hypotension in each group. Additional data including onset of sensory block, side effects such as nausea and vomiting, bradycardia, back pain, itching and headache were recorded.

### III. STATISTICAL ANALYSIS

Quantitative and qualitative data were analysed using SPSS version 20. Data are presented as frequency and percentages. Tests of statistical significance were carried out using appropriate statistical tests. Chi Square and Fisher exact test was used to compare differences between proportions. The statistical tests were carried out at significance of less than 0.05. The primary objective of the study was to decrease the incidence of hypotension following induction of spinal anaesthesia from 40% reported by Desalu et al<sup>11</sup>, when preload was used alone, to 24% when combined loading (preload plus coload) is used in the presence of delayed induction of spinal anaesthesia. On the basis of this, a power analysis indicated that a minimum of 50 subjects per group would be sufficient to detect 40% difference, with a study power of 80% and  $\alpha=0.05$ .

### IV. RESULTS

A total of one hundred parturients: 50 in group N and 50 in group D were recruited for the study. Demographic and obstetric clinical variables were comparable among the study population as shown in Tables 1 and 2. As shown in Table 3, incidence of hypotension is higher at 5 min (5 versus 0), at 10 min (29 versus 3), and at 15 min (44 versus 6) among patients in group D compared to patients in group N, the difference at 10<sup>th</sup> or 15<sup>th</sup> minutes is statistically significant ( $P<0.001$ ). At 25<sup>th</sup> minute a significant amount of patients (45 versus 9) in group D had had hypotension compared to patients in group N, The difference is statistically significant ( $P<0.001$ ). Total average rescue dose of fluid administered to manage hypotension is significantly higher in patients in group D ( $841\pm480$  versus  $1015\pm529$ ) than the ones administered to patients in group N. The total fluid management is significantly higher in patients in group D ( $3571\pm320$ ) than in parturients in group N ( $2783\pm703$ ). Mean ephedrine dosage consumed is significantly higher in parturients in group D ( $16.4\pm1.8$ ) than in patients in group N ( $5.0\pm1.9$ ). Total blood loss were comparable among the participants.

### V. DISCUSSION

Our findings showed that incidence of haemodynamic shift lability is higher among patients who had delay in having induction of spinal anaesthesia after one hour of receiving one litre crystalloid preloading than in patients who had no delay. Patients in the normal group had no delay because they had their induction of spinal anaesthesia immediately after crystalloid preloading. Incidence of hypotension was significantly higher among parturients in group with delay than in parturients in normal group. Those in group with delayed spinal anaesthesia had their induction of spinal anaesthesia and caesarean section delayed for one hour after crystalloid preload had been administered.

In our centre, few unreported cases of severe hypotension and even cardiac arrest had occurred in some patients who had had crystalloid preloading but were abandoned as a result of shift in attention to other patients who needed more urgent attention. For instance, anaesthetists might have positioned a pregnant woman billed for caesarean section on operating table in the theatre. The team of anaesthetists might have administered fluid preloading to the pregnant woman. All of a sudden, news can filter into the operating room that the caesarean section should be put on hold because of the urgent need to attend to another pregnant woman in critical condition who may also need urgent caesarean section due to life threatening situations in the mother, baby or both. We carried out our study because of the fact that it has not been studied in the past and owing to the life threatening conditions associated with this kind of spinal anaesthesia after a delay of more than 30 minutes following administration of crystalloid preload.

Pathophysiology of the severe hypotension resulting from this fluid management is traceable to its effect on extracellular fluid volume (ECF).<sup>[7,8]</sup> There is increase in diuresis whenever extracellular fluid volume is expanded.<sup>8</sup> This expansion of ECF volume usually occurs whenever fluid preloading or coload is taking

place. This increase in ECF volume then triggers activities of Atrial Natriuretic Peptide to cause diuresis in order to reduce the extracellular fluid volume to its original state or below its original state. Its effect can be milder on the patients billed for surgery. Its effect is usually aggravated on the patients who might have suffered delay in having their caesarean delivery after crystalloid preloading has taken place. In some situations caesarean section can be delayed for more than 30 minutes, even up to 2 hours after administration of fluid. In some cases, operating procedures can be delayed as long as two hours, giving rise to continuous activities of Sodium Natriuretic Peptide and diuresis which may reduce the extracellular fluid volume to below normal level. In view of this delay, it is reasonable to administer another crystalloid preload to prevent incidence of severe hypotension in this group of patients. Apart from this, ephedrine must be on standby, diluted and made available should the patient need urgent intervention to treat her hypotensive condition. It was observed in our study that in most patients in this category that additional preloading, prior to caesarean section, did not ameliorate the incidence of severe hypotension in them. In these patients, additional vasoactive agents were also administered to them.

Atrial Natriuretic Peptide (ANP) or atrial natriuretic factor is a natriuretic peptide hormone secreted from cardiac atria in human. The main function of ANP is causing a reduction in expanded extracellular fluid ECF volume by increasing renal sodium excretion.<sup>[7,8,9]</sup> ANP is synthesized and secreted by cardiac muscle cells in the walls of atria in heart. These cells contain volume receptors which respond to increasing stretching of the atria walls due to increased atrial blood volume.<sup>[8]</sup> Reduction of blood volume by ANP can result in secondary effects, such as reduction of extracellular fluid volume, improved cardiac ejection fraction with resultant improved organ perfusion, decreased blood pressure and increased serum potassium.<sup>[7,8]</sup> Over time, these secondary effects may be blunted or negated by various counter-regulatory mechanisms operating concurrently on each of these secondary effects. Modulation of the effects of ANP is achieved through gradual degradation of the peptide by the enzyme neutral endopeptidase.<sup>[7,8,10]</sup>

According to this present study, a significant amount of patients (45 versus 9) in group D had severe hypotension compared to patients in group N, The difference is statistically significant ( $P < 0.001$ ). Total average rescue dose of fluid administered to manage hypotension is significantly higher in patients in group D than the one administered to patients in group N. The total fluid management is significantly higher in patients in group D than in parturients in group N. Mean ephedrine dosage consumed is significantly higher in parturients in group D than in patients in group N. Total blood loss were comparable among the participants.

In the study conducted by Bishop and colleagues, they found that the overall incidence of obstetric spinal anaesthesia induced severe hypotension to be 30.4% despite the use of crystalloid preloading and without any form of delay. According to Zwane et al.<sup>[6]</sup> they reported 33% incidence of spinal anaesthesia induced severe hypotension, even with the help of preloading. In Asia, a study conducted by Ataousa and colleagues<sup>[9]</sup> in 2008 reported incidence of spinal anaesthesia induced severe hypotension to be 40%. Desalu et al.<sup>[11]</sup> in an independent study in Nigeria reported incidence of spinal anaesthesia induced severe hypotension to be 40%. However, in our present study, in the normal group, the incidence of spinal anaesthesia induced severe hypotension was much lower (18%) than the incidence observed in above-cited the different studies of Bishop et al, Zwane et al, Ataousa et al and Desalu et al. The difference between our study and other studies was probably because both preload and coload were used to manage the incidence of hypotension in our study, unlike these other studies that utilized only preloading.

Afolayan et al.<sup>[10]</sup> had earlier documented that the use of combined therapy of preload and coload in the management of hypotension following spinal anaesthesia is significantly better than when only preload or coload is administered.<sup>[10]</sup> In our study, the incidence of spinal anaesthesia induced severe hypotension was very high (45/90%) among patients who had delay of one hour in instituting spinal block after crystalloid preload had been given. However, there was no morbidity and mortality among the study participants. Some authors<sup>[12-15]</sup> were of the opinion that maternal hypotension following spinal anaesthesia for caesarean section can occur in up to 80% without prophylactic measures. They recommended that in order to avoid morbidity and mortality, among pregnant women scheduled for caesarean section, adequate prophylactic measures must be put in place.

Delayed induction of spinal anaesthesia following crystalloid preloading can exacerbate the hypotensive state induced by spinal anaesthesia. There is need to put some resuscitative equipment and drugs on stand by whenever such situation is envisaged.

The limitation of this present study is premised on the fact that in Nigeria and any other country, there is no data about the incidence of severe hypotension occasioned by delay in induction of spinal block after about one hour to two hours of administering crystalloid fluid. We did not have previous works on this subject matter to compare with our work. There is need to carry out further research in the future to determine the correlation between period of delay and the incidence of severe hypotension in this group of people.

## VI. CONCLUSION

This study showed that incidence of hypotension during spinal anaesthesia becomes more severe when surgery and anesthesia are postponed for one hour or more after initial administration of crystalloid preloading during spinal anaesthesia for caesarean section. In view of this delay, it is reasonable to administer another crystalloid preload to prevent incidence of severe hypotension in this group of patients. Apart from this, ephedrine must be on standby, diluted and made available should the patient need urgent intervention to treat her hypotensive condition.

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Table 1: Patients demographic characteristics

	Group N (n=50)	Group D (n=50)	p. value
Age (year) ( M/SD)	30.0 ± 6.5	29.0 ± 5.9	0.83
Weight (Kg) ( M/SD)	72.5 ± 11.8	70.1 ± 15.3	0.47
Height (cm) (M/SD)	158.6 ± 3.1	160.0 ± 6.2	0.70
Prenatal Status:			
Booked (N/% )	50/100	50/50	1.0
Elective (N/%)	50/100	50/100	1.0
Gestational age (wks) ( M/SD)	37.5 ± 1.6	38.2 ± 1.3	0.97
Parity:(N/%)			
Nulliparous	22/44	20/40	0.65
Multiparous	28/56	30/60	0.83
Singleton	50/100	50/100	1.0

Table 2: Intraoperative clinical variables

Parametre	Group N (M/range)	Group D (M/Range)	P.value
Duration of fluid preload (min)	10 (9-13)	11(10-12)	0.830
Preloading-incision time (min)	10 (7-11)	70 (65-71)	0.003
Induction – delivery time (min)	32 (17-35)	31 (15-33)	0.841
Block height (seg)	T4 (T3-T4)	T4 (T3-T4)	1.000
Duration of anaesthesia (min)	94 (86-105)	91 (82-111)	0.870
Duration of Surgery (min)	49 (48-58)	51 (39-55)	0.652
Duration for induction of anaesthesia	13 (8-16)	11 (9-15)	0.819
APGAR Score (1 min)	8 (8-10)	9 (6-10)	0.741

APGAR Score (5 min)                      10(8-10)                      10 (8-10)                      1.000

Table 3: Haemodynamic variables and intravenous fluid management

Parameter	Group N (n=50)	Group D(n=50)	P.value
Incidence of hypotension (N/%):			
At 5th min.	0/0	5/10	0.0668
At 10 <sup>th</sup> min.	3/6	29/58	0.0002
At 15 <sup>th</sup> min	6/12	44/88	0.0002
At 25 <sup>th</sup> min	9/18	45/90	0.0063
Rescue fluid (ml) (M/SD)	841±480	1015±529	0.0071
Total fluid (ml) (M/SD)	2783±703	3571±320	0.0839
Mean ephedrine used (mg)	5.0±1.9	16.4±1.8	0.0484
Total blood loss (M/SD)	552.34±33.3	600.2±67.5	0.5730