

A Randomised Prospective Double Blind Study to Compare The Effects of Fluid Preloading and Co-Loading During Spinal Anaesthesia for Caesarean Delivery.

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ABSTRACT

Background: Spinal anaesthesia (SA) induced hypotension can result in reduced uterine blood flow and cause foetal hypoxia and acidosis. We performed this prospective, randomized, double-blind study to assess the efficacy of crystalloid coload over preloading in reducing the incidence of hypotension. **Methods:** Forty parturients scheduled for elective caesarean section were randomized in two groups: Group P (preload with Ringer's Lactate (RL) 20 ml/kg over 15-20 minutes before SA) or Group C (coload with RL 20 ml/kg over 15-20 minutes at the initiation of spinal anaesthesia). Haemodynamic parameters were recorded at baseline, at 2 min for the first 20 min and then at every 5 min till the end of surgery. Secondary outcome in terms of incidence of nausea and vomiting, pre-delivery ephedrine requirements and neonatal outcome were noted. **Results:** Demographic, anaesthetic, surgical and baseline haemodynamic characteristics were comparable between two groups. The incidence of hypotension (P=0.07), lowest mean systolic Blood Pressure recorded (p=0.44), and incidence of nausea and vomiting (group P: 20% vs group C: 5%) were comparable statistically. However, the incidence of hypotension was 40% in group P as compared to 15% in group C (p<0.05), total mean dose of ephedrine required in group P was 0.80 ± 0.83 and in group C (Coload) was 0.65 ± 0.74 with p value >0.05. The incidence of tachycardia was significant (p<0.008) in preloaded parturients. Neonatal characteristics were similar in the two groups. **Conclusion:** Coload imparts a better maternal haemodynamic stability as compared to preloading.

Keywords: Hypotension, Spinal Anaesthesia, Caesarean Section, Crystalloid Preloading, Coload.

INTRODUCTION

Spinal anaesthesia is commonly used for Caesarean delivery and hypotension is the commonest serious problem following spinal anaesthesia. The reported incidence is upto 85%^[1], if severe, it can be associated with maternal and foetal morbidity. Maternal hypotension lasting more than 2 min may be associated with lower Apgar scores.^[2,3] Hypotension is caused by an increase in venous capacitance and reduction in systemic vascular resistance. On the other hand, uterine blood flow is dependent on perfusion pressure, so the reduced blood flow due to hypotension, leads to compromise in foetal oxygenation.^[4,5] Anaesthetic texts continue to emphasize methods for the prevention of hypotension, for example, leg wrapping, anti-thromboembolic stockings, patient positioning, fluid and vasopressor administration as prophylactic measures to reduce the incidence of hypotension.^[6-9]

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However, the incidence of hypotension was not much reduced with the prior rapid intravenous fluid administration (20 ml/kg over 10 min compared to 20 ml/kg over 20 min)^[6,10] with the suggestion that the fluid given as pre-hydration was unlikely to

have much impact.^[10-12] Afterwards, an alternative technique emerged with the concept of fluid administration at the initiation of spinal anaesthesia; the Co-loading.^[13] Crystalloid has short intravascular half life and gets rapidly redistributed into interstitial space.^[13-17] Moreover, preloading may induce the release of atrial natriuretic peptide (ANP), resulting in peripheral vasodilatation followed by an increased rate of excretion of the preloaded fluid, hence increased incidence of hypotension.^[17] Crystalloid co-load technique appears to be superior to preload, as the co-load provides additional intravascular fluid at the time of maximal vasodilatation.^[13-16] Thus, the aim of this study is to test whether crystalloid coload is more effective than the crystalloid preload in reducing the spinal induced hypotension. We designed a prospective randomised double blind study to compare the incidence of hypotension in women undergoing Caesarean delivery under spinal anaesthesia, who received crystalloid solution both as volume preload and volume coload. Secondary outcomes included the severity of hypotension, need of vasopressors, as well as the incidence of nausea and/or vomiting and neonatal outcome.

MATERIALS AND METHODS

After approval by Board of Studies, Institutional ethical committee and written informed consent from all patients, we designed a randomised prospective double blind study in 40 parturients

scheduled for elective caesarean section. Exclusion criteria include: patients having pregnancy-induced hypertension, chronic hypertension, multiple gestation, known foetal compromise, diabetes mellitus, polyhydramnios, weight >100 kgs, height <140 cms, major systemic disease, anaemia (haemoglobin concentration <8 gm/dl), clotting diathesis or any contraindication to spinal anaesthesia. Parturients were assigned to one of the two groups having 20 patients each. The enrolment of patient into the study was done by opening sealed opaque envelopes that had been sorted by computer generated random allocation. Group P patients received volume Preloading with crystalloid, @20 ml/kg in over 15-20 min, before spinal anaesthesia. Group C received volume Coload with crystalloid, @20 ml/kg with initiation of spinal anaesthesia.

On arrival to the operating room, 18G intravenous cannula was placed on the arm / hand of the patient. Patient did not receive any IV fluid or premedication before entering the study as per study protocol. In the operating room, the patients were placed comfortably in supine position with the wedge under right hip in order to give left uterine displacement and monitored by automated non-invasive arterial blood pressure (NIBP), and peripheral pulse oximeter. Baseline Blood pressure (BP) was calculated after taking mean of three consecutive readings during which the systolic blood pressure (SBP) does not vary by more than 10% from the average value.

The patient, the anaesthesiologist performing the subarachnoid block, collecting the data, and treating the side effects, and the paediatrician assessing the neonatal outcome were unaware of the patient's group assignment. A two-operator technique was used to maintain blinding. The principal investigator recorded the baseline haemodynamic variables, left the Operating Room (OR), and re-entered the OR immediately after initiation of anaesthesia. The second investigator administered the fluids and spinal anaesthetic and had no role in patient assessment. Bags of IV fluids and the proximal part of the IV tubing were covered with an opaque cloth and shielded from the outcome assessor's view. Haemodynamic parameters were recorded at baseline, at 2 min interval for the first 20 min and then at every 5 min interval till the end of surgery. Vasopressor were administered by an anaesthesiology resident blinded to group assignment whenever the SBP decreased 25% from baseline. Data were later coded and entered into a computer by a resident doctor blinded to patient allocation.

All patients received Metoclopramide 10mg i.v. and Ranitidine 50mg i.v. as premedication. The lumbar area was prepared aseptically and draped. Spinal anaesthesia was initiated in the sitting position at the L2-3 or L3-4 interspace with 26G

Quincke's spinal needle. 0.5% hyperbaric bupivacaine 12.5mg (2.5 ml) was administered after cerebrospinal fluid was seen. Parturients in both groups were promptly placed in the supine position with 15 degree left lateral tilt, and supplemental oxygen was delivered at 6lt/min through facemask. After preloading and coload, as per randomization, all patients were given lactated Ringer's at a rate of 10ml/kg/hr per-operatively. The principal investigator, who was blinded to patient group allocation, evaluated hemodynamic status and spinal anaesthesia characteristics.

All patients were observed for any change in heart rate and blood pressure. Bradycardia (Heart Rate < 50 beats/min) was treated with inj. Atropine 0.5 mg IV bolus. Hypotension was considered if systolic BP fell below 90 mm of Hg or > 25% of the baseline SBP value. Intraoperative hypotension was treated with intermittent boluses of Inj. Ephedrine (6 mg i.v stat) every time. Vasopressor treatment was repeated every 1 min if hypotension persisted or recurred. Smaller decreases in BP were similarly treated if accompanied by nausea, vomiting, or dizziness. An additional rapid bolus infusion of lactated Ringer's solution was administered at the time of hypotension (approximately 100 ml at each episode of hypotension).

The cephalad extent of sensory blockade was assessed first at 2.5min then at every 5 min after intrathecal injection. Onset of Sensory block was tested with pinprick discrimination (with tooth pick) method, the shin corresponding to L4 level. Height of sensory block was tested starting at L4 level and ascending above with a tooth pick. Surgery was allowed to proceed after T6 sensory blockade was established. Motor blockade was assessed by MODIFIED BROMAGE SCALE at every 5 min interval by an independent observer. 0--Able to move hip, knee and ankle, 1--Unable to move hip, able to move knee and ankle, 2--Unable to move hip and knee, able to move ankle and 3--Unable to move hip, knee and ankle. Regular monitoring of Blood pressure (BP) and Oxygen saturation (SpO₂) was done at 2 min intervals for the first 20 min and then at 5 min intervals. The doses of vasopressor required and foetal characteristics (Apgar score at 1 min and 5 min) were noted by independent observer who was unaware about the study. The study period was started when the patients in preload group started receiving their preload and finished at the end of skin closure. After delivery of the baby, 5 IU of oxytocin was given I.V. and 15 IU was added to 500 ml normal saline solution given within one hour.

Statistical analysis

Sample size was computed on considering the incidence of hypotension as primary outcome. While considering the 25% difference in the mean

arterial pressure during the first 10 min after initiation of anaesthesia as a clinically significant end-point and assuming $\alpha= 0.05$ 2-sided, $\beta= 0.2$ (i.e., 80% power), 18 subjects per group were required. Hence we have taken 20 parturients in each group. The following tests were used to compare data between the two groups: Student's t-test for patient demographics, and other parametric data; Chi square test for nonparametric data. All statistical analyses were performed using Excel 2007TM (Microsoft, Redmond, WA). Data were expressed as mean \pm SD unless otherwise stated. A P value of < 0.05 was considered significant.

RESULTS

Forty patients were recruited from April 2010 to September 2010. All subjects were successfully enrolled, received treatment as allocated and completed the study. No failed/inadequate block was recorded. There were no dropouts. The groups were similar with respect to age, weight and height, anaesthetic or surgical characteristics [Table 1]. The baseline hemodynamic characteristics including SBP, Diastolic blood pressure (DBP), Mean arterial pressure (MAP) and Heart rate (HR) were statistically comparable in both the groups ($p>0.05$).

Median height of sensory block attained was at the level of T5 dermatome in both the groups with range varying from (T3-T6) and (T2 -T6) in preload and coload groups respectively which were comparable statistically [Table 1]. Onset time of mean maximal sensory block achieved in both the preload and coload groups were 8.2 ± 0.4 mins and 7.4 ± 0.2 mins respectively which were found to be statistically insignificant. Time of onset for maximal motor block achieved was 4.6 ± 2.2 mins in preload group and 4.0 ± 1.4 min in coload group which were also found to be statistically insignificant [Table 1].

The mean systolic BP in preload patients was increased and does not required inj. Ephedrine for the first 5 minutes of spinal anaesthesia, but this increase was not sustained after 5 minutes and peak decline in SBP was noted at 6 min after induction of spinal anaesthesia. However, in case of coload group after initiation of spinal anaesthesia, mean systolic blood pressure was gradually decreasing for the first 5 min but it was well maintained for the next 10 or 20 min after spinal anaesthesia [Figure 1]. The incidence of hypotension was 40% (8/20) in preload group as compared to 15% (3/20) in coload group. The mean maximal fall in systolic blood pressure was 86 ± 7 mmHg in preload group and 88 ± 8 mmHg in coload group, which was statistically insignificant ($p>0.05$) [Table 2].

Table 1: Demographic, Sensorimotor and hemodynamic characteristics {mean \pm SD, median (range)}

Characteristics	Group P	Group C	P value
Age (yrs.)	24.7 \pm 2	25.4 \pm 2	0.74
Height (cms.)	153.6 \pm 2	153 \pm 2	0.63
Weight (kgs.)	53 \pm 2	53.6 \pm 2	0.56
Baseline SBP (mm of Hg)	115.4 \pm 5	116.6 \pm 4	0.60
Baseline DBP (mm of Hg)	74.2 \pm 4	78.4 \pm 4	0.97
Baseline MAP (mm of Hg)	87.8 \pm 4	90.9 \pm 4	0.93
Baseline HR (/min)	108.8 \pm 4	103 \pm 6	0.98
Height of sensory block	T5 (T3-T6)	T5 (T2 -T6)	0.871
Time to maximum sensory block (min)	8.2 \pm 1.57	7.4 \pm 1.63	0.931
Time to maximal motor block (min)	4.6 \pm 1.46	4.0 \pm 1.71	0.284

Table 2: Parameters after spinal anaesthesia {mean \pm SD}

Parameters	Group P	Group C	P value
Incidence of Hypotension	40%	15%	0.07
Lowest SBP (mm Hg)	86 \pm 8	88 \pm 7	0.44
Lowest DBP (mm Hg)	71.3 \pm 2	71.6 \pm 3	0.44
Lowest MAP (mm Hg)	76.4 \pm 5	78.5 \pm 4	0.99
Maximum HR (bpm)	110.6 \pm 3	102.9 \pm 5	0.0078*
Incidence of nausea and vomiting	4/20=20%	1/20=5%	0.15
Total dose of Ephedrine required (mg)	0.80 \pm 0.83	0.65 \pm 0.74	0.58
Apgar score (5 min) $<$ 7	0/20	0/20	--

The mean HR in preloaded group decreased below the baseline in the first 5 mins after spinal anaesthesia which increased subsequently in the next 10 or 20 mins, but in case of coload patients mean heart rate was increased further above the baseline for the first 5 mins. However, it decreased and tachycardia settled in the next 10 - 20 mins [Fig 4]. The mean maximal rise in heart rate in preloaded

parturients was 110.6 ± 3 per min and 102.9 ± 5 per min in case of coload group which was statistically significant ($p<0.05$) [Table 2].

In both the study groups, mean maximal fall in diastolic blood pressure and mean arterial pressure was statistically insignificant [Fig 2&3]. Total mean dose of ephedrine required in Group P (Preload) was

0.80 ± 0.83 and in Group C (Coload) was 0.65 ± 0.74, which was statistically insignificant [Table 2]. Nausea occurred in four patients in preload group and one patient in coload group. All incidences were associated with hypotension hence, treated with inj. Ephedrine. Neonatal outcome was similar and uneventful in both the groups. None of the neonate had Apgar score of <7 at 1 or 5 minutes [Table 2].

DISCUSSION

Spinal-induced hypotension (SIH) is the most documented and discussed response to local anaesthetic induced sympathectomy. Since hypotension has detrimental effects on the mother and the neonate, several strategies have been investigated to prevent its occurrence.

Fluid preloading for Caesarean section under regional anaesthesia has been established as a routine and considered to be a safe and effective method of reducing the incidence of hypotension. Hahn et al.^[18] studied the volume kinetics of lactated Ringer's (LR) solution found that the effect of LR solution on ↑ CO & restoring blood volume would be largest while the infusion is running. These findings have led to emergence of an alternative technique with the administration of fluid at the initiation of spinal anaesthesia i.e the concept of Co-loading. Muzlifah et al.^[19] conducted a study for prevention of hypotension during spinal anaesthesia for Caesarean section, infusing 20ml/kg and 10ml/kg of Ringer's lactate which had given similar results.

The role of crystalloid preloading in prevention of SIH was re-evaluated by Rout et al.^[6]; found small reduction in the incidence of hypotension with preloading. Crystalloid preloading appears to be ineffective due to rapid redistribution and "coload" given at the time of cerebrospinal fluid identification may be more effective. Since date, several studies have been conducted^[6,10,20,21] to reconsider the role of crystalloid preload in the prevention of hypotension for elective caesarean section and found that hypotension associated with spinal anaesthesia for caesarean section cannot be eliminated by volume preload in supine wedged patient. Dyer et al.^[15] compared the hemodynamic effects of crystalloid preload versus rapid crystalloid administration after induction of spinal anaesthesia during caesarean section, concluded with similar neonatal outcomes among two groups, significantly more patients in the coload group did not require vasoconstrictor. Therefore, they concluded rapid crystalloid administration after the induction of spinal anaesthesia may be advantageous in terms of managing maternal blood pressure. Our study has also demonstrated the beneficial effects of a crystalloid coload on maintaining SBP during sympathetic blockade and vasodilatation after spinal anaesthesia in comparison to a crystalloid preloading. However, we did not find any significant difference between groups in lowest maternal mean arterial pressure recorded (p=0.99). We found that a 20 ml/kg crystalloid preload in 15-20 min before spinal anaesthesia, was unable to significantly increase the maternal SBP within 10 min after spinal anaesthesia for caesarean delivery and incidence of hypotension was found to be more (40% vs 15%)

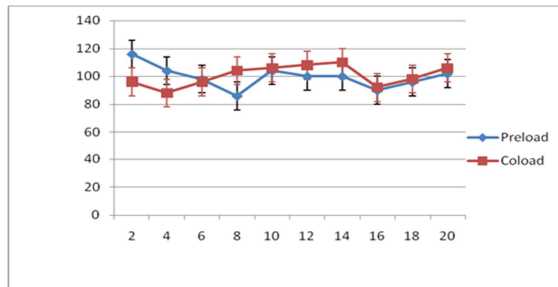


Figure 1: Serial changes in systolic blood pressure for first 20 min, data are presented as mean ±SD.

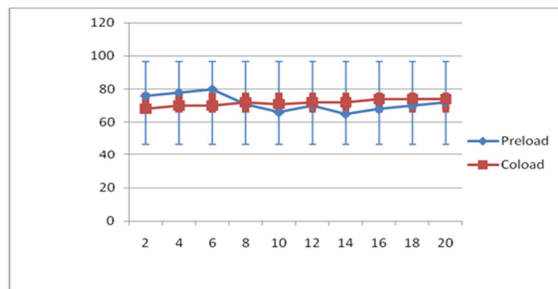


Figure 2: Serial changes in DBP for first 20 min data are presented as mean ±SD.

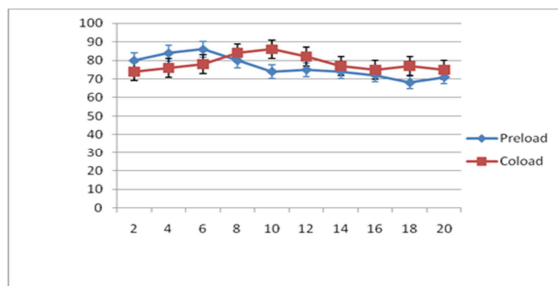


Figure 3: Serial changes in MAP for first 20 min data are presented as mean ±SD.

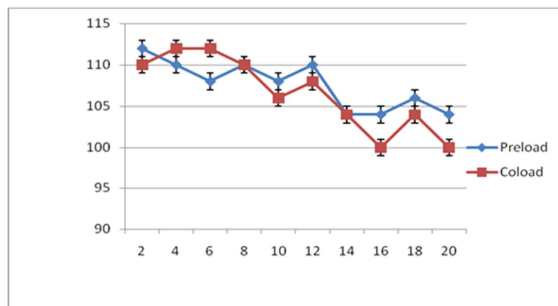


Figure 4: Serial changes in heart rate for first 20 min., data are presented as mean ±SD.

together with the incidence of nausea and vomiting as compared to the coload group. Similar to Sahar et al.^[16], statistically no significant difference was found between the two groups in maternal BP, Vasopressor requirement and neonatal outcome.

Despite the large number of studies available, evidences are still inconclusive in proving the superiority of crystalloid coload for preventing spinal induced hypotension. Neither do these studies provide conclusive guidelines regarding the appropriate timing of administration of these fluids to have best possible results.

However, our data, in combination with those of Rout and colleagues, confirm the lack of efficacy of an infusion preload in preventing the incidence of hypotension. As per our hypothesis coload seems to be more effective in preventing maternal hypotension as compared to preloading. Hence, it is unnecessary to delay surgery in order to deliver a preload of fluid. However, regardless of fluid loading strategy, proper hydration is still recommended because of improved maternal and neonatal outcome.

CONCLUSION

Preloading has a clinically advantage over the coload strategy in reducing hypotensive episodes, under low dose spinal anaesthesia for cesarean delivery. Preload should be advocated for situations where large haemodynamic fluctuations are expected, although coload is better suited for emergency situations because of shortage of enough time for fluid preloading in such circumstances. Understanding the individual benefit with each strategy allowing for better planning of anaesthesia and selection of either approach should be based upon the need of the hour against the chances of maternal hypotension.

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