Effect of Timing of Fluid Bolus on Reduction of Spinal-Induced Hypotension in Patients Undergoing Elective Cesarean Delivery

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Spinal-induced hypotension remains the most common complication associated with spinal anesthesia for cesarean delivery. Recent evidence indicates that a 20-mL/kg bolus via pressurized infusion system administered at the time of subarachnoid block (SAB) (coload) may provide better prophylaxis than the traditional administration of a 20-mL/kg crystalloid infusion (preload) approximately 20 minutes before SAB; however, this method raises some concerns. We hypothesized that administering half of the fluid bolus (10 mL/kg) before and half immediately following injection of the SAB would provide benefit. Variables included demographics, spinal anesthetic dermatome level obtained, additional intravenous (IV) fluid bolus and vasopressor requirements, and maternal vital signs.

We enrolled 87 subjects in this prospective, randomized investigation, 43 preload (control) and 44 preload/coload (experimental). There were no demographic differences between groups. The increased supplemental vasopressors required to treat maternal hypotension in the preload group were not statistically significant. Total IV fluids and supplemental IV bolus requirements were significantly higher in the preload group. No differences in neonatal outcomes were noted between groups. Maternal vital signs were not significantly different between groups; hypotension was treated as it occurred.

We recommend replacing standardized prophylactic crystalloid fluid administration with the preload/coload method described herein.

Keywords: Cesarean, fluid timing, hypotension, obstetrics, spinal.

Spinal-induced hypotension (SIH) remains the most common complication associated with subarachnoid block (SAB) for cesarean delivery, with an incidence ranging from 25% to 75%.[1-8] In keeping with previous studies, we defined SIH as a 20% drop from baseline and/or a systolic blood pressure (SBP) less than 100 mm Hg following administration of the anesthetic agent.[1-3,7,9] Spinal-induced hypotension is primarily due to sympathetic blockade, which leads to peripheral vasodilatation and venous pooling.[3,10] In a parturient, SIH is a significant problem leading to sequelae including nausea and vomiting, pulmonary aspiration, syncope, maternal cardiac dysrhythmias, and decreased intrauterine blood flow, thereby placing the fetus at risk.[7,8,11,12]

Practitioners use various methods to offset the effects of SIH. The most basic approach used is placement of a wedge under the right hip to facilitate left uterine displacement, a method that has been proven to reduce hypotension by minimizing aortocaval compression.[7] However, left uterine displacement alone is often ineffective in preventing hypotension in a patient undergoing spinal anesthesia because of the rapid onset of sympathectomy. Therefore, other methods are also used to prevent and treat hypotension. Foremost among these methods is the practice of prophylactically treating the patient with an intravenous (IV) fluid bolus before implementation of an SAB in an effort to offset the effects of the sympathectomy caused by the spinal anesthetic. These effects, while apparent in any patient receiving an SAB, are even more problematic in the parturient population because of the high level of sensory block required for a cesarean delivery (T4) and the unique anatomical and physical characteristics of pregnant patients. Another method used to reduce the incidence of SIH is the prophylactic administration of vasopressors.

Although there are a multitude of vasopressors that can be administered to prevent or treat SIH, the agents that have been most closely studied include ephedrine, phenylephrine, and metaraminol. Of these, ephedrine has been studied the most extensively and has been shown to be successful in prevention and treatment of

SIH in parturients.[4,7,13] Ephedrine, predominantly a beta-adrenergic agonist, is more commonly used because animal studies have shown that ephedrine can reverse SIH while preserving uteroplacental blood flow.[13] However, recent studies have indicated that ephedrine can also cause uteroplacental vasoconstriction, which may potentiate fetal acidosis. Therefore, some practitioners caution that administration of ephedrine prophylactically should not be the standard of care.[4,7,13] Recent studies have called into question the adverse effects of phenylephrine on uteroplacental blood flow. In a study published in 2005, the researchers pointed out that SIH was nearly eliminated by the combination of rapid crystalloid cohydration and a phenylephrine infusion.[8] Furthermore, in this study, there were no adverse effects on neonatal outcome as measured by Apgar scores and umbilical cord blood gases.[8] Due to the possibility of uteroplacental vasoconstriction, we believe that the use of vasopressors should be reserved for treatment of SIH, not for prophylaxis, and that IV fluid loading is the most benign method of reducing the incidence of SIH.

The first study to describe the fluid preloading technique was by Wollman and Marx[14] in 1968, in which they reported the administration of 10 to 20 mL of crystalloid solution approximately 30 minutes before the placement of an SAB resulted in a significant reduction in the incidence and severity of SIH in a parturient population receiving an SAB for a cesarean delivery. Based on these findings, many practitioners began preloading patients undergoing an SAB, and it has become the standard of practice for many anesthesia practitioners. However, multiple studies have questioned the efficacy of routine preloading with crystalloid solution as described by Wollman and Marx[14] and have reported that prehydration or preloading with a crystalloid solution provides no prophylactic benefit for SIH.[1,6,12,15,16] Despite these contradictory findings, most anesthesia practitioners have not abandoned the concept of fluid preloading, arguing that, in theory, fluid preloading makes sense.

Anesthesia providers have sought alternative methods and solutions for fluid preloading with a mixture of results. For example, there have been multiple studies examining the effect of changing the rate or timing of fluid administration before SAB in an effort to decrease the incidence and severity of SIH, but these studies have mixed results in relation to efficacy.[1,6,12,15,16] Other methods explored include the use of colloidal and noncolloidal solutions administered before the placement of an SAB. It has been reported that using a colloidal solution before SAB results in a significant reduction in the incidence of SIH in a variety of patients.[10,17] In general, studies of colloids indicate that the incidence of SIH is reduced because colloids remain in the intravascular space. However, colloids are not routinely used clinically because of the increased cost, the possibility of dilutional dysfunction of coagulation, suppression of platelet activity, and risk for anaphylaxis, which could be devastating in this patient population.[3,5,7]

At least 1 study may explain why preloading with a crystalloid solution 20 to 30 minutes before placement of an SAB is ineffective. Ueyama et al[10] evaluated the administration of 1.5 L of lactated Ringer's (LR) solution 30 minutes before administration of an SAB. They reported that at the time of SAB injection, only 28% of the LR solution remained in the vasculature, thereby providing some direct evidence as to why fluid preloading is ineffective for providing complete prophylaxis against SIH.[10]

However, it has been noted that fluid preloading 30 minutes before SAB injection provides limited prophylaxis against SIH. Previous research of SIH indicates that subjects given fluid preloading have a decreased incidence of hypotension for the first 5 minutes following injection compared with a similar group provided no fluid preloading boluses.[18,19] This finding is significant because the parturient population receiving an SAB for cesarean delivery experiences the most severe drop in maternal blood pressure 3 to 10 minutes after injection of the spinal anesthetic, thereby offering some rationale to continue the routine administration of fluid preloading.[1,4,20,21]

Because of this obvious limited advantage, some investigators began analyzing what effect the timing of the fluid preload would have on overall maternal hemodynamics. The most promising studies performed analyzing the effects of the timing of fluid preloading were conducted by Mojica et al[6] and Dyer et al,[12] in which they reported that the administration of a rapid fluid bolus administered at the time of SAB injection resulted in a significant reduction in the incidence of SIH compared with groups of patients receiving standardized fluid preloading. However, the results reported by Mojica et al[6] were for patients undergoing prostatectomy, which calls in to question their applicability to a cesarean delivery population. Although the study by Dyer et al[12] was performed on groups of patients undergoing cesarean deliveries, the coload (fluid bolus at time of SAB injection) was administered using a rapid infusion device under pressure, bringing into question the relative safety of using this method in a cesarean delivery population that is predisposed to pulmonary edema.

On analysis, while reporting an overall decrease in maternal hypotension, both of these studies reported a drop in blood pressure in the coload group in the immediate period following SAB injection, thereby suggesting that administration of a preload would be advantageous for this short period.[6,12] Also, because complications that can result from the rapid administration of a coload of fluid to a parturient population exist, the routine administration of a coload as described by Dyer et al[12] makes it difficult to assimilate this method into clinical practice. In an effort to combine the favorable aspects of the preload and coload techniques, we designed a study to determine

if splitting the fluid bolus of crystalloid solution, in which half of the normal 20-mL/kg bolus was given 10 minutes before SAB injection (preload) and half was given after SAB injection (coload), would be more effective in reducing the incidence of SIH, total fluid volume infused, and vasopressor requirements in groups of cesarean delivery patients receiving an SAB compared with a similar group of patients receiving the standard fluid preload of 20 mL/kg of LR solution given 20 minutes before SAB injection.

Methods

Following institutional review board approval, 89 parturients scheduled for elective cesarean delivery with SAB consented to participation in this study. Other inclusion criteria included a weight of less than 120 kg, singleton pregnancy of at least 37 weeks' gestation, and an ASA physical status classification of I or II. Subjects with evidence of preexisting comorbidity, essential hypertension, decreased lung compliance, preeclampsia, decreased uterine perfusion, or preexisting coagulopathy were excluded from the study. All subjects were randomized into a control (preload) group or an experimental (preload/coload) group by a computer-generated randomization process. After placement of a 16-gauge or 18-gauge IV catheter, all subjects received a baseline IV infusion of LR solution at 100 mL/h. The IV flow rate was calculated manually, and the amount of fluid administered was estimated by the bag markings. Preoperative medications included 30 mL of sodium citrate orally and 10 mg of IV metoclopramide. Baseline maternal heart rate, blood pressure, oxygen saturation, and fetal heart rate were recorded.

Subjects assigned to the control group received a 20-mL/kg fluid bolus of LR during approximately 20 minutes in the preoperative holding area. This bolus was timed to be completed just before transport to the operative suite. Fluid boluses for both groups were given via a 16-gauge or 18-gauge IV catheter with a fully open control valve and gravity alone providing the driving pressure. The start and finish times of the fluid bolus, arrival in the operating room, and other relevant event times were recorded. Once the fluid bolus was given, the infusion rate was decreased to a maintenance rate of 100 mL/h. Subjects assigned to the experimental group received a 10-mL/kg LR preload beginning approximately 10 minutes before transport to the operative suite, and then received a maintenance infusion of 100 mL/h during placement of the SAB. Immediately following injection of the SAB, all subjects in the experimental group were administered an IV bolus of 10 mL/kg of LR during approximately 10 minutes and then received a maintenance infusion of 100 mL/h until the conclusion of the cesarean delivery.

ASA standard monitors were used to record initial vital signs, and the fetal heart rate was also recorded. All subjects were placed in a sitting position for the SAB place-

ment. Medications used in the SAB were at the discretion of anesthesia providers. A total of 8 to 15 mg of hyperbaric bupivacaine, 0 to 50 μg of fentanyl, and 0 to 300 μg of preservative-free morphine sulfate were injected into the subarachnoid space. Following SAB, all subjects were placed into a supine position, and left uterine displacement was obtained by using a roll of sheets under the right hip. The time and location of SAB placement were recorded. The level of sensory block of the spinal anesthetic was recorded every 1 to 2 minutes for the first 10 minutes following SAB. After the spinal anesthetic was injected, the blood pressure and heart rate were recorded every minute for the first 10 minutes, followed by every 5 minutes until transfer to the postanesthesia care unit (PACU).

For the purposes of this study, *hypotension* was defined as an SBP of less than 100 mm Hg or a decrease in mean arterial pressure (MAP) of 20% from baseline. If the MAP dropped more than 20% from baseline or the SBP was less than 100 mm Hg, the hypotension was treated by the anesthesia provider. The decision to use ephedrine or phenylephrine to treat hypotension was at the discretion of anesthesia providers and based on maternal hemodynamics. All medications administered to treat hypotension and the time from completion of the SAB until medication administration was recorded. In addition, hypotension (20% decrease in baseline BP or SBP <100 mm Hg) could be treated with additional IV fluid boluses of 250 to 500 mL of LR solution.

Additional bolus requirements and time intervals were established for each group using specific criteria. For subjects assigned to the control group, time to additional boluses required was determined by measuring the time (in minutes) from completion of the SAB to additional boluses, whereas the time to additional boluses required in the experimental group was determined by measurement of the time from completion of the coload bolus to additional fluid requirements because a fluid bolus was already in progress at completion of the SAB. Treatment using additional fluid (as a sole treatment or in conjunction with ephedrine or phenylephrine) was at the discretion of anesthesia providers. All additional fluid boluses were recorded.

Following delivery of the neonate, all subjects received an oxytocin infusion and antibiotics as directed by the obstetrician. The total amount of IV fluid administered intraoperatively was recorded. All additional medications administered for breakthrough pain or nausea during the operative procedure were recorded on the data collection sheet for both groups.

At the conclusion of the cesarean delivery, all subjects were transferred to the obstetrical PACU and vital signs were recorded according to the standardized protocol. Any additional treatments for hypotension in the PACU were recorded. Admission and discharge Aldrete scores, spinal dermatome levels, and vital signs were obtained

	Preload (n = 43)	Preload/coload (n = 44)	P
Age, y	28.7 ± 5.1	28.9 ± 5.4	.821
Height, in	63.5 ± 2.3	64.0 ± 3.6	.462
Weight, kg	83.6 ± 23.1	83.63 ± 15.5	.986
Gestational age, wk	38.65 ± 0.81	39.0 ± 0.98	.076
Gravida (range)	(1-7)	(1-8)	.950
Race, No. of patients			.346
Caucasian	28	27	
African American	3	7	
Pacific Islander	0	1	
Asian	3	0	
Hispanic	7	7	
Other	2	2	
Time to place SAB, min	7.4 ± 8.7	6.45 ± 3.5	.509
SAB injection to delivery time, min	26.4 ± 7.9	26.1 ± 9.7	.874
Surgical time, min	60.2 ± 17.8	57.6 ± 14.7	.464
Anesthesia time, min	86.9 ± 19.4	85.3 ± 17.9	.705
PACU time, min	119.5 ± 41	126.3 ± 52	.433
Median dermatome level achieved (range)	T4 (T1-T5)	T4 (T1-T5)	.590

Table. Demographic and Independent Variables*

SAB indicates subarachnoid block; PACU, postanesthesia care unit.

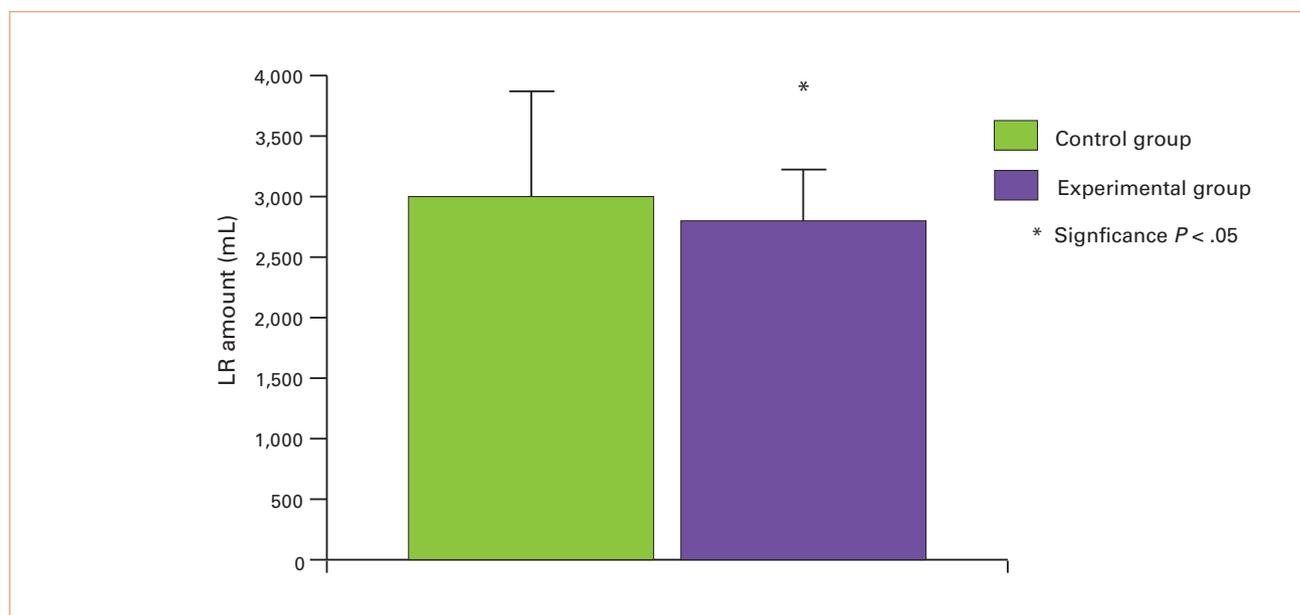* Data are given as mean ± SD unless otherwise indicated.

Figure 1. Total Amount of Lactated Ringer's (LR) Solution Infused

from the PACU records. Hypotension in the PACU was treated by using standardized PACU protocols. All treatment regimens used were recorded.

The sample size for this study was estimated based on a previous study by Dyer and colleagues[12] using the following assumptions: The incidence of SIH for patients as-signed to the control (preload) group would be approximately 50%, whereas patients assigned to the experimental (preload/coload) group would experience only a 25% incidence of SIH. By using an α level of .05 and a β level of .20, it was determined that we would need approximately 45 subjects per group (90 subjects total) after a 10% attrition
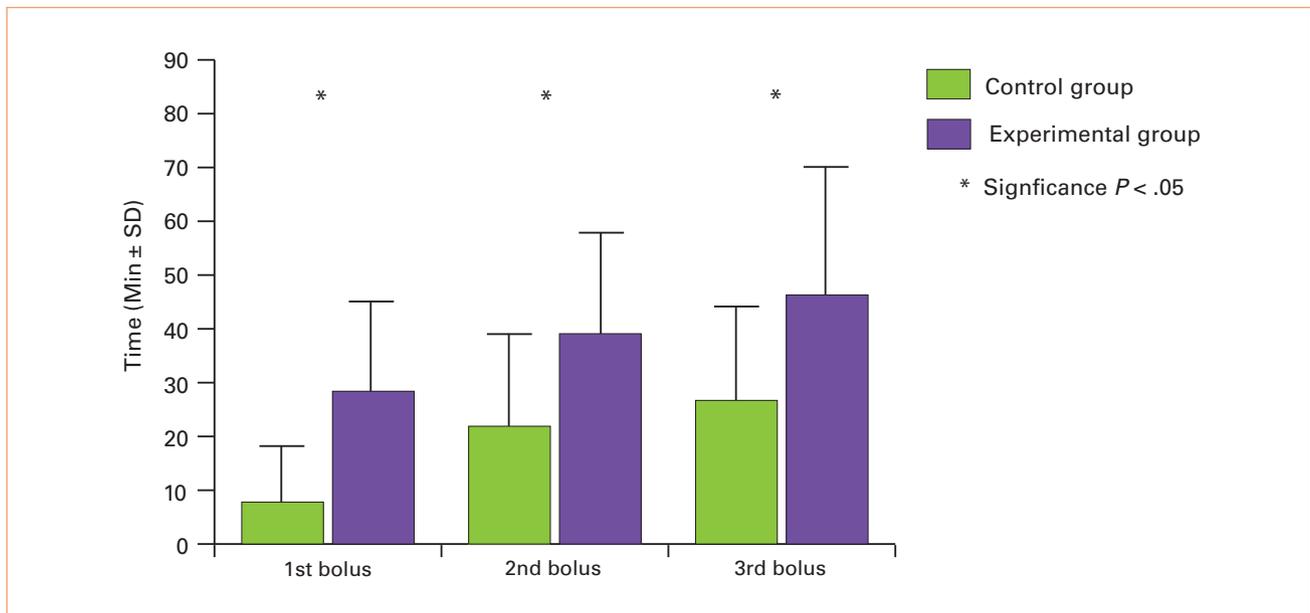
Figure 2. Time to Bolus Requirements

rate was added to the total sample size. Descriptive and inferential statistics were used to analyze data, and a *P* value of less than .05 was considered significant.

Results

A total of 89 subjects were enrolled in the study, but the data for 2 subjects were dropped from analysis, leaving a total of 87 subjects for final analysis (43 in the control group and 44 in the experimental group). The data for 1 patient from each group were dropped from the analysis due to failed spinal anesthetic; one subject was administered a general anesthetic (experimental group), and the other subject received a second spinal anesthetic successfully (control group). There were no significant differences between groups in demographic data, time to place the SAB, SAB to delivery time, SAB dermatome level achieved, or the duration of anesthesia, surgery, or PACU stay (Table).

Compared with the control group, the total volume of LR infused was significantly less (*P* = .02) in the experimental group (Figure 1). Analysis of the percentage of subjects in each group requiring supplemental boluses revealed that 31 (72%) of 43 subjects in the control group required supplementation compared with only 17 (39%) of 44 subjects in the experimental group (*P* = .004). The experimental group required a maximum of 3 additional supplemental boluses, whereas some subjects in the control group required as many as 7 additional boluses; therefore, a comparative analysis of time to supplemental IV boluses was done for the first 3 boluses only. The time to first bolus for the preload group was measured from the time of the SAB to the first additional fluid bolus. The time to first bolus in the experimental group was after the completion of the SAB and the coload bolus. The timin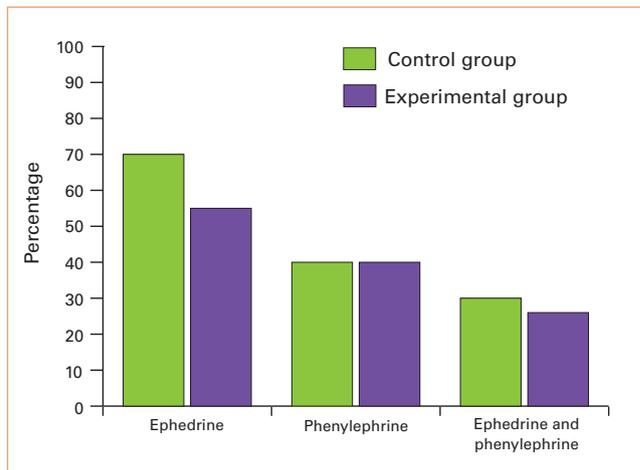g for the first 3 additional IV boluses required was significantly shorter in the control group compared with the experimental group for all 3 interval measurements (*P* < .05) (Figure 2).

Analysis of vasopressor use revealed that 31 (72%) of 43 subjects in the control group required ephedrine for blood pressure support compared with 24 (55%) of 44 subjects in the experimental group (*P* = .090). The amount of ephedrine and phenylephrine used was higher in the control group than in the experimental group, but this finding did not achieve statistical significance. (*P* > .05; Figure 3). Analysis of SBP and MAP readings showed no significant differences between the groups at any time (Figure 4). There was no difference between groups in surgical and anesthesia times, neonatal Apgar scores, neonatal weights, maternal blood loss, urinary output, intraoperative and postoperative sensory levels, or postoperative anesthesia satisfaction scores.
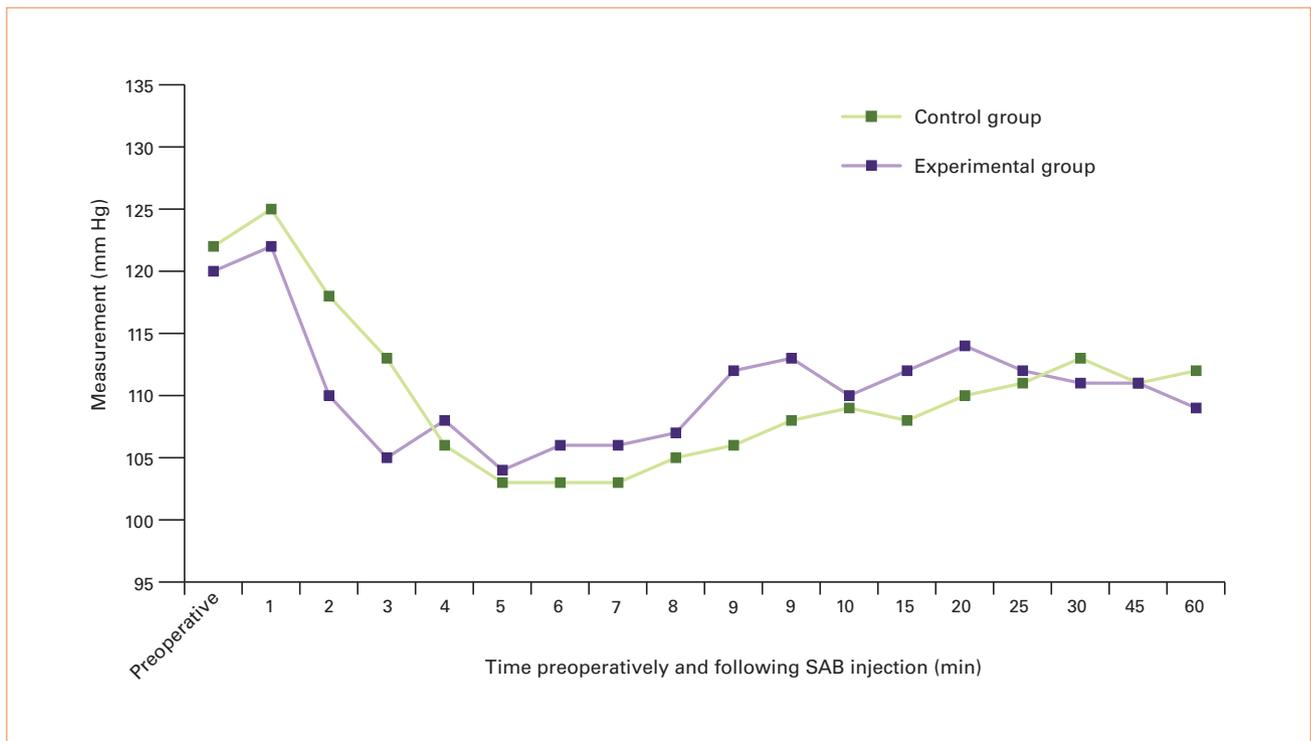

Figure 3. Pharmacologic Support Given

Figure 4. Systolic Blood Pressure Readings

Discussion

In this study of the effect of the timing of fluid boluses on the reduction of SIH in patients undergoing elective cesarean delivery, there was a significant difference between groups in the amount of fluid boluses and total LR infused. Due to physiologic changes associated with pregnancy, parturient patients are at an increased risk for the development of pulmonary edema.[22] This risk is increased in the setting of large fluid boluses that are often required during spinal anesthesia. The experimental group required a significantly larger total volume of crystalloid perioperatively and also required more fluid boluses intraoperatively to maintain blood pressure, despite having no difference in the level of spinal blockade. Although no subjects in either group showed signs of pulmonary edema, minimizing the total fluid requirements is necessary to ameliorate the risk.

There were no differences between groups in demographic variables. However, because this was a healthy population, future research is necessary to determine the effects in parturients with coexisting conditions. These data suggest that there may be a benefit to patients with preeclampsia or parturients with preexisting cardiac disease who have the added risk of the development of pulmonary edema.

The stability of the blood pressure that was shown in the results of this study may be clinically significant during an urgent cesarean delivery by decreasing the initial bolus time to 10 minutes before the spinal anesthetic followed by a coload, which was shown in this study to be an effective alternative to the standard 20-mL/kg preload.

We did not control for the treatment of hypotension, allowing vasopressors and/or fluid boluses to be used at the discretion of the anesthesia providers. Despite this lack of control in the study design, there was no significant difference between groups in the amount used or time to treat with vasopressors.

The lack of a significant difference in MAP readings between groups may be because this difference is difficult to see due to the hypotension being treated by the providers when indicated. However, the stability of the MAP readings after placement of the SAB indicates that the preload/coload method avoids the decrease in blood pressure noted by Dyer et al.[12] Also, there was no significant difference in the neonatal Apgar scores; the median scores at 1 and 5 minutes were 8 and 9 respectively, indicating general neonatal well-being.

Although the methods used in this study were not blinded or tightly controlled, the method reflected situations commonly seen in clinical practice, ie, different IV catheter size, room delays, and different provider preferences in the treatment of hypotension. Despite these limitations to the study design, clinically significant results were achieved that could be applied in clinical practice. Patients who are scheduled to have an elective or a scheduled cesarean delivery could be given a 10-mL/kg preload followed by a 10-mL/kg coload after initiation of spinal anesthesia.

An extensive review by Cyna et al[7] to evaluate methods used to eliminate SIH determined that hypotension is a risk of spinal anesthesia regardless of the method of prophylaxis and that no one method reliably eliminates this risk. Our findings indicate that the amount of perioperative fluid received by patients undergoing cesarean delivery can be safely decreased by combining a preload and coload bolus of fluid without increasing postoperative morbidity and mortality. This method of SIH prophylaxis can also decrease the amount of vasoactive medications required.

Conclusion

Based on the results of this study, we believe that a combination preload and coload of fluid is a beneficial method of minimizing SIH. Further studies with tighter controls of fluid administration and a prescribed anesthetic plan that includes strict parameters to treat hypotension are needed to further explore this effect. In addition, future research is necessary to determine if this effect is similar in parturients with coexisting disease.

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