Colloid Preload Versus Coload for Spinal Anesthesia for Cesarean Delivery: The Effects on Maternal Cardiac Output

Wendy H. L. Teoh, FANZCA

Alex T. H. Sia, M.MED

BACKGROUND: Spinal anesthesia for cesarean delivery may cause severe maternal hypotension, and a decrease in cardiac output (CO) and blood flow to the placenta. Fluid preloading with crystalloid is ineffective due to rapid redistribution. A "coload" given at the time of cerebrospinal fluid identification may be more effective. Our null hypothesis was that there would be no difference between the effect of a colloid preload (15 mL/kg hydroxyethyl starch (HES) 130/0.4 [Voluven® 6%]) and an identical coload on maternal CO and the incidence of hypotension after spinal anesthesia for cesarean delivery. Secondary outcomes studied were neonatal acid- base status and predelivery vasopressor requirements.

METHODS: Forty ASA PS I and II women scheduled for elective cesarean delivery were recruited. Patients were randomized to Group P (preload of 15 mL/kg HES) or Group C (coload, given when cerebrospinal fluid identified). Heart rate, arterial blood pressure, stroke volume and CO measurements were recorded at baseline, every minute for 10 min, and every 2.5 min interval for 10 min with the USCOM™ ultrasonic CO monitor. Spinal anesthesia was performed at the L3/4 interspace in the right lateral position. Arterial blood pressure was maintained at 90%–100% of baseline values using IV phenylephrine boluses.

RESULTS: Demographic, anesthetic, and surgical characteristics were similar. There were no between-group differences in baseline systolic blood pressure, heart rate, and colloid volume. CO and stroke volume were significantly increased in Group P ($P = 0.01$) in the 5 min after spinal anesthesia. This increase in CO was not sustained at 10 min. There were no significant between-group differences in the incidence of hypotension, absolute arterial blood pressure values ($P = 0.73$), predelivery median (range) phenylephrine requirements (300[0–1000] in Group P versus 150 [0–850]μg in Group C, $P = 0.24$), or neonatal outcome as measured by Apgar scores and umbilical arterial and venous blood gas values.

CONCLUSION: Intravascular volume expansion with 15 mL/kg HES 130/0.4 given as a preload, but not coload, significantly increased maternal CO for the first 5 min after spinal anesthesia for cesarean delivery, however, maternal and neonatal outcomes were not different.

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Hypotension during spinal anesthesia for cesarean delivery is a common and troublesome complication, both from the maternal and fetal-neonatal point of view. Commonly used methods for the prevention of hypotension, for example, leg wrapping, antithromboembolic stockings, patient positioning, and fluid and vasopressor administration have met with mixed success. Traditionally, crystalloid IV fluids are administered in the 20 min before the induction of spinal anesthesia for cesarean delivery (preload). The literature suggests that this is relatively ineffective since preload is rapidly redistributed.[1–3] Also, this method may induce atrial natriuretic peptide (ANP) secretion, resulting in peripheral vasodilatation followed by an increased rate of excretion of the preloaded fluid.[4] A more rational approach is to administer the fluid bolus at the time that the local anesthetic block is starting to take effect. This might maximize intravascular volume expansion during vasodilatation from the sympathetic blockade and limit fluid redistribution and excretion. This practice has been termed "coload."[5]

Preload augmentation of blood volume, regardless of the type of fluid, should be substantial enough to

From the Department of Women's Anesthesia, KK Women's and Children's Hospital, Singapore.

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Address correspondence and reprint requests to Dr. Wendy H.L. Teoh, Department of Women's Anesthesia, KK Women's and Children's Hospital, 100 Bukit Timah Rd., Singapore 229899. Address e-mail to teohwendy@yahoo.com.

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result in a significant increase in cardiac output (CO), to prevent hypotension.[6] Maternal arterial blood pressure (BP) has always been used as a surrogate index of CO. However, because of changes in peripheral resistance, changes in maternal BP do not necessarily reflect changes in maternal CO.[7] Significant correlation among decreases in maternal CO after spinal anesthesia, increased umbilical artery pulsatility index and umbilical arterial acidemia at delivery suggest that changes in these variables are better predictors of reduced uteroplacental perfusion than changes in maternal BP.[8] This is further supported by placental scintigraphy which showed no correlation between maternal BP and placental blood flow.[9]

Colloid preload seems to be more effective than crystalloid in the prevention of spinal anesthesia-induced hypotension[6] and crystalloid coload is more effective than preload.[5] Thus, we tested the hypothesis that there is no significant difference between a colloid preload (15 mL/kg hydroxyethyl (HES) 130/0.4 [Voluven® 6%, Fresenius Kabi, Bad Homburg, Germany]) and an identical coload on maternal CO. Secondary outcomes included predelivery vasopressor requirements and neonatal acid-base status.

METHODS

After obtaining approval from our IRB, and written informed consent, 40 ASA physical status I and II women with term singleton pregnancies who were scheduled to undergo elective cesarean delivery under spinal anesthesia were recruited. Exclusions were chronic or pregnancy- induced hypertension, diabetes on medication, cardiovascular or cerebrovascular disease, known fetal abnormalities, extremes of weight (<40 or >100 kg) and height (<140 cm or >180 cm) and any contraindications to neuraxial anesthesia. Ranitidine 150 mg was administered orally the night before and 2 h before surgery. Thirty milliliters of 0.3 M sodium citrate was also given just before patient arrival in the operating room (OR). Otherwise, all patients fasted 8–10 h.

A 16-gauge IV catheter was inserted under local anesthesia in the left hand, and connected to an IV infusion which was not commenced. Lights were dimmed and staff movement minimized in the OR. Standard monitors of electrocardiography, pulse oximetry (Spo_2), and noninvasive BP (Dinamap, Critikon, FL) were applied on the right arm. After a 15 min rest period, all patients had the following baseline variables measured in the supine position with 15° of left lateral tilt: heart rate (HR), systolic BP (SBP), calculated as the mean of three successive measurements taken 1–2 min apart, and, using a noninvasive CO monitor (Ultrasonic Cardiac Output Monitor [USCOM™]), the baseline stroke volume (SV) and CO.

The USCOM ultrasonic CO monitor (USCOM Pty, Coffs Harbor, NSW, Australia) provides noninvasive transcutaneous measurement of CO based on the continuous-wave Doppler ultrasound. A transducer is placed on the chest in the suprasternal notch to measure transaortic blood flow. The flow profile is presented as a time-velocity spectral display. CO is calculated from the equation CO = HR × SV, where the SV is the product of the velocity time integral (VTI) and the cross-sectional area (CSA) of the aortic valve. VTI is the stroke distance of a column of blood and is calculated from the peak velocity detected. The CSA of the aortic valve is determined by height-indexed regression equations.

Patients were randomized into two groups to receive either preload (Group P) or coload (Group C) after enrolment into the study by opening sealed opaque envelopes that had been sorted by computer-generated random allocation. Group P patients received a preload of 15 mL/kg of HES 130/0.4. As soon as the preload was completed, spinal anesthesia was initiated. Group C patients received an identical fluid load of 15 mL/kg initiated at the time of identification of cerebrospinal fluid. An IV administration set (Infusable® pressure infusor, Vital Signs, NJ) pressurized to 250 mm Hg was used in all patients to administer the fluid at the maximal possible rate, after which no additional fluid was given other than that required to maintain IV patency.

Spinal anesthesia was induced in the right lateral position using 5% hyperbaric bupivacaine 10 mg and morphine 100 μg, injected over 20 s at the L3/4 level with a 27 gauge Whitacre spinal needle (Becton Dickinson, NJ). Patients were immediately positioned supine with a 15° left lateral tilt. The principal investigator (WHLT), who was blinded to patient group allocation, evaluated hemodynamic status and spinal anesthesia characteristics. HR, SBP, SV, and CO measurements were recorded in both groups at 1 min intervals after the intrathecal injection for 10 min and at 2.5 min intervals for the subsequent 10 min. HR and SBP monitoring were continued at 5 min intervals until the completion of surgery as part of our routine anesthetic care.

A two-operator technique was used to maintain blinding. The principal investigator (WHLT) recorded the baseline hemodynamic variables, left the OR, and reentered the OR immediately after initiation of anesthesia. The second investigator administered the fluids and spinal anesthetic and had no role inpatient 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. Vasopressor was administered by an anesthesiology resident blinded to group assignment whenever the SBP decreased 10% from baseline. Data were later coded and entered into a computer by a research nurse blinded to patient allocation.

Oxygen was not routinely given unless the Spo_2 decreased to <95%, when oxygen 5 L/min was administered via a clear facemask. The extent of the

sensory block was tested using an ice pack in the midline 5 min after induction of spinal anesthesia. This was further confirmed by assessing loss of pinprick discrimination. Neuraxial blockade assessment continued at 2.5 min intervals and surgical incision was allowed when T6 dermatome was attained (both to cold and pinprick).

Subjects received IV boluses of phenylephrine 50 μg to maintain BP more than 90% of baseline. The study was terminated at delivery. Nausea and vomiting not associated with hypotension (<90% of baseline BP) were treated with ondansetron 4 mg. Apgar scores were assessed by a pediatrician blinded to group assignment at 1 and 5 min, and blood was taken from a double-clamped segment of the umbilical cord for immediate blood gas analysis.

The following data were collected:

a. Patient demographics: age, weight, height, duration of surgery, estimated blood loss.
b. Fluids and anesthesia data: total volume infused, duration of infusion, highest dermatomal sensory level achieved, induction to delivery interval, skin incision to delivery interval, uterine incision to delivery interval.
c. Hemodynamic data: HR, SBP, SV, CO, the minimum and maximum SBP, number of hypotensive patients predelivery (defined as a 10% decrease from baseline SBP), the total number of episodes of hypertension (defined as 20% more than baseline SBP), and the incidence of vomiting or nausea (as reported by patients).
d. Phenylephrine requirements (predelivery) and side effects.
e. Neonatal outcome: incidence of Apgar scores <7 at 1 and 5 min, umbilical arterial and venous blood gas variables (pH, P_{CO_2}, P_{O_2}, base excess).

Statistical analysis:

The primary outcome was CO. Sample size was computed to detect a 25% difference in mean CO during the first 5 min after initiation of anesthesia as a clinically significant end-point. Based on our preliminary pilot study where mean CO was 7.0 (SD 1.9) during the first 5 min in the coload group, and assuming $\alpha = 0.05$ 2-sided, $\beta = 0.2$ (i.e., 80% power), 18 subjects per group were required. The following tests were used to compare data between the two groups: Student's *t*-test for patient demographics, neonatal acid base data, and other parametric data; Mann-Whitney *U*-test for nonparametric data; Fisher's exact test for proportion of subjects with hypotension predelivery and nausea or vomiting. The general linear model for repeated measures was used to analyze serial changes in the primary outcome variable (CO), including SBP, HR, SV in the 5 and 10 min interval after completion of spinal anesthetic at time = 0. Individually significant data points were identified using paired *t*-tests with Bonferroni correction for multiple comparisons. All statistical analyses were performed using Excel 97™ (Microsoft, Redmond, WA) and SPSS 11.5™ (SPSS, Chicago, IL). Data are expressed as mean ± SD (SD) unless otherwise stated. A *P* value of <0.05 was considered significant.

Table 1. Baseline Demographic, Fluid and Anesthesia Data

	Preload group ($n = 20$)	Coload group ($n = 20$)	*P*
Age (yr)	33 ± 5	31 ± 5	0.15
Weight (kg)	73 ± 13	72 ± 13	0.78
Height (cm)	157 ± 7	157 ± 5	0.85
Duration of surgery (min)	34 ± 13	38 ± 10	0.31
Estimated blood loss (mL)	370 ± 283	368 ± 167	0.98
Total fluids infused (mL)	1100 ± 200	1085 ± 200	0.82
Duration of infusion (min)	8 ± 2	9 ± 3	0.17
Time from preload initiation to cerebrospinal fluid identification (min)	11 ± 3	NA	NA
Maximal sensory block level to cold (median [range])	T3 [T1–T4]	T3 [C6–T4]	0.08
Spinal anesthesia to delivery time (min)	35 ± 9	33 ± 8	0.41
Skin incision to delivery time (min)	7 ± 3	7 ± 3	0.68
Uterine incision to delivery time (s)	68 ± 51	77 ± 42	0.55

Values are mean ± SD.

NA = not applicable.

RESULTS

Forty patients were recruited between February and July 2006. All subjects were successfully enrolled, received treatment as allocated and completed the study. Results from all subjects were analyzed. There were no dropouts. The groups were not different with respect to age, weight and height (Table 1) or anesthetic or surgical characteristics. There were no between-group differences in the volume of colloid infused and the duration of infusion. Initiation of preload to identification of cerebrospinal fluid occurred at a mean of 10.6 (2.8) min in Group P.

Maternal SV and CO were successfully recorded in all patients as per protocol. Baseline CO and HR were similar for both groups but by chance, baseline SV was significantly lower in the coload group. Within the first 5 min after induction of spinal anesthesia, CO was significantly higher in the patients who had received a preload ($P = 0.01$) but this increase was not sustained at 10 min, $P = 0.08$ (Fig. 1) or 20 min after spinal anesthesia, $P = 0.13$. SV followed a similar trend in the first 5 min ($P = 0.02$) (Fig. 2).

There were also no significant differences between groups in baseline SBP and at any point within the first 10 min after spinal anesthesia ($P = 0.99$) (Fig. 3). Ninety percent of patients who received a colloid preload and 75% of those receiving coload experienced more than a 10% decrease from baseline SBP

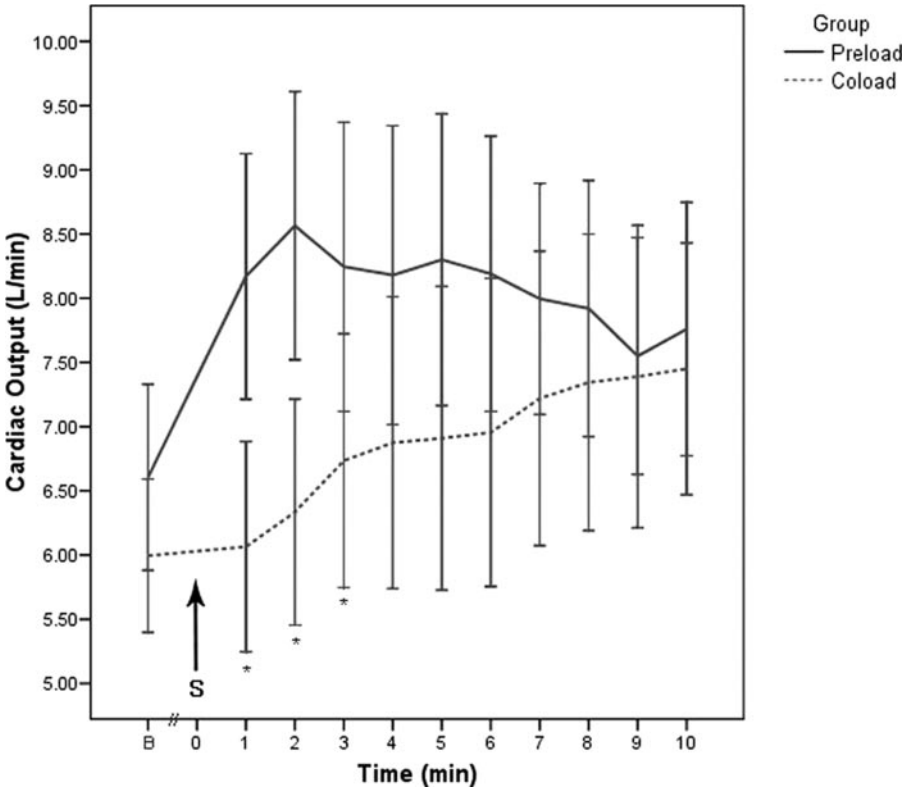

Figure 1. Mean (95% CI) cardiac output (CO) from baseline and after induction of spinal anesthesia. Patients receiving a 15 mL/kg colloid preload had a significant increase in CO within 5 min ($P = 0.01$) which was not sustained over 10 min ($P = 0.08$) using general linear model for repeated measures. There were significant intergroup differences in CO at 1, 2, 3 min (*$P < 0.05$). B = baseline; S = spinal anesthesia at time 0; Time = minutes after injection of intrathecal bupivacaine.

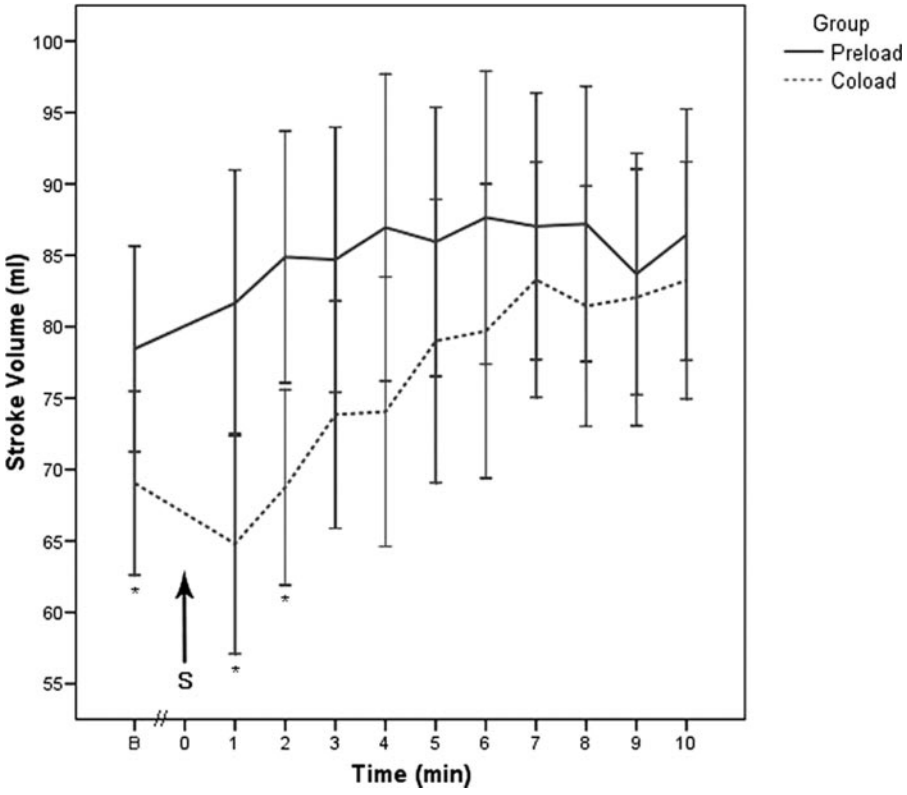

Figure 2. Mean (95% CI) stroke volume (SV) changes. Patients receiving a 15 mL/kg colloid preload had a significant increase in SV within 5min ($P = 0.02$) which was not sustained over 10 min ($P = 0.10$) using general linear model for repeated measures. There were significant intergroup differences in SV at baseline (B), 1 and 2 min after spinal anesthesia (*$P < 0.05$). B = baseline; S = spinal anesthesia at time 0; Time = minutes after injection of intrathecal bupivacaine.

($P = 0.41$), but the minimum recorded SBP was not significantly different. The median dose of phenylephrine administered predelivery was not different between groups (Table 2).

Nausea occurred in one patient in Group P and in two patients in Group C. All incidences were associated with hypotension predelivery and treated with vasopressor. No patients vomited or required oxygen supplementation. Neonatal outcome was not different between groups. All neonates had Apgar scores of 9 at 1 and 5 min (Table 3). There were no significant differences in umbilical artery or vein pH, CO_2, O_2, and base excess.

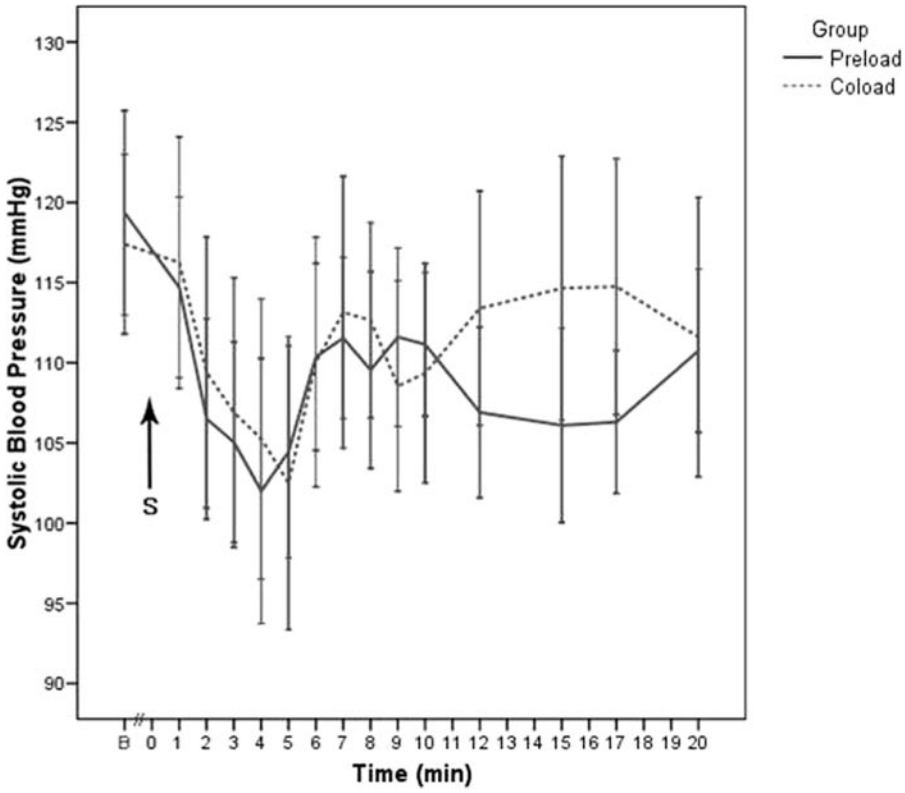

Figure 3. Mean (95% CI) maternal systolic blood pressure (SBP) during the study. There were no significant intergroup differences in baseline SBP or at any 1 point within the first 10 or 20 min of regional block (P = 0.99). B = baseline; S = spinal anesthesia at time 0; Time = minutes after injection of intrathecal bupivacaine.

Table 2. Hemodynamic Data

	Preload group (n = 20)	Coload group (n = 20)	P
Baseline heart rate (bpm)	88 ± 12	87 ± 14	0.85
Minimum SBP (mm Hg)[a]	91 ± 12	93 ± 17	0.82
Maximum SBP (mm Hg)[a]	122 ± 11	127 ± 12	0.14
Patients with >1 hypertensive episodes[b]	1 (5)	2 (10)	1.00
Predelivery phenylephrine dose (μg)	300 [0–1000]	150 [0–850]	0.24
Predelivery nausea or vomiting	1 (5)	2 (10)	1.00

Values are mean ± SD, median (range) or number (%).

SBP = systolic blood pressure.

[a] From start of spinal anesthesia until 20 min later.

[b] Defined as 20% more than baseline systolic blood pressure (SBP).

No neonates had fetal acidosis, as defined by pH <7.2 (Table 3).

DISCUSSION

Our study has demonstrated the beneficial effects of a colloid preload on maintaining CO during sympathetic blockade and vasodilation after spinal anesthesia in comparison to a colloid coload. However, we did not find a difference between groups in maternal BP changes and measures of uteroplacental perfusion (umbilical cord gases).

We have also demonstrated the use of a portable continuous-wave Doppler ultrasonic CO monitor to noninvasively track the CO and SV changes of parturients in the first 20 min after induction of spinal anesthesia. Using the USCOM device, we were able to track the CO changes every minute after spinal anesthesia. The device calculates CO as the product of HR and SV, where the SV is the product of the VTI and the CSA of the aortic valve. To our knowledge, there have been no published reports of its use in pregnant patients and after spinal anesthesia. This particular device has not been validated during pregnancy; one of the factors it uses to calculate CO is the CSA of the aortic valve, determined by height-indexed regression equations in nonpregnant individuals. However, cross-sectional echocardiographic measurement of the aortic orifice area and Doppler ultrasound measurement of ascending aortic blood velocity have been shown to provide accurate noninvasive measurements of CO, validated in pregnancy.[10–12] This combined technique, however, requires expert personnel trained in echocardiography; CO measurements could only be made at 5 min intervals after spinal anesthesia as each Doppler reading required 2–3 min to complete and cross-sectional echocardiographic recordings took another 2 min.[8] We believe that the USCOM device was a useful bedside trend monitor, capable of rapid serial CO measurements.

The accuracy of the device has been investigated in anesthetized dogs[13] and validated in mechanically ventilated postcardiac surgery patients.[14] The authors of the latter study found very good agreement between the CO measurements determined by the USCOM device and the thermodilution method. Using the Bland- Altman technique, the mean of the differences (estimate of bias) was 0.18 L/min (95% CI:−0.09 to 0.44) and the limits of agreement for the 2 techniques −1.43 to 1.78.

Table 3. Neonatal Outcome

	Preload group (n = 20)	Coload group (n = 20)	P
Umbilical arterial blood gases			
pH	7.28 ± 0.05	7.29 ± 0.03	0.48
pCO_2 (mm Hg)	57.2 ± 13.7	57.7 ± 5.5	0.89
pO_2 (mm Hg)	22.4 ± 24.0[a]	15.1 ± 5.1	0.62
Base excess (mmol/L)	0.4 ± 5.5	−1.0 ± 1.3	0.31
O_2 saturation (%)	24 ± 26	17 ± 7	0.30
Umbilical vein blood gases			
pH	7.34 ± 0.02	7.34 ± 0.05	0.83
pCO_2 (mm Hg)	47.9 ± 7.1	46.8 ± 5.7	0.89
pO_2 (mm Hg)	25.0 ± 7.2	26.0 ± 9.1	0.70
Base excess (mmol/L)	0.00 ± 5.8	−1.4 ± 1.8	0.30
O_2 saturation (%)	43 ± 14	47 ± 11	0.41
Fetal acidosis (umbilical arterial pH <7.2)	0	0	1.0
1 min Apgar score <7	0	0	1.0
5 min Apgar score <7	0	0	1.0

Values are mean ± SD or number (%).

[a] Two outliers: 90.3 and 88.5 mm Hg.

In our study, we found that a 15 mL/kg colloid preload significantly increased maternal CO and SV within 5 min after spinal anesthesia for cesarean delivery. This concurs with work by Ueyama et al.[6] in which intravascular volume preloading with 500 mL and 1000 mL of 6% HES significantly increased CO by 14% and 43%, respectively, from baseline. Our work differs from Ueyama et al.'s in the following ways: the amount of HES infused was fixed and not based on a body weight. They used indocyanine green and pulse spectrophotometry to measure the effects of volume preload on blood volume and CO. This technique required a 40-min interval between measurements and hence no CO data were obtained after spinal anesthesia was induced and trends could not be followed.

A colloid preload may augment the blood volume enough to offset the effects of increased ANP and rapid redistribution of fluid, diminishing the effects of peripheral vasodilatation and decreased venous return after the central sympathetic blockade of spinal anesthesia. Colloid solutions are not as rapidly redistributed to the extracellular compartment as crystalloids, thus better maintaining intravascular volume and hence CO. Although our study demonstrated a significant increase in maternal CO after a colloid preload, no differences in SBP were observed. Ogata et al.[15] also found no significant reduction in postspinal hypotension after a 8 mL/kg HES preload compared to the control group, who received no prehydration. This volume of infusion did result, however, in an increased concentration of ANP by 86% versus a 23% decrease in ANP when no preload was given. They concluded that colloid preloading with moderate volume might prevent the decrease in cardiac preload with increasing ANP, whereas it did not prevent spinal-induced hypotension.

Dyer et al.[5] had previously found that a 20 mL/kg crystalloid coload significantly reduced postspinal hypotension with reduced vasopressor requirements, compared with an identical volume preload. Unlike Dyer et al.'s work, we did not see a reduction in predelivery vasopressor use with coload. This may have been due to the strict criterion for maintenance of near normal BP (<10% decrease from baseline) with vasopressor, as well as differences in colloid and crystalloid, as colloid preload increases intravascular volume.

Maintaining baseline maternal BP with an infusion of phenylephrine at a rate of 100 μg/min has been shown to reduce CO at 10 and 15 min compared with an ephedrine infusion at 5 mg/min.[16] Despite equivalent SBP control in that study, it was at the expense of greater fetal acidosis with ephedrine. Any changes in CO that might result from the colloid preload or coload may have been decreased by the use of phenylephrine to maintain SBP near normal in the current study.

Other investigators have found that colloid preload is better than crystalloid preload resulting in increased CO and less hypotension.[6] Crystalloid coload is better than preload,[5] but a direct comparison between the benefits of crystalloid and colloid coload has yet to be made. Colloid solutions are generally expensive and run a small risk of allergy. Significant increases in central venous pressure after both crystalloid and colloid preloading have also been recorded,[17] but there have been no reports of pulmonary edema.[18]

Our study had several limitations. The lack of a control group precluded determination of an absolute reduction in the incidence of hypotension.[19] We chose to omit it as withholding fluids would not have been in keeping with our clinical practice. Second, after colloid preloading and before the initiation of spinal anesthesia, we did not record CO, SV and SBP. Third, we did not record mean and diastolic BPs which are more likely to be related to uteroplacental perfusion. Fourth, one may argue that CO and SV were higher in the preload group as the baseline SV started significantly lower in the coload group. However, there were

no SV intergroup differences after 3 min, and there were no differences in baseline HR (Table 2).

In conclusion, a 15 mL/kg of colloid preload significantly increases maternal CO in the first 5 min after spinal anesthesia for cesarean delivery. However, we could not detect any differences in maternal BP, vasopressor requirement and neonatal outcome between the preload and coload groups. It may be argued that, since a preload takes more time, and there was no difference in outcome between the two groups (CO being an intermediate variable and maternal nausea/vomiting and neonatal outcomes the outcomes of interest), then a coload should be used. We suggest that the use of a modest colloid preload or coload (e.g., 500 mL), plus support of BP close to baseline with phenylephrine, results in minimal maternal nausea/vomiting and no obvious difference in neonatal outcomes. This may be a reasonable option for hemodynamic management of women presenting for cesarean delivery under spinal anesthesia.

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