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Original Article

Effects of isothermic crystalloid coload on maternal hypotension and fetal outcomes during spinal anesthesia for cesarean section: A randomized controlled trial[☆]Mehmet Canturk^{a, *}, Fusun Karbancioglu Canturk^b^a Department of Anesthesiology and Reanimation, Kirsehir Ahi Evran University Training and Research Hospital, Kervansaray Mahallesi, 2019. Sokak, D:1 40200, Merkez, Kirsehir, Turkey^b Department of Obstetrics and Gynecology, Kirsehir Ahi Evran University Training and Research Hospital, Kervansaray Mahallesi, 2019. Sokak, D:1 40200, Merkez, Kirsehir, Turkey

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ABSTRACT

Objective: Spinal anesthesia induced hypotension (SAIH) is a common occurrence during spinal anesthesia for cesarean section resulting in perturbing effects on maternal and fetal outcomes. Previous studies conducted to attenuate SAIH focused on the timing of intravenous fluid infusion and demonstrated the superiority of coload strategy on traditional preload strategy but neither of them focused on the effect of the temperature of crystalloid infused on SAIH and fetal outcomes. The current study aimed to assess the effect of the temperature of the crystalloid infused with coload strategy on the incidence of SAIH and fetal outcomes.

Materials and methods: Seventy-six parturients were enrolled into the study and data of 60 parturients were analyzed. Patients were randomly assigned to receive crystalloid coload at room temperature (Group RT, n = 30) or warmed at 37 °C (Group W, n = 30). The incidence of hypotension, cumulative hypotension episodes, heart rate, core body temperature, ephedrine dose, and fetal outcomes were recorded.

Results: There was no significant difference in the incidence of maternal hypotension, cumulative hypotension episodes, and ephedrine dose (p = 0.625, p = 0.871, p = 0.460 respectively). Umbilical arterial pH and fetal Apgar scores at first and fifth minutes were higher in Group W than in Group RT (p = 0.013, p = 0.006 and p = 0.045 respectively). One fetus in Group RT but none in Group W had umbilical arterial pH lower than seven. Fetal birth weight and rectal temperature measurements were comparable in both groups (p = 0.639 and p = 0.675 respectively). Demographic data, patient characteristics, and surgery data were comparable between groups.

Conclusions: Isothermic crystalloid coload strategy results in higher umbilical pH values and Apgar scores in parturients scheduled for cesarean section under spinal anesthesia.

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Introduction

Single-shot spinal anesthesia is widely used for cesarean anesthesia [1–3]. It has superiorities on epidural anesthesia since it is less time consuming, provides relatively dense anesthesia, and less amount of local anesthetic is necessary to achieve adequate anesthesia for cesarean section. Spinal anesthesia induced hypotension (SAIH) is a common occurrence seen in about 60–70% of parturients undergoing elective cesarean section with spinal anesthesia [4]. Severe and sustained hypotension may pose perturbing side effects. Maternal side effects include bradycardia, loss of consciousness, dyspnea, nausea and vomiting, pulmonary aspiration

and cardiovascular collapse. Fetal side effects include uteroplacental hypoperfusion, fetal hypoxia, acidosis, and neonatal depression [1,2].

Several measures have been used to overcome SAIH during cesarean section with spinal anesthesia. Patient positioning to left lateral tilt up to 15°, lower limb compression and antithromboembolic stockings are non-pharmacological measures with limited affectivity [3]. Vasopressor medication and intravenous fluid administration are the pharmacological interventions to prevent SAIH. Recently there is a great interest on prophylactic use of ondansetron to decrease the incidence of SAIH [5,6].

We know that the mechanism of hypotension is vasodilatation due to sympathetic blockade rather than a decreased venous return and cardiac output which activates Bezold–Jarish reflex [7,8]. Preganglionic sympathetic blockade results in increased venous capacitance and decreased arterial resistance by decreasing vascular smooth muscle tone [2]. The relative volume gap produced by sympathetic blockade during spinal anesthesia is treated with intravenous hydration. The timing and type of intravenous fluid is still a controversy, but preloading is no longer used in clinical practice. In two review articles, combining a prophylactic vasopressor regimen with colloid preloading, colloid co-loading or crystalloid co-loading is stated to be the best method of preventing maternal hypotension after the initiation of spinal anesthesia [4,9]. In a recent research article it is reported that when crystalloids are used for intravenous hydration during cesarean section under spinal anesthesia, the coload strategy is superior to preloading [10]. Oh et al. [11] reported that in case of using crystalloids for intravenous hydration during cesarean delivery, the coload strategy is more effective than preload strategy for the prevention of maternal hypotension after spinal anesthesia. The former studies focused on the timing of intravenous fluid administration and the type of intravenous fluid infused to attenuate maternal hypotension during cesarean section with spinal anesthesia, but none of them explicated the effect of the temperature of the intravenous fluid on preventing maternal hypotension and fetal outcomes during cesarean section with spinal anesthesia.

The current study is conducted on term parturients scheduled for elective cesarean section with spinal anesthesia to assess if there is an effect of the temperature of infused crystalloid with the coload strategy on the incidence of SAIH and fetal outcomes.

Materials and methods

The current prospective randomized controlled trial was in accordance with Consolidated Standards of Reporting Trials (CONSORT) guidelines and declaration of Helsinki. After obtaining Institutional Review Board and Ethics Committee approval (Ahi Evran Üniversitesi Tıp Fakültesi Klinik Araştırmalar Etik Kurulu, Kırşehir, Turkey, 2018-07/74), the study was prospectively registered at Australian New Zealand Clinical Trials Registry Service (ACTRN12618000739213).

Patients

Seventy-six parturients with American Society of Anesthesiologists' (ASA) physical status class II with a term, uncomplicated singleton pregnancies aged 18–40 years scheduled for elective cesarean section with spinal anesthesia were enrolled in the study. Of the seventy-six parturients, sixty patient completed the study, and their data were analyzed. Written informed consent to participate in the study was obtained from all parturients. Patients were excluded from the study if they met any of the following: patient refusal to participate in the study or spinal anesthesia, any contraindication for spinal anesthesia, complicated pregnancies,

known maternal or fetal cardiac disease, emergency cases, eclampsia, preeclampsia, gestational diabetes or diabetes mellitus.

Group allocation

The parturients were evaluated at their preoperative visit by an anesthesiologist. This anesthesiologist was not connected with clinical care and data collection of the study but randomized parturients by computer-generated random number table. Printout of the randomization number was put in an opaque sealed envelope, and the envelope was brought in to operation room with the patient. The anesthesia nurse opened the envelope and prepared the crystalloid fluid according to group allocation on parturients' arrival to operation room for infusion with coload strategy.

Anesthesia and surgery

Parturients were monitored with standard ASA monitors [heart rate, non-invasive blood pressure, pulse oximeter (SpO₂)] and core body temperature was measured with an infrared thermometer (Riester ri-thermo®N; Rudolf Riester GmbH, Germany) from the tympanic membrane. Operation room ambient temperature was kept constant at 22 °C by preset climate. A 16G intravenous line was secured on the dorsum of the left hand. Isothermic coload group (Group W, n = 30) received crystalloid coload at 37 °C with a fluid warmer (ASTOFLO PLUS eco, Stihler Electronic GmbH, Stuttgart, Germany) switched on and covered with an opaque cover at a rate of 10 ml/kg starting with the induction of spinal anesthesia. Control group (Group RT, n = 30) received intravenous crystalloid coload at room temperature with the same fluid warmer but switched off, covered by an opaque cover at a rate of 10 ml/kg with the induction of spinal anesthesia. The anesthesia nurse switched on or off the fluid warmer according to parturients' study group. The anesthesiologist collecting data was not allowed to touch the infusion line or change the finished crystalloid fluid bags. All patients received Lactated Ringers' solution as crystalloid fluid with coload strategy.

Spinal anesthesia was performed at sitting position with a 26G spinal needle (Atraucan, BBraun, Melsungen, Germany) introduced from L3-L4 interspace navigated by ultrasound with 13.5 mg hyperbaric bupivacaine 0.5% without opioids after observation of free flow of clear cerebrospinal fluid. Parturients were immediately placed supine on the operation table with 15° left lateral tilt and surgery was commenced when spinal anesthesia level reached to T5 dermatome level assessed by loss of sensation to sharp pain with pinprick test at both midclavicular lines.

As soon as the parturient was positioned to supine with left lateral tilt, the surgical team completed antiseptic skin preparation and sterile draping. The fetus was delivered with Pfannenstiel incision, and layers were sutured anatomically. After delivery, oxytocin was given to every parturient according to protocols of obstetrics and gynecology clinic. The wound was covered with a sterile cover, and the patient was discharged to the post-anesthesia care unit.

Data collection

Demographic data (age, weight, height, BMI, ASA, and gravida) were recorded for every parturient. Baseline data for heart rate, blood pressure [systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), oxygen saturation (SpO₂), and core body temperature was recorded as the mean of patients' last three measurements at the ward. Time zero for data collection is accepted as the time when intrathecal injection of the local anesthetic drug is completed. Vital parameters were recorded every minute for 10 min following induction of spinal anesthesia

and every 5 min until the end of surgery. Fetal Apgar scores were assessed by a pediatrician who was not involved in the study and did not have information of group assignment of the parturients. Fetal cord blood gas analysis was studied from umbilical artery samples for every fetus.

The incidence of SAIH, the primary outcome of the study, defined as 80% of baseline arterial blood pressure was recorded and treated with an incremental 5 mg bolus of ephedrine. Cumulative hypotension episodes (i.e., the mean number of hypotensive episodes) were also recorded. Bradycardia defined as a heart rate less than 50 beats per minute was recorded and treated with atropine when necessary. Oxygen saturation was continuously monitored with pulse oximeter and data recorded at every data collection periods. Core body temperature was measured from the same tympanic membrane with the same infrared thermometer that had a disposable sleeve for every parturient and recorded at data collection intervals. A pediatrician assessed the fetuses with Apgar scores at first and fifth minutes after birth and umbilical arterial blood gas analysis which was the secondary outcome of the study. Fetal birth weight and rectal temperature were also recorded. The time from spinal anesthesia induction to skin incision, uterus incision, cord clamping, and the time to the end of surgery was recorded.

Statistical analysis

IBM SPSS 23.0 package program (SPSS, Inc., Chicago, IL, USA) was used for data analysis. Descriptive data are presented as frequencies, percentages, mean and standard deviation. Qualitative data was analyzed with Pearson Chi-square, Yates or Fischer's tests. Normal distribution of data was assessed by Kolmogorov-Smirnov and Shapiro-Wilk tests. Intergroup comparison of data was achieved by independent samples-t-test, Mann Whitney-U test, and repeated measures analysis of variance (ANOVA) tests followed by post-hoc Bonferroni correction. Correlations between variables were tested with Pearson Correlation or Spearman's rho Correlation tests. A probability level (p) less than 0.05 was accepted as statistically significant.

Sample size

Power analysis was assessed with G*Power 3.1.9.2 statistical package program. According to the analysis of the preliminary results of the study, 60 patients were necessary to achieve a power level of 0.86 with an effect size of 0.8 and a probability level of 0.05.

Results

Seventy-six parturients were enrolled for the study, and sixty parturients completed the study and their data were analyzed (Fig. 1). Patient characteristics such as age, weight, height, BMI, ASA, and gravida were comparable between groups. The time from induction of spinal anesthesia to skin incision, uterus incision, umbilical cord clamping, and the completion of cesarean section were not significantly different between groups (Table 1).

The incidence of SAIH, the primary outcome of the study, was observed in 17 parturients (56%) in Group W and 18 parturients (60%) in Group RT ($p = 0.625$) and treated with incremental 5 mg ephedrine boluses. The ephedrine dose was 18.5 ± 10.4 mg in Group W and 25.2 ± 22.0 mg in Group RT which was comparable between groups ($p = 0.460$). SAIH was observed 3 min after spinal anesthesia induction in both groups, and the cumulative episodes of hypotension were comparable between groups ($p = 0.871$; Figs. 2–5). Heart rate changes were not significantly different between groups ($p = 0.825$; Fig. 6). SpO₂ values were comparable

between groups ($p = 0.518$). Core body temperature at the end of surgery was higher in Group W than Group RT ($p = 0.003$; Fig. 6).

Umbilical arterial pH, fetal Apgar scores at first and fifth minute after birth, the secondary outcome of the study, was higher in Group W than in Group RT ($p = 0.013$, $p = 0.006$ and $p = 0.045$ respectively.) One fetus in Group RT but none in Group W had umbilical arterial pH lower than seven. Fetal birth weight and rectal temperature measurements were comparable in both groups ($p = 0.639$ and $p = 0.675$ respectively; Table 2).

All patients reached a spinal block level above T5 dermatome, and the number of blocked segments were comparable between groups ($p = 0.26$; Fig. 7). Time to reach sensory block at T5 dermatome level lasted three to 4 min after induction of anesthesia in both groups. Maximum sensory block level was achieved between eight to 10 min after induction of spinal anesthesia. Three parturients in Group W and two patients in group RT needed 0.5 mg atropine for the treatment of bradycardia ($p = 0.414$).

The time from spinal anesthesia induction to skin incision, uterine incision, fetal cord clamping, and wound dressing were similar between groups ($p = 0.720$; $p = 0.467$; $p = 0.813$; and $p = 0.669$ respectively).

Discussion

This prospective randomized controlled trial demonstrated that warmed crystalloid infusion at 37 °C with coload strategy during cesarean section with spinal anesthesia has comparable effects with crystalloid coload at room temperature on attenuation of SAIH incidence. However isothermic crystalloid coload results in higher umbilical artery pH values and Apgar scores at first and fifth minutes.

Several infusion strategies have been studied to overcome SAIH during cesarean section with spinal anesthesia [4,9,11–18]. Colloids stay longer in the intravascular space compared to crystalloids and therefore when used with preload strategy, logically it compensates intravenous volume depletion due to vasodilatation induced by spinal anesthesia at lower extremities and splanchnic vasculature as demonstrated by previous studies [19–21]. However, the potential risks of using colloids such as coagulation problems, cost, and allergic reactions advocate many anesthesiologists to prefer crystalloids for intravenous hydration to attenuate the incidence of SAIH during cesarean section.

Studies on the timing of colloids had confusing results. Varshney et al. [18] reported that colloid preload had a clinical advantage over the coload strategy in reducing hypotensive episodes under low dose spinal anesthesia. Teoh et al. [22] have reported that colloid preload increased maternal cardiac output for the first 5 min but maternal and fetal outcomes were not different, and Siddik-Sayyid et al. [23] concluded that there was no difference in the incidence of hypotension in parturients receiving colloids either with coload or preload strategy.

Studies comparing colloid and crystalloids also had conflicting results. Bannasr et al. [13] have compared co-loading with colloids to crystalloids and reported that colloid coload was superior to crystalloid coload to prevent maternal hypotension during cesarean section under spinal anesthesia. Tawfik et al. [16] compared colloid preload and crystalloid coload in the cesarean section under spinal anesthesia and concluded that 1000 ml crystalloid coload has similar effects to 500 ml colloid preload in reducing maternal hypotension in cesarean delivery with spinal anesthesia. In another study by Tawfik et al. [17] they compared combined colloid and crystalloid coload to crystalloid coload and reported that the combination of colloids and crystalloids had no superiority on improving maternal outcomes compared to crystalloids alone

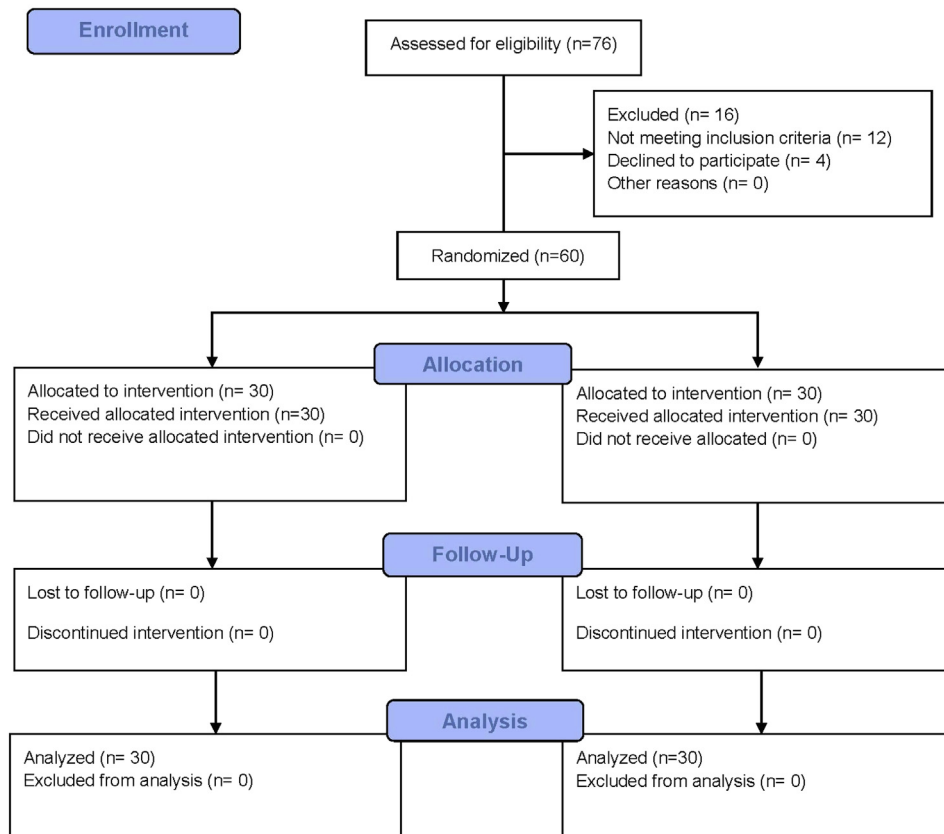


Fig. 1. Consort flow diagram.

when infused with coload strategy in parturients undergoing cesarean section with spinal anesthesia.

In the reviews reported by Mercier and Mercier et al. [4,9] combining a vasopressor regimen with colloid preloading, colloid co-loading or crystalloid co-loading is suggested to be the best method of preventing maternal hypotension after the initiation of spinal anesthesia for cesarean section under spinal anesthesia. McDonald et al. [15] also reported there was no difference in cardiac output of parturients randomized to either colloid or crystalloid coload following spinal anesthesia for elective cesarean delivery.

Table 1
Demographic and surgical data of parturients.

	Group W (n = 30)	Group RT (n = 30)	p
Age(y)	27.83 ± 4.66	27.86 ± 4.06	0.977
Height(cm)	162.60 ± 6.35	163.47 ± 5.72	0.581
Weight(kg)	78.96 ± 10.82	79.66 ± 13.55	0.826
BMI (kg/m ²)	29.97 ± 4.73	29.80 ± 4.65	0.888
Gravida (n)	2.33 ± 1.02	2.06 ± 0.86	0.282
ASA II	30 (%100)	30 (%100)	1.000
Crystalloid Coload (L)	1.10 ± 0.3	1.12 ± 0.3	0.996
Spinal anesthesia to			
Skin incision (min)	3.36 ± 1.21	3.28 ± 1.17	0.720
Uterus incision (min)	6.10 ± 1.43	5.73 ± 1.72	0.467
Umbilical clamp (min)	6.86 ± 1.50	6.76 ± 1.75	0.813
Wound dressing (min)	24.76 ± 8.81	25.63 ± 6.65	0.669

Values are expressed as mean ± SD and percentage as appropriate. There was no statistically significant difference between groups ($p > 0.05$ for all comparisons). Group W = crystalloid infused at 37 °C with coload strategy, Group RT = crystalloid infused at room temperature with coload strategy. BMI = body mass index, ASA = American Society of Anesthesiology Physical Status Score.

A recent study has reported that crystalloid infusion with coload strategy is superior to preload for the prevention of SAIH during spinal anesthesia for cesarean section [10]. Oh et al. [11] also have reported the superiority of crystalloid co-loading over preloading to prevent maternal hypotension after spinal anesthesia.

The challenging difference in our study from the previous studies was the assessment of the temperature of the crystalloid infused with coload strategy in attenuating the incidence of SAIH and its effects on fetal outcomes. We found comparable results for SAIH between groups. Peripheral vasodilatation due to warmed intravenous fluid administration did not result in a statistically significant difference in maternal blood pressure.

Umbilical arterial pH and fetal Apgar scores were higher in Group W when compared to Group RT. The probable explanation of higher fetal Apgar scores and umbilical pH in Group W may be the

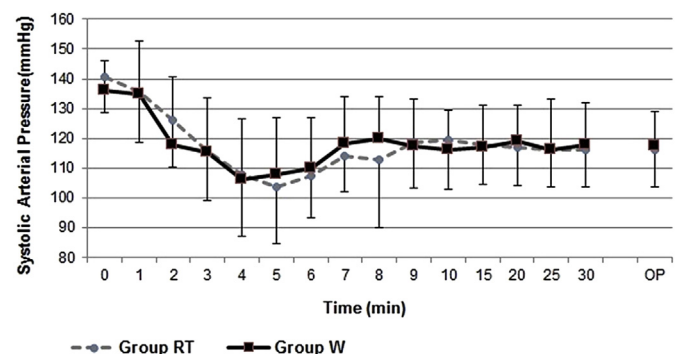


Fig. 2. Systolic arterial blood pressure against time.

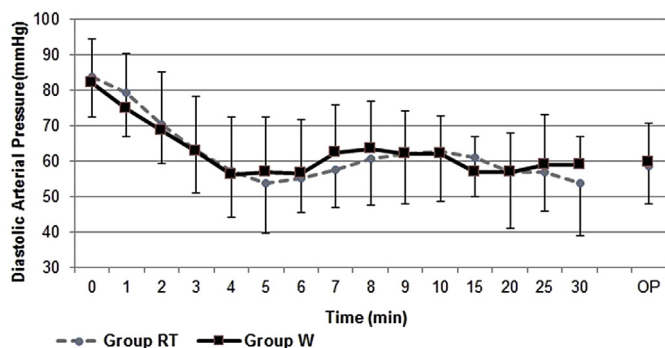


Fig. 3. Diastolic arterial blood pressure against time.

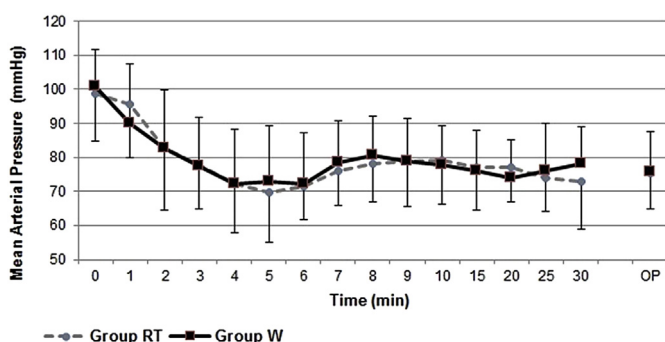


Fig. 4. Mean arterial blood pressure against time.

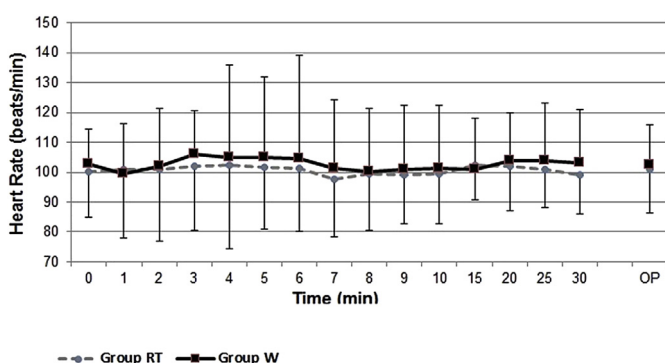


Fig. 5. Heart rate changes against time.

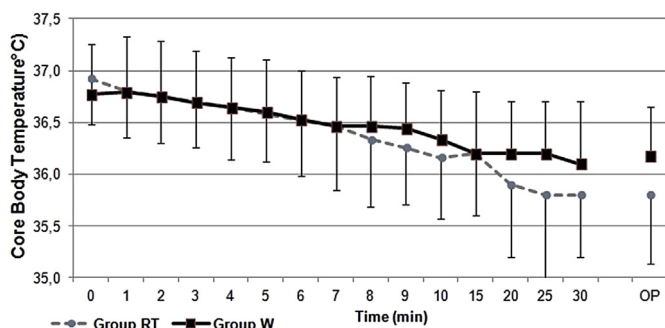


Fig. 6. Change in core body temperature against time.

Table 2
Fetal outcomes.

	Group W (n = 30)	Group RT (n = 30)	p
Apgar 1st minute	8.76 ± 0.43	8.40 ± 0.56	0.006
Apgar 5th minute	9.80 ± 0.20	9.60 ± 0.40	0.045
Umbilical arterial pH	7.3762 ± 0.0558	7.3433 ± 0.0422	0.013
Newborn weight (g)	3295.8 ± 385.2	3348.5 ± 476.3	0.639
Rectal Temperature	36.96 ± 0.69	36.87 ± 0.88	0.675

Values are expressed as mean ± SD percentages and numbers as appropriate. Group W = crystalloid infused at 37 °C with coload strategy, Group RT = crystalloid infused at room temperature with coload strategy. There was no statistically significant difference between groups for pH, newborn weight and gender. Apgar scores were significantly different at first and fifth minute after delivery.

lower incidence of maternal hypothermia due to the infusion of warmed crystalloid coload. In a former study by Yokoyama et al. [24], the effect of pre-warmed intravenous fluids on the frequency of hypothermia following spinal anesthesia for cesarean delivery was studied and in that study fetal Apgar score at the first minute, and umbilical arterial pH was higher in the warmed infusion group. The nadir blood pressure in both groups was comparable in both groups, and the amount of atropine and ephedrine used was also similar between groups. Therefore they suggested that the difference in umbilical arterial pH may be due to the difference in the temperature of infusion. The results of the present study and that of Yokoyama et al. [24] are in accordance to report a statistically higher umbilical pH value and higher Apgar score. This result may even be more critical in emergency cesarean sections where the fetus is under stress. This topic may be the scope of a further clinical study.

A very striking point in the current study was the time interval between the induction of spinal anesthesia to the delivery of the fetus which was shorter compared to the previous studies conducted to assess strategies to attenuate the incidence of SAIH. This time interval was 12–13 min in the study reported by Karacaer et al. which was the shortest amongst other previous studies [13,15–17,22,23,25] however in the current study the time from spinal anesthesia induction to delivery was shorter than 7 min in both groups. Also, umbilical cord blood gas analysis revealed most of the pH values were in physiologic pH range, which was also higher than the previous studies. As pointed out by Sumikura [6] shortening the time lapse from induction of spinal anesthesia to delivery may be of great importance considering the well-being of fetus which needs to be validated by further controlled trials.

Limitations regarding our study are as follows: first, we did not assess other side effects of spinal anesthesia as nausea, vomiting, and shivering. Second, the time interval from the induction of spinal anesthesia to skin incision, uterine incision, delivery of the fetus, and wound dressing was shorter in the current study than previous studies. Further studies are needed to assess the

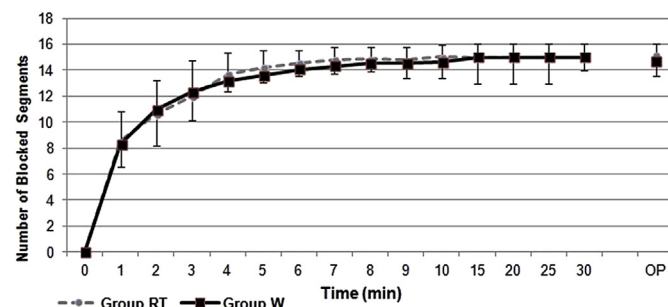


Fig. 7. Number of blocked segments against time.

relationship between SAIH and fetal outcomes with the time lapse from induction of spinal anesthesia to delivery.

Conclusion

In conclusion, isothermic crystalloid coload strategy results in higher umbilical pH values and Apgar scores which may play a critical role when the fetus is under stress conditions. Therefore pre-warmed crystalloids should be infused to obtain better fetal outcomes in patients undergoing cesarean section with spinal anesthesia.

Conflict of interest

None.

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