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Effect of warming different intravenous fluids on maternal and neonatal outcomes during cesarean section - comparison of crystalloids and colloids

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Ethics Committee Approval
The study protocol was approved by Zekai Tahir Burak Women's Health Training and Research Hospital's Ethical Committee (2011-KAEK-19, Approval code: 155/2017).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Fluid warming is a useful method to prevent maternal and neonatal hypothermia. Because colloids stay in the intravascular space longer than crystalloids, their protective effect against hypothermia may be more emphasized. The aim of this study is to compare the effects of using warmed colloids or crystalloids on maternal and neonatal core temperatures, neonatal blood gas values, and maternal thermal comfort scores.

Methods: After ethical approval, 220 ASA I or II pregnant women, scheduled for cesarean section with spinal anesthesia were enrolled in the study. Patients were assigned to receive hydroxyethyl starch (group HES) or Ringer's lactate solution (group RL) throughout the intraoperative study period. Once the patient entered the room, fluids were actively warmed with fluid warmer to 41 °C in both groups. Measurement of maternal core temperature (MT) and thermal comfort score (TCS) were performed before starting intravenous fluid administration (control), at the time of delivery of the neonate (delivery), 15th, 30th minutes, and at the end of the surgery. Tympanic temperature of the neonates was measured 1 minute after delivery. Blood gas samples from the umbilical artery of the neonates at the 1st minute and Apgar scores at 1st and 5th minutes after delivery were evaluated.

Results: Maternal tympanic temperatures, maternal thermal comfort scores were higher at all measurement values other than control measurement in group HES. Neonatal tympanic temperatures (P = 0.051), neonatal umbilical artery cord pH (P < 0.001) and pO_2 (P = 0.001) values were higher and pCO_2 (P < 0.001) and HCO_3 (P < 0.001) values were lower in group HES.

Conclusion: Colloids are more effective than crystalloids in terms of maternal and neonatal temperatures and thermal comfort scores. Even if there was no difference between Apgar scores in our study, for neonates with potential vulnerabilities, better umbilical artery cord values may provide clinical advantages.

Keywords: Hypothermia, Crystalloids, Colloids, Maternal core temperature, Neonatal core temperature, Apgar score

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Introduction

Hypothermia occurs in 30-60% of parturients who delivers with cesarean section with neuroaxial anesthesia and maternal hypothermia contributes to hypothermia of the newborn [1, 2]. Neonatal hypothermia is commonly defined as a core temperature below 36.5°C [3]. Hypothermia has an impact on neonatal mortality and morbidity, especially in preterm and low birth weight infants [4].

Neuroaxial anesthesia has been shown to demonstrate a negative correlation between block levels and core temperature by inhibiting vasomotor function which results in peripheral vasodilatation [5].

In the study in which intestinal temperature was measured in 28 patients who underwent spinal anesthesia for elective cesarean section, hypothermia was observed in half of the patients, and baseline values could not be restored in 8 of these patients during the 8-hours follow-up [6].

Infusion of warmed intravenous fluids is used to prevent hypothermia. Use of colloids instead of crystalloids may be more effective in cesarean section operations, since colloids are four times long lasting in the intravascular space [7].

Yokoyama et al. [8] showed that using prewarmed (41°C) intravenous fluids reduced the occurrence of maternal hypothermia during cesarean section. In that study, maternal core temperature, neonatal Apgar scores, and blood gas values have been shown as significantly improved with warmed colloids.

The aim of this study is to compare the effects of using either warmed colloids or warmed crystalloids on maternal and neonatal core temperatures, neonatal blood gas values and maternal thermal comfort scores.

Materials and methods

The study protocol was approved by Zekai Tahir Burak Women's Health Training and Research Hospital's Ethical Committee (2011-KAEK-19, Approval code: 155/2017) and study was conducted according to the Helsinki Declaration principles.

After Ethics Committee approval, 220 ASA I or II pregnant women, scheduled for cesarean section with spinal anesthesia were enrolled in the study. An informed written consent was taken from the patients before participation. Exclusion criteria were refusal or contraindication for regional anesthesia, age under 18 or over 40 years, body weight over 100 kg and body height below 150 cm, pregnancy with gestational age under 36 weeks and multiple gestations, fetal anomaly, placental invasion anomalies, history of preeclampsia/eclampsia, and abnormal values of fibrinogen, coagulation tests, hemoglobin, hematocrit and platelet.

Using a computer-generated randomization list, patients were assigned to receive hydroxyethyl starch (6% Voluven® 130/0.4, Fresenius, Pharma Austria GmbH, Graz, Austria) (group HES) or Ringer's lactate solution throughout the intraoperative study period (group RL). Patients in the group HES received hydroxyethyl starch 130/0.4 10 mL/kg/h and group RL received Ringer lactate solution 20 mL/kg/h. The volume regimen was based on the presumption that hydroxyethyl starch and Ringer lactate solution show different volume effects. As soon as the patient entered the room, fluids were actively warmed with fluid warmer (en Flow® Controller Model 121, USA) to 41°C. The safety of usage and stability of HES that had been warmed has been shown in previous studies [9].

With patients in the sitting position, spinal anesthesia was performed with 26 gauge atraucan (atrau-com®, Egemen International, Izmir) needle. A standard solution of 12 mg hyperbaric bupivacaine was injected in 30 seconds to cerebrospinal fluid. After the procedure, the patients lied supine with 20° tilt to left to prevent hypotension caused by aorta-caval pressure.

Hypotension was defined as a decrease of 20% or more below baseline mean arterial pressure value and treatment was achieved with ephedrine bolus of 10 mg until the mean arterial pressure returned to normal values. Bradycardia was defined as heart rate < 50 beats/min and treatment was achieved with atropine 0.5 mg.

Measurement of maternal core temperature and thermal comfort score was performed before starting intravenous fluid administration (control), at the time of delivery of the newborn (delivery), 15th, 30th minutes and at the end of the surgery. Tympanic temperature of the neonate was measured 1 minute after delivery. A blood gas sample from the umbilical artery was obtained and analyzed by a blood gas analyzer. Apgar scores were evaluated 1 and 5 minutes after delivery by a pediatrician.

Statistical analysis

Statistical analyses were performed using SPSS Software (Version 21.0, SPSS Inc., IL, USA. Continuous data were expressed as mean(SD) (range). After determining normal distribution using Kolmogorov-Smirnov test for quantitative data, analysis were performed using either Student's t-test or Mann–Whitney U-test. $P < 0.05$ was considered significant.

The primary outcome was the difference in mean Tc between study groups at the time of delivery of newborn (Tcdel) Secondary outcomes were all Tc measurements, neonatal Tc, neonatal arterial blood pH. The sample size of study was calculated based on a performed pilot study of 20 patients (n = 10 in each group). A clinically significant difference in Tcdel between study groups was 0.2 and groups had a standard deviation (SD) of 0.4 and 0.6. The minimum sample size required to detect a significance difference was calculated as at least 104 in each group, (208 in total), considering type I error (alfa) of 0.05, power (1-beta) of 0.8, effect size of 0.39 and two-sided alternative hypothesis.

Results

There was no statistically significant difference between the demographic characteristics of patients in group HES and group RL. Duration of anesthesia-induction, duration of surgery and cord-clamping time were not different between two groups. The amount of administered intravenous solutions was 390.0 (107.4) mL for group HES, and 646.6 (255.9) mL for group RL (Table 1).

In neonatal umbilical artery cord pH analysis, the pH ($P < 0.001$) and pO_2 ($P = 0.001$) values were higher, and pCO_2 ($P < 0.001$) and HCO_3 ($P < 0.001$) values were lower in group HES when compared to group RL. The Apgar scores at 1st and 5th minute were not different between two groups. Tympanic

temperature of the neonates at birth was also higher in group HES (P = 0.051) (Table 2).

Table 1: The demographical and surgical characteristics of patients

	Group HES n = 110 mean(SD) (min-max)	Group RL n = 110 mean(SD) (min-max)	P-value
Height (cm)	161.8(4.3) (157-170)	161.4(6.8) (150-170)	0.935
Weight (kg)	84. (13.2) (67-108)	80.3(12.7) (60-107)	0.461
Age (years)	32.0(4.1) (27-38)	31.1(4.9) (23-42)	0.683
Gestational age (weeks)	38.7(0.3) (38-39)	38.7(1.1) (36-40)	0.261
Infused intravenous fluid (ml)	390.0(107.4) (250-500)	646.6(255.9) (400-1100)	0.007*
Anesthesia-surgery initiation duration (min)	7.4(2.6) (5-13)	7.1(1.8) (5-11)	0.849
Duration of surgery (min)	40.1(7.7) (30-55)	48.2(16.9) (27-87)	0.216
Cord clamping time (min)	5.8(1.8) (3-9)	6.2(3.0) (4-10)	0.412

*P < 0.05

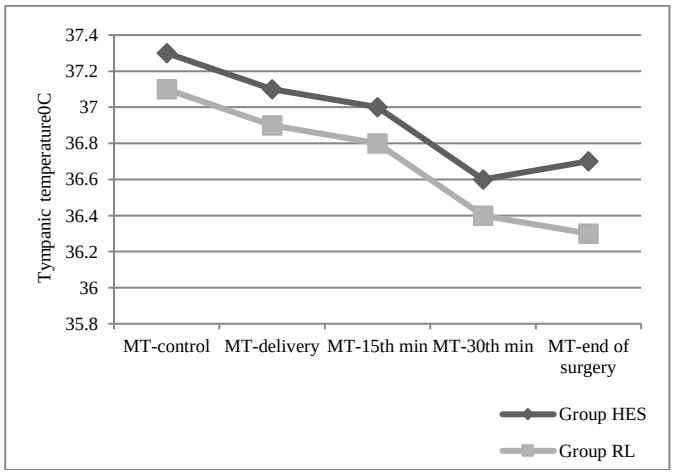
Table 2: Neonatal outcomes

	Group HES n = 110 mean(SD) (min-max)	Group RL n = 110 mean(SD) (min-max)	P-value
Apgar (1st min)	8.7(0.4) (8-9)	8.5(0.7) (7-9)	0.765
Apgar (5th min)	9.9(0.3) (9-10)	9.8(0.3) (9-10)	0.892
Tympanic temperature (ºC)	37.9(0.3) (37.5-38.5)	37.7(0.9) (34.6-39.1)	0.051*
pH	7.34(0.04) (7.26-7.41)	7.32(0.04) (7.22-7.38)	< 0.001*
pO_2 (mmHg)	24.2(6.9) (16.4-35.8)	20.3(4.8) (12.4-30.6)	0.001*
pCO_2(mmHg)	40.5(6.7) (33.6-52.4)	43.6(7.2) (31.1-56.9)	< 0.001*
HCO_3 (mmol/L)	21.4(2.7) (18.2-27.9)	22.1(2.6) (15.4-26.3)	< 0.001*
BE (mmol/L)	-3.25(2.8) (-6.6- -2)	-3.45(2.3) (-9.5- -1)	0.865

*P < 0.05

Maternal core temperatures at delivery (P = 0.017), at 15th minute (P < 0.001), at 30th minute (P = 0.002) and at the end of the surgery (P < 0.001) were higher in group HES when compared to group RL (Table 3) (Figure 1).

Figure 1: Maternal core temperatures (MT)



When the groups were compared in terms of thermal comfort score, TCS-delivery (P < 0.001), TCS -15th minute (P = 0.004), TCS-30th (P = 0.001) and TCS- end of surgery (P = 0.017) were higher in group HES (Table 3) (Figure 2).

There was no difference between the groups in terms of maternal hemodynamic variables and ephedrine use (Table 4).

Figure 2: Maternal thermal comfort scores (TCS)

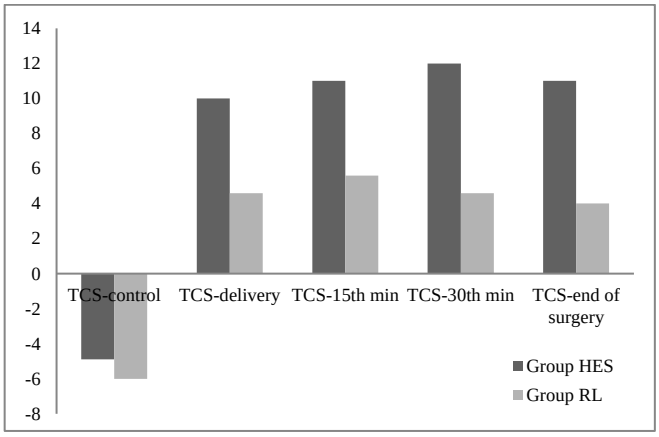


Table 3: Maternal tympanic temperature and thermal comfort score

	Group HES n = 110 mean(SD) (min-max)	Group RL n = 110 mean(SD) (min-max)	P-value
Maternal temperature (ºC) -control	37.3(0.4) (37.6-37.9)	37.1(0.3) (36.3-37.4)	0.230
Maternal temperature (ºC) -delivery	37.1(0.6) (36.3-38.1)	36.9(0.4) (36.1-37.5)	0.017*
Maternal temperature (ºC) -15th minute	37.0(0.6) (35.9-37.8)	36.8(0.3) (36.1-37.5)	< 0.001*
Maternal temperature (ºC) -30th minute	36.6(0.6) (35.7-37.6)	36.4(0.4) (35.7-37.6)	0.002*
Maternal temperature (ºC) -end of surgery	36.7(0.8) (35.5-37.7)	36.3(0.5) (35.6-37.3)	< 0.001*
TCS-control	-4.9(15) (-20-20)	-6.0(9.8) (-20-10)	0.857
TCS-delivery	10(14) (0-40)	4.6(1.7) (-10-40)	< 0.001*
TCS- 15th minute	11(15.2) (0-40)	5.6(12.9) (-10-40)	0.004*
TCS-30th minute	12.0(16.8) (0-40)	4.6(11.8) (-10-40)	0.001*
TCS- end of surgery	11.0(17.9) (-10-40)	4.0(11.2) (-10-40)	0.017*

*P < 0.05, TCS: Thermal comfort score

Table 4: Maternal hemodynamic variables and ephedrine use

	Group HES n = 110 mean(SD) (min-max)	Group RL n = 110 mean(SD) (min-max)	P-value
MAP (mmHg) -control	94.5(9.3) (81-106)	98.4(8.8) (73-108)	0.311
HR (beat/min) -control	90.4(12.1) (75-111)	99.2(15.5) (78-137)	0.103
MAP (mmHg) -start of surgery	67.5(12.0) (56-97)	74.2(14.1) (43-98)	0.08
HR (beat/min) -start of surgery	105.2(22.5) (86-162)	93.6(21.9) (64-129)	0.397
MAP (mmHg) -delivery	79.4(14.5) (60-102)	78.6(11.2) (57-97)	0.987
HR (beat/min) -delivery	97.3(25.3) (76-162)	94.8(16.5) (65-132)	0.723
Amount of ephedrine used (mg)	10.6(4.1) (5-20)	12.5(7.0) (10-30)	0.057

*P < 0.05, MAP: Mean arterial pressure, HR: Heart rate

Discussion

Pregnant women undergoing cesarean section are susceptible to hypothermia. There are many reasons causing heat loss during cesarean section under neuroaxial anesthesia. Vasodilation below sensory block causes heat loss, due to decreased core-periphery temperature gradient and redistribution of the blood [10, 11]. Neuraxial anesthesia also results in reduction of thermoregulatory vasoconstriction and shivering thresholds above the level of the block by approximately 0.5°C [12].

Sultan et al. [13] reported improved umbilical artery cord pH by active warming in a meta-analysis yet the rest of the neonatal outcomes were remained unchanged. Maternal temperature decrease was smaller in this warmed group. During cesarean delivery, patients may receive liters of intravenous fluids intra-operatively to minimize spinal hypotension. Fluid warming may be effective in the cesarean delivery to reduce any

decrease in core temperature and reduce the degree of heat loss from core to periphery.

When colloids are administered, the most of the solution is expected to remain in intra vascular space, and heat distribution may have occurred in a limited area such as the heart, trunk, and vascular space. In last trimester, 85% of the heat produced by the fetus exits by the placenta [14]. Therefore, we hypothesized that using warmed intravenous colloid solutions instead of crystalloid solutions may enhance the fetus to receive warm blood supply through the placenta. The oxyhemoglobin dissociation curve shifts to the right with warmed blood [15]. Thus neonates in the warmed colloid group may have received higher oxygen supply before birth.

In another study using warmed colloids, Apgar scores at one minute and umbilical artery pH were reported significantly higher in the warmed colloid group than the unwarmed colloid group [8].

The main finding of this study is that maternal tympanic temperature, maternal thermal comfort score and the neonatal tympanic temperature, pH, pO_2 values were higher and pCO_2 and HCO_3 values were lower in group HES when compared to group RL. There was no difference between Apgar scores.

Although neonatal umbilical artery cord pH and tympanic temperature of the neonates at birth were significantly higher in group HES than group RL, the difference between measurements was not very high. Still, these small differences may be clinically useful for neonates with potential neonatal vulnerabilities such as prematurity, cardiac abnormalities, low birth weight and fetal distress, and may alter Apgar scores.

As seen in the literature, our study of comparing the effects of using either warmed colloids or warmed crystalloids on maternal temperatures and maternal thermal comfort scores and neonatal outcomes was the first study that planned in this way.

Limitations of the study include not measuring the time between patient's entrance to the room and the onset of anesthesia. However, no difference was found between other measured durations. Therefore, there is a need for further studies to clarify the effect of the timing of the warming.

Conclusion

Choosing the warmed fluid given to pregnant women during cesarean section as colloids is more effective against hypothermia by providing superiority to crystalloids in terms of maternal and neonatal temperatures and thermal comfort scores. Although there is no difference in terms of Apgar scores in this study, we think that the difference in neonatal umbilical artery cord pH in favor of group HES may have a positive effect on neonates with risk factors.

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