DOES WARMING INTRAVENOUS FLUIDS DURING SPINAL-INDUCED HYPOTENSION DECREASE THE INCIDENCE OF HYPOTENSION AND REDUCE THE AMOUNT OF FLUID, TRANSFUSION AND EPHEDRINE REQUIREMENTS?

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Abstract

Background/Aim: This study was undertaken to test whether warming IV fluids (37ºC) results in lower incidence of hypotension, less ephedrine and transfusion requirement and lower fluid consumption than use of room-temperature fluids (22°C) in cesarean delivery patients undergoing spinal anesthesia.

Materials and Methods: We studied 63 parturients with uncomplicated pregnancies undergoing elective cesarean delivery under spinal anesthesia. Parturients were allocated randomly as un-warmed fluid group (Group C, n=30) and warmed fluid group (Group W, n=30). Maternal body temperatures, the incidence of hypotension, ephedrine and transfusion requirements, total fluid volumes, and side effects were recorded.

Results: Maternal body temperatures were significantly higher in the warmed group compared with the un-warmed group only at 15 min (p=0.02). There was no significant difference between the two groups in the incidence of hypotension (70% (21/30), 56.7% (17/30) in Group C and W respectively). Fluid requirement and ephedrine consumptions were similar between the two groups and no patient needed blood transfusion.

Conclusion: In cesarean section patients undergoing spinal anesthesia, warming IV fluids (37°C) resulted in lower incidence of decreased core temperature but did not affect the incidence of maternal hypotension, ephedrine and transfusion requirement and volume consumption.

Keywords: Cesarean delivery, hypothermia, hypotension, ephedrine consumption, fluid and transfusion requirement.

Introduction

Inadvertent perioperative hypothermia (IPH) during cesarean delivery is not rare and frequently neglected, despite the recommendations by clinical guidelines[1]. Even a mild degree of hypothermia (<1°C) can be associated with significant adverse complications including increased wound infection rates, length of hospital stay, operative blood loss, anesthetic recovery time and intraoperative hypotension[2].

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Hypothermia-related hypotension may emerge with various factors during surgery. First, inverse relation has been demonstrated between hypothermia and cardiac contractility during cardiac surgery[3]. Second, negative inotropic and chronotropic effect in humans, secondary to a declined sarcoplasmic reticulum-Ca^{++} storage and decreased atrial calcium sensitivity during hypothermia has also been reported previously[4]. Third, mild hypothermia significantly induces coagulopathy, increases blood loss, reduces blood pressure and results in hypotension in surgical patients. In a prospective randomized study, mild therapeutic hypothermia significantly increased surgical blood loss (16%) and transfusion requirement (22%) in normothermic and mildly hypothermic patients[5]. In another retrospective study, perioperative hypothermia caused significantly higher fluid, transfusion, vasopressor and inotrope requirement in patients undergoing elective abdominal aortic aneurysm repair[6].

Apart from surgery, neuraxial anesthesia used for cesarean delivery has also been demonstrated to impair normal autonomic thermoregulatory control, exacerbate inadvertent perioperative hypothermia and thereby may increase the risk of blood loss, hypotension and fluid requirement[7,8]. Finally, studies have shown that patients with warmer body temperatures tend to experience less acidosis, better cardiac contractility and lower incidence of hypotension[2,4]. We assumed that preventing hypothermia not only decreases the incidence of hypotension but also reduces the fluid and transfusion requirements.

Various measures such as pre-warming of patients or fluids before anesthesia, perioperative warming of iv fluids and active/passive cutaneous warming techniques have all been used to prevent or to reduce IPH[9,10]. However, to date, as far as we know, the effect of intravenous fluid warming on the incidence of hypotension, ephedrine requirement and total volume consumption during cesarean section has not previously been investigated.

This prospective, double-blinded, randomized, controlled study was undertaken to test whether warming IV fluids (37°C) results in lower incidence of hypotension, less ephedrine and transfusion requirements and lower fluid consumption than use of room-temperature fluids (22°C) in patients undergoing cesarean section under spinal anesthesia.

Materials and Methods

This trial is registered with Clinical Trials. gov with registration number: NCT02582112. Following approval by faculty and ministry of health ethics committee (23.09.2010 / 30, date / decision number) and written informed patient consent, 63 healthy parturients undergoing elective cesarean section with spinal anesthesia were invited to participate in the study. Inclusion criteria were previous cesarean section and breech presentation. Exclusion criteria included parturients younger than 18 and older than 43 years, significant co-morbid disease such as preeclampsia or eclampsia, thyroid disorders, neurological disorders, increased risk of intra-operative hemorrhage (such as placenta accreta), and any contraindication to spinal anesthesia such as bleeding disorders or local infection at injection site. Preoperatively and just before beginning the study, parturients were instructed on the use of pain scale (Verbal Rating Scale (VRS)) for pain assessment. All parturients had fasted for at least 6 hours and no premedication was given except routine antacid prophylaxis.

Following arrival in theatre, intravenous access was achieved via an 18 Gauge venous cannula and patients were monitored with automated blood pressure cuff, lead II electrocardiogram, thermo digital clinical thermometer, non-contact forehead thermometer and pulse oximetry. Convective warming blankets were used in all patients to maintain maternal temperature.

Parturients were allocated using computer generated random numbers and sealed envelopes to one of two groups as follows: Un-warmed fluid group (Group C) and warmed fluid group (Group W).

Body temperatures in parturients were measured before the induction of spinal anesthesia and at 15 and 30 min after the start of operation using both digital oral thermometer (C402; Terumo Corporation, Tokyo, Japan) and forehead skin thermometer (Thermofocus, model 01500, TECNIMED, Varese, Italy) and the highest reading was used for analysis. The operating room ambient temperature was set and maintained near 22°C by central air conditioning system. Ambient

(Room) temperature was monitored continuously by a thermometer (Klimalogg Pro). All iv fluids were stored in a water-bath sufficient to maintain the temperature of fluids at 22°C. They were taken out from storage and covered with an invisible package just before infusion.

The spinal anesthesia was performed with the parturient in the sitting position using a midline approach at the L_{3-4} or L_{4-5} intervertebral level by experienced, qualified anesthetists using a standard spinal anesthetic technique. Following identification of the intervertebral space and return of clear spinal fluid, a standard spinal anesthetics consisting of 0.5% heavy bupivacaine 10 mg combined with 25 mcg of fentanyl was given. After intrathecal injection of anesthetics, the parturients were placed in the supine position and operating table was tilted by a 15°-20° left side for the prevention of aortocaval compression. Maximum sensory block height was tested using pinprick and recorded at 1, 3, 5 10, 15, 20, 30, and 45 min after patients placed supine following spinal anesthesia. Surgery was allowed to start after obtaining a sensory block higher than T_5 dermatome.

Lactated Ringer's infusions were started at the maximal possible rate before the induction of spinal anesthesia in both groups. In order to maintain blinding, all intravenous fluids in the two groups were given via a Hotline fluid warmer (Smiths Medical ASD, inc. Rockland, MA 02370, USA), which was only switched off in Group C and switched on in Group W by an anesthetist in charge of the case. To provide blinding, all hotline monitors and giving sets were also covered in tubular bandage or invisible package so that investigator was unable to see if there was any condensation.

An anesthetist in charge of the case performed the spinal anesthesia, administered fluid and supervised the clinical management according to our clinical routine practice, whilst a separate investigator blinded to the treatment groups recorded hemodynamic parameters (systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR)) and peripheral oxygen saturation (SpO_2) preoperatively and at 1, 3, 5 10, 15, 20, 30 and 45 min after IT injection intraoperatively.

Hypotension, defined as systolic blood pressure less than 80% of baseline (prenatal) or <90 mm Hg, was treated with repeated doses (10 mg) of IV ephedrine. Bradycardia (defined as any rhythm disorder with a heart rate less than 50 beats min^{-1}) was corrected with iv 0.5 mg of atropine sulfate.

The occurrence of hypotension (administration of at least one dose of ephedrine), mean amount of blood loss (measured by visual estimation), ephedrine requirements (number of patients requiring ephedrine and mean dose of ephedrine consumption), total fluid consumptions, bradycardia, hypoxemia (SpO_2 < 90), pain (VRS), shivering, nausea and vomiting were recorded intraoperatively. A less than 24% hematocrit (or 8 gr of hemoglobin) was regarded as transfusion requirement.

Pain was assessed using a pain scale (verbal rating scale (VRS) from 0 to 10 (0=no pain, 10= most intense pain imaginable) by an anesthetist blinded to the treatment group. If pain score exceeded four or the patient requested supplement analgesia, 1 mg/kg of tramadol was given intravenously for postoperative pain relief. Side effects such as hypoxemia, shivering, nausea and vomiting was graded as present or absent as well. Maternal body temperatures were also recorded preoperatively, and at 15, 30 min intraoperatively, and 5, 15, 30, 60 and 120 minutes postoperatively.

After delivery, umbilical artery blood gas samples (PO_2, pCO_2, pH, Base excess (BE) and hematocrit (Htc)) were taken and Neonatal Apgar scores at 1 and 5 min after delivery were recorded by an attending pediatrician who was unaware of the groups.

Demographic data (age, weight, and height), parturient characteristics (parity and gravity) and duration of surgery were recorded by an anesthesiologist blinded to groups. When the surgery is done, the Hotline fluid warmer was switched off and disconnected, and a standard IV fluid infusion set was attached.

On arrival to postanesthesia care unit (PACU), pain, level of sensory and motor blockage, hemodynamic variables (SBP, DBP, HR and SpO_2) and side effects were evaluated. Discharge criteria for the ward were resolved motor block, hemodynamic stability (blood pressure within 20% of the preanesthetic levels), absence of clinically significant pain, no nausea or vomiting.

The primary study endpoint was the incidence

of intraoperative maternal hypotension (ephedrine requirement). We calculated that 60 women, 30 for each group would be needed to demonstrate a 35% difference in the incidence of intraoperative maternal hypotension or ephedrine requirement between groups (beta=0.2, alpha= 0.05). Normality was evaluated for each continuous variable, and normally distributed values were presented as mean (SD), others as median (range) where appropriate. Categorical variables were summarized as number and percent. Demographic (maternal age, height and weight) variables were analyzed using Student's T test. Clinical data were analyzed using the Student-t / Mann-Whitney's U test where appropriate. The incidence of hypotension in the groups was compared by Chi-square test. Hemodynamic variables were analyzed by repeated measure analyses (RMA). The incidences of side effects were analyzed using Chi-square tests. P values lower than 0.05 were considered significant. IBM SPSS 20.0 (IBM SPSS, inc., Chicago, IL) was used to perform statistical analyses.

Results

Sixty-three patients were enrolled but only 60 patients completed the study. There were 3 withdrawals: 2 were because of a protocol violation in Group C, and 1 in Group W because of inadequate data collection. These patients were dropped from further analysis (Figure 1).

There were no significant differences between the two groups in demographic data, parturient characteristics and duration of surgery (Table 1). Neonatal Apgar scores at 1 and 5 min after delivery and umbilical artery blood gas samples were also similar (Table 2). There was no statistically significant difference in the hemodynamic data (SBP, DBP, HR and SpO_2) between groups. Perioperative SBP and DBP values are shown in Figure 2-3. HR and SpO_2 values during all study periods were within the normal range. Maximum sensory block height was achieved within 10 min in both groups and no significant difference in the level of maximum sensory block height was found between the two groups (Table 3).

Fig. 1
Flowchart of the patients

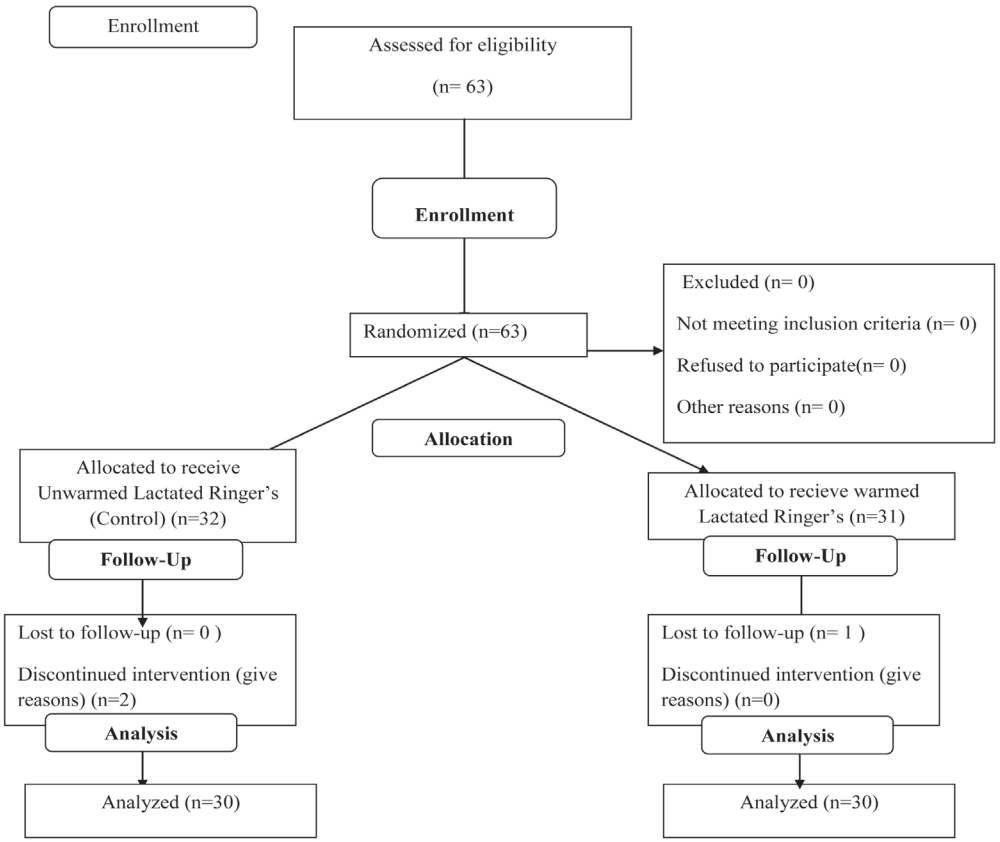


Table 1

Demographic data and duration of surgery in groups. Data are presented as mean ± SD or median (range).

	Group C (n=30)	Group W (n=30)	P-value
Age (year)	32.4±6.3	31.6±4.7	0.58
Height (cm)	1.60±5.0	162±5.7	0.32
Weight (kg)	79.9±12	75.5±11.3	0.15
Parity	2.5 (1-6)	2 (1-4)	0.55
Gravidity	3 (1-11)	3 (1-5)	0.11
Duration of surgery (min)	47.9±12	46.2±13.3	0.58

Data are presented as mean ± SD or median (range).

Table 2

Neonatal Apgar scores and umbilical artery gas values. pO_2: Oxygen pressure, pCO_2: Carbon dioxide pressure, Htc: Hematocrit Data are presented as mean±SD or median (range)

	Group C (n=30)	Group W (n=30)	*P-value*
Apgar score @ 1. min	8 (3-9)	9 (5-10)	0.94
Apgar score @ 5. min	8 (6-10)	9 (9-10)	0.40
Umbilical artery pH pO_2 (mmHg) pCO_2 (mmHg) BE	 7.35±0.03 25.1±6.8 43±5.7 -1.9 (-8.6 0.6)	 7.34±٠,٠٥ 23.9±5.7 43.1±6.5 -1.5 (-4.9 3.8)	 0.49 0.47 0.93
Htc	43±4.5	44±5.7	0.44

pO_2: Oxygen pressure, pCO_2: Carbon dioxide pressure, Htc: Hematocrit

Data are presented as mean±SD or median (range)

Table 3

Maximum sensory block heights. Data are presented as median (min-max). K- Wallis Test was used

	Group C (n=30)	Group W (n=30)	*P*-value
Time 1 min 3 min 5 min 10 min 15 min 20 min	 T10 (T5-T12) T6 (T4-T12) T5 (T2-T10) T4 (T2-T6) T4 (T2-T6) T4 (T2-T6)	 T8 (T4-T12) T6 (T4-T12) T4 (T2-T10) T4 (T2-T8) T4 (T2-T7) T4 (T2-T7)	 0.76 0.42 0.36 0.72 0.70 0.29
30 min	T4 (T2-T6)	T4 (T2-T7)	0.19
45 min	T5 (T2-T7)	T4 (T2-T7)	0.24

Data are presented as median (min-max)

Table 4

Estimated blood Loss, total amount of volume infused, incidence of hypotension and ephedrine requirements. Data are presented as mean±SD, median (min-max) or n (%)

	Group C (n=30)	**Group W (n=30)**	**P-value**
Total volume (mL)	1870±386	1796±251	0.38
Hypotension (n %)	21(70%)	17(56.7%)	0.42
Mean dose of ephedrine (mg)	20.6±18.5 20 (0-50)	13.6±15.4 10 (0-50)	0.11

Data are presented as mean±SD, median (min-max) or n (%)

Table 5

The number of patients requiring ephedrine in groups. Data were presented as count (% within group).

mg			Group		Total
			Control	Warming	
Ephedrine	00	Count (%)	9 (30%)	13 (43,3%)	22 (36,7%)
	10	Count (%)	4 (13,3%)	5 (16.7%)	9 (15%)
	20	Count (%)	6 (20%)	5 (16.7%)	11 (18.3%)
	30	Count (%)	3 (10%)	3 (10%)	6 (10%)
	40	Count (%)	3 (10%)	3 (10%)	6 (10%)
	50	Count	5 (16.7%)	1 (3.3%)	6 (10%)

Data were presented as count (% within group).

Table 6

Tramadol consumption, incidence of nausea and shivering. Data are presented as n or n (%)

	Group C (n=30)	**Group W (n=30)**	**P-value**
Tramadol (n)			
120 min	6	7	0.67
6 hr	16	13	0.50
12 hr	7	3	0.33
24 hr	2	0	0.30
Shivering (n %)	6 (20%)	1 (3.3%)	0.10
Nausea (n %)	9 (30%)	7 (23.3%)	0.55

Data are presented as n or n (%)

Fig. 2

Perioperative systolic blood pressures in the two groups.

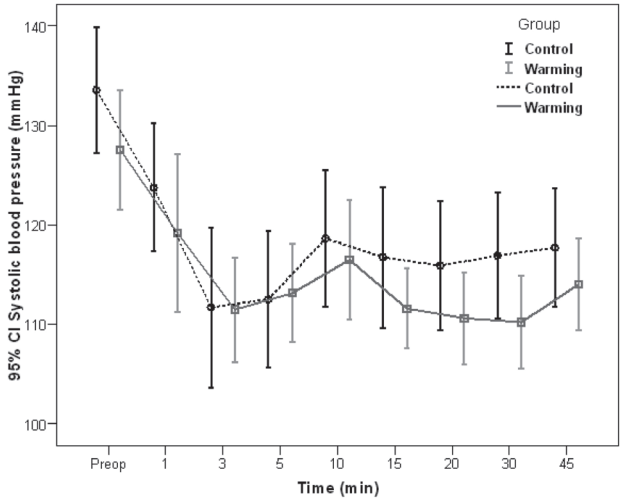
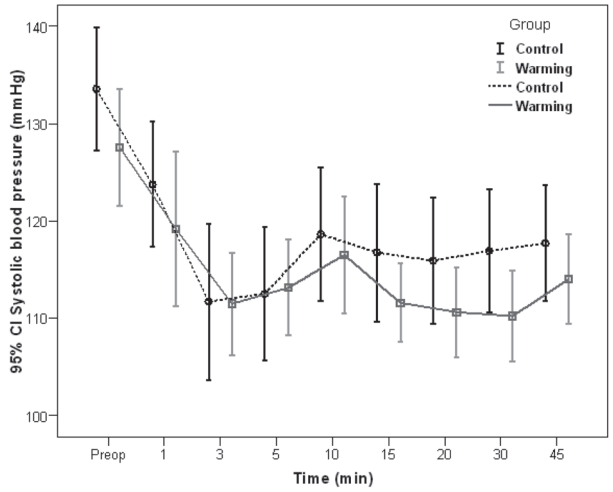


Fig. 3

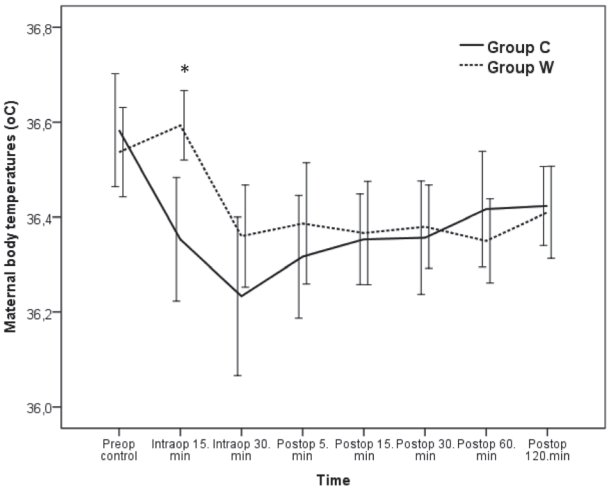
Perioperative diastolic blood pressures in the two groups.



Transient hypotension occurred in each group despite iv fluid therapy and ephedrine administration. The incidence of hypotension after spinal anesthesia was 70% (21/30) in-Group C and 56.7% (17/30) in Group W. There was no significant difference between the two Groups in the incidence of hypotension (Table 4). The total amount of fluid infused throughout study period was also similar between the two groups (Table 4). Although fewer patients in Group W needed ephedrine, there was no significant difference in the number of patients requiring ephedrine and in the mean dose of ephedrine consumption between the two groups (Table 4, 5). No patient needed blood transfusion.

Fig. 4

*Maternal body temperatures in the two groups. Maternal body temperatures in parturients randomized to two groups: IV fluid warming at 37°C and controls (at approximately 22°C). Time is after induction of anesthesia (preoperative control, 15 and 30 min), followed by time in the postanesthesia care unit (5, 15, 30, 60 and 120 min). *P =0.02 between groups.*



The number of patients requiring supplement analgesic (tramadol) for postoperative analgesia and shivering was similar and no significantly different pain scores (data not presented) were recorded throughout the study period between the two groups (Table 6).

Maternal body temperatures were found significantly higher only at 15 min in Group W than in group C (p=0.02) (Figure 4). Six patients (20%) in Group C and one patient (3.3%) in Group W shivered. All required treatment with iv tramadol (25 mg) (Table 6). Although much shivering was observed in group C, no significant difference was found between the two groups.

Nausea was experienced by nine patients (30%) in Group C and seven in Group W (23.3%). All of these patients were successfully treated by correcting hypotension (Table 6). No complication or major side effect related with spinal anesthesia was recorded.

Discussion

Despite a plethora of published clinical guidelines and manuals, the incidence of Inadvertent Perioperative Hypothermia (IPH) varies from 6-90%,

depending on the use of active/passive warming techniques[11-13]. Concerns for the development of IPH are still high and routine use of warming techniques during cesarean delivery is not widely practiced.

The administration of 1 L of crystalloid solution at room temperature has been demonstrated to decrease mean body temperature approximately by 0.25°C[14]. Therefore, prevention of IPH by using warming techniques is important. Even prevention of small changes in temperature (e,g, 0.25°C) decreases the degree of hypothermia and associated side effects[14]. Some reports have advocated that warming iv fluids prevents hypothermia in parturients undergoing elective cesarean delivery, whereas others have reported no benefit at all[15]. Woolnough et al[2] and Goyal et al[16] evaluated the effect of warming intravenous fluids during elective cesarean delivery under regional anesthesia and reported that warming iv fluids does not preserve baseline core temperature of the patients, but significantly mitigates the decrease in maternal temperature during cesarean section.

These results were similar to our findings, in which warming IV fluids resulted in lower incidence of decreased core temperature. Although maternal body temperatures in both groups were not significantly lower than preoperative baseline values, it was significantly higher in the warm fluid group only at 15 min compared with the control group.

To date, many studies examining the effect of warming iv fluids on maternal comfort and fetal outcomes during cesarean delivery have been conducted. However, as far as we know, the effects of warming iv fluids on hemodynamic variables have not been investigated in details. Thus, this is the first study comparing the effects of warmed (37°C) and non-warmed (22°C) fluid infusions during cesarean section undergoing spinal anesthesia on the incidence of hypotension, fluid, transfusion and ephedrine requirement.

Various studies in humans have shown that hypothermia can lead to hypotension by depressing left ventricular contractility and exerting negative inotropic effect in myocardium[3,4]. Patients with warmer body temperatures tend to experience less hemodynamic and rheological side effects. Unlike other surgical population, IPH more easily develops in pregnants undergoing cesarean delivery with neuraxial anesthesia. Furthermore, cesarean delivery distinguishes from any other surgical intervention as neuraxial anesthesia produces a sympathectomy in lower part of body that reduces the threshold for vasoconstriction and results in significant heat loss and hypothermia[17]. Additionally, parturients often receive greater volumes of iv fluid to compensate for the decrease in systemic vascular resistance provided by sympathetic block during spinal anesthesia when compared with general anesthesia. Therefore, warming iv fluids is particularly important in cesarean delivery performed spinal anesthesia because of the relatively high fluid volumes infused. With warming fluids, the magnitude of any decrease in body temperature and hypothermia-related hemodynamic fluctuations can be reduced or prevented. In our study, although transient hypotension occurred in each group, no significant difference was detected in the incidence of hypotension between the two groups.

Studies evaluating the hemodynamic and rheological effect of fluid warming during cesarean delivery have shown conflicting results. Although some studies have demonstrated beneficial effect of warming fluids, others have failed to demonstrate any effect at all[15,18].

In a retrospective study, IPH caused significantly greater fluid transfusion, vasopressor and inotrope requirements in patients undergoing elective abdominal aortic aneurysm repair[6].

These results were supported by a meta-analysis evaluating the effect of IPH on surgical blood loss and transfusion requirement. In that meta-analysis, although hemodynamic data were not presented, authors reported that even a mild hypothermia (<1°C) significantly increase blood loss and the relative risk for transfusion[5].

In contrast, in another meta-analysis evaluating the effect of warming patients during cesarean section on maternal and neonatal outcomes, authors reported that warming did not significantly reduce the incidence of hypotension, vasopressor requirement and vomiting. However, in those studies neither data were presented nor commented on whether the incidence of hypotension differed between groups[19]. In our study, although maternal body temperatures were significantly

higher at 15 min in Group W compared with Group C, we couldn't find any significance between the two groups as to the incidence of hypotension, fluid, blood transfusion and ephedrine requirement.

IPH during cesarean section not only results from un-warmed fluid infusion, but also mainly results from redistribution of heat from the core to the periphery, and subsequently from heat loss greater than metabolic heat production[7,20]. Because neuraxial anesthesia impairs central thermoregulatory control and decreases the thresholds triggering vasoconstriction and shivering, the incidence of decreased core temperature is possibly exacerbated by spinal anesthesia[7]. Although shivering is not always associated with a reduction of body temperature, the incidence of intraoperative shivering during cesarean delivery has been reported as around 60%[2]. In our study, although much shivering was observed in Group C, the incidence of shivering was as low as 20% in Group C and 3.3% in Group W. Lower incidence of shivering seen in the present study was attributed to the routine use of convective warming blankets, autonomic blockade of spinal anesthesia and the pharmacologic effects of intrathecal drugs in both groups.

Fetal temperature is mainly related to maternal temperature, and therefore maternal heat loss and hypothermia is most likely to be associated with neonatal hypothermia and acidosis[21]. In the present study neonatal Apgar scores at 1 and 5 min after delivery and umbilical artery blood gas samples were also similar and there were no statistically significant difference in Apgar scores and umbilical artery blood gas variables between groups.

There were three limitations of our study. First, the National Institute for Health and Clinical Excellence (NICE) has published a guideline concerning prevention of perioperative hypothermia and suggested that all intravenous fluids (more than 500 mL) should be warmed routinely to 37°C for all surgical procedures[1]. However, at the time of this trial, using active warming devices was not routine during elective cesarean section in our clinic since intraoperative and postoperative hypothermia is rarely a significant clinical problem. The second limitation of this study is the routine use of convective warming blankets in both groups. If we hadn't used blankets, we might have found significance between the two groups as to incidence of hypotension, fluid, blood transfusion and ephedrine requirement. The third limitation is our power analysis. As there were no previous studies evaluating the significant percentage of differences, we chose a 35% difference in the incidence of intraoperative maternal hypotension. If we had decreased the percentage of differences, possibly, we could have found significant differences between the two groups. As such future large series of studies are needed to demonstrate possible beneficial effect of fluid warming on the incidence of hypotension and ephedrine requirement.

In conclusion, in cesarean section patients undergoing spinal anesthesia, warming IV fluids (37°C) resulted in lower incidence of decreased core temperature but did not affect the incidence of maternal hypotension, ephedrine and transfusion requirement and total volume consumption. Although we failed to demonstrate any beneficial effect of fluid warming on the incidence of hypotension and ephedrine requirement, we strongly support the idea that all iv fluids should be warmed routinely in patients undergoing cesarean delivery.

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