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Comparative effect of 6% hydroxyethyl starch (containing 1% dextrose) and lactated Ringer's solution for cesarean section under spinal anesthesia

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Abstract

Purpose. This study aimed to compare low-molecular weight hydroxyethyl starch containing 1% dextrose (HES) infusion and lactated Ringer's solution (LR) in the prevention of hypotension associated with spinal anesthesia for cesarean section.

Methods. Sixty-seven patients scheduled for cesarean section under spinal anesthesia were randomly allocated to receive either LR ($n = 35$) or HES ($n = 32$) infusion before cesarean delivery. Infusion of the fluid was started immediately after arrival at the operating room, through two fully open i.v. routes of 18 or 16 gauge. The two groups were compared in terms of the incidence of hypotension; ephedrine dose; cord and maternal blood gas, hemoglobin, and glucose; and Apgar scores.

Results. Intravenous fluid volume until delivery in the LR group was significantly greater than that in the HES group (1298 ± 503 and 973 ± 339 ml, respectively) in spite of the similar periods of intravenous infusion (18.1 ± 3.9 and 18.2 ± 4.1 min). The incidence of hypotension, and the ephedrine dose, blood gas analyses, and Apgar scores were not significantly different between the groups. The ephedrine dose correlated with the anesthesia level by spinal anesthesia ($P < 0.05$).

Conclusion. This study did not show an advantage of HES compared with LR in the prevention of hypotension or in the reduction of ephedrine dose during cesarean section under spinal anesthesia. The anesthesia level, rather than the choice of intravenous fluid solution, might be related to the ephedrine dose.

Key words Hydroxyethyl starch · Cesarean section · Spinal anesthesia · Spinal hypotension

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Introduction

Hypotension during spinal or epidural anesthesia for cesarean section is considered to be a detrimental factor for the infant's outcome. Although colloid fluid has advantages over crystalloid infusion for preventing hypotension [1,2], there are still some controversies concerning this issue [3,4]. A recent report even failed to confirm the advantageous effect of crystalloid fluid infusion for the prevention of hypotension [5]. Therefore, we designed this study to compare the effects of infusion of low-molecular weight hydroxyethyl starch containing 1% dextrose and lactated Ringer's solution during spinal anesthesia for cesarean section.

Methods

After obtaining the approval of the Human Research Ethics Committee of our institute, we studied 67 consecutive patients without toxemia of pregnancy scheduled for cesarean section. All patients received 0.5 mg atropine sulfate about 30 min before their arrival in the operating room. The administration of either lactated Ringer (LR) or hydroxyethyl starch containing 1% dextrose (HES; Hespander, mean molecular weight 70000; Kyorin, Tokyo, Japan) was randomly allocated to the patients (the LR group; $n = 35$ and the HES group; $n = 32$, respectively). Infusion was commenced on arrival at the operating room until delivery, through two fully open i.v. routes of 18 or 16 gauge. HES infusion was limited to 1000 ml and subsequently LR solution was infused. After the baseline measurement of blood pressure, the patients were placed in the right lateral decubitus position. Spinal anesthesia was induced with (height [m] ×1.2 ml) of 0.3% dibucaine at the L3/4 interspace. Then the patients were placed in the supine position with the operating table rotated toward the left in order to avoid supine hypotensive syndrome. The

upper anesthesia level was checked by cold sensation 5 min after the induction of spinal anesthesia. All patients received 40% oxygen via a facemask throughout the surgery. Blood pressure and heart rate were measured every minute for 20 min after the induction of spinal anesthesia, and every 2.5 min subsequently. Hypotension, defined as systolic arterial pressure of less than 90 mmHg, was immediately treated with the administration of 5 mg of intravenous ephedrine. Blood samples were taken from parturient arterial blood, umbilical vein (UV), and umbilical artery (UA) at delivery for measurements of blood gases and blood glucose (BS). Pediatricians who did not know the choice of solutions defined the Apgar scores 1 and 5 min after delivery.

Data values for measurements of blood samples were expressed as means ± SD, and intergroup differences were analyzed by unpaired *t*-test. The number and the percentage of infants whose Apgar scores were less than 7 were recorded, and group differences were analyzed with the Mann-Whitney test. Correlation between the ephedrine dose and anesthesia level was analyzed by Spearman's correlation coefficient by rank.

Results

There were no significant differences in the characteristics of the patients between the groups (Table 1). Three of the 35 patients in the LR group and 2 of the 32 patients in the HES group had preoperative labor pain. No patients received β stimulants preoperatively. The intravenous fluid volume administered until delivery in the LR group (1298 ± 503 ml) was significantly greater than that in the HES group (total, 973 ± 339 ml [HES, 852 ± 200 ml and LR, 123 ± 196 ml]) in spite of similar periods of intravenous infusion in the LR group and the HES group (18.1 ± 3.9 and 18.2 ± 4.1 min, respectively; Table 2). There were no significant differences between the groups in level of anesthesia, total ephedrine dose,

Table 1. Characteristics of the patients

	LR group	HES group	*P*
n	35	32	
Age (years)	30 ± 5	30 ± 4	NS
Weight (kg)	61 ± 7	62 ± 8	NS
Gestation (days)	257 ± 34	267 ± 19	NS
Birth weight (g)	2661 ± 811	2740 ± 509	NS
Time from incision to delivery (min)	8.1 ± 3.7	8.1 ± 2.3	NS
Time from uterine incision to delivery (s)	85 ± 32	86 ± 35	NS
Preoperative i.v. fluid (ml)	287 ± 174 ($n = 6$)	375 ± 189 ($n = 8$)	NS

Data values are expressed as means ± SD
LR, Lactated Ringer; HES, hydroxyethyl starch; NS, not significant

Table 2. Results: maternal and fetal data

	LR group	HES group	*P*
	$n = 35$	$n = 32$	
Volume of i.v. fluid until delivery (ml)	1298 ± 503	973 ± 339 (HES, 852 ± 200; LR, 123 ± 196)	$P < 0.05$
Period of infusion (min)	18.1 ± 3.9	18.2 ± 4.1	NS
Apgar score (1 min) <7 (*n* [%])	4 (11.4%)	1 (3.1%)	NS
Apgar score (5 min) <7 (*n* [%])	3 (8.6%)	0 (0%)	NS
Apgar minus cyanosis score (1 min) <7 (*n* [%])	5 (14.7%)	2 (6.3%)	NS
Apgar minus cyanosis score (5 min) <7 (*n* [%])	4 (11.4%)	0 (0%)	NS
Incidence of hypotension (%) (SBP <90 mmHg)	26 (74.3%)	27 (84.4%)	NS
Ephedrine dose (mg) (including the patients without ephedrine use)	10.3 ± 9.4	12.5 ± 11.4	NS
Volume of i.v. fluid until first ephedrine use (ml)	461 ± 307	318 ± 300	NS
Time from SAB to hypotension (min)	3.2 ± 2.1	2.8 ± 2.1	NS
Duration of hypotension (min)	2.4 ± 1.4	2.8 ± 1.8	NS
Anesthesia level (median [range])	6 (2–12)	6 (2–10)	NS
Blood loss (ml)	643 ± 618	870 ± 560	NS

The incidences of Apgar scores of less than 7 and Apgar minus cyanosis scores of less than 7 are expressed in terms of numbers of patients and percentages. The incidence of hypotension is expressed as a percentage. Other data values are expressed as means ± SD
LR, Lactated Ringer; HES, hydroxyethyl starch; NS, not significant; SBP, systolic blood pressure; SAB, subarachnoid block

Table 3. Blood sample data

	Parturient artery		Umbilical vein		Umbilical artery	
Group	LR	HES	LR	HES	LR	HES
n	35	32	35	32	35	32
pH	7.41 ± 0.04	7.41 ± 0.04	7.33 ± 0.04	7.32 ± 0.05	7.29 ± 0.05	7.26 ± 0.07
PO_2 (mmHg)	167 ± 43	160 ± 37	26.6 ± 7.5	29.0 ± 7.1	16.2 ± 5.2	17.9 ± 6.5
PCO_2 (mmHg)	32 ± 4	32 ± 4	44 ± 5	44 ± 6	52 ± 6	54 ± 11
Base excess ($mEq \cdot l^{-1}$)	−3.9 ± 1.4	−3.9 ± 1.4	−3.8 ± 0.4	−4.0 ± 0.4	−3.5 ± 2.4	−4.3 ± 2.3
BS ($mg \cdot dl^{-1}$)	93 ± 23	155 ± 38*	54 ± 4	101 ± 8*	50 ± 11	79 ± 21*
Hb ($g \cdot dl^{-1}$)	10.0 ± 1.3	8.9 ± 1.3*	17.4 ± 2.2	16.6 ± 2.0	17.0 ± 1.8	16.4 ± 1.8

* $P < 0.05$ compared with LR group
Values are means ± SD
LR, Lactate Ringer; HES, hydroxyethyl starch; BS, blood sugar; Hb, hemoglobin

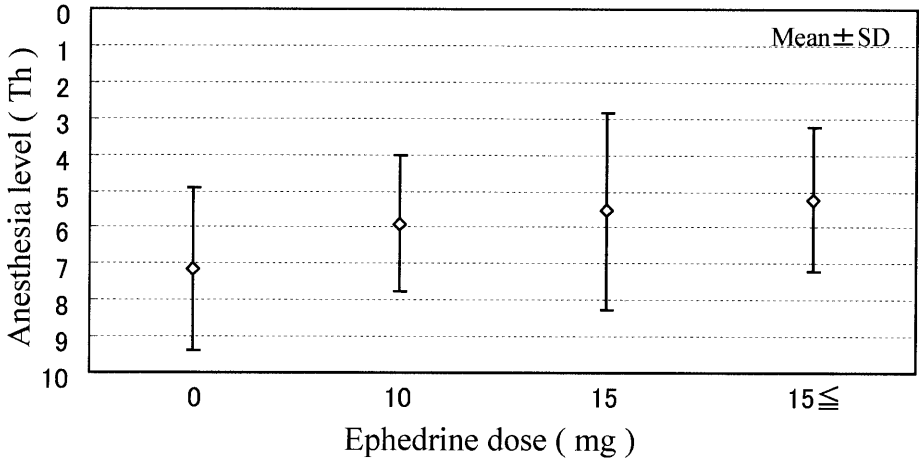

Fig. 1. Correlation between anesthesia level and ephedrine dose. Spearman's correlation coefficient by rank revealed a relationship between ephedrine dose and anesthesia level 5 min after the induction of spinal anesthesia ($\rho = -0.28$; tied $P = 0.041$). The higher the anesthesia level, the more ephedrine was used

incidence of hypotension, or onset and duration of hypotension (Table 2). No significant differences were noted between the groups in blood pressure and heart rate changes. Blood gas analyses and Apgar scores were not significantly different between the groups (Tables 2 and 3). Higher blood glucose levels were noted in the HES group than in the LR group (Table 3). The HES group showed lower hemoglobin concentrations in the maternal artery than the LR group (Table 3). The pediatricians diagnosed no infant with hypoglycemia after the delivery.

Spearman's correlation coefficient by rank revealed a relationship between ephedrine dose and anesthesia level 5 min after the induction of spinal anesthesia ($\rho = -0.28$; tied $P = 0.041$; Fig. 1) showing that the higher the anesthesia level, the more ephedrine was used.

Discussion

We could not show a beneficial effect of colloid infusion to prevent spinal anesthesia-induced hypotension compared with crystalloid. Although a similar dose of ephedrine was required for treating maternal hypotension, a lower solution load was obtained in the HES group; this might be because HES has higher viscosity than LR. In addition, because the HES contained 1% dextrose, the HES group preserved a higher level of blood glucose in UV, UA and parturient arterial blood, which might have an advantageous effect in avoiding both fasting hypoglycemia and insulin-induced hypoglycemia in the fetal circulation. Moreover, because there was no significant difference in the total amount of bleeding between the groups, the hemodilution indicated by the lower hemoglobin concentration in the HES group might be beneficial in terms of prevention of hemoglobin loss in the maternal blood.

Although some other studies have suggested an advantageous effect of colloid infusion for the prevention of hypotension during cesarean section under spinal anesthesia, they allowed at least 15 to 20 min to load the solution before the induction of anesthesia [1,2], which would not be practical in an emergency case. In this study, we planned to load fluid only during the anes-

thetic procedure, which has a limited time of infusion; about 18 min in this study, in order to apply the result of this study even to emergency cases.

HES is a colloid solution that is widely used for plasma volume expansion in patients with trauma, shock, or sepsis [6–8]. The reasons we used HES as colloid infusion are as follows. First, HES has a lower incidence of anaphylactic reaction than dextran [9]. Second, it is less cost-demanding than dextran or other colloid fluids. Third, HES is one of the commercially available colloid fluid materials, which contains 1% glucose. Rapid infusion of 5% glucose solution increases the production of CO_2 and lactate, resulting in acidemia [10]. On the other hand, maternal fasting reportedly decreases fetal breathing movements and fetal electrocortical activity, both of which are improved by maternal glucose infusion [11]. Peng et al. [12] reported that 1% glucose infusion had a good effect in maintaining euglycemia in the UA, the UV, and the parturient patient's artery, avoiding both fasting hypoglycemia and hypoglycemia in the infant induced by an increase in maternal insulin secretion. Mendiola et al. [13] have reported that when the rate of maternal glucose administration does not exceed 20 g/h, the incidence of neonatal hypoglycemia is negligible. In this study, no infant showed either hypo- or hyperglycemia, and the glucose values were similar to those in a previous report [12], which suggested that 1% glucose solution was advantageous in rapid infusion before cesarean section under epidural anesthesia. Although parturient and infant blood glucose might be affected by β stimulants, which induce glycolysis [14], blood glucose values were not significantly different whether ephedrine was used or not in this study.

An animal study reported that infusion of HES significantly increased uterine blood flow, total oxygen-delivery capacity, and uterine artery oxygen delivery, whereas, infusion of LR did not have these effects [15]. Although our study did not show higher oxygenation in fetal blood in the HES group compared with the LR group, HES has a potential benefit for the fetal circulation.

A higher anesthesia level correlated with a high ephedrine dose. This may imply that hypotension is at least partially related to high spinal anesthesia level. Therefore, adequate prophylactic use of ephedrine, based on checking of the anesthesia level, might be beneficial to prevent hypotension.

In conclusion, we could not show a beneficial effect of colloid infusion to prevent spinal anesthesia-induced hypotension compared with lactated Ringer infusion. The anesthesia level was correlated with the ephedrine dose rather than with the choice of intravenous fluid solution.

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