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A Study of Volume Replacement in Intraoperative Hemodilution Technique -A Comparison of Crystalloidal and Colloidal Solution-

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INTRODUCTION

Intraoperative hemodilution method with crystalloid or colloidal solutions is widely used to reduce blood transfusion requirements and decrease the potential incidence of complications, arising from homologous blood transfusion. The blood which is lost during surgery contains loss cells and plasma factors, hence, the diluted patient looses less blood constituents as compared to undiluted patients.

The purpose of this study was to assess the hemodynamic effects and circulating blood volume of hemodilution techniques. Blood loss and replacement therapy with two fluid groups were simulated experimentally.

MATERIALS AND METHODS

Fourteen adult mongrel dogs weighing 12 to 19 kg were randomly allocated into two groups of animals: a Ringer group (lactated Ringer's solution) and an HES group (hydroxyethyl starch of 6 % weight/volume, average molecular weight of 200 kDa, molar substitution of 0.62 [ratio hydroxyethyl groups/glucose unit] in 0.9 % sodium chloride). The experimental animals were anesthetized with sodium pentobarbital 30 mg/kg iv. Pancuronium bromide (0.2 mg/kg) was administered after an endotracheal tube was inserted. The animals were ventilated with 0.5 % isoflurane in 60 % nitrous oxide using a Harvard respirator (DOG Respirator Model 613, Harvard Apparatus, USA). The tidal volume was monitored with an infrared CO_2 analyzer and adjusted to maintain end expiratory $ETCO_2$ at 35~40 mmHg. The animals were maintained in the supine position under anesthesia.

The left femoral vein was cannulated for infusion of lactated Ringer's solution (maintenance dose of 10 ml/kg/h) and for withdrawal of blood and volume replacement for induced hemodilution. The left femoral artery was cannulated for the continuous monitoring of systemic arterial pressure and for blood samplings. Left ventricula pressure (LVP) was monitored with a 7-French pigtail catheter cannulated via the right femoral artery. The maximum rate of the left ventricular pressure change (LV dp/dt max) was measured electrically deriving a LVP wave using an electric differentiator. A 7.5-French balloon-tripped triple-lumen pulmonary catheter was inserted via the right external jugular vein and its top was positioned in a branch of the pulmonary artery for circulatory parameter measurements. Cardiac output (CO) was determined by the thermodilution method using 5 ml of 0.9 % saline at 0 ℃ injected into the right atrium at the end of expiration. Heart rate (HR) was monitored using a cardiotachometer from lead áUof an electrocardiograph.

Circulating blood volume (CBV) was measured by pluse-dye densitometry (PDD) method. PDD was performed using a DDG analyzer (DDG-2001 Nihon Kohden Corp, Japan). A nostrial probe which is connected to the integrated pulse-spectrophotometry monitoring system was fixed on the tongue to detect the blood concentrations of indocyanine green (ICG) based on pulse-spectrometry. Twenty-five milligrams of ICG in 10 ml saline were injected as a bolus followed by a flush of 0.16 ml/kg into the right atrium at the end of expiration. The arterial dye concentration was continuously computed by reference to the previously mesured blood hemoglobin (Hb) concentration.

The dogs were allowed to stabilize for at least 60 minutes (min) after the surgical procedure, and baseline mesurements were taken. Hemodilution was produced by exchanging blood (25 ml/kg) within 5 min, which was achieved by introducing either lactated Ringer's solution at 3 times the volume (Ringer group) or HES 200 in an equivalent volume of blood lost (HES group). Mesurements and sampling were taken at baseline, end of hemodilution, 30, 60, 120, 180, 240, and 300 min.

Hb, HR, mean arterial pressure (mAP), pulmonary arterial wedge pressure (PAWP), LVP, CO, arterial partial oxygen pressure (PaO_2), arterial partial carbon dioxide pressure ($PaCO_2$), plasma colloidal osmotic pressure (Posm), plasma crystalloidal osmotic pressure (Posm), and CBV. The cardiac index (CI), systemic vascular resistance (SVR), and LV dp/dt max were calculated using standard formulas. Blood samples were drawn at the point of the experimental mesurements for analysis of Pcop and Posm. Blood samples were kept on ice and centrifuged at 2,000 g for 10 min at 4 °C. The plasma was removed and analyzed for Pcop using a colloid osmometer (Colloid Osmometer 4400, WESCOR Corp., USA). Posm was mesured by a cryoscope (Osmotic Pressure AUTO & STAT OM-6030, Kyoto Daiichi Kagaku Corp., Japan).

Data are expressed by mean ± SEM. The data were analyzed for significant differences within groups between the baseline values and those for the subsequent phases (HD; 30~300 min), using Student's paired t-test, with $P<0.05$ considered as statistically significant. Differences between the two groups were analyzed using Student's unpaired t-test. Values of $P<0.05$ were considered statistically significant.

RESULTS

Hb values did not differ significantly between the Ringer and HES groups under baseline conditions (Ringer group 11.2 ± 0.8 g/dl: HES group 11.4 ± 0.6 g/dl).

Hemodynamic variables are shown in Table I. Under baseline conditions, there was no significant difference in the hemodynamic variables between the two groups. A significant increase in PAWP and CI, and a significant decrease in HR and SVR values occurred after hemodilution in Ringer group. However, mAP, PAWP, CI values in group Ringer decreased significantly with the lapse of time as compared with the baseline condition. On the other hand, in HES group, after hemodilution, a significant increase in CI and LV dp/dt max, and a significant decrease in SVR values occurred. HR, mAP, PAWP in group HES did not differ significantly compared with the baseline condition during any of the experimental periods. After hemodilution, the mAP, PAWP, CI and LV dp/dt max values in Ringer group were significantly lower than those in HES group. On

Table I
Hemodynamic variables in response to Hemodilution with lactated Ringer's solution (Ringer) or 6% hydroxyethyl starch 200 (HES)

Variable	Group	Baseline	HD	30	60	120	180	240	300
HR	Riner	163±9	129±6'	159±8	152±10	144±11'	139±11'	134±10'	128±11'
	HES	156±8	143±9	153±9	154±8	156±10	155±10	145±12	144±11
mAP	Ringer	118±4	117±12	105±10	98±8'	93±10'	104±9'	88±8''	86±8''
	HES	112±3	108±4	110±3	103±3	107±3	110±3	110±4	109±3
PAWP	Ringer	12±2	17±3'	11±1	11±1	10±1''	10±1''	10±1''	10±1''
	HES	12±2	14±2	13±1	13±1	13±1	13±1	13±1	13±1
CI	Ringer	1.6±0.1	2.1±0.3'	1.8±0.1	1.5±0.1'	1.2±0.1''	1.2±0.1''	1.0±0.1''	0.9±0.1''
	HES	1.6±0.1	1.9±0.1'	2.0±0.1'	2.0±0.1'	1.9±0.1'	1.9±0.1'	1.9±0.1'	1.8±0.1'
SVR	Ringer	8301±463	6911±656'	7194±443'	7911±450'	8926±757'	10190±728''	12743±458''	15287±303''
	HES	7620±364	5991±306'	6030±335'	5780±296'	5785±263'	5990±242'	6310±276'	6540±272
LVdp/dt	Ringer	2066±204	2033±238	2556±354	2366±247'	2233±230'	2300±260'	2100±209'	2022±201'
max	HES	2080±186	2320±245'	2976±292'	3004±286'	2940±276'	2894±302'	2856±292'	2755±306'

(n=7)
Data are expressed as mean ± standard error (SE)

HR: heart rate ($beats \cdot min^{-1}$); mAP: mean arterial pressure (mmHg); PAWP: pulmonary arterial wedge pressure (mmHg); CI: cardiac index ($l \cdot min^{-1} \cdot m^{-2}$); SVR: systemic vascular resistance ($dyn \cdot sec \cdot cm^{-5}$); LV dp/dt max: maximum rate of left ventricular pressure change ($mmHg \cdot sec^{-1}$)
Ringer: lactated Ringer's solution group ; HES: 6% hydroxyethyl starch 200 group
Baseline: pre-hemodilution ; HD : after hemodilution
30 min, 60 min, 120 min, 180 min, 240 min, 300 min: 30, 60, 120, 180, 240, 300 minutes after hemodilution.
'$P<0.05$: from Baseline
'$P<0.05$: between group Ringer and HES

Table II
Plasma Osmotic Pressure and Circulating blood volume in Response to Hemodilution with lactated Ringer's solution (Ringer) or 6% hydroxyethyl starch 200 (HES)

Variable	Group	Baseline	HD	30	60	120	180	240	300
Pcop	Riner	12±1	5±1"	7±1"	7±1"	7±1"	7±1"	8±1"	8±1"
	HES	12±1	15±1'	13±1'	13±1'	12±1	12±1	12±1	11±1
Posm	Ringer	304±2	299±2	301±2	301±2	299±2	299±2	297±2	298±2
	HES	306±2	310±3	309±1	309±1	310±1	310±1	309±1	304±2
CBV	Ringer	1.4±0.2	1.4±0.2	1.4±0.2	1.4±0.2	1.1±0.1"	1.1±0.1"	1.0±0.1"	1.0±0.1"
	HES	1.3±0.1	1.6±0.1'	1.7±0.1'	1.7±0.1'	1.7±0.1'	1.8±0.1'	1.8±0.1'	1.8±0.1'

(n=7)
Data are expressed as mean ± standard error (SE)
Pcop: plasma colloid osmotic pressure (mmHg); Posm: plasma crystalloid osmotic pressure ($mOsm \cdot kg^{-1} \cdot H_2O^{-1}$); CBV : circulating blood volume (litter)
Ringer: lactated Ringer's solution group ; HES: 6% hydroxyethyl starch 200 group
Baseline: pre-hemodilution ; HD : after hemodilution
30 min, 60 min, 120 min, 180 min, 240 min, 300 min: 30, 60, 120, 180, 240, 300 minutes after hemodilution.
'P<0.05: from Baseline
'P<0.05: between group Ringer and HES

the other hand, SVR in group Ringer was significantly greater than that in group HES.

With regard to the respiratory variables, PaO_2 and $PaCO_2$ under the baseline condition did not differ between the two groups: In the Ringer group, PaO2 was 183 ± 28 mmHg and PaCO2 was 37.7 ± 2.2 mmHg, whereas in the HES group, the corresponding values were 201 ± 22 mmHg and 36.5 ± 2.6 mmHg, respectively.

Pcop, Posm and CBV are shown in Table II. Pcop, Posm and CBV values did not differ significantly between the two groups under baseline condition. After hemodilution, Pcop and CBV values decreased significantly compared with the baseline condition in Ringer group. On the other hand, those values increased significantly in HES group. Moreover, Pcop and CBV in group Ringer were significantly lower than those in group HES. Posm did not change significantly compared to the baseline condition in both groups.

DISCUSSION

Normovolemic hemodilution indicates dilution of the blood, while the circulating blood volume remains in its normal range. The rationale for its use is that, if intraoperative blood loss is relatively constant with or without normovolemic hemodilution, it is better to lose blood at a lower hematocrit than at a higher hematocrit.

In this study, hemorrhage of 25 ml/kg was then effected and this volume was replaced stimultaneously with either at 3 times the volume of lactated Ringer's solution or at same volume of HES 200. Plasma expansion after infusion of lactated Ringer's solution was relatively short-lived (1,2). The time courses of the changes in mAP, PAWP and CI were significantly decreased as compared with the baseline condition. In contrast, increases in CBV after administration of HES 200 paralleled increases in CI. The data suggest that the improvements in hemodynamics after administration of HES 200 are produced by the increased CBV. Hemodynamic responses were greater and more prolonged HES group than Ringer group. These responses were related to concomitant improvement in CBV and Posm (3). The increased CBV after HES group and the decreased CBV after Ringer group suggests that the escape of fluid from plasma is greater after the latter. Hausen et al. (4) suggested that aggressive use of crystalloid extracellular fluid expansion to expand the plasma volume is contraindicated.

Acute normovolemic hemodilution induced changes in cardiovascular and regional myocardial hemodynamics, such as increases in cardiac output and myocardial blood flow, have been previously known. These alterations in hemodynamics result in the preservation of oxygen delivery by increasing peripheral and myocardial blood flow to compensate for the decreased arterial oxygen content. The most acceptable explanation is the effect of hemodilution on viscosity and peripheral resistance. Some investigators (5,6) reported that at least part of the acute normovolemic hemodilution decrease in SVR might be due to an increase in endothelium-dependent nitric oxide (NO), since acute normovolemic hemodilution results in a reduction of the contribution of hemoglobin to NO scavenging capacity. On the other hand, Hirose et al. (7) have reported that NO does not play a major role in mediation or modulation of the syatemic vascular responses to acute normovolemic hemodilution.

In the present study, CBV was measured by PDD method. PDD enables ICG concentrations to be measured non-invasively and continuously without calibration. Many investigators (8-10) concluded that PDD provides a non-invasive estimate of CBV, which in this investigation appeared to be at least as accurate as the thermodilution method.

Hydroxyethyl staech (HES) is commonly used as a plasma volume expander in the surgical patients. HES improve microcirculation blood flow and is less expansive than human albumin. Moreover, HES is very well tolerated and the incidence of anaphylactic reactions is lower than with dextran 11). Vogt et al. (12) with respect to efficacy and side effects on coagulation and renal function, medium molecular HES is an appropriate and economic alternative to albumin at daily doses of up to at least 36 ml/kg. In the present study, small volume (25 ml/kg) of 6 % HES 200 may cause no clinically relevant disturbances of the coagulation and fibrinolysis system.

CONCLUSION

These results suggest that HES group may be more effective than Ringer group for the hemodilution technique. These responses were related to concomitant improvement in Pcop and CBV.

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ABSTRACT

The purpose of this study was to experimentally compare the hemodynamic variables, plasma colloidal and crystalloidal osmotic pressure (Posm and Posm), and circulating blood volume (CBV) under hemodilution in isoflurane anesthetized dogs. We divided anesthetized dogs into two groups: a Ringer group (lactated Ringer's solution), and an HES group (hydroxyethyl starch, MW=200 kDa, 6 % in saline). Hemodilution was produced by exchanging blood (25 ml/kg), which was achieved by introducing either lactated Ringer's solution at 3 times the volume (Ringer group) or HES 200 in an equivalent volume of blood lost (HES group). Measurements and samplings were taken before hemodilution, at the end of hemodilution, and 30, 60, 120, 180, 240, and 300 minutes after hemodilution. After hemodilution, the mean arterial pressure (mAP), pulmonary arterial wedge pressure (PAWP), cardiac index (CI), the maximum rate of the left ventricular pressure change (LV dp/dt max), Pcop, and CBV values in Ringer group were significantly lower than those in HES group. Systemic vascular resistance (SVR) was significantly greater than that in group HES. Heart rate (HR) and Posm did not differ significantly between two groups. Hemodynamic responses were greater and more prolonged HES group than Ringer group.

Theses results suggest that HES group may be more effective than Ringer group for the hemodilution technique. These responses are due to an improvement and a maintainance in hemodynamic variables, CBV and Pcop.

Key words: volume replacement, intraoperative hemodilution, circulating blood volume, pluse dye-densitometry, plasma colloidal osmotic pressure