[Original]

Responses of hemodynamics, plasma oncotic pressure, and circulating blood volume following the administering a isooncotic or a hyperoncotic colloidal solution

Masao KOBORI, Hiroe NAGAI, Hideru NEGISHI

Department of Anesthesiology, Showa University School of Medicine, Tokyo Japan

INTRODUCTION

To increase preload, volume loading is frequently appropriate. For hemodynamic reasons, it is important to expand the circulating volume in the intravascular space. Accordingly, the use of colloidal solution is more preferable than crystalloidal solution.

This investigation examined the circulating blood volume and plasma osmotic pressure effects of a isooncotic colloidal solution or a hyperoncotic colloidal solution administered to anesthetized dogs.

MATERIALS AND METHODS

Eighteen adult male mongrel dogs weighing 12 to 20 kg were assigned randomly to receive a 6 % 200 kDa hydroxyethyl starch (HES) in saline (A group) or a 12 % 200 kDa HES in saline (B group).

The dogs were sedated initially with pentobarbital sodium 30 ml/kg administered intravenously. Pancuronium bromide 0.2 ml/kg was administered to facilitate tracheal intubation. The dogs were placed in a supine position and anesthetized using a continuous intravenous infusion of ketamine chloride 5 mg/kg/h. The animals were ventilated with oxygen using a Harvard respirater (DOG Respirator Model 613, Harvard Apparatus, USA). The respiratory tidal volume was adjusted to maintain an end-expiratory carbon dioxide pressure of 30 to 40 mmHg and was monitored with an infrared carbon dioxide analyzer (Multigas Monitor, OMA-8101, Nihon Kohden, Tokyo, Japan).

The left femoral vein was cannulated for infusion of lactated Ringer's solution at a maintenance dose of 5 ml/kg/h, and for an intravenous bolus injection. The left femoral artery was cannulated for continuous monitoring of systemic arterial pressure and for blood sampling. Left ventricular pressure (LVP) was monitored with a 7-French pigtail catheter introduced through the right femoral artery. The maximum rate of left ventricular pressure change (LV dp/dt max) was measured by electrically deriving the LVP wave using an electronic differentiator (Pressure Processor Model EQ-601G, Nihon Korden, Tokyo, Japan). A 7.5-French balloon-tripped triple-lumen pulmonary catheter (Swan-Ganz) was inserted via the right external jugular vein and its tip positioned in a branch of the pulmonary artery for measurement of hemodynamic variables. 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 áU of an electrocardiograph.

Circulating blood volume (CBV) was measured by the pulse-dye densitometry (PDD) method. PDD was performed using a DDG analyzer (DDG-2001 Nihon Korden Corp., Tokyo, 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-spectophotometry. In a preliminary experiment, the tongue probe was found to direct pulsation better than probes placed on the finger, ear, and nostril. Twenty-five milligrams of ICG in 10 ml of 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 measured blood hemoglobin (Hb) concentration.

The dogs were allowed to stabilize for at least 60 minutes (min) after the surgical procedure; physiological measurements were then taken (baseline). Thereafter, intravenous bolus injection was started within 2 min by an intravenous bolus injection (4 ml/kg) of either group A or group B. Measurements were taken at baseline, 5, 15, 30, 60 and 120 min after bolus injection.

The following variables were measured in all dogs: Hb, HR, mean arterial pressure (mAP), mean pulmonary arterial pressure (mPAP), LVP, CO, partial pressure of arterial oxygen (PaO_2), partial pressure of arterial carbon dioxide ($PaCO_2$), plasma colloidal osmotic pressure (Pcop), plasma crystalloidal osmotic pressure (Posm) and CBV. The cardiac index (CI), systemic vascular resistance (SVR), left ventricular stroke work index (LVSWI) and LV dp/dt max were carculated using the standard formulas. Blood samples were drawn at the point of the experimental measurements for analysis of Pcop and Posm. Blood samples were kept on ice and centrifuged at 2000 g for 20 min at 4℃. The plasma was removed and analyzed for Pcop using an osmometer (Colloid Osmometer 4400 WESCOR, Baxter Corp., USA). Posm was measured by a cryoscope (osmotic pressure AUTO & STAT OM-6030, Kyoto Daiichi Kagaku Corp., Japan).

Data are expressed as mean ± standard error (SE). The data were analyzed for significant differences each group between the baseline values and those for the subsequent phases (5-120 min), using the Student's paired t-test, with $P<0.05$ considered as statistically significant. Differences between the two groups were analyzed using the Student's unpaired t-test. Values of $P<0.05$ were considered statistically significant.

RESULTS

Hb did not differ significantly between the A and B groups at baseline condition (12.9 ± 0.8 and 12.5 ± 0.5 g/dl, respectively).

Hemodynamic variables are shown in Table 1. At baseline, no significant between group differences were noted in the hemodynamic variables. After the bolus injection, the HR in both groups did not differ significantly as compared with the baseline value. mAP did not change in the A group after bolus injection, but increased significantly in the B group from the baseline value. However, mPAP, CI, LVSWI and LV dp/dt max values in both groups increased significantly, while SVR decreased significantly compared with the baseline value after the bolus injection. After bolus injection, mAP and LV dp/dt max values in group B were significantly at 60

Table 1
Hemodinamic variables at 5, 15, 30, 60 and 120 min after bolus injection with 6% 200KDa HES or 12% 200KDa HES

Variable	Group	Baseline	5 min	15 min	30 min	60 min	120 min
HR	A	168±8	167±7	167±8	169±7	175±6	166±5
	B	163±8	158±7	170±8	172±7	175±6	167±6
mAP	A	131±5	135±4	137±4	141±4	135±6†	140±6†
	B	136±6	145±6*	147±6*	152±5*	151±5*	155±6*
mPAP	A	17±2	19±2*	19±2*	20±3*	20±3*	20±2*
	B	19±1	22±1*	22±1*	23±1*	23±1*	24±2*
CI	A	1.5±0.1	2.0±0.1*	2.1±0.2*	2.1±0.1*	2.1±0.1*	2.0±0.1*
	B	1.6±0.1	2.1±0.1*	2.2±0.1*	2.2±0.1*	2.4±0.1*	2.2±0.1*
SVR	A	8486±373	7064±418*	6872±484*	6876±317*	6741±299*	7484±384*
	B	8938±468	7376±477*	7216±503*	7294±532*	6697±466*	7339±403*
LVSWI	A	15.5±0.6	20.3±1.4*	21.6±1.8*	22.6±1.3*	20.6±1.5*	21.3±1.6*
	B	17.2±0.8	24.7±1.8*	24.7±2.0*	25.9±2.3*	27.0±2.4*	27.4±2.9*
LVdp/dt max	A	2467±149	2867±207*	3033±249*	3133±260*	3200±225*†	3000±205*†
	B	2589±200	2944±209*	3200±197*	3456±206*	3544±215*	3467±216*

(n=7)
Data are expressed as mean ± standard error (SE)
HR: heart rate (beats·min^{-1}); mAP: mean arterial pressure (mmHg); mPAP: mean pulmonary arterial pressure (mmHg); CI: cardiac index (l·min^{-1}·m^{-2}); SVR: systemic vascular resistance (dyn·sec·cm^{-5}); LV dp/dt max: maximum rate of left ventricular pressure change (mmHg·sec^{-1})
A: 6% 200KDa HES group ; B: 12% 200KDa HES group
Baseline: after surgical procedure. 5min, 15min, 30min, 60min, and 120min : 5, 15, 30, 60, and 120 min after bolus injection.
*$P<0.05$: from Baseline
†$P<0.05$: between group A and B

Table 2
Respiratory variables plasma osmotic pressure, and circulating blood volume at 5, 15, 30, 60, 120 min after bolus injection with 6% 200KDa HES or 12% 200KDa HES

Variable	Group	Baseline	5 min	15 min	30 min	60 min	120 min
PaO_2	A	582±8	576±8	574±8	570±10	573±17	560±7
	B	573±10	564±8	564±13	552±9	535±15	545±18
$PaCO_2$	A	39±1	39±1	39±1	40±1	38±1	38±1
	B	36±1	36±1	37±1	38±1	38±1	38±1
Pcop	A	14.1±0.6	15.0±0.6''	14.8±0.6''	14.7±0.5''	14.1±0.5''	13.4±0.4'
	B	14.5±0.6	17.3±0.8'	16.5±0.7'	16.0±0.7'	15.9±0.7'	15.4±0.7
Posm	A	305±3	305±3	304±2	304±2	303±2	302±2
	B	308±1	310±1	309±1	308±2	306±2	307±2
CBV	A	1.2±0.1	1.7±0.2'	1.6±0.1'	1.8±0.1'	1.8±0.1'	1.7±0.1'
	B	1.2±0.1	1.5±0.1'	1.6±0.1'	1.7±0.1'	1.7±0.1'	1.7±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)
A: 6% 200KDa HES group ; B: 12% 200KDa HES group
Baseline: after surgical procedure. 5min, 15min, 30min, 60min, and 120min : 5, 15, 30, 60, and 120 min after bolus injection.
'P<0.05: from Baseline
''P<0.05: between group A and B

min to 120 min greater than those in the group A.

Blood gas, Pcop, Posm and CBV are shown in Table 2. At baseline, no significant between group differences were noted. After the bolus injection, the PaO_2, $PaCO_2$ and Posm in both groups did not differ significantly as compared with the baseline values. After bolus injection, the Pcop and CBV values in both groups increased significantly compared with the baseline values. Pcop in the group B were significantly greater than that in the group A.

DISCUSSION

Plasma substitutes are used for the prevention and treatment of hypovolemia after the loss of blood. The main reason for using colloidal volume replacements is to maintain the circulating blood volume by stabilizing plasma colloidal osmotic pressure. Need et al.(1) have found that hemodynamic and oxygen transport responses were related to concomitant improvement in circulating blood volume and plasma colloidal osmotic pressure.

HES is commonly used as a plasma volume expander, in part because of its therapeutic safety, its stable effect on plasma volume, and its association with a low incidence of anaphylactic reactions. At present, we used HES in this experiment. Dieterich H-J et al.(2) reported that HES is very well tolerated, and the incidence of anaphylactic reactions is lower than with dextran or gelatin. Furthermore, HES is less expensive than human albumin.

In the present study, after the bolus injection, hemodynamic variables, except mAP and LV dp/dt max, did not differ significantly between two groups, as a result of CBV did not differ significantly between two groups. However, Pcop in group A increased significantly at 5 and 30 minutes after injection of plasma substitutes. On the other hand, high and prolonged colloidal osmotic pressure levels were noteworthy in group B. Although CBV increased after injection of plasma substitutes, no change PaO_2 and $PaCO_2$ in both groups could be documented. This suggested that the amount of pulmonary interstitial water was not significantly increased despite increased CBV.

HES is available in high (~400 kDa), medium (~200 kDa), and low (40~100 kDa) molecular weight type. We used 200 kDa HES in this study. In Japan, at present low molecular weight type HES are used overwhelmingly as a first choice in the volume replacement therapy. Low molecular artificial colloid is cleared rapidly from the blood. The present authors reported(3,4) previously that medium molecular weight HES is more effective than low molecular weight HES as volume replacement therapy, as measured by improvements in hemodynamic variables, CBV and Pcop. We are convinced that the hyperoncotic colloidal solution is a useful plasma substitutes which overcomes the disadvantages of isooncotic colloidal solution. Particularly, a satisfactory result may be anticipated in the volume replacement therapy using low molecular colloidal solution.

The intravenous bolus injection of hypertonic saline solution (4 ml/kg) represents a new concept for primary resuscitation from shock: it is called small-volume resuscitation. However, some investigators (5-7) suggested that the superiority of small-volume resuscitation using hypertonic hyperoncotic solution as compared with hypertonic solution consists of its effects on the hemodynamic variables and splanchnic organ blood flow. The authors are confident that small-volume resuscitation using hyperoncotic solution are capable of restoring hemodynamic and CBV for hemorrhagic shock.

CONCLUSION

These results suggest that the group B is superior to the group A in Pcop. This phenomenon occurred despite the relatively similar time couse of the effects of systemic hemodynamics and CBV.

ACKNOWLEDGMENT

The authors thanks Doctor Akiyoshi Hosoyamada for his valuable comments on the contents of his manuscript.

Reference

1. Need JE, Hauser CJ, Shippy C, et al.: Comparison of cardiorespiratory effects of crystalline, hemoglobin, whole blood, albumin, and Ringer's lactate in the resuscitation of hemorrhagic shock in dogs. Surgery 83: 639-647, 1978
2. Dieterich H-J, Kraft D, Sirtl C, et al.: Hydroxyethyl starch antibodies in human: Incidence and clinical relavance. Anesth Analg 86: 1123-6, 1998
3. Nagai H & Kobori M: A study of plasma substitutes for volume replacement in intraoperative hemodilution technique: Estimation of circulating blood volume by pulse dye-dentistometry. Cire Cont 21: 47-53, 2000
4. Kobori M, Negishi H, Nagai H, et al.: Plasma substitutes for volume replacement in hemorrhagic shock: Comparison of low and medium molecular weight hydroxyethyl starch. Curr Ther Res Clin Exp 61: 414-421, 2000
5. Kreimeier U & Messmer K: Einsatx hypertoner NaCl-losunger zur primaren volumentherapie. Zentralbl Chir 117: 532-9, 1992
6. Brock H, Rapf B, Necek S, et al.: Vergleichende untersuchungen zur postoperativen volumentherapie bei kar diochirurgischen patienten. Anaesthesist 44: 486-92, 1995
7. Kobori M, Negishi H, Kuno M: Comparison of hypertonic saline and hypertonic oncotic saline solutions for small-volume resuscitation under hemorrhagic hypotensive shock: Effect on hemodynamic variables and splanchnic organ blood flow. J Soc Res Body Fluid Meta 15: 26-31, 1999

ABSTRACT

This investigation examined the effect on hemodynamics, plasma osmotic pressure, and circulating blood volume (CBV) after administering a isooncotic colloidal solution or a hyperoncotic colloidal solution. We divided anesthetized dogs into two groups. The anesthetized dogs were given with a single bolus injection, 4 ml/kg, of a 6 % 200 kDa hydroxyethyl starch (HES) in saline (A group) or 12 % 200 kDa HES in saline (B group). Mesurements were taken at baseline, 5, 15, 30, 60 and 120 minutes after the bolus injection. After bolus injection, mean pulmonary pressure (mPAP), cardiac index (CI), left ventricular stroke work index (LVSWI), maximum rate of left ventricular pressure change (LV dp/dt max), plasma colloidal osmotic pressure (Pcop), and CBV in both groups increased significantly, while systemic vascular resistance (SVR) decreased significantly compared with the baseline values. Heart rate (HR), partial pressure of arterial oxygen (PaO_2), partial pressure of arterial carbon dioxide ($PaCO_2$), plasma crystalloidal osmotic pressure (Posm) in both groups did not differ significantly as compared with the baseline values. mAP (60-120 min), LV dp/dt max (60-120 min), Pcop (5-120 min) in the group B were significantly greater than those in the group A after bolus injection.

These results suggest that the group B is superior to the group A in Pcop. This phenomenon occurred despite the relatively similar time couse of the effects of systemic hemodynamics, blood gas, and CBV.

Key words: isooncotic colloidal solution, hyperoncotic colloidal solution, circulating blood volume (CBV), plasma colloidal osmotic pressure (Pcop)