Original Article

A Comparative Study of Crystalloid and Colloid Solutions for Volume Replacement in Hypovolemic Shock

Masao KOBORI Hideru NEGISHI
Department of Anesthesiology, School of Medicine, Showa University
Kinuko GOTOH Masatoshi KUNO Hiroyoshi YAMAZAKI
Department of Anesthesia, School of Dentistry, Showa University

Abstract

We studied the relative efficacy of two volume replacement therapies in a canine model for induced hemorrhagic shock. The subjects were randomly allocated to two groups. The R group received lactated Ringr's solution at four times the volume of withdrawn blood and the D group received 6% dextran (MW=70 kDa) in saline at a volume equivalent to blood withdrawn. The efficacy of both therapies in maintaining hemodynamic parameters and splanchnic organ blood flows (renal cortex, renal medulla, liver and pancreas) stability were investigated over a 180 min period.

Cardiovascular parameters were well maintained in the D group as compared to the R group. Particularly, cardiac index in the D group increased significantly within 15 min after initiation of replacement therapy and was well maintained throughout the study relative to the R group. All splanchnic organ blood flows decreased significantly with hemorrhage, while they increased with volume replacement. However, the stability of splanchnic organ blood flows were better maintained over a longer period with dextran, rather than lactated Ringer's replacement.

These results suggest that replacement therapy using colloid dextran solution is more effective than crystalloid lactated Ringer's solution in preventing irreversible shock resulting from reduced splanchnic organ blood flows.

Introduction

There has been a persistent controversy over the relative merits of using crystalloids and colloids in fluid resuscitation. The fractional distribution of the cardiac output following bleeding indicated differences in the local vascular response, with an increased fraction of blood flow allocated to vital organs such as the heart and brain. However, an irreversible shock is precipitated by the reduction of splanchnic organ blood flows.

The purpose of this study was to experimentally compare the hemodynamic effects and splanchnic organ blood flows under conditions of hemorrhagic shock and volume replacement therapy with lactated Ringer's solution or dextran 70 solution. The efficacy of both fluids in maintaining hemodynamics and splanchnic blood flows were investigated in mongrel dogs with hemorrhagic shock and volume replacement therapy over a 180 min period.

Materials and Methods

The experiments were performed on 14 adult male mongrel dogs (10-18kg) allocated randomly to 2 groups consisting of 7 dogs each: R group (lactated Ringer's solution); D group (dextran,MW 70,000, 6% in saline).

The experimental animals were anesthetized with sodium pentobarbital (30 mg/kg i.V.). Pancuronium bromide at 0.2 mg/kg was administered after an endotracheal tube was inserted, and the dogs were ventilated via a cuffed endotracheal tube

with oxygen using a Harvard respirator. Tidal volumes were adjusted to maintain end-expiratory ETCO2 at 30-40 mmHg, as monitored with an infrated CO2 analyzer. The animals were maintained in the supine position under anesthesia with continuous intravenous infusion of ketamine at 3 mg/kg/h.

Bilateral femoral veins were cannulated for the infusion of lactated Ringer's solution at a rate of 5 ml/kg/h as a maintenance dose, for withdrawal of blood, and for the volume replacement therapy. The left femoral artery was cannulated for continuous systemic arterial pressure monitoring and for blood sampling. Left ventricular pressure (LAP) was monitored with a 7-French pigtail catheter cannulated via the right femoral artery. The maximum rate of pressure change in the left ventricle (LV dp/dt max) was electrically derived from the LVP wave signal using an electronic differentiator. A 7.5-French balloon-tripped triple lumen pulmonary catheter (Swan-Gantz catheter) was cannulated via the right external jugular vein and positioned in a branch of the pulmonary artery for measuring circulatory parameters and for mixed venous blood sampling. Cardiac output (CO) was determined by the thermodilation technique (5 ml of 0.9% saline at 0°C into the right atrium at end-expiration). The heart rate (HR) was calculated from lead II of an electrocardiogram by using a cardiotachometer.

Splanchnic blood flow was determined by the hydrogen gas clearance method. Laparotomy was performed for the placement of electrodes. Hydrogen gas clearance electrodes were inserted into the kidney (renal cortex and medulla), liver and pancreas.

After steady-state anesthesia was achieved, surgery, control (C) measurements, and blood sampling were performed. The animals were then subjected to hemorrhagic shock, which was achieved by withdrawal of blood until the mean arterial pressure was reduced by approximately 50 mmHg during 30 min and were measured all the parameters (SO). The volume of blood withdrawn did not differ significantly between the two groups (R group=534±80 ml, D group=615±77 ml). Next, the dogs were subjected to volume replacement therapy within 5 min, which was achieved by introducing either lactated Ringer's solution at 4 times the volume (R group) or by dextran 70 in an equivalent volume of blood lost (D group). All sampling and measurements were carried out at 15, 30, 60, 120, and 180 min (S15-S180) after initiation of the volume replacement therapy.

Heart rate, mean arterial pressure (mAP), LAP, CO, partial arterial oxygen pressure (PaO2), partial arterial carbon dioxide pressure (PaCO2), and mixed venous oxygen saturation (SvO2) were measured. The hematocrit (Hct) value was measured by centrifuging sampled blood at 5,000 rpm for 5 min. The cardiac index (CI), LV dp/dt max, and systemic vascular resistance (SVR) were calculated using standard formulas. Renal cortex, renal medulla, liver and pancreas blood flow were measured. Splanchnic blood flows were calculated as a percent of respective control (C) values (RCBF, RMBF, LBF, and PBF).

Data are expressed as mean±standard error (SE) and stastistical comparisons between the control and SO-S180 values of each dog group were made using the Student's paired t-test with $P<0.05$ considered as statistically significant. Differences between both groups were analyzed of variance by using the unpaired t-test with $P<0.05$ considered as statistically significant.

Results

The control values did not differ significantly between both groups.

[1] Hct value

Hct values are shown in Table 1. Hct values decreased significantly by the

hemorrhagic technique and the replacement therapy in two groups. Furthermore, S60 and S180 measurements statistlcally differed between the two groups.

[2] Hemodynamic parameters

Hemodynamic parameters are shown in Table 1. No significant changes in HR were observed by the hemorrhagic technique, but HR decreased significantly by the volume replacement therapy in both groups. mAP decreased significantly during the hemorrhagic period, but then returned to control values in the D group within 60 min. In contrast, the mAP was hypotensive in the R group throughout the experimental period as compared with the control (mAP was also slightly hypotensive in the D group). Furthermore, S60 measurements of the mAP statistically differed between both groups. Cardiac

Table 1. Hematocrit value and hemodynamic parameters

		C	S_0	S_{15}	S_{30}	S_{60}	S_{120}	S_{180}
Hct	R	45±2	40±3*	19±1**	21±2**	22±2**†	25±1**†	27±2**†
	D	39±2	36±2*	18±3**	16±3**	16±3**	17±3**	18±3**
HR	R	173±9	191±8	147±4**	148±8	142±5**	150±13	151±14
	D	185±10	207±10	164±5*	163±5*	160±5**	161±7*	170±9
mAP	R	143±8	50±1**	130±5*	129±8*	111±11**†	122±10*	131±9**
	D	153±6	50±1**	138±5*	142±5*	141±6	140±6	139±7
CI	R	1.8±0.2	0.7±0.1**	3.3±0.5*	2.5±0.3*	1.8±0.1†	1.3±0.1*†	1.1±0.1**
	D	2.0±0.3	0.6±0.1**	3.3±0.5**	3.3±0.4**	2.9±0.4**	2.1±0.4	1.8±0.4
SVR	R	10402±2157	8535±1065	5295±1236**	6613±1077	6969±836	11343±1275	14090±1384*
	D	9410±1248	8182±416	5068±622**	5166±652**	5979±721**	8880±1487	10964±2062
LV dp/dt max	R	2786±243	1271±117**	3414±389	3571±78	2500±256†	2514±198	2557±419
	D	3343±372	1343±156**	3457±239	3543±265	3243±183	2957±307	2743±317

Data are expressed as mean±standard error (SE)

Hct (hematocrit;%), HR (heart rate;beats·min^{-1}), mAP (mean arterial pressure;mmHg), CI (cardiac index;l·min^{-1}·m^{-2}), SVR (systemic vascular resistance;dyn·sec^{-1}·cm^{-5}), LV dp/dt max (left ventricular maximum rate of pressure change;mmHg·sec^{-1})
R:lactated Ringer's group, D:dextran group
C:control, S_0:hemorrhagic shock, S_{15}～S_{180}:after the volume replacement therapy.
**:P<0.01, *:P<0.05 versus control value (C)
† :P<0.05 between group R and group D

Table 2. Respiratory parameters and changes in splanchnic blood flows

		C	S_0	S_{15}	S_{30}	S_{60}	S_{120}	S_{180}
PaO_2	R	578±15	562±35	588±11	588±12	583±16	550±17	543±28
	D	533±18	511±25	535±25	554±14	529±20	525±16	528±20
$PaCO_2$	R	34±1	33±2	35±2	36±1	34±1	35±1	34±1
	D	35±1	31±2	37±2	39±2	35±1	35±1	34±1
SvO_2	R	84±2	27±2**	97±2**	92±3	85±3	74±5	67±3**
	D	85±3	29±5**	93±2**	93±3**	91±3*	79±3	73±3
RCBF	R	100 %	42±7**	95±6	88±5*	84±5*†	74±3*††	50±6**††
	D	100 %	41±10**	103±2	95±3	100±2	90±2**	83±3**
RMBF	R	100 %	38±6**	188±29*	180±39	202±57	147±28	96±12
	D	100 %	38±10**	195±52**	212±59**	240±57**	228±71**	185±63
LBF	R	100 %	47±6**	117±27	144±27	129±21	84±17	59±14*
	D	100 %	32±7**	127±15	118±14	110±12	91±10	77±12
PBF	R	100 %	36±8**	80±4**†	77±7*†	62±10*†	41±6**†	33±8**†
	D	100 %	46±9**	186±35*	183±28*	166±35	143±30	103±20

Data are expressed as mean±standard error (SE)

PaO_2 (arterial partial oxygen pressure;mmHg), $PaCO_2$ (arterial partial carbon dioxide pressure;mmHg), SvO_2 (mixed venous oxygen saturation;%), RCBF (changes in renal cortex blood flow;%), RMBF (changes in renal medulla blood flow;%), LBF (changes in liver blood flow;%), PBF (changes in pancreas blood flow;%)
R:lactated Ringer's group, D:dextran group
C:control, S_0:hemorrhagic shock, S_{15}～S_{180}:after the volume replacement therapy.
**:P<0.01, *:P<0.05 versus control value (C)
††:P<0.01, †:P<0.05 between group R and group D

index decreased significantly in both groups by the hemorrhagic technique. With volume replacement, CI increased significantly in both groups. Greater CI stability in the D group was seen relative to the R group. Hemorrhage produced insignificant changes in SVR, while volume replacement caused SVR to decrease significantly in both groups. However, a significant increase in SVR was observed at S180 in the R group relative to the control. LV dp/dt max decreased significantly by the hemorrhagic technique, but promptly returned to control values after volume replacement therapy in both groups.

[3] Respiratory parameters

Respiratory parameters are shown in Table 2. In both groups, no significant changes in PaO2 and PaCO2 values were observed with hemorrhage and also with volume replacement. However, SvO2 decreased signifieantly with hemorrhage, which was corrected by volume replacement in both groups. SvO2 deviated from this general trend at S180 in the R group where a decrease relative to the control was observed.

[4] Changes in splanchnic blood flows

Changes in splanchnic blood flows are shown in Table 2. RCBF decreased significantly by the hemorrhagic technique. Despite volume replacement by lactated Ringer's solution, RCBF did not returned to control values during S30-S180 measurements. Furthermore, S60-S180 measurements statistically differed between both groups. In contrast to RCBF values, volume replacement caused RMBF values to return immediately to control values after a significant decrease induced by the hemorrhagic technique. In general, RMBF values were slightly higher in the D group than in the R group. LBF decreased significantly by the hemorrhagic technique, but upon volume replacement therapy, LBF values rebounded to control values. As with other splanchnic parameters, PBF decreased significantly with hemorrhage. During volume replacement therapy, PBF in the R group decreased significantly relative to control values during the experimental period. In contrast, PBF in the D group increased significantly between S15-S30 by volume replacement. PBF differed statistically between both groups after volume replacement.

[5] Urine volume during the experimental period

The urine output differed significantly between the two groups during the experimental period (R group=309± 219 ml vs D group=158±137 ml:$P<0.05$).

Discussion

Although hemodilution can be performed with a crystalloid solution instead of a colloid solution, it is important to note that with crystalloid hemodilution, the patient's blood has to be exchanged in a 1:4 ratio for crystalloids to ensure normovolemia. Need et al.[1] found that hemodynamic and oxygen transport responses were greater and more prolonged after replacement with colloidal rather than lactated Ringer's solution. Similarly, Shoemaker et al.[2,3] observed that increases in cardiac output, oxygen delivery and oxygen consumption were much greater after an equal volume of colliod therapy than with two to four times the volume of lactated Ringer's solution. In this study, we further studied the efficacy of colloid versus cryatalloid volume replacement therapies. Our experimental model was one in which blood withdrawn by the hemorrhagic technique was replaced simultaneously by infusion of an equal volume of colloidal solution (6% dextran 70 in saline) or four times the volume of lactated Ringer's solution. Hct values differed statistically between the two groups during S60-S180 measurements. Furthermore, our results showed greater CI and SVR stability in the D group relative to the R group. The observed stability of cardiovascular parameters after colloid infusion and the lack there of after infusion of the crystalloid solution suggested

that the escape of fluid from plasma was greater after cristalloid infusion. In addition, the urine output was significantly more in the R group than in the D group during the experimental period. Hauser et al.[4] suggested that colloid therapy improved cardiovascular performance and oxygen transport by plasma expansion while the effect of lactated Ringer's solution was relatively short lived. It has also been shown in several investigations that volume replacement with colloid solution better maintained hemodynamic stability, whereas administration of crystalloid solution jeopardized tissue perfusion and oxygenation[4,5]. Moreover, Kobori et al.[6] demonstrated that hemodynamic stability is better maintained after dextran 70 (MW 70,000) than after dextran 40 (MW 40 kDa) administration.

In our study, volume replacement therapy by both fluids did not significantly change the distribution of ventilation or perfusion within the lung as measured by changes in PaO2 and PaCO2 in the two groups. However, SvO2 decreased gradually as a function of time with volume replacement therapy. In particular, the SvO2 measurement at S180 in the R group showed a significant drop as compared with the control. These results suggest that relative to colloid replacement, crystalloid volume replacement therapy results in inadequate tissue oxygen supply.

Many investigations have found that in acute hemorrhage, the fractional distribution of cardiac output is increased to the brain[7-9], heart[7-9], adrenal gland[7,9] and liver (via the hepatic artery)[7-9] at the expense of blood distribution to the skin[7,9] spleen[7,9], pancrease[9], kidney[7] and lung[7]. The gastrointestinal, portal, and total liver fractions showed little change[7]. However, blood flow to all organs decreased due to the overall decreased in cardiac output. In the heart, brain, and hepatic artery the absolute blood flow decreased, despite the increased fractional distribution[8]. In our study, blood flow to all splanchnic organs decreased significantly by the hemorrhagic technique and increased with volume replacement therapy. However, RCBF (S60-S180) and PBF (S15-S180) differed statistically between both groups. Since RCBF and PBF were better maintained in the D group, we speculate that volume replacement therapy by the colloid solution instead of the crystalloid solution is a possible means to avoid irreversible shock resulting from reduced splanchnic organ blood flow. Regarding this hypothesis, Shoemaker et al.[3] showed that resuscitation times were almost always shorter with a regimen of about one fourth colloid than with crystalloid only. This is consistent with our observations of greater increases in hemodynamic an oxygen transport variables after an equal volume replacement of colloid than 4 times the volume of lactated Ringer's solution.

Rocha-e-silva et al.[10] reported that a small volume of hypertonic saline can normalize circulatory function in cases of severe blood loss. In another study, Kramer et al.[11] found that a small volume of hypertonic saline with dextran fully restored cardiovascular and metabolic functions for hypovolemia. In general, hypertonic solutions have been used as a treatment for severe blood loss since they are known to cause an increase in myocardial contractility, widespread precapillary dilation, and an increase in circulating blood volume though a shift of fluid into the vasculature driven by osmotic forces. However, it has also been shown that infusion of hyperosmotic saline resulted in decreased platelet function[12]. This could lead to additional blood loss in hemorrhagic patients.

In conclution, our results demonstrate that hemodynamic parameters and splanchnic organ blood flows are better maintained and more stable with colloid, rather than crystalloid solution therapy in laparotomized mongrel dogs with hemorrhagic shock.

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