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Hemodynamic effects of fluid resuscitation with 6% hydroxyethyl starch and whole blood in experimental hypovolemic shock in Beagle dogs

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Abstract: The short-term effects of 6% hydroxyethyl starch (HES) and whole blood (WB) resuscitations in hypovolemic shock (HS) on invasive and noninvasive hemodynamic variables were studied from the clinical point of view in 20 mature healthy male Beagle dogs. After anesthesia, the animals were randomly divided into 2 groups, HES (n = 10) and WB (n = 10), and were surgically instrumented with an arterial catheter and a thermodilution cardiac output catheter. For induction of HS, the right carotid artery was catheterized and approximately 40% of the blood volume was drawn over a period of 30 min, until a mean arterial blood pressure (MAP) of about 50 mmHg was reached. After that, the HES group received 6% HES and the WB group received autologous whole blood resuscitation (30 mL/kg/h). The measurement of hemodynamic variables was performed in normovolemic (baseline, BL), severe hypovolemic, and resuscitation state (from R1 to R4 at an interval of 30 min). Significant changes in some of the hemodynamic variables systolic arterial pressure (SAP), diastolic arterial pressure (DAP), MAP, central venous pressure (CVP), cardiac output (CO), cardiac index (CI), stroke volume (SV), stroke volume index (SVI), oxygen delivery (DO_2), and oxygen consumption (VO_2) were observed during hypovolemic shock and resuscitation, which could reflect the condition of the patient. Resuscitation with WB seemed to resolve the hemodynamic variables to or above BL, whereas that with HES could resolve most but not all of the hemodynamic variables. The WB was found to be superior to restore the hemodynamic variable to the BL or above in comparison to that of the HES, for the clinical management of HS in dogs. The findings of this study suggest that dogs in HS can be successfully resuscitated with HES and WB.

Key words: Hypovolemic shock, hemodynamic variables, resuscitation, whole blood, hydroxyethyl starch, Beagle dogs

Introduction

Hypovolemic shock (HS) is an emergency condition in which severe blood and fluid loss results in a critical decrease in intravascular blood volume and makes the heart unable to pump sufficient blood to the body. HS is one of the major causes of morbidity and mortality in patients suffering acute hemorrhage (1). Hemorrhage is a natural consequence of injury and surgical procedures and is considered the most common clinical cause of HS (2). Acute blood loss leads to circulatory dysfunction causing lower tissue oxygenation and accumulation of oxygen debt, which can ultimately result in multi-organ system failure if left untreated (3). Vital organ perfusion, most nota-

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bly renal perfusion, is severely compromised in low-flow states in shock and much of the morbidity and mortality related to acute hemodynamic decompensation is the consequence of end-organ failure (4).

Subsequent monitoring to screen ongoing hemorrhage and to evaluate the efficacy of resuscitation is vital for avoiding morbidity in shock patients. Vital signs, such as blood pressure (BP) and heart rate (HR), are the initial parameters used to test for possible hemorrhage in trauma. The early recognition of shock using vital signs alone may be difficult, even in the presence of significant blood loss, due to compensatory mechanisms in otherwise healthy patients (5). Though there is a long history of research on fluid resuscitation in trauma victims, there is still debate concerning the optimal fluid solution, its dose, rate, and timing of administration (6). To date, the target end points of resuscitation remain vague, e.g. to what BP, HR, or other clinical criteria should be aspired to achieve while treating a trauma victim (1). An understanding of the rate, magnitude, and duration of the expanding effects of each fluid on blood volume would allow clinical decisions for predicting the efficacy of fluid resuscitation in the management of HS, but the real-time assessments have been poorly documented (7).

There is still not a clear understanding of the time course of events leading from hypovolemia to irreversible hypoxic tissue injury, circulatory collapse, and multiple organ failure, hindering significant progress in the development of effective therapy, in particular with respect to early interventions (8). Aggressive fluid therapy, elimination of cardiac tamponade, and catecholamine administration are among the traditional therapies for restoring adequate tissue perfusion and oxygen delivery. In HS, the circulating blood volume must be restored with aggressive administration of colloids, crystalloids, and/or blood. Crystalloids have been recommended as the initial resuscitation fluid in the treatment of hemorrhagic shock, but these solutions are poor plasma volume expanders and less than 20% of the administered volume stays in the intravascular space (9). Therefore, to maintain cardiovascular stability, consequent infusion of a large volume of crystalloids is necessary. Hydroxyethyl starch (HES), a substituted starch (amylopectin) available as a 6% solution, has been used to treat HS with results similar to those of gelatin and albumin (10). These solutions are more effective plasma expanders than crystalloids (4,11). It is generally recommended to not exceed 20 mL/kg/day in the dog and 10 mL/kg/day in the cat (11,12).

In this experiment, the short-term effects of 6% HES and whole blood (WB) resuscitations in HS on invasive and noninvasive hemodynamic variables were studied from the clinical point of view.

Materials and methods

In this experiment, 20 mature healthy male Beagle dogs, aged 1 to 2 years and weighing 10 to 16 kg, were divided into 2 groups: HES (n = 10) and WB (n = 10). Physical, hematologic, radiographic, and ultrasonographic examinations were performed to ensure the absence of heart, lung, liver, and urologic diseases. The dogs were fasted overnight but had free access to water up to 2 h prior to induction of anesthesia and experimentation.

The animals were premedicated with atropine sulfate (Atropie Sulfate Inj*, Dai Han Pharmaceutical Co., Ltd., Korea) 0.02 mg/kg, SC, followed by catheterization of the left cephalic vein for blood sampling, and continuous infusion of fluid at a rate of 30 mL/kg/h throughout the preparation and instrumentation period. Anesthesia was induced with intravenous (IV) administration of propofol 2-4 mg/kg (Pofol inj*, Jeil Pharm. Co. Ltd., Korea) and maintained with isoflurane (Forane Soln*, Choongwae Co. Ltd., Korea), and oxygen (O_2) was delivered through a cuffed endotracheal tube. During animal preparation and instrumentation, isoflurane in O_2 was delivered at an end-tidal concentration of 0.8%-1.2%. The animals were spontaneously ventilated to ensure an arterial partial pressure of carbon dioxide ($PaCO_2$) in the range of 35-45 mmHg.

The animals were instrumented in dorsal recumbency for continuous recording of the electrocardiogram (ECG; Datex-Engstrom*, 3 cables) and arterial oxygen saturation (SpO_2; Datex-Engstrom*, sat sensor cable and rectal temperature cable). Body temperature was maintained between 37 and 39 °C by means of a heating pad and circulating warm air blanket placed underneath and on top of the animal, respectively. End-tidal partial pressure of

CO_2 ($P_{ET}CO_2$), end-tidal concentration of isoflurane (ISO_{ET}), and inspired O_2 concentration (FiO_2) were continuously monitored using a Datex 254 airway gas monitor (Datex-Engstrom*, Helsinki, Finland).

The first surgical instrumentation included placement of catheters into the right femoral artery for determination of systemic arterial pressures, percutaneously (Figure 1). Then the right jugular vein and carotid artery were dissected, isolated, and catheterized (Figure 2). Next a 5-Fr balloon-tipped flow-directed thermodilution pulmonary arterial catheter (Swan-Ganz*, 132F5, Edwards Life Sciences, Irvine, CA, USA) was inserted via the jugular vein and floated into the pulmonary artery (Figure 3), for direct monitoring of pressure traces and fluoroscopic monitoring for measurements of mean pulmonary arterial pressure (MPAP), central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), core body temperature, and cardiac output (CO).

The pulmonary arterial catheter with CO set was connected to a CO computer (Datex-Engstrom* M-COP, Finland) for continuous CO monitoring. Finally, instrumentation included placement of a 5-Fr introducer catheter set (CHECK-FLO Performer*, COOK*, Bloomington, IN, USA) into the right carotid artery for blood withdrawal. The proximal port and distal port in the pulmonary arterial catheter and the femoral arterial catheter were connected to a disposable multiple pressure transducer (Auto Transducer*, Blood Pressure Monitoring Set, Acemedical Co. Ltd., Seoul, Korea). Disposable transducers to calibrate pulmonary arterial pressure (PAP) and mean arterial blood pressure (MAP) were connected to a heparinized saline bag with an IV pressure bag, and those to calibrate CVP and CO were connected to 5% dextrose in water. Prior to each experimental procedure, all of the pressure transducers were calibrated against a mercury manometer and against atmospheric pressure using the mid-thoracic inlet of the supine dog as zero level. Systolic, diastolic, and mean arterial blood pressure (ABP), PAP, PAOP, and CVP were recorded. The pulmonary arterial catheter was connected to a CO computer (Datex-Engstrom*, M-COP, Finland) for continuous CO monitoring.

After a 45 min adjustment period at the end of all of the preparations, a baseline (BL) set of measurements were taken, which included the standard invasive and noninvasive hemodynamic parameters: HR, respiration rate (RR), arterial partial pressure of oxygen (PaO_2), mixed venous partial pressure of oxygen ($PmvO_2$), arterial hemoglobin saturation with oxygen (SaO_2), venous hemoglobin saturation with oxygen ($SmvO_2$), arterial oxygen content (CaO_2), mixed venous oxygen content ($CmvO_2$), arterial hemoglobin (Hba), venous hemoglobin (Hbmv), systolic arterial blood pressure (SAP), diastolic arterial blood pressure (DAP), mean arterial blood pressure (MAP), CVP, MPAP, PAOP, CO, cardiac index (CI), stroke volume (SV), stroke

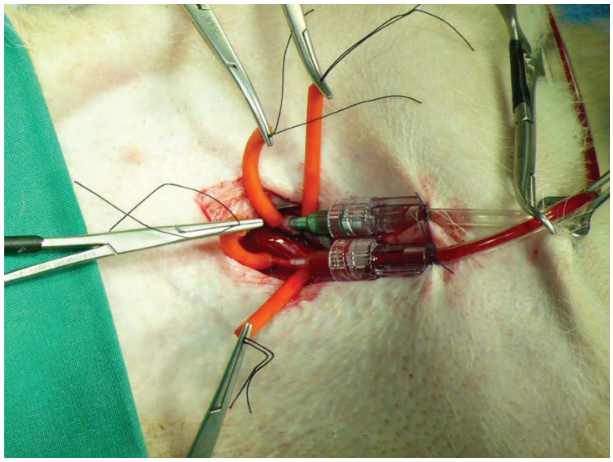

Figure 1. Photograph showing catheterization of the right femoral artery.

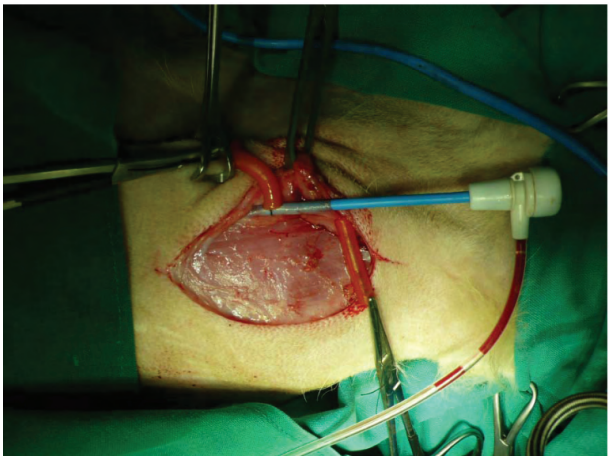

Figure 2. Photograph showing catheterization of the right jugular vein.

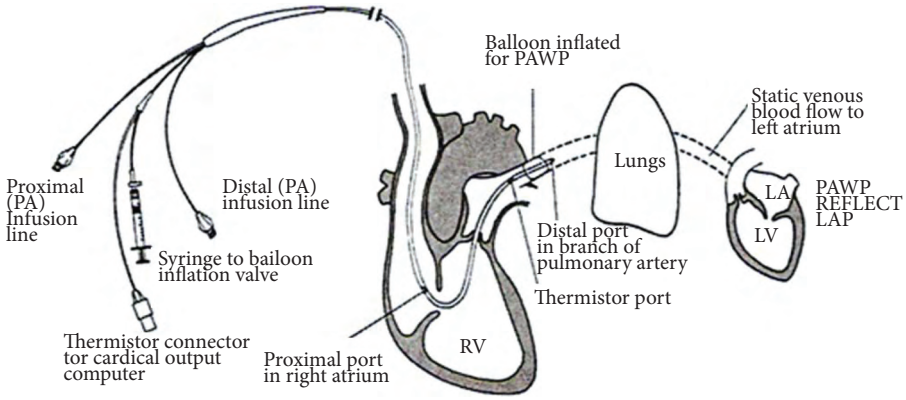

Figure 3. Schematic diagram of a 5-Fr balloon-tipped flow-directed thermodilution pulmonary arterial catheter placement via the right jugular vein.

volume index (SVI), oxygen delivery (DO_2), oxygen consumption (VO_2), and oxygen extraction (O_2ER). Subsequently, approximately 40% (30 ± 2 mL/kg) of the dogs' blood volume (total blood volume: 85 mL/kg), was collected in a citrate phosphate dextrose blood bag from the right carotid artery over 30 min until an MAP of about 50 mmHg was reached. An additional small amount of blood (about 5 mL/kg) was drawn to maintain the MAP at 50 mmHg for 60 min, and after this a second set of measurements, posthemorrhagic (PH), were performed.

Then fluid resuscitation with IV administration of 6% HES (HES group) and autologous WB (WB group), at the rate of 30 mL/kg/h, was continued for 1 h. A third set of measurements (R1) was taken followed by a fourth (R2), fifth (R3), and sixth (R4) set of measurements, at 30 min intervals. The experimental animals were euthanized following the last measurement with an overdose of potassium chloride without regaining consciousness.

Statistical analysis

The data obtained in the present study were analyzed using ANOVA and Student's t-test. $P < 0.05$ or less was considered as statistically significant by SAS package. The data are presented as mean ± SEM values.

Results

Changes in HR and RR

The HR was found to increase in both the groups during the experiment. This increase was not statistically significant in the HES group, whereas that of the WB group was significant ($P < 0.01$) at PH and during resuscitation from R1 to R4, in comparison to the baseline measurement. There were no significant changes in the values of RR during the experiment in the HES group, whereas that of the WB group was significantly ($P < 0.05$) increased during resuscitation from R1 to R4 in comparison to the baseline measurement. The results are presented in the Table.

Changes in PaO_2 and $PmvO_2$

There were no significant changes in the mean arterial partial pressure of oxygen (PaO_2, mmHg) and mixed venous partial pressure of oxygen ($PmvO_2$, mmHg) in either of the groups during the experiment (Table).

Changes in SaO_2 and $SmvO_2$

The values of arterial hemoglobin saturation with oxygen (SaO_2, %) and venous hemoglobin saturation with oxygen ($SmvO_2$, %) were decreased after hemorrhage but returned to normal during the resuscitation in both groups (Table). However, the changes in the mean values of SaO_2 and $SmvO_2$ were not statistically significant during the experiment.

Changes in CaO_2 and $CmvO_2$

There was no significant change in the arterial oxygen content (CaO_2, mL/dL) in either of the groups during the experiment. The values of the mean mixed venous oxygen content ($CmvO_2$, mL/dL) were decreased after hemorrhage, which increased and became normal during resuscitation in both of the groups during the experiment (Table).

Table. Hemodynamic variables at the baseline, during hypovolemic shock, and after treatment with HES and WB in the experimental animals (n = 20).

Variables	Group	Baseline	Post hemorrhage	After resuscitation			
				R1	R2	R3	R4
Heart rate	HES	128 ± 4.5	145 ± 9.6	139 ± 6.1	147 ± 4.3	150 ± 3.4	148 ± 4.2*
	WB	148 ± 7.3	171 ± 4.9*	165 ± 6.7*	151 ± 6.1	154 ± 6.5	165 ± 2.7*
Respiration rate	HES	16 ± 1.8	15 ± 1.5	12 ± 1.5	11 ± 1.6	11 ± 1.8	18 ± 1.1
	WB	19 ± 2.5	15 ± 1.5	31 ± 2.6*	24 ± 4.1	29 ± 5.7*	30 ± 5.2*
PaO_2 (mmHg)	HES	106.5 ± 1.5	100. 6 ± 0.8	107.4 ± 2.1	106.2 ± 1.5	103.2 ± 2.0	100.6 ± 1.2
	WB	106.3 ± 2.2	98. 2 ± 0.8	110.4 ± 3.3*	109.8 ± 2.9*	108.3 ± 2.7*	108.4 ± 1.5*
$PmvO_2$ (mmHg)	HES	50.1 ± 0.3	27.7 ± 1.6	53.1 ± 7.0	31.2 ± 1.9	29.0 ± 1.5	29.3 ± 1.4*
	WB	49.1 ± 1.9	26.6 ± 1.6	44.6 ± 3.4	45.0 ± 2.2	49.0 ± 2.2	49.4 ± 1.7*
SaO_2 (%)	HES	95.9 ± 1.3	90.1 ± 0.7	96.8 ± 0.6	94.0 ± 1.3	92.9 ± 2.0	90.6 ± 1.0
	WB	95.8 ± 0.6	88.5 ± 0.7	99.5 ± 0.9*	98.2 ± 1.1	97.9 ± 0.9	97.6 ± 0.4*
$SmvO_2$ (%)	HES	78.7 ± 0.1	33.3 ± 1.5*	69.7 ± 0.2	67.9 ± 0.9	68.0 ± 0.8	66.0 ± 1.7
	WB	77.9 ± 0.2	33.8 ± 0.9*	70.8 ± 0.3	74.8 ± 0.7	76.8 ± 0.9	77.9 ± 0.6
CaO_2 (mL/dL)	HES	18.9 ± 0.4	15.7 ± 0.5*	12.2 ± 0.6	12.8 ± 0.7	12.7 ± 0.6	12.1 ± 0.5
	WB	18.3 ± 0.2	15.9 ± 0.3*	18.6 ± 0.2	18.9 ± 0.6	18.8 ± 0.5	18.8 ± 0.4
$CmvO_2$ (mL/dL)	HES	15.8 ± 0.5	6.5 ± 0.5*	9.1 ± 0.4	9.0 ± 0.3	9.1 ± 0.5	9.7 ± 0.7
	WB	14.6 ± 0.4	6.1 ± 0.4*	13.2 ± 0.6	13.8 ± 0.5	13.9 ± 0.8	14.9 ± 0.5
Hba (g/dL)	HES	14.5 ± 0.3	12.2 ± 0.3	9.5 ± 0.4	9.9 ± 0.7	9.9 ± 0.9	10.2 ± 0.5
	WB	14.0 ± 0.2	13.1 ± 0.3	13.7 ± 0.2	14.0 ± 0.2	14.1 ± 0.8	14.1 ± 0.3
HBmv (g/dL)	HES	14.9 ± 0.5	14.5 ± 0.3	9.6 ± 0.4	9.9 ± 0.9	10.8 ± 0.6	10.0 ± 0.5*
	WB	13.9 ± 0.3	13.3 ± 0.3	13.8 ± 0.2	13.9 ± 0.8	14.3 ± 0.5	14.2 ± 0.3
SAP (mmHg)	HES	158.8 ± 10.2	75.4 ± 6.2*	139.6 ± 8.1	174.4 ± 7.3	176.6 ± 5.2*	164.0 ± 5.2
	WB	150.6 ± 4.2	90.6 ± 3.8*	130.6 ± 3.8	167.4 ± 0.4	175.4 ± 1.3*	171.0 ± 0.3*
DAP (mmHg)	HES	90.8 ± 4.7	32.8 ± 1.2*	60.4 ± 2.7	73.0 ± 2.3	80.0 ± 4.8	71.8 ± 3.1
	WB	92.2 ± 0.9	29.4 ± 1.5*	68.0 ± 3.0	95.4 ± 4.5	99.0 ± 3.3*	96.0 ± 3.3*
MAP (mmHg)	HES	113 ± 6.4	47 ± 2.5*	101 ± 2.7	107 ± 3.7	112 ± 4.9	103 ± 3.2
	WB	111 ± 1.3	43.2 ± 1.5*	88.9 ± 1.9	119 ± 3.6	125 ± 2.3*	121 ± 2.9*
CVP (mmHg)	HES	-4.5 ± 0.5	-7.5 ± 0.9*	-5.7 ± 0.8	-5.7 ± 1.3	-6.4 ± 0.5	-7.1 ± 1.2
	WB	-4.7 ± 0.4	-6.5 ± 0.4*	-5.1 ± 0.2	-5.9 ± 0.4	-6.7 ± 0.3	-4.5 ± 0.4
MPAP (mmHg)	HES	4.1 ± 0.6	4.3 ± 1.2	4.5 ± 1.3	6.9 ± 0.6	1.3 ± 0.4*	1.4 ± 1.2*
	WB	6.9 ± 0.7	2.2 ± 0.4*	3.2 ± 0.4	5.5 ± 0.6	5.9 ± 0.5	5.1 ± 0.5
PAOP (mmHg)	HES	-1.0 ± 0.7	0.6 ± 0.6	1.4 ± 0.9	0.6 ± 0.5	-2.0 ± 0.4*	-1.4 ± 0.3
	WB	-3.4 ± 0.6	-4.8 ± 0.5	-3.2 ±0.9	-3.8 ± 0.2	-4.2 ± 0.1*	-4.0 ± 0.3*
CO (mL/min)	HES	2414 ± 164.7	864 ± 27.8	2337 ± 334.6	3018 ± 253.0	2372 ± 183.6	2086 ± 246.6
	WB	2401 ± 310.9	804 ± 49.1	1852 ± 78.3	2460 ± 31.5	2624 ± 79.1	2770 ± 91.9*
CI (L/min/m^2)	HES	4.6 ± 0.1	1.7 ± 0.1*	3.1 ± 0.7	5.8 ± 0.4	4.5 ± 0.2	3.9 ± 0.4
	WB	4.5 ± 0.6	1.5 ± 0.1*	3.5 ± 0.2	4.6 ± 0.1	4.9 ± 0.2*	5.2 ± 0.2*
SV (mL/beat/min)	HES	18.7 ± 0.5	6.2 ± 0.5*	11.9 ± 2.8	12.4 ± 1.4	15.8 ± 1.6	14.0 ± 1.5
	WB	16.7 ± 2.2	4.8 ± 0.4*	11.4 ± 0.8	16.6 ± 1.0	17.3 ± 0.8	16.8 ± 0.7
SVI (mL/beat/min/m^2)	HES	35.9 ± 0.5	12.2 ± 1.1*	24.1 ± 5.8	48.9 ± 5.9*	30.1 ± 1.6	26.5 ± 2.3
	WB	31.5 ± 1.4	8.9 ± 0.7*	29.5 ± 1.6	31.1 ± 2.1	32.3 ± 1.7	31.5 ± 1.4
SVRI (dyn s/cm^5/m^2)	HES	2054.3 ± 70.7	2663.1 ± 18.4	4632.1 ± 85.9*	1612.9 ± 88.3	2167.8 ± 160.7	2402.3 ± 199.9
	WB	1876.9 ± 111.2	2698.4 ± 104.4	2202.2 ± 103.4	2191.8 ± 106.5	2132.1 ± 81.6	1980.7 ± 123.4
DO_2 (mL/min/m^2)	HES	866.7 ± 34.4	296.1 ± 16.4	554.2 ± 122.4	498.2 ± 186.6	495.7 ± 132.1	484.1 ± 52.8
	WB	820.4 ± 105.6	240.2 ± 19.5	878.2 ± 44.1	890.6 ± 65.5	885.9 ± 67.4	966.7 ± 29.9*
VO_2 (mL/min/m^2)	HES	121 ± 15.5	82.3 ± 8.1*	10.9 ± 2.6	10.0 ± 2.2	9.9 ± 1.7*	9.4 ± 0.8*
	WB	161 ± 24.2	61.3 ± 1.8*	19.8 ± 1.5	19.7 ± 1.7	19.5 ± 1.3	19.5 ± 0.5*
O_2ER (mL/min/m^2)	HES	14.4 ± 1.9	27.5 ± 1.4	19.2 ± 4.1	19.8 ± 3.4	20.9 ± 3.7	21.5 ± 2.6
	WB	20.1 ± 1.5	26.4 ± 1.1	22.4 ± 1.0	22.2 ± 2.3	21.2 ± 1.9	20.3 ± 0.6

The data were analyzed using ANOVA and Student's t-test, and $P < 0.05$ or less was considered statistically significant. The data are presented as mean ± SEM values. *Significant difference.

Changes in Hba and Hbmv

The values of arterial hemoglobin (Hba, g/dL) and venous hemoglobin (Hbmv, g/dL) decreased after hemorrhage in both the HES and WB groups. However, in the HES group, the parameters remained decreased even after resuscitation, whereas they increased and returned to normal in the case of WB resuscitation in the WB group (Table).

Changes in SAP and DAP

The mean systolic arterial blood pressure (SAP, mmHg) and diastolic arterial blood pressure (DAP, mmHg) were significantly decreased ($P < 0.05$) posthemorrhage, which gradually increased during resuscitation and this increase became statistically significant ($P < 0.05$) on R2, R3, and R4 in both of the groups (Table).

Changes in MAP, CVP, MPAP, and PAOP

The mean arterial blood pressure (MAP, mmHg) and central venous blood pressure (CVP, mmHg) were significantly decreased ($P < 0.05$) posthemorrhage, which gradually increased during resuscitation. However, in the HES group, the MAP and CVP remained below the BL values even after resuscitation, but in the WB group, they increased significantly ($P < 0.05$) on R4. There were no significant changes in the mean pulmonary arterial blood pressure (MPAP, mmHg) in the WB group during the experiment. That of the HES remained almost the same up to R2 but a significant decrease ($P < 0.05$) was recorded on R3 and R4. There were no statistically significant changes in the pulmonary occlusion blood pressure (PAOP, mmHg) in either of the groups during the experiment (Table).

Changes in CO and CI

The cardiac output (CO, mL/min) and cardiac index (CI, L/min/m^2) decreased significantly posthemorrhage, which was gradually restored during resuscitation and increased significantly ($P < 0.05$) on R3 and R4 in both of the groups (Table).

Changes in SV, SVI, and SVRI

The stroke volume (SV, mL/beat/min) and stroke volume index (SVI, mL/beat/min/m^2) decreased significantly ($P < 0.05$) posthemorrhage, which increased gradually from R1 to R4 and was restored with fluid resuscitation in both of the groups. However, no significant changes were recorded in the systemic vascular resistance index (SVRI, dyn s/cm^5/m^2) during the experiment in either of the groups (Table).

Changes in DO_2, VO_2, and O_2ER

The mean oxygen delivery (DO_2, mL/min/m^2) and oxygen consumption (VO_2, mL/min/m^2) decreased significantly ($P < 0.05$) posthemorrhage, in both of the groups. After that the DO_2 increased gradually from R1 to R4 with fluid resuscitation but still remained below the BL value in the HES group, whereas a significant increase was recorded in the WB group on R4 in comparison to the BL values. The mean values of oxygen extraction (O_2ER, mL/min/m^2) were increased posthemorrhage, which gradually decreased and was restored to normal during fluid resuscitation in both of the groups (Table).

Discussion

Hemorrhagic shock is a major life-threatening trauma-related clinical case encountered in human medicine and veterinary practice. Despite many years of research, the role of presurgical fluid resuscitation remains open to debate (1). This study was focused on changes in the invasive and noninvasive hemodynamic variables in HS due to experimental controlled hemorrhage, and the short-term effects of 6% HES and WB resuscitations on these variables from the clinical point of view in anesthetized Beagle dogs. In the present study, the average blood volume loss was 30 ± 2 mL/kg, corresponding to about 40% of the estimated circulating blood (85 mL/kg) volume. An additional small amount of blood (about 5 mL/kg) was drawn to maintain the MAP at 50 mmHg for 60 min. This controlled hemorrhage was found to exert remarkable effects on various hemodynamic variables. The fluid resuscitation with 6% HES and WB was instituted after complete withdrawal of the estimated blood volume and maintaining the MAP 50 mmHg for 1 h. That is why this model revealed HS (due to controlled bleeding) rather than revealing hemorrhagic shock due to uncontrolled bleeding. However, the findings of Haskins et al. (13) were a little bit different from those of this study. They had

drawn 32 ± 8 mL/kg blood (43% of the circulating blood) to induce HS and observed remarkable effects on the hemodynamic parameters. This difference was due to the differences in the experimental protocol with Haskins et al. (13), who induced HS in unanesthetized mongrel dogs, whereas, in the present study, HS was induced in anesthetized Beagle dogs.

The HR and RR were found to increase in this experiment posthemorrhage, which is in agreement with a previous report (1). After a massive hemorrhage, the HR and RR are thought to increase to maintain the homeostasis of the body. In mild hypovolemia, reduced blood flow is frequently hidden by the normal values of the MAP. It is reported that 10% of the circulating blood volume can be removed without remarkable changes in the CI or MAP. A large volume of blood loss reduces the SV and CO initially, whereas the MAP is maintained by sympathetic reflexes, which also change later (14). In this experiment, a large amount (40%) of the blood volume was withdrawn to make the shock model, which was enough to bring about remarkable changes in the MAP, SV, CO, and CI, which justified the model.

Immediate restoration of intravascular volume with bolus administration of intravenous fluid is a basic tenet of the treatment of HS in order to reestablish cellular perfusion. Selection of the fluid type is based on an assessment of its anticipated distribution and effects to expand blood volume (7). To resuscitate clinical patients with severe shock, the goals of treatment were based on oxygen delivery parameters, including the metabolic markers and organ function indicators (15). The hemodynamic parameters using a pulmonary artery catheter, including CI, CO, SV, and VO_2, are reported to show good specificity and sensitivity for predicting survival. However, in this study we also found remarkable changes in these parameters, which is in agreement with the previous reports (16,17)

The posthemorrhagic decrease in the DO_2 and VO_2 is thought to be due to the decrease in the SV. The decrease in the SV is probably the result of lower CVP. However, the DO_2 increased after resuscitation in both of the groups, but in the HES group, it still remained below the BL value. This is thought to be due to the hemodilation with HES administration, which resulted in decreased oxygen carrying capacity. This finding is in agreement with that of Friedman et al. (1). The Hba and Hbmv also decreased posthemorrhage, which increased after resuscitation with WB but remained below BL in the HES group. This is because the WB contains the carrier of oxygen, the hemoglobin in the transfused RBCs, whereas, with HES, hemodilation occurs. The posthemorrhagic decrease in SV and SVI was due to the loss of a large amount of circulating blood volume, which seemed to be restored with fluid resuscitation in both of the groups. A better restoration observed in the WB group was due to the resuscitation with autologous WB.

A significant posthemorrhagic decrease in SAP and DAP was due to the discrepancy between the volume of the vascular bed and the volume of the effective circulating blood, resulting from the large amount of blood loss. The SAP and DAP were found to be restored to about BL values with resuscitation in both of the groups; however, a better restoration was observed in the WB group. The restoration of the SAP and DAP reflexes the potentiality of the HES and WB for effective volume expansion in severe shock. Muir and Wiese also observed similar results with resuscitation using HES in anesthetized dogs with HS (18). The volume expansion with WB is simple and expected as autologous WB was transfused, but it is difficult to postulate whether the volume expansion was sustained with HES resuscitation or not. To observe this phenomenon, a long-term observation is needed. The limitation of this study was the short observation period and small number of animals. It was not clear whether or not any of the differences in the hemodynamic variables existed between the HES and WB resuscitated animals after the experimental period. Volume loading with large amounts of HES may lead to potential deleterious effects on coagulation, renal, or hepatic function. The final outcome may or may not be better even in the presence of better initial hemodynamic effects. For a clearer understanding, studies measuring the long-term effects on various hemodynamic variables and on mortality and morbidity are needed.

The findings of this study suggest that dogs in HS can be successfully resuscitated with HES and WB administration. Resuscitation with WB seemed

to resolve hemodynamic variables to or above BL, whereas that with HES could resolve most but not all of the hemodynamic variables. The WB was found to be superior to restore hemodynamic variable to the BL or above in comparison to that of the HES for the clinical management of HS in dogs.

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