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Responses of systemic hemodynamics and circulating blood volume following the administration of a hypertonic saline solution-A comparison with physiological saline solution-

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INTRODUCTION

Small volumes of hypertonic saline solution have been effectively used in the primary resuscitation from hemorrhagic shock. However, the precise mechanism for the efficacy of hypertonic saline solutions are unknown.

This investigation examined the hemodynamic and circulating blood volume effects of a hypertonic saline solution administered to anesthetized dogs.

MATERIALS AND METHODS

Fourteen adult male mongrel dogs were randomly allocated to either one of 2 groups of animals; namely the physiological saline group (PS: 15.0 ± 0.5 kg), and the hypertonic saline group (HS: 15.3 ± 0.9 kg).

The animals were anesthetized with sodium pentobarbital (30 mg/kg i.v.). Pancuronium bromide (0.2 mg/kg) was administered after insertion of an endotracheal tube. The dogs were placed in a supine position under anesthesia with a continuous intravenous infusion of ketamine chloride at 5 mg/kg/hour. 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 $ETCO_2$ of 35-40 mmHg which was monitored with an infrared CO_2 analyzer (Multigas Monitor, OMA-8101, Nihon Kohden, Tokyo, Japan).

Both femoral veins were cannulated for infusion of lactated Ringer's solution with a maintenance dose of 5 ml/kg/h, and for an intravenous bolus injection. The left femoral artery was cannulated for continuously monitoring the systemic arterial pressure and for blood sampling. Left ventricular 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 by electrically deriving the LVP wave using an electronic differentiator (Pressure Processor Model EQ-601G, Nihon Kohden). A 7.5-French balloon-tipped triple-lumen pulmonary catheter (Swan-Gantz catheter) was inserted via the right external jugular vein and its top was positioned in a branch of the pulmonary artery to measure the hemodynamic variables. Cardiac output (CO) was determined using the thermodilution technique (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 (ECG AMP/Pulse Counter Model 611-G, Nihon Kohden) from lead II 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 nostril probe which was 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 detect 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 concentra-

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tion was continuously computed by reference to the previously measured blood hemoglobin (Hb) concentration.

The dogs were allowed to stabilize for at least 60 min after the surgical procedure before the physiological measurements (baseline values) were taken. Thereafter, intravenous bolus injection was started within 2 min by an intravenous bolus injection (4 ml/kg) of either the physiological saline (PS; 0.9 % NaCl) or the hypertonic saline (HS; 7.5 % NaCl). Measurements were taken at baseline, 5, 15, 30, 60, and 120 min after bolus injection.

HR, mean arterial pressure (mAP), mean pulmonary arterial pressure (mPAP), pulmonary arterial wedge pressure (PAWP), LVP, CO, arterial partial oxygen pressure (PaO_2), arterial partial carbon dioxide pressure ($PaCO_2$), plasma colloidal osmotic pressure (Pcop), plasma crystalloidal osmotic pressure (Posm), and CBV were all measured. The cardiac index (CI), systemic vascular resistance (SVR), left ventricular stroke work index (LVSWI) and LV dp/dt max were calculated using 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 within groups between the baseline values and those for the subsequent phases (5-120 min), using Student's paired t-test, with $P<0.05$ considered as statistically significant. Differences between both groups were analyzed in terms of variance using the Student's unpaired t-test, with $P<0.05$ considered as statistically significant.

RESULTS

Blood hemoglobin (Hb) did not differ significantly between the PS and HS groups under the baseline condition (11.7 ± 0.8 and 11.9 ± 0.6 g/dl, respectively).

Hemodynamic variables are shown in Table 1. Under the baseline condition, the hemodynamic variables did not differ significantly between the two groups. After the bolus injection, the HR, mAP, and

Table 1
Hemodynamic variables at 5, 15, 30, 60 and 120 min after bolus injection with physiological saline (0.9 % NaCl) or hypertonic saline (7.5 % NaCl)

Variable	Group	Baseline	5 min	15 min	30 min	60 min	120 min
HR	PS	177±5	178±6	182±6	181±5	184±9	176±8
	HS	167±6	173±8	165±8	164±7	160±7	155±8
mAP	PS	135±11	137±11	138±11	140±10	127±17	131±9
	HS	135±12	138±16	137±14	133±14	128±15	128±15
mPAP	PS	15±2	16±3	16±3	17±3	16±3	15±2
	HS	17±2	19±3[a]	18±3	18±2	18±2	17±2
PAWP	PS	9±2	9±2	10±2	10±2	9±2	8±2
	HS	11±1	11±1	11±2	11±1	10±1	10±1
CI	PS	1.6±0.1	1.6±0.1[b]	1.6±0.1[b]	1.5±0.1[b]	1.5±0.1	1.4±0.1[a]
	HS	1.7±0.1	2.1±0.1[a]	1.9±0.1[a]	1.8±0.1	1.6±0.1	1.4±0.1[a]
SVR	PS	8473±519	8619±525[b]	8894±523[b]	9559±500[ab]	9757±698[a]	10648±1030[a]
	HS	8007±628	6706±608[a]	7176±610[a]	7560±658	8271±562	9630±924[a]
LVSWI	PS	17.6±0.8	17.0±0.6[b]	15.6±1.2[b]	16.7±0.9	14.7±0.3[a]	14.1±0.5[a]
	HS	17.3±1.4	21.3±2.8[a]	20.4±1.8[a]	18.4±1.7[a]	15.6±2.1	14.7±2.2
LVdp/dt max	PS	2863±168	2888±168[b]	2950±170	2925±171	2850±166	2588±167[a]
	HS	2729±283	3443±252[a]	3214±255[a]	3086±282[a]	2900±311	2571±207

(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); PAWP: pulmonary arterial wedge pressure (mmHg); CI: cardiac index (l·min^{-1}·m^{-2}); SVR: systemic vascular resistance (dyn·sec·cm^{-5}); LVSWI: left ventricular stroke work index (g·m·beat^{-1}·m^{-2}); LV dp/dt max: maximum rate of left ventricular pressure change (mmHg·sec^{-1})
PS: physiological saline group ; HS: hypertonic saline group
Baseline: after surgical procedure. 5min, 15min, 30min, 60min, and 120min : 5, 15, 30, 60 and 120 min after bolus injection.
[a]$P<0.05$: from Baseline
[b]$P<0.05$: between group PS and HS

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Table 2
Plasma osmotic pressure and circulating blood volume at 5, 15, 30, 60, and 120 min after bolus injection with physiological saline (0.9 % NaCl) or hypertonic saline (7.5 % NaCl)

Variable	Group	Baseline	5 min	15 min	30 min	60 min	120 min
Pcop	PS	14.3±0.8	14.0±0.9[b]	13.8±0.9[b]	14.0±0.9[b]	13.9±0.9[b]	13.9±1.0
	HS	14.0±0.5	11.4±0.5[a]	11.5±0.5[a]	11.8±0.5[a]	11.7±0.6[a]	12.1±0.5[a]
Posm	PS	310±4	307±3[b]	309±3[b]	307±3[b]	310±2[b]	304±3[b]
	HS	312±2	329±2[a]	325±2[a]	321±2[a]	322±2[a]	321±2[a]
CBV	PS	1.3±0.1	1.3±0.1[b]	1.2±0.1[b]	1.2±0.1	1.2±0.1	1.2±0.1
	HS	1.3±0.1	1.6±0.2[a]	1.6±0.1[a]	1.5±0.1	1.3±0.1	1.3±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)
PS: physiological saline group ; HS: hypertonic saline group
Baseline: after surgical procedure. 5min, 15min, 30min, 60min, and 120min : 5, 15, 30, 60 and 120 min after bolus injection.
[a]$P<0.05$: from Baseline
[b]$P<0.05$: between group

PAWP values in both groups did not differ significantly as compared with the baseline condition, but not so the mPAP in the HS group. Immediately after bolus injection, CI, SVR, and LV dp/dt max values in group PS did not differ significantly compared with those of the baseline condition. However, with the lapse of time, a significant decrease in CI, LVSWI, LV dp/dt max and a significant increase in SVR values occurred in group PS. On the other hand, CI, LVSWI, and LV dp/dt max values in group HS increased significantly, while SVR decreased significantly compared with the baseline condition during the experimental period. However, with the lapse of time, a significant decrease in CI and a significant increase in SVR values occurred as compared with the baseline condition values in group HS. After the bolus injection, CI, LVSWI, and LV dp/dt max in group HS were all significantly greater than those in group PS. SVR in group HS was significantly lower than that in group PS.

With regard to the respiratory variables, PaO2 and PaCO2 under the baseline condition did not differ significantly between the two groups. In group PS, PaO2 was 585 Å} 12 mmHg and PaCO2 was 38.9 ± 0.8 mmHg, whereas in group HS the corresponding values were 589 ± 15 mmHg and 39.8 ± 1.2 mmHg, respectively.

Pcop, Posm and CBV are shown in Table 2. Under the baseline condition, the Pcop, Posm and CBV values did not differ significantly between the two groups. After the bolus injection, the Pcop, Posm and CBV values in group PS did not differ significantly. On the other hand, a significant decrease in the Pcop and a significant increase in the Posm and CBV values occurred in group HS. Moreover, after the bolus injection, the Pcop, Posm and CBV values differed significantly between the two groups.

DISCUSSION

Hypertonic saline solution, when given either initially in the prehospital period or shortly after arrival, might improve a patient's survival by rapidly restoring tissue perfusion while conventional treatment modalities are begun. Some investigators (1-4) have found that hypertonic saline treatment substantially improved cardiovascular variables in a model of hemorrhagic shock. In the present study, CI, LVSWI and LV dp/dt max values increased significantly by a bolus injection of hypertonic saline, but did not differ from these produced by an injection of physiological saline. On the other hand, SVR in group HS decreased significantly. The results showed that the hypertonic saline solution caused an increase in myocardial contractility and widespread precapillary dilation. This restoration of cardiovascular function has been attributed to a neurogenic reflex (5,6), but it may also result from an osmotically induced redistribution of intracellular water into the extracellular space (7,8). On the other hand, Ogata et al.(9) demonstrated that hematocrit did not decrease markedly after the administration

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of hypertonic saline solution. This suggests that the improvement of circulation produced by hypertonic saline solution may have been caused by blood redistribution, rather than by the plasma expander effect. Similarly, Velasco et al.(10) reported that the intravenous infusion of hypertonic saline solution, given to anesthetized dogs in hemorrhagic shock, rapidly restored hemodynamic variables and moved acid base equilibrium toward normality. However, no appreciable plasma volume expansion occurrs for at least 12 hours.

At present, the ICG blood concentration is monitored noninvasively with pulse spectrophotometry, which is based on the same principle as pulse oximetry. In the present study, CBV increased significantly after the bolus infusion of hypertonic saline. Our results were not always satisfactory because the use of hypertonic saline as a volume replacement therapy may only be effective for a period of about 15 minutes. The authors are dubious as to whether or not hypertonic saline therapy can be applied to the relief of severe hypovolemic shock. However, it appears that hypertonic saline therapy is very effective in the treatment of hemorrhagic shock for a short period. On the other hand, in the early resuscitation of patients in hemorrhagic shock, when time is all important and the rate of infusion is limited, hypertonic saline may improve their circulatory condition, allowing more conventional methods of resuscitation to be initiated. With regard to neurological resuscitation, Prough et al.(11) reported that intracranial pressure was lower in dogs resuscitated with hypertonic saline than resuscitated with lactated Ringer's solution. Moreover, Gunner et al.12 demonstrated that the use of hypertonic saline early in resuscitation may enhance the return of cell membrane and blood-brain barrier function, and may prove beneficial to the patient in hemorrhagic shock who has also substained neurologic trauma.

CONCLUSION

These results suggest that the administration of hypertonic saline solution causes an increase in myocardial contractility, widespread precapillary dilation, and an increase in circulating blood volume. Our results were not always satisfactory bacause hypertonic saline therapy's effectiveness is of such short duration.

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ABSTRACT

This investigation examined the effect on hemodynamics and circulating blood volume (CBV) after administering a hypertonic saline solution. We divided anesthetized dogs into two groups. The anesthetized dogs were given with a single bolus injection, 4 ml, of a physiological saline solution (PS; 0.9 % NaCl) or a hypertonic saline solution (HS; 7.5 % NaCl). Mesurements were taken at baseline, 5, 15, 30, 60, and 120 minutes after the bolus injection. The post bolus injection, cardiac index (CI), left ventricular stroke work index (LVSWI), maximum rate of the left ventricular pressure change (LV dp/dt max), plasma crystalloidal osmotic pressure (Posm), and CBV values in group HS increased significantly, while systemic vascular resistance (SVR) and plasma colloidal osmotic pressure (Pcop) decreased significantly as compared with the baseline condition. Moreover, CI, LVSWI, LV dp/dt max, Posm and CBV values in the HS group were significantly greater than those in the group PS. SVR and Pcop in group HS were significantly lower than the values found in the PSgroup. These results suggest that a hypertonic saline solution causes an increase in myocardial contractility, widespread precapillary dilation, and an increase in circulating blood volume. However, our results were not always satisfactory because the benefits of hypertonic saline therapy may be of short duration.

Key words: hypertonic saline solution, circulating blood volume, pulse-dye densitometry

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