NOTE *Internal Medicine*

The Effect of 7.2% Hypertonic Saline Solution on M-Mode Echocardiographic Indices in Normovolemic Dogs

Kazuyuki SUZUKI[1)], Shinobu AOYAGI[1)], Hiroshi KOIE[1)] and Ryuji ASANO[1)]

[1)]*Department of Veterinary Medicine, College of Bioresource Sciences, Nihon University, 1866 Kameino, Fujisawa, Kanagawa 252–8510, Japan*

(Received 29 September 2005/Accepted 7 March 2006)

ABSTRACT. This study investigated whether a small volume of 7.2% hypertonic saline solution (HSS) could affect M-mode echocardiographic indices in dogs. HSS induced significant increase in heart rate, stroke volume and cardiac index, when the fluid infusion was completed ($P<0.05$). In the HSS group, the left ventricular end-diastolic volume index, as an index of preload, significantly increased ($P<0.05$), whereas left ventricular end-systolic volume index were not altered. HSS induced slight increases in ejection fraction at end of infusion despite significantly differences were not observed. In conclusion, HSS did not induce a demonstrable effect on M-mode echocardiographic indices of systolic functionenhance cardiac contractility, but it caused preload augmentation that may contribute to an abrupt and transient increase in cardiac output just after HSS infusion.

KEY WORDS: canine, cardioechography, hypertonic saline solution.

J. Vet. Med. Sci. 68(7): 749–751, 2006

Small volume hypertonic saline solution (HSS) has been successfully used to resuscitate dogs with experimentally induced hypovolemic shock [11, 21, 22]. The beneficial haemodynamic effects of HSS have been attributed to rapid plasma volume expansion caused by body fluid shift from intracellular space [2, 7], transient decrease in systemic and pulmonary vascular resistance [20], a vagally-mediated reflex dependent on stimulation of pulmonary osmoreceptors [11, 23], and increased cardiac contractility [22].

Some studies found a positive inotropic effect after HSS infusion [9, 10, 13, 15]. HSS induces cellular dehydration through an osmotic effect, thus decreasing cellular water content and consequently increasing the calcium level [25]. This could produce a positive inotropic effect of HSS because the increase in intracellular calcium concentration resulted in increased cardiac contractility. However, many *in vitro* studies have demonstrated that a sudden increase in extracellular sodium concentration ($[Na^+]_{out}$) produces a transient and mild negative inotropic effect that lasts up to 10 min, with $[Na^+]_{out}$ directly influencing cardiac contractility [3, 4, 24]. The improvement of cardiac contractility, therefore, is still considered questionable because some reports have revealed no apparent positive effect on it.

This study aimed to investigate whether a small volume of HSS could affect M-mode echocardiographic indices that could monitor cardiac functions non-invasively and in real time in normovolemic anesthetized dogs.

All procedures were undertaken in accordance with the National Research Council on Guide for the Care and Use of Laboratory Animals [16]. The experiments were performed on 5 male Beagles, 1.6 ± 0.1-year-old, weighing 13.2 ± 2.0 kg (mean ± SD). These dogs were deemed healthy on the basis of a physical examination, thoracic auscultation, and radiological and echocardiographic analysis. The dogs were given two treatments as follows: the HSS group was given HSS (7.2%-NaCl, IV infusion of 5 m*l*/kg) and the isotonic saline solution (ISS) group was given isotonic saline solution (0.9%-NaCl, IV infusion of 5 m*l*/kg) at a flow rate of 20 m*l*/kg/hr. The order of treatment was at random and interval between experiments was more than 3 weeks. Each dog was anesthetized by thiopental sodium (Ravonal 0.3 for injection, Tanabe Seiyaku, Osaka) at a dose of 18 mg/kg IV, and anaesthesia was maintained with 2.0 MAC isoflurane (Forane, Abbott Japan, Tokyo) in 100% oxygen. All dogs were monitored until the end of the experiment.

M-mode echocardiographic images (EUB565A, Hitachi Medical Co., Tokyo) of the right parasternal short-axis view at chordae tendineae level and the long-axis four-chamber view were obtained by the standard transthoracic echocardiography with 5.0 MHz transducers (EUP-S32, Hitachi Medical Co., Tokyo). Venous samples and echocardiographic images were obtained at t=0 (pre), 5, 15, 30, 45, 60, 90 and 120 min after the initiation of fluid infusion. The heart rates (HR) at each sampling point were obtained from a simultaneously recorded electrocardiograph. Venous samples were used to determine hemoglobin concentration and hematcrit value by an automatic cell counter (Celltac-alfa, Nihon Kohden Co., Tokyo). Changes in relative plasma volume (rPV) were calculated from haemoglobin concentrations and haematocrit values [19].

Derived from the M-mode recordings of the left ventricular short axis, the left ventricular (LV) end-systolic volume (ESV) and end-diastolic volume (EDV) were obtained by the Teichholz formula [14]. The stroke volume (SV), cardiac output (CO), ejection fraction (EF) and percent fractional shorting (%FS) were also calculated by acceptable formulas [14]. M-mode echocardiographic parameters were indexed to body surface area (BSA) as follows [18].

$$BSA\ (m^2) = (body\ weight^{2/3} \times 10.1) / 100$$

Data are expressed as mean ± standard deviation. Measured dependent variables were compared between the two

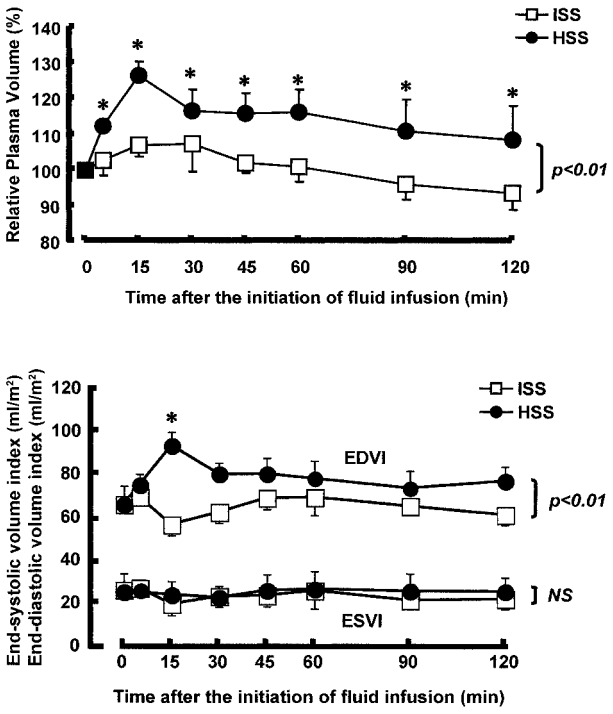

Fig. 1. Sequential changes in the relative plasma volume (rPV), and left ventricular end-systolic (ESVI) and end-diastolic volume index (EDVI) by hypertonic saline solution (HSS) infusion in dogs. Levels of significance ($P<0.05$) indicated; *: versus pre-value by Bonferroni test. Data are mean ± SD of five dogs per group.

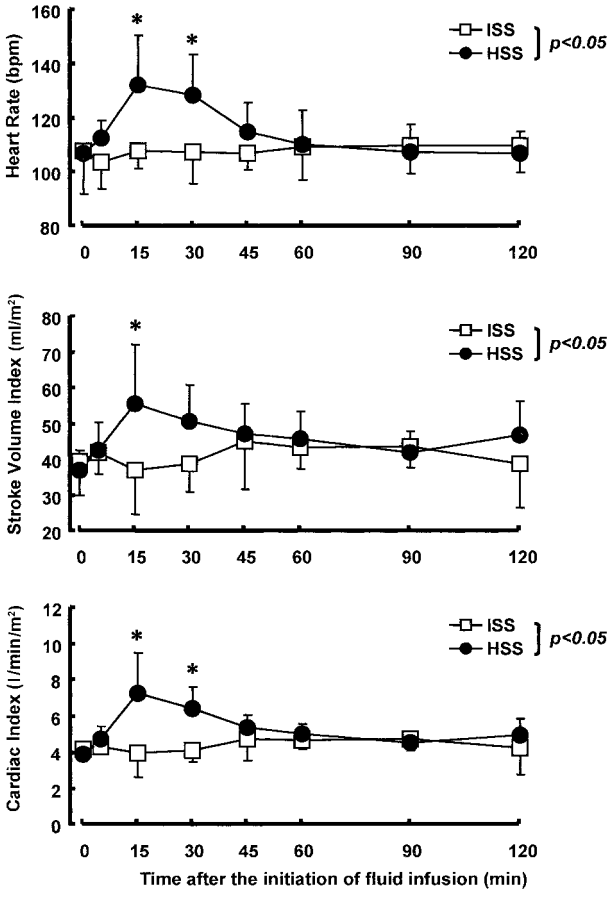

Fig.2. Sequential changes in the heart rate (HR), stroke volume per BSA (SVI) and cardiac index (CI) by hypertonic saline solution (HSS) infusion in dogs. Levels of significance ($P<0.05$) indicated; *: versus pre-value by Bonferroni test. Data are mean ± SD of five dogs per group.

groups for each sample collection period, using repeated-measures 2-way analysis of variance (ANOVA). Within groups, mean values for each dependent variable were compared with the pre values, using the Bonferroni test as a post-hoc test after ANOVA. A value of $P<0.05$ was considered significant.

Figure 1 shows sequential changes in rPV, ESV index (ESVI) and EDV index (EDVI) in the dogs received HSS. The rPV in the ISS group increased significantly, reaching 107.2 ± 3.4% at t=15 min when the fluid infusion was completed, and this value recovered to the pre value at t=45 min ($P<0.05$). In contrast, a significant increase in the rPV was observed in the HSS group, which reached a peak of 125.6 ± 2.5% at t=15 min ($P<0.05$). The significant increase in rPV was maintained for the rest of the experiment.

The pre values of ESVI and EDVI in the HSS group were 25.1 ± 8.5 m*l*/m^2 and 65.8 ± 15.9 m*l*/m^2, respectively. The EDVI in the HSS group increased transiently but significantly compared with the pre-value, reaching 93.2 ± 13.0 m*l*/m^2 at t=15 min ($P<0.05$), whereas there was no significant change in the ESVI in the HSS group. Those parameters were not affected by ISS infusion and remained constant throughout the experiment in ISS groups.

HSS infusion induced a slight and transient increases in EF and %FS despite significant differences were not observed, with the values reaching 64.5 ± 9.7% and 34.0 ± 8.4% at t=15 min, respectively, from 55.8 ± 9.8% and 29.3 ± 5.2% at t=pre, respectively. The mean values of EF and %FS in the ISS group were not changes by ISS infusion and remained constant throughout the experiment in ISS group.

HSS infusion induced a transient but significant acceleration of HR and an increase in SV index (SVI), with the values reaching 132.4 ± 18.2 bpm and 55.9 ± 16.4 m*l*/m^2 at t=15 min, respectively, from 107.0 ± 3.6 bpm and 37.0 ± 6.0 m*l*/m^2 at t=pre, respectively ($P<0.05$, Fig. 2). The cardiac index (CI) in the HSS group increased transiently but significantly compared with the pre value, from 4.0 ± 0.7 *l*/min/m^2 at t=pre to 7.3 ± 2.2 *l*/min/m^2 at t=15 min ($P<0.05$), whereas there was no significant change in the CI in the ISS group.

We studied the effect of HSS on systolic function in anesthetized dog by using the noninvasive and real time M-mode echocardiography. In the present study, HSS infusion did not show enough increases in EF and %FS, despite satisfactory plasma volume and EDV expansion. These results agree with earlier studies that showed that HSS dose not

influence echocardiographic parameters of systolic function [6, 17]. However, the EF and %FS which can be obtained from the M-mode data are dependent on inherent preload and afterload [14]. This may be explained in part by the findings that HSS administered IV will be diluted in a short period and equilibrated in the systemic circulation [12], so that its contractile effect may not be persistent enough to be detected [17]. Horton and Mitchell [8] examined the left ventricular dimensional changes during hemorrhagic shock and found that the changes in left ventricular geometry were related to a disproportionate decrease in the septal-lateral axis more than apex-base axis. Although the EF is a global index of LV fibre shortening and highly regarded measures of LV systolic function [14], the EF obtained from the M-mode data has no advantage over the %FS because those parameters are derived from one diameter of the LV across the septal-lateral axis [17]. Therefore, additional studies using two-dimensional echocardiograph to confirm whether HSS improve a cardiac contractility before definitive recommendations can be make regarding the optimal fluid to use for initial resuscitation of dog with shock.

Changes in the hemodynamic parameters, such as rPV, EDVI and CI just after HSS infusion, had a tendency to increase much higher than those in the ISS group. The increase in those parameters in the dogs received HSS may have been due to increase in preload [10]. In fact, many researchers have reported a significantly expanded plasma volume caused by HSS infusion [1, 22]. Because CI was calculated for the product of HR by SVI, it was supposed that HR and/or SVI were the factors for the increased CI. Our results indicated that HSS infusion induced both a transient but significant acceleration of HR and an increase in SVI during HSS infusion. The SVI increased at the end of HSS infusion without significant change in EF. This may be explained in part by the findings that HSS administered IV did not show any ESV decreases, whereas there was a significant increase in EDV due to preload augmentation. These results agree with earlier studies that showed that resuscitation of shocked animals with HSS caused a significant increase in HR and SV [5, 9, 21].

In conclusion, the present study suggests that the increases in rPV and EDVI, as indices of preload caused by HSS infusion, induced the increases in both HR and SVI to manage the volume-load and resulted in an increase in CI.

This work was partially supported by the Ministry of Education, Science, Sports and Culture through the Grant-in-Aid for Scientific Research given to K. Suzuki (No. 15780204).

REFERENCES

1. Ajito, T., Suzuki, K. and Iwabuchi, S. 1999. *J. Vet. Med. Sci.* **61**: 637–641.
2. Baue, A.E., Tragus, E.T. and Parkins W.M. 1967. *J. Trauma* **7**: 743–756.
3. Ben-Haim, S.H., Edoute, Y., Hayam, G. and Better, O.S. 1992. *Am. J. Physiol.* **263**: H1154–1160.
4. Brown, J.M., Grosso, M.A. and Moore, E.E. 1990. *J. Trauma* **30**: 646–651.
5. Constable, P.D., Schmall, L.M., Muir, W.W., Hoffsis, G.F. and Shertel, E.R. 1991. *Am. J. Vet. Res.* **52**: 981–989.
6. Constable, P.D., Muir, M.W.III. and Binkley, P.F. 1994. *Am. J. Physiol.* **267**: H667–H677.
7. Drobin, D. and Hahn, R.G. 2002. *Anesthesiology* **96**: 1371–1380.
8. Horton, J.W. and Mitchell, J.H. 1992. *Am. J. Physiol.* **260**: H1433–H1422.
9. Kien, N.D. and Kramer, G.C. 1989. *Braz. J. Med. Biol. Res*. 22: 245–248.
10. Kien, N.D., Reitan, J.A., White, D.A., Wu, C.H. and Eisele, J.H. 1991. *Circulatory Shock* **35:** 109–116.
11. Lopes, O.U., Pontieri, V., Rocha-E-Silva, M. and Velasco, I.T. 1981. *Am. J. Physiol.* **241**: H883–890.
12. Mazzoni, M.C., Borgstrom, P., Arfors, K.E. and Intaglietta, M. 1988. *Am. J. Physiol.* **255:** H269–H637.
13. Mouren, S., Dalayance, S., Mion, G., Souktani, R., Fellahi, J.L., Arthaud, M., Baron, J.F. and Viars, P. 1995. *Anesth. Analg.* **81**: 777–782.
14. Moise, N. S. and Fox, P. R. 1999. Echocardiography and doppler imaging. pp. 130–171. *In*: Textbook of Canine and Feline Cardiology, 2 ed. (Fox, P.R., Sisson, D. and Moise, N.S., eds.), W.B. Saunders Co., Philadelphia, PA, U.S.A.
15. Muir, W.W. and Sally, J. 1989. *Am. J. Vet. Res.* **50**: 1883–1888.
16. National Research Council. 1996. pp. 1–70. Guide for the Care and Use of Laboratory Animals. National Academy Press, Washington, D.C., U.S.A,
17. Ogino, R., Suzuki, K., Kohno, M., Nishina, M. and Kohama, A. 1998. *J. Trauma* **44**: 59–67.
18. Pypendop, B. and Verstegen, J. 1999. *Am. J. Vet. Res.* **60**: 1148–1154.
19. Suzuki, K., Ajito, T., Kadota, E., Ohashi, S. and Iwabuchi, S. 1997. *J. Vet. Med. Sci.* **59**: 689–694.
20. Suzuki, K., Suzuki, T., Miyahara, M., Iwabuchi, S. and Asano, R. 2005. *J. Vet. Sci.* **6**: 111–116.
21. Us, M.H., Ozkan, S., Oral, L., Ogus, T., Acar, H.V., Cakir, O. and Keskin, O. 2001. *J. Inter. Med. Res*. **29**: 508–515.
22. Velasco, I.T., Pontieri, V., Rocha-E-Silva, M. and Lopes, O.U. 1980. *Am. J. Physiol.* **239**: H664–673.
23. Velasco, I.T. and Baena, R.C. 2004. *Braz. J. Med. Biol. Res.* **37**: 419–425.
24. Waagstein, L., Wennberg, E., Waagstein, F. and Haljamae, H. 1999. *Crit. Care Med.* **27**: 605–616.
25. Wildenthal, K., Adcock, R.C., Crie, J.S., Templeton, G.H. and Willerson, J.T. 1975. *Am. J. Physiol*. **229**: 1505–1509.