The Thai Journal of Veterinary Medicine

Volume 52
Issue 2 *52(2)*

Article 16

6-1-2022

Optimal infusion rate of hypertonic saline to encephalic vessel vasodilatation using magnetic resonance imaging in normovolemic dogs

Yoshiki Murakami

Kenji TSUKANO

Haruyuki HIRATA

Hiroshi KOIE

Kazuyuki SUZUKI

Short Communication

Optimal infusion rate of hypertonic saline to encephalic vessel vasodilatation using magnetic resonance imaging in normovolemic dogs

Yoshiki Murakami[1] Kenji TSUKANO[1] Haruyuki HIRATA[1]

Hiroshi KOIE[2] Kazuyuki SUZUKI[1*]

Abstract

This study aimed to investigate, using magnetic resonance imaging, whether continuous hypertonic saline (**HSS**) infusion induces a superior vasodilating effect on the encephalic vessels compared to bolus infusion in dogs. The relative cross-sectional area of superior sagittal sinus increased to 1.96±0.09 and 1.69±0.31 times of the pre-value in the continuous and bolus groups, respectively, at t=30 min (p<0.001). However, the relative cross-sectional area of superior sagittal sinus was larger in the continuous group than that in the bolus group (p<0.001). The results suggest that continuous infusion of HSS might be superior to bolus infusion in inducing vasodilatation of the encephalic circulation.

Keywords: encephalic circulation, fluid therapy, hypertonic saline, magnetic resonance imaging, superior sagittal sinus

[1]*School of Veterinary Medicine, Rakuno Gakuen University, 582 Bunkyoudai-Midorimachi, Ebetsu, Hokkaido 069-8501, JAPAN*
[2]*Department of Veterinary Medicine, College of Bioresource Sciences, Nihon University, 1866 Kameino, Fujisawa, Kanagawa 252-0880, JAPAN*
***Correspondence**: kazuyuki@rakuno.ac.jp* (K. SUZUKI)
Received September 12, 2021
Accepted February 4, 2022
https://doi.org/10.14456/tjvm.2022.41

Introduction

A hypertonic saline solution (**HSS**) has been investigated for the treatment of cerebral edema and elevated intracranial pressure (**ICP**) (Gunnar *et al*., 1988; Qureshi *et al*., 1998; Schwarz *et al*., 1998; Suarez *et al*., 1998). The administration of 7.5%-HSS in rabbits with cryogenic cerebral regions caused a prompt and substantial decrease in cerebral water content as assessed by spin-echo T2-weighted magnetic resonance imaging (MRI) (Bacher *et al*., 1998). HSS may prove to be more beneficial than osmotic diuretics such as mannitol because they augment intravascular volume and cardiovascular performance in addition to improving intracranial elastance (Suarez *et al*., 1998). Horn *et al*. (1999) suggested that repeated bolus application of HSS (7.5%, 2 ml/kg) is an effective measure to decrease ICP which is otherwise refractory to standard therapeutic approaches using 20%-mannitol.

Materials and Methods

HSS is given as a rapid intravenous (**IV**) bolus (1 m*l*/kg/min) at a dose of 4 to 6 m*l*/kg for improving cardiovascular dysfunctions in small animal practice (Rozanski and Rondeau, 2002). In some of the literature, however, an infusion rate of 0.25-0.50 m*l*/kg/min for 10 to 20 mins is recommended for the initial resuscitation of hypotensive trauma patients (Chiara *et al*., 2003; Kramer, 2003; Krausz and Hirsh, 2003). The optimal infusion rate of HSS for improving cerebral circulation is still considered questionable. Therefore, this study aimed to investigate, using spin-echo T1-weighted MRI, whether a continuous HSS infusion is superior to bolus HSS infusion in inducing vasodilatation of encephalic vessels such as the superior sagittal sinus in dogs.

All procedures were in accordance with the College of Bioresource Sciences Nihon University Guide for the Care and Use of Laboratory Animals (approval number: 079). Experiments were performed on 18 healthy, 2.9±1.5 year-old purpose-bred female Beagle dogs weighing 10.9±1.8 kg. The dogs were anesthetized with IV infusion of thiopental sodium (Ravonal® for Injection, Tanabe Seiyaku Co., Ltd., Osaka, Japan) at a dose of 18 mg/kg before being tracheole intubated with a cuffed endotracheal tube. After intubation each dog was put under general anesthesia and maintained in oxygen throughout the experiment using the isoflurane (Forane®; Abbott Laboratories, Illinois, U.S.A.). The end-tidal concentration of isoflurane and end-tidal partial pressure of carbon dioxide were continuously monitored using an airway gas monitor (Datex Instrument Co., Helsinki, Finland) and maintained at 2.0% and 40 torr (35 – 45 torr) by mechanical ventilation.

Results and Discussion

6 dogs were randomly allocated to one of the following groups: control (5 m*l*/kg of isotonic saline solution at an infusion rate of 20 m*l*/kg/hr for 15 mins), continuous and bolus groups. Dogs in the continuous group received 5 m*l*/kg of HSS at an infusion rate of 20 m*l*/kg/hr for 15 mins and those in the bolus group received the same dose of HSS at a flow rate of 60 m*l*/kg/hr for 5 mins. The time of the initiation of fluid infusion was designated as t=0 min. Venous blood samples were collected at pre-fluid infusion (pre) and at a time of 5, 15, 30, 45, 60, 75, 90, 105 and 120 mins after initiation of fluid infusion to measure sodium and hemoglobin concentrations and hematocrit value. Blood sodium concentrations were determined using an automatic gas and electrolyte analyzer (Bayer 348, Bayer Medical Japan Co., Tokyo, Japan). Hemoglobin concentration and hematocrit value were measured by an automatic cell counter (Celltac alfa, Nihon Koden, Tokyo). Changes in rPV were calculated from hemoglobin concentrations and hematocrit values, using the accepted formulas (Greenleaf *et al*., 1979; Suzuki *et al*., 1998). Immediately after sampling, spin-echo T1-weighted MRI recordings were started. The relative cross-sectional area of superior sagittal sinus, which is represented by area of cerebral falx, in the axial transverse section of pituitary were measured by spin-echo T1-weighted MRI using a 0.5 tesla-superconducting MRI system (Frexart MRT-50GP, Toshiba Medical Systems Co., Tokyo, Japan) set at TR/TE=375/15 milliseconds in T1-weighted image with 4-mm-thick slices and 6 mins per recording time. Changes in the cross-sectional area of superior sagittal sinus were analyzed using image analysis software (Frexart MRT-50GP, Toshiba Medical Systems Co., Tokyo, Japan). Relative changes in the cross-sectional area of the superior sagittal sinus compared with the pre-value were analyzed using image analysis software (Toshiba Medical Systems). Suzuki *et al*. (2008), demonstrated that it was easy to measure the upper sagittal blood vessel of a dog by MRI (T1-weighted image) because the blood vessel diameter is larger than that of other intracerebral blood vessels.

Data is expressed as mean ± standard deviation. Measured dependent variables were compared among groups for each sample collection period, using one-way factorial ANOVA with post hoc Tukey HSD test as appropriate. Within groups, mean values for each dependent variable were compared with the pre-values, using the Tukey HSD test after analysis of repeated measures ANOVA as a post-hoc test. Those statistical analyses were performed using a software package (IBM SPSS Statistics, Ver.19, IBM Co, Somers, NY, USA). A value of $p<0.05$ was considered significant.

Sequential changes in rPV, sodium concentration and the cross-section of the superior sagittal sinus in the dogs receiving 5 m*l*/kg of HSS are shown in Fig. 1. The rPV in the continuous and bolus groups increased significantly, reaching 131.0±11.6% at t=15 mins ($p<0.001$) and 143.0±7.3% at t=5 mins ($p<0.001$), respectively. The rPV subsequently declined toward the pre-value in the continuous group but remained significantly higher than the pre-value for the rest of the experiment in the bolus group ($p<0.001$). On the completion of fluid infusion, the venous sodium concentrations increased significantly in continuous and bolus groups, reaching 167.4±2.7 and 168.0±3.3 mM, respectively ($p<0.001$). Then venous sodium concentration in the continuous group remained at

significantly higher levels than that in the bolus group until t=60 min (p<0.05).

The relative cross-sectional area of the superior sagittal sinus in the control group was not altered significantly throughout the experimental period. The relative cross-sectional area of the superior sagittal sinus in the continuous and bolus groups increased significantly, reaching 1.96±0.09 at t=15 min (p<0.001) and 1.66±0.21 times of the pre-value (p<0.001), respectively. Then, the relative cross-sectional area of the superior sagittal sinus subsequently declined towards the pre-value in the continuous group. In contrast, the relative cross-sectional area of the superior sagittal sinus remained in the continuous group significantly higher than that for the bolus group (p<0.001). Therefore, the area under the curve of the cross-sectional area of the superior sagittal sinus was significantly larger in the continuous group than that in the bolus group during the experimental period (p<0.001).

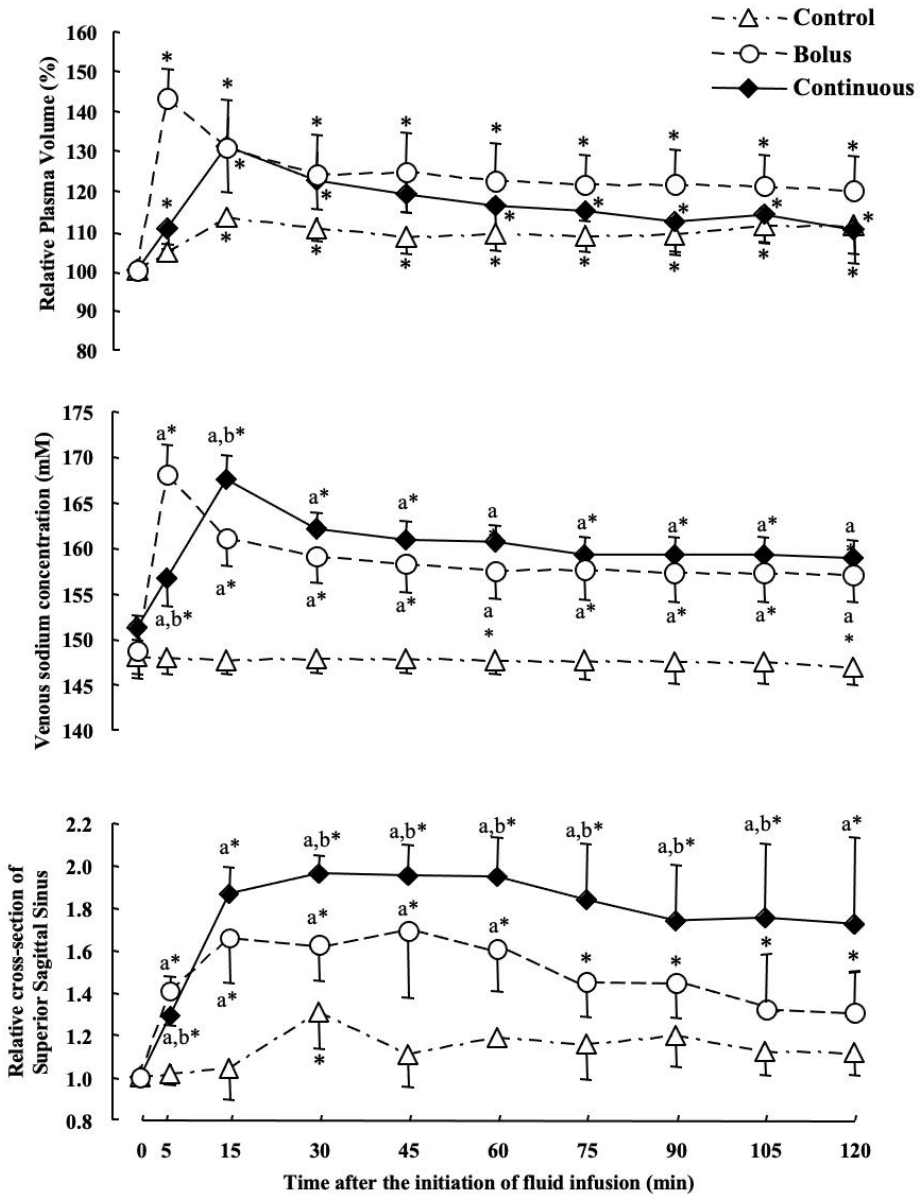

Figure 1 Sequential changes in the relative plasma volume (**rPV**), venous sodium concentration and relative cross-section of the superior sagittal sinus at the axial transversal section of pituitary. Levels of significance (p<0.05) were as follows; a: versus control group, b: versus bolus group, and*: versus pre-value by Tukey HSD test. Data is mean ± standard deviation of six dogs per group.

Our finding that the continuous HSS infusion is superior to bolus infusion in inducing vasodilatation of the encephalic vessel could be attributed to the sustained high levels of venous sodium concentration in the continuous group. One of the primary mechanisms by which HSS exerts its action on the cerebral circulation is mainly through an osmotic effect (Doyle *et al*., 2001). Multiple animal models of trauma brain injury have demonstrated a decrease in cerebral water content with the use of HSS (Doyle *et al*., 2001). Other agents such as mannitol have also been reported to dehydrate edematous tissue. However, the blood-brain barrier is better able to HSS because of tight gap junctions and its higher polarity, resulting in a reflection coefficient of 1.0 for sodium chloride as compared with 0.9 for mannitol (Doyle *et al*., 2001;

Nagasawa *et al*., 2006). Cerebral osmolytes are important to consider when discussing the action of HSS for several reasons. Remaining high levels of extracellular sodium help restore the co-transporters and restore normal cell polarity (Doyle *et al*., 2001). The cell responds to an increase in extracellular osmolarity by pulling osmolytes intracellularly, a process that occurs via active sodium-osmolyte co-transporter at the blood brain barrier (Doyle *et al*., 2001). This is consistent with human trials in which a 10 to 15 mM rise in serum sodium lowered the ICP (Qureshi *et al*., 1998).

In conclusion, the present study demonstrated that continuous HSS infusion significantly induced vasodilatation of the superior sagittal sinus more than the bolus infusion. This finding suggests that continuous HSS infusion might be superior to bolus infusion in improving cerebral circulation. Therefore, it may be effective in the treatment of cerebral edema and increased intracranial pressure.

Acknowledgements

This study was supported by a grant-in-aid for Science Research from the Ministry of Education, Culture and Sciences of Japan (21580393) to Suzuki K.

References

Bacher A, Wei J, Grafe MR, Quast MJ and Zornow MH 1998. Serial determinations of cerebral water content by magnetic resonance imaging after an infusion of hypertonic saline. Critical Care Med. 26: 108-114.

Chiara O, Pelosi P, Brazzi L, Bottino N, Taccone P, Cimbanassi S, Segala M, Gattinoni L and Scalea T 2003. Resuscitation from hemorrhagic shock: experimental model comparing normal saline, dextran, and hypertonic saline solutions. Critical Care Med. 31: 1915-1922.

Doyle JA, Davis DP and Hoyt DB 2001. The use of hypertonic saline in the treatment of traumatic brain injury. J Trauma. 50: 367-383.

Greenleaf, JE, Convertino VA and Mangeseth GR 1979. Plasma volume during stress in man: osmolality and red cell volume. J Appl Physiol. 47: 1031-1038.

Gunnar W, Jonasson O, Merlotti G, Stone J and Barrett J 1988. Head injury and hemorrhagic shock: studies of the blood brain barrier and intracranial pressure after resuscitation with normal saline solution, 3% saline solution, and dextran-40. Surgery. 103: 398-407.

Horn P, Münch E, Vajkoczy P, Herrmann P, Quintel M, Schilling L, Schmiedek P, Schürer L 1999. Hypertonic saline solution for control of elevated intracranial pressure in patients with exhausted response to mannitol and barbiturates. Neurol Res. 21(8):758-764.

Kramer GC 2003. Hypertonic resuscitation: physiologic mechanisms and recommendations for trauma care. J Trauma. 54: S89-S99.

Krausz MM and Hirsh M 2003. Bolus versus continuous fluid resuscitation and splenectomy for treatment of uncontrolled hemorrhagic shock after massive splenic injury. J Trauma. 55: 62-68.

Nagasawa K, Chiba H, Fujita H, Kojima T, Saito T, Endo T and Sawada N 2006. Possible involvement of gap junctions in the barrier function of tight junctions of brain and lung endothelial cells. J Cell Physiol. 208: 123-132.

Qureshi AI, Suarez JI, Bhardwaj A, Mirski M, Schnitzer MS, Hanley DF and Ulatowski JA 1998. Use of hypertonic (3%) saline/acetate infusion in the treatment of cerebral edema: Effect on intracranial pressure and lateral displacement of the brain. Critical Care Med. 26: 440-446.

Rozanski E and Rondeau M 2002. Choosing fluids in traumatic hypovolemic shock: the role of crystalloids, colloids, and hypertonic saline. J Am Anim Hosp Assoc. 38: 499-501.

Schwarz S, Schwab S, Bertram M, Aschoff A and Hacke W 1998. Effects of hypertonic saline hydroxyethyl starch solution and mannitol in patients with increased intracranial pressure after stroke. Stroke. 29: 1550-1555.

Suarez JI, Qureshi AI, Bhardwaj A, Williams MA, Schnitzer MS, Mirski M, Hanley, DF and Ulatowski JA 1998. Treatment of refractory intracranial hypertension with 23.4% saline. Critical Care Med. 26: 1118-1122.

Suzuki K, Ajito T and Iwabuchi S 1998. Effect of infusion of hypertonic saline solution of conscious heifers with hypoxemia caused by endotoxin infusion. Am J Vet Res. 59: 452-457.

Suzuki K, Koie H, Matsumoto T, Asano R 2008. The effect of hypertonic saline solution on vasodilatation of the superior sagittal sinus using magnetic resonance imaging in normovolemic dogs. Res Vet Sci. 84(3):465-470.