EXPERIMENTAL STUDY

Hypertonic saline, normal saline or neither: which is best for uncontrolled hemorrhagic shock? An experimental study in goats

Morteza Saeedi, M.D.,[1] Houman HajiseyedJavadi, M.D.,[2] Samad Shams Vahdati, M.D.,[2] Vahid Eslami, M.D.,[1] Mohamad Mokhtarpour, M.D.,[3] Mehdi Momeni, M.D.,[1] Mohammad Reza Farnia, M.D.,[1] Nima Hafezi Nejad, M.D.[1]

[1] Department of Emergency Medicine, Tehran University of Medical Sciences, Tehran, Iran
[2] Department of Emergency Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
[3] Department of Emergency Medicine, Aja University of Medical Sciences, Tehran, Iran

ABSTRACT

BACKGROUND: To evaluate the effects of various fluids on uncontrolled hemorrhagic shock (UHS). Controversy exists over the appropriate doses and types of fluids for best treating UHS. This study evaluated the effects of hypertonic saline (HTS), normal saline (NS), and no fluid resuscitation (NFR) on UHS.

METHODS: Thirty goats were anesthetized and underwent right leg ablation. The animals were randomly assigned to equal NFR, HTS, and NS groups. The following features of UHS were analyzed: hemoglobin, heart rate, blood loss, mean arterial pressure, bleeding time, and pH. Animals were sacrificed two hours after ablation.

RESULTS: All of the goats who received HTS died within 60 minutes. Four goats in the NS group and one goat in the NFR group died within 120 minutes. The NFR group had significantly higher hemoglobin values than the NS and HTS groups at the end of the trial. Blood loss in the HTS group was greater than in the other two groups ($p<0.05$). The NS group had higher blood loss than the NFR group ($p<0.05$). Mean arterial pressure in the HTS group decreased sharply toward zero within the first 60 minutes. In the NFR and NS groups, mean arterial pressure was higher than in the HTS group ($p<0.05$), and remained constant at 60mmHg after 35 minutes. The NFR group had higher pH values compared to the other two groups ($p<0.05$).

CONCLUSION: Our study demonstrated that HTS is not suitable for treating UHS when compared to NFR and NS. Goats treated with NFR had superior values for all UHS features, including hemoglobin, pH, blood pressure, and bleeding time, compared to those treated with HTS and NS. Pre-hospital field treatment with NS or HTS may worsen the condition until surgical repair is accomplished.

Key words: Fluid; goat; hypertonic saline; resuscitation; uncontrolled hemorrhagic shock.

INTRODUCTION

The rate of death from injury, for which hemorrhagic shock is a major contributing factor, is estimated to reach more than 8 million per year globally by 2020.[1,2] Fluid therapy is a commonly accepted treatment for resuscitating trauma patients. However, controversy exists over the choice of fluid therapy, (such as colloids or crystalloids) to manage uncontrolled hemorrhagic shock (UHS) in a pre-hospital setting.[3] Although fluid resuscitation is often the main treatment for UHS, the benefits are doubtful, as demonstrated in both animal and human studies.[4,5]

The rationale for upholding blood pressure in trauma patients is to maintain tissue oxygenation; however, more bleeding may result due to impairing the coagulation process.[6] Excessive fluid administration may cause brain edema, abdominal compartment syndrome, and acute respiratory distress syndrome.[7] Studies have shown that hypertonic saline (HTS) is useful for treating UHS patients.[8,9] Moreover, HTS is thought to decrease lung tissue damage and pulmonary inflammation,

Address for correspondence: Morteza Saeedi, M.D.
Tehran University of Medical Sciences,
North Amirabad Street Tehran, Iran
Tel: 00982144263995 E-mail: m_saeedi@tums.ac.ir

Qucik Response Code

Ulus Travma Acil Cerr Derg
2013;19(6):500-506
doi: 10.5505/tjtes.2013.31799

and increase cellular protection in animal models of UHS.[10,11] Studies of rats, dogs, swine, and pigs showed the relative efficacy of HTS fluid compared to normal saline (NS) for treating UHS.[12-17] Studies in the literature have proven the benefits of HTS in cases of brain and cord trauma.[18-20]

Modeling UHS in animals can lead us to a definite decision on the optimal fluid therapy for UHS in humans. Therefore, studies demonstrating the benefits of using hypertonic fluid in cases of human UHS[21,22] led us to design a goat study to compare hypertonic and isotonic fluid, as well as no fluid treatment, in a clinically relevant model.

MATERIALS AND METHODS

a. Animal Care Committee Approval

The study was approved by the Animal Care Committee of Tabriz University of Medical Sciences and reviewed by a group other than the authors according to procedures approved by the Report Review Committee.

b. Study Design

The study was a randomized trial conducted in a goat model. The model was based on a pre-hospital setting in which there is no access to packed red blood cells or other resuscitation options except fluids.

After the insertion of a 20G venous cannula in the vein of the goat's right ear, blood was obtained for primary and homogeneity comparison. All goats were anesthetized completely before the intervention with 5 mg/kg intravenous ketamine and 0.2 mg/kg diazepam, which was repeatedly administered every 10 minutes, as necessary. Following anesthesia, tracheostomy was performed on the goats.[23] Ventilators designed for humans were used. Ventilator settings were as follows: respiratory rate, 8; FiO_2, 50%; positive end-expiratory pressure, 3; and tidal volume, 15 cc/kg. The goats were monitored intensively using heart rate and invasive continuous blood pressure monitoring.[24]

c. Materials

The administered fluids included 20 cc/kg of normal saline (NS)[25] for the NS group, and 8 cc/kg of 3% saline for the HTS group.

d. Uncontrolled Hemorrhagic Shock Model

Thirty healthy male Mako goats with a mean weight of 28 kg (range: 15-40 kg) were included in the study. To decrease the incidence of regurgitation, goats underwent 12-hour preoperative fasting (except for water) before surgery.[24] After weighing the goats and obtaining the blood samples, ketamine and diazepam were administered. The goats underwent tracheostomy, and ventilation was performed using portable ventilators. Goats were randomly chosen to receive a specific resuscitation fluid. The 30 goats were assigned into three groups (10 in each group). The first group had no fluid resuscitation (NFR); the second group received NS; and the third group received HTS resuscitation.

After the insertion of an arterial line in the left carotid artery, mean arterial pressure was monitored continuously. Heart rate was monitored by ECG monitoring and recorded every five minutes. The right leg was ablated beneath the knee, so it caused bleeding from arteries, veins, muscles, and skin. No attempt was undertaken to mitigate the bleeding in order to simulate a real pre-hospital setting. Blood was collected and measured in a graded suction bottle.

Blood samples were obtained from the arterial line every 15 minutes to measure hemoglobin and pH. Goats have a blood volume of approximately 70 to 72 ml/kg blood.[26] To simulate the UHS setting, researchers waited for a blood loss equal to one-third of the goat's expected blood volume in all three groups (24 ml/kg).[27] Then, 20 ml/kg NS, 8 ml/kg HTS fluid (3%), or no fluids (for the NFR group) were administered rapidly. The starting point for the study was after saline infusion completion and was similar in all groups. The total infusion time was about 10 minutes in the NS group and less than 5 minutes in the HTS group. When their heart rates fell below 40 beats/min, the goats were announced dead and data collection was stopped. If a goat stayed alive for more than two hours, the resuscitation was deemed successful, and data collection for that goat was terminated. Throughout the whole procedure, bleeding was not controlled by the researcher in order to simulate UHS.

e. Statistical Analysis

All gathered information (i.e., the duration of the goat's life, tissue pH range, mean arterial pressure, and heart rate) was analyzed using the Statistical Package for the Social Sciences (SPSS, Windows version 15.0, SPSS, Inc., Chicago, IL). Of the non-parametric statistical tests, repeated measure analysis was used to evaluate the comparability of HTS, NS, and NFR groups and to compare the duration of life, amount of bleeding, blood pressure, and acidosis level. Survival analysis was performed by deriving Kaplan-Meier statistics and plots. The differences in survival of the three groups were investigated using log-rank (Mantel-Cox) testing, pooled over the strata. Analysis of variance was used to compare the groups. Significance was defined as $p < 0.05$.

RESULTS

The main features of UHS, including hemoglobin, heart rate, blood loss, mean arterial pressure, and pH were analyzed at 0, 15, 30, 45, 60, 75, 90, 105, and 120 minutes. Baseline characteristics and laboratory values were similar for all groups.

a. Bleeding Time

Because of massive bleeding, all the goats in the HTS group

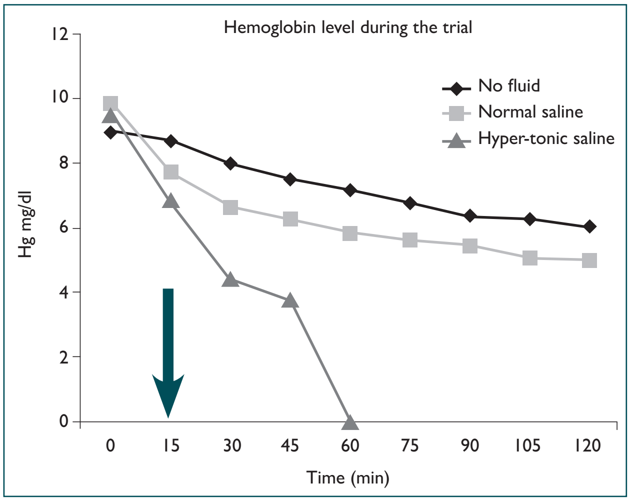

Figure 1. Comparison of hemoglobin levels during the trial between groups. The arrow shows when differences started to become statistically meaningful.

died in under one hour and the test was terminated for the HTS group. The bleeding time for the HTS group was 53±2.4 minutes. The bleeding stopped in the NS and NFR groups after 37±4.8 and 18.4±3.9 minutes, respectively, but the trial continued for both groups until the 120th minute. There was no significant difference between the NS and NFR groups ($p>0.05$). There was a significant difference between the NS and HTS groups, as well as between the NFR and HTS groups, at 60 minutes ($p=0.015$ and $p<0.001$, respectively).

b. Hemoglobin

There was no initial significant difference between the hemoglobin values of the groups. However, between 15 and 60 minutes, during which the HTS goats died, a significant difference appeared between the groups ($p<0.001$). The NFR group had much higher hemoglobin levels than the NS group, and the lowest hemoglobin values occurred in the HTS group. From the 60th minute to the 120th minute, the NFR group continued to have higher hemoglobin values than the NS group ($p<0.001$). Although decreasing hemoglobin levels were observed in all three groups, a rapid and severe decline occurred in the HTS group. Hemoglobin values for the NFR and NS groups remained parallel during the 120 minutes, but NFR group levels were statistically higher during the trial, except for during the first 15 minutes (Figure 1).

c. Heart Rate

Heart rate in the NFR and HTS groups increased at first, but heart rates were lower in the NFR group. Heart rate trends were irregular during the 120 minutes. In the HTS group, from the beginning until the 45th minute, heart rate increased rapidly and then fell rapidly toward zero until the 60th minute. At the 60th minute, heart rate fell below 40 beats/min, and the goats were excluded from the rest of the study. In the NS group, heart rate decreased during the first 35 minutes. In general, heart rates in both the NS and NFR groups increased gradually. Heart rate differences were not statistically significant between the three groups, and no well-defined pattern was observed (Figure 2).

d. Blood Loss

The blood loss gathered in the suction bottle was measured from minutes 15 to 120. Blood loss in the HTS group reached a mean of 1600 ml at the 30th minute. The HTS group had more than twice the blood loss of the other two groups, and blood loss in the NS group was higher than in the NFR group (minutes 15 to 30, $p=0.021$; minute 30 to end, $p<0.001$). The mean blood loss in the NS group was 1220 ml at the 35th minute. The mean blood loss in the NFR group was 610 ml at the 25th minute and did not increase considerably. Blood loss data are presented in Figure 3.

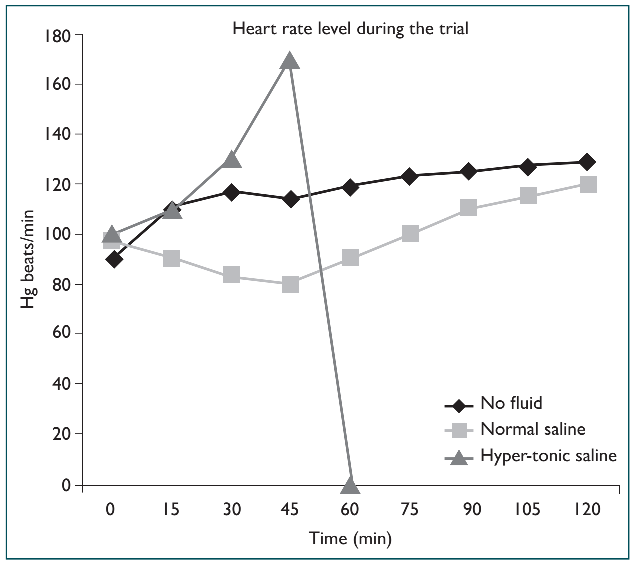

Figure 2. Comparison of heart rates during the trial between groups.

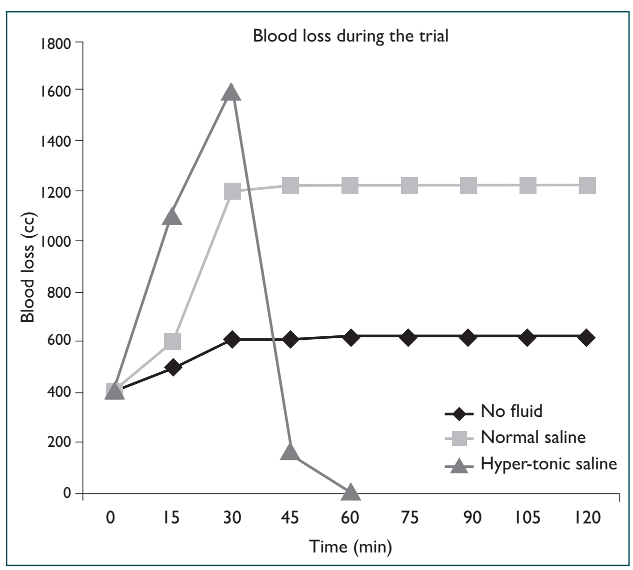

Figure 3. Comparison of blood loss during the trial between groups.

e. Mean Arterial Pressure

In all groups, mean arterial pressure decreased in the first approximately 10 minutes. However, after receiving fluid therapy, mean arterial pressure in the NS group continued to fall until the 35th minute, after which, values in the NS group were continuously around 60 mmHg. Similarly, the NFR group experienced a drop in BP until the 28th minute. Mean arterial pressure in the HTS group decreased sharply toward zero in the first 60 minutes, and HTS goats were excluded since all died. All of these results were statistically significant ($p<0.05$), and mean arterial pressure values are presented in Figure 4.

f. pH

No statistical difference between the pH values of the groups was observed in the beginning (p=0.21). Statistically significant differences occurred at the 15th minute (p=0.020) and were present during the rest of the study period ($p<0.001$). The NFR group had the least acidity compared to the other two groups. The pH values in the HTS group were lower than in the NS group until the 60th minute. Data for pH are presented in Figure 5.

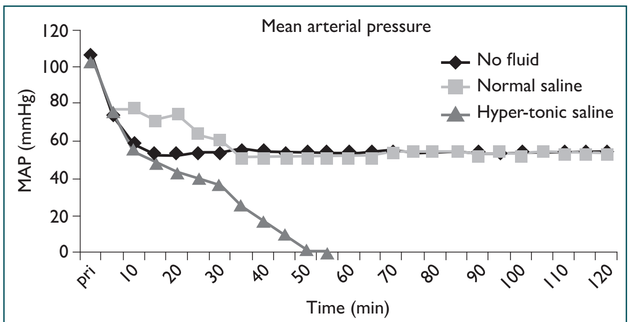

Figure 4. Comparison of mean arterial pressure levels during the trial between groups. "Pri" stands for primary and denotes the starting point of the study.

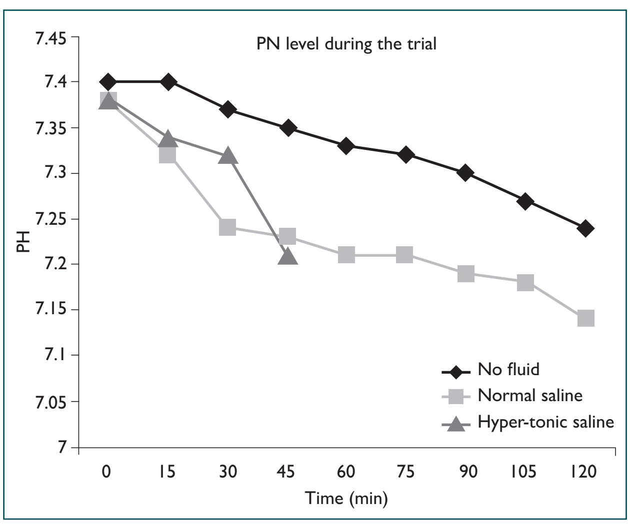

Figure 5. Comparison of pH levels during the trial between groups.

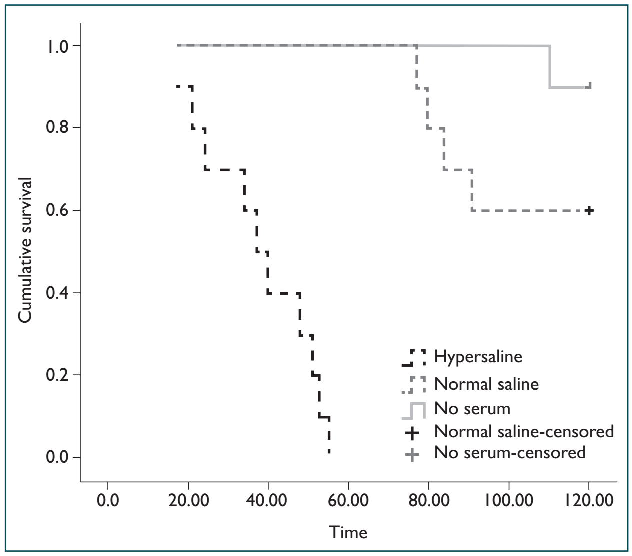

Figure 6. Kaplan-Meier analysis revealing cumulative survival plotted against time and differentiated by study groups. * indicates a significant difference ($p<0.05$) between the NFR and NS groups. + indicates a significant difference ($p<0.05$) between the NS and HTS groups. # indicates a significant different ($p<0.05$) between the NFR and HTS groups.

In this trial, all the goats in the HTS group died before the 60th minute. In the NS and NFR groups, four goats and one goat died, respectively, during the 120 minutes of evaluation.

g. Survival Analysis

Figure 6 shows the cumulative survival time for each treatment group. Kaplan-Meier analysis of survival until the 120th minute revealed an overall mean survival time of 87.4 minutes (S.E = 6.9). Mean survival times for the three groups were as follows: 119.0 (S.E = 0.95) for the NFR group, 105.2 (S.E = 5.83) for the NS group, and 38.0 (S.E = 4.38) for the HTS treatment group. Overall, 50% of all the goats survived. None of the goats that received HTS treatment survived; 60% of the NS group goats survived; and 90% of the untreated group survived the full 120 minutes. Log-rank (Mantel-Cox) statistics were significant when comparing the three groups pooled over the strata (chi-square = 41.72, $p<0.001$).

DISCUSSION

Previous protocols and advanced trauma life support teachings[28] have recommended that the primary treatment of UHS include controlling the source of external bleeding, and intravenous administration of crystalloids followed by packed blood cells through a catheter.[29] This approach has been challenged, and researchers have focused on different doses and types of fluids for treating UHS patients.

Goats are an appropriate mammal for modeling biomedical studies. Goats have relatively low fat proportions, so goats have similar weights to humans with low body mass. Their anatomy is the most similar to humans after monkeys and dogs. Therefore, tracheostomy and other procedures are easier to perform. Surgeries and ablations on dogs are difficult, and few monkeys are available. Goats are mammals and respond to shock more similarly to humans compared to rats. As a result, we chose to use a goat model. As far as we know, no previous studies have been performed of fluid therapy for UHS cases using a goat model.

Few studies have shown that resuscitation without fluid provides superior results in the treatment of UHS. In their rat study, Krausz et al.[30] showed that infusion of HTS and NS leads to more bleeding and hemodynamic instability. Studies of humans have shown that patients should not receive fluids at the accident scene in a UHS setting, and excessive fluid therapy leads to coagulopathy, increased acidosis, hypothermia, abdominal compartment syndrome, elevated intracranial pressure, and immunologic disorders.[17,31-33] Fluid therapy increases the mortality rate in such conditions.[34]

In our study, blood loss in the NFR group was lower than in the NS and HTS groups. Furthermore, the administration of fluid raised blood pressure levels, which interfered with the coagulation process. Contrastingly, not manipulating blood pressure and venous pressure caused less blood to leave the body; so pH levels in the NFR group decreased subsequently to values lower than in the NS and HTS groups. Theoretically, fluids increase blood volume. However, since more blood left the body, the increase in volume was offset by a decrease in hemoglobin in goats which received NS compared to the NFR goats. Hemoglobin levels decreased because of the addition of crystalloid. Heart rates in the NFR group increased slower than in the NS group during UHS. Thus, in cases of uncontrollable hemorrhage, such as abdominal or chest cavity bleeding or pelvic fracture, for which packed red blood cells are not available, the infusion of NS may not be beneficial.

Studies have demonstrated the benefits of administering hypertonic fluid to trauma patients.[7-9,35] For example, HTS has been found to facilitate cerebral perfusion, decrease intracranial pressure,[36] restore blood pressure, and improve cardiac performance.[37] In their study of mice, Bahrami et al.[38] concluded that resuscitation with hypertonic fluid decreases the inflammatory process, but neither lung tissue damage nor mortality follow the same pattern following severe UHS. Krausz et al.[39] concluded that, compared to lactated ringer's solution, HTS was associated with less blood loss and improved survival in most groups of rats. Yu et al.[40] reported that limited fluid resuscitation improved the thermodynamics of pregnant rabbits, decreased inflammatory markers, and improved survival rate. In our study, using a model of UHS based on land-mine explosion and no access to packed blood cells, the infusion of HTS was the worst treatment option. HTS decreased hemoglobin levels and mean arterial pressure, and increased blood loss, heart rate, and pH severely and rapidly. No goat in the HTS group was still living after the 60th minute. Using HTS may be a valuable option for resuscitation in cases of controlled hemorrhagic shock, but our study demonstrated a model of UHS in which fluid therapy was not useful.

Ciesla et al.[41] showed that HTS attenuates the neutrophil cytotoxic response which leads to other complications. Additionally, Watters et al.[42] suggested that any fluid therapy dose may cause dysfunctional inflammatory response, which may explain the higher blood loss in the HTS group in our study. The development of a hypercoagulable state following an injury may also explain the blood loss.[17] Fluid therapy, especially HTS, attenuates this hypercoagulability, leading to more bleeding and other complications. In addition, HTS raises blood pressure and increases blood flow. These findings are in accordance with our study, in which more bleeding and higher blood pressure were observed in the HTS group. Additionally, HTS resuscitation causes more liquid to exit the intercellular space and enhances tissue acidosis. Similarly, in our study, the arterial blood gas results for the HTS group were comparable to those of the NFR and NS groups.

Our study has several limitations. We could not control for the effects of anesthesia, which would not be present in human cases of UHS. We did not use different doses of HTS or evaluate dextran. Due to the expense of goats and our limited funding, it was not possible to obtain a large number of animals for more exhaustive testing. Our study showed the role of fluids only in cases of early intervention. An extended evaluation is definitely needed to properly observe late outcomes and survival results. We limited the trial to 120 minutes, but all the goats in the HTS group died by the 60th minute. Therefore, we could not completely compare the three groups for the full two hours. However, no preliminary study using a smaller number of experimental subjects was performed.

Further studies and larger randomized clinical trials are required to confirm that, in cases of UHS, the administration of fluids is detrimental. More studies are also needed to determine the physiologic reasons that HTS and NS are worse than no fluid therapy in a UHS setting. Additional studies should focus on resuscitation methods and determining the situations in which fluid administration may augment tissue oxygenation and counterbalance potential harmful effects.

Conclusion

Our study shows that HTS may not be a suitable treatment for UHS when compared to NFR and NS groups, especially in settings where bleeding is uncontrollable. The NFR group had considerably better results compared to the HTS and NS groups for all features of UHS, such as hemoglobin levels, pH, bleeding time, and mean arterial pressure. NS and HTS fluids may worsen the condition in the pre-hospital field until surgical repair can be accomplished in the hospital.

Acknowledgments

This study was financially supported by a medical research grant of the Military Research Service Department of Iran. The authors thank Dr. Fred Naraghi for his review and critical comments. The authors would also like to thank Mrs. Pourmand (Sina Hospital, Research Development Center) for her careful edits of the manuscript.

REFERENCES

1. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet 1997;349:1498-504. [CrossRef]
2. Sato H, Kita T, Tanaka T, Kasai K, Tanaka N. Marker of death from hemorrhagic shock. Leg Med (Tokyo) 2009;11:241-3. [CrossRef]
3. Moore FA, McKinley BA, Moore EE. The next generation in shock resuscitation. Lancet 2004;363:1988-96. [CrossRef]
4. Bickell WH, Bruttig SP, Millnamow GA, O'Benar J, Wade CE. The detrimental effects of intravenous crystalloid after aortotomy in swine. Surgery 1991;110:529-36.
5. Bickell WH, Wall MJ Jr, Pepe PE, Martin RR, Ginger VF, Allen MK, et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. N Engl J Med 1994;331:1105-9. [CrossRef]
6. Dries DJ. Hypotensive resuscitation. Shock 1996;6:311-6. [CrossRef]
7. van den Elsen MJ, Leenen LP, Kesecioglu J. Hemodynamic support of the trauma patient. Curr Opin Anaesthesiol 2010;23:269-75. [CrossRef]
8. Ghafari MH, Moosavizadeh SA, Moharari RS, Khashayar P. Hypertonic saline 5% vs. lactated ringer for resuscitating patients in hemorrhagic shock. Middle East J Anesthesiol 2008;19:1337-47.
9. Bender R, Breil M, Heister U, Dahmen A, Hoeft A, Krep H, et al. Hypertonic saline during CPR: Feasibility and safety of a new protocol of fluid management during resuscitation. Resuscitation 2007;72:74-81.
10. Gao J, Zhao WX, Xue FS, Zhou LJ, Yu YH, Zhou HB. Effects of different resuscitation fluids on acute lung injury in a rat model of uncontrolled hemorrhagic shock and infection. J Trauma 2009;67:1213-9. [CrossRef]
11. Fernandes TR, Pontieri V, Moretti AI, Teixeira DO, Abatepaulo F, Soriano FG, et al. Hypertonic saline solution increases the expression of heat shock protein 70 and improves lung inflammation early after reperfusion in a rodent model of controlled hemorrhage. Shock 2007;27:172-8.
12. Kentner R, Safar P, Prueckner S, Behringer W, Wu X, Henchir J, et al. Titrated hypertonic/hyperoncotic solution for hypotensive fluid resuscitation during uncontrolled hemorrhagic shock in rats. Resuscitation 2005;65:87-95. [CrossRef]
13. Prough DS, Whitley JM, Taylor CL, Deal DD, DeWitt DS. Small-volume resuscitation from hemorrhagic shock in dogs: effects on systemic hemodynamics and systemic blood flow. Crit Care Med 1991;19:364-72.
14. Velasco IT, Pontieri V, Rocha e Silva M Jr, Lopes OU. Hyperosmotic NaCl and severe hemorrhagic shock. Am J Physiol 1980;239:664-73.
15. Stanford GG, Patterson CR, Payne L, Fabian TC. Hypertonic saline resuscitation in a porcine model of severe hemorrhagic shock. Arch Surg 1989;124:733-6. [CrossRef]
16. Younes RN, Deutsch F, Itinoshe M, Fontes B, Poggetti R, Birolini D. Responsiveness to different volume therapies following hemodilution and hemorrhagic shock: a Acta Cir Bras 2007;22:355-60.
17. Watters JM, Tieu BH, Differding JA, Muller PJ, Schreiber MA. A single bolus of 3% hypertonic saline with 6% dextran provides optimal initial resuscitation after uncontrolled hemorrhagic shock. J Trauma 2006;61:75-81. [CrossRef]
18. Nout YS, Mihai G, Tovar CA, Schmalbrock P, Bresnahan JC, Beattie MS. Hypertonic saline attenuates cord swelling and edema in experimental spinal cord injury: a study utilizing magnetic resonance imaging. Crit Care Med 2009;37:2160-6. [CrossRef]
19. Patanwala AE, Amini A, Erstad BL. Use of hypertonic saline injection in trauma. Am J Health Syst Pharm 2010;67:1920-8. [CrossRef]
20. Qureshi AI, Suarez JI, Bhardwaj A, Mirski M, Schnitzer MS, Hanley DF, et al. Use of hypertonic (3%) saline/acetate infusion in the treatment of cerebral edema: Effect on intracranial pressure and lateral displacement of the brain. Crit Care Med 1998;26:440-6. [CrossRef]
21. Holcroft JW, Vassar MJ, Turner JE, Derlet RW, Kramer GC. 3% NaCl and 7.5% NaCl/dextran 70 in the resuscitation of severely injured patients. Ann Surg 1987;206:279-88. [CrossRef]
22. Angle N, Hoyt DB, Coimbra R, Liu F, Herdon-Remelius C, Loomis W, et al. Hypertonic saline resuscitation diminishes lung injury by suppressing neutrophil activation after hemorrhagic shock. Shock 1998;9:164-70.
23. Wingfield WE. Veterinary emergency medicine secrets. 2nd ed. Elsevier Health Sciences; 2001. p. 431-5.
24. Greene SA. Veterinary anesthesia and pain management secrets. Elsevier Health Sciences; 2002. p. 260-3.
25. Surgeons ACo: ATLS, Advanced Trauma Life Support Program for Doctors, 7th ed., 2004.
26. Reece W. Duox physiology of domestic animals. 12 ed. Comstock; 2004. p. 50.
27. Robert MJAH. Rosen's emergency medicine: Concepts and clinical practice. Vol. 1, 6th ed. Mosby; 2006. p. 46.
28. Committee on Trauma: Advanced Trauma Life Support Course for Physicians. Chicago: American College of Surgeons; 1993.
29. Trunkey DD. Is ALS necessary for pre-hospital trauma care? J Trauma 1984;24:86-7. [CrossRef]
30. Krausz MM, Bar-Ziv M, Rabinovici R, Gross D. "Scoop and run" or stabilize hemorrhagic shock with normal saline or small-volume hypertonic saline? J Trauma 1992;33:6-10. [CrossRef]
31. Turner J, Nicholl J, Webber L, Cox H, Dixon S, Yates D. A randomised controlled trial of prehospital intravenous fluid replacement therapy in serious trauma. Health Technol Assess 2000;4:1-57.
32. Sampalis JS, Tamim H, Denis R, Boukas S, Ruest SA, Nikolis A, et al. Ineffectiveness of on-site intravenous lines: is prehospital time the culprit? J Trauma 1997;43:608-17. [CrossRef]
33. Yaghoubian A, Lewis RJ, Putnam B, De Virgilio C. Reanalysis of prehospital intravenous fluid administration in patients with penetrating truncal injury and field hypotension. Am Surg 2007;73:1027-30.
34. Kaweski SM, Sise MJ, Virgilio RW. The effect of prehospital fluids on survival in trauma patients. J Trauma 1990;30:1215-9. [CrossRef]
35. Nolan J. Fluid resuscitation for the trauma patient. Resuscitation 2001;48:57-69. [CrossRef]
36. Xiao HP, Gu MN, Xiao JF, Xu X, Zhao ZL. Effects of hypertonic sodium chloride hydroxyethyl starch 40 injection in treatment of acute intracranial hypertension complicated by hemorrhagic shock in dogs. [Article in Chinese] Nan Fang Yi Ke Da Xue Xue Bao 2008;28:385-8. [Abstract]
37. Kramer GC, Perron PR, Lindsey DC, Ho HS, Gunther RA, Boyle WA, et al. Small-volume resuscitation with hypertonic saline dextran solution. Surgery 1986;100:239-47.
38. Bahrami S, Zimmermann K, Szelényi Z, Hamar J, Scheiflinger F, Redl H, et al. Small-volume fluid resuscitation with hypertonic saline prevents inflammation but not mortality in a rat model of hemorrhagic shock. Shock 2006;25:283-9. [CrossRef]
39. Krausz MM, Semenikhina L, Hirsh M. Lactated Ringer's solution and

hypertonic saline improve survival in uncontrolled hemorrhagic shock in female rats in metestrus. J Surg Res 2006;132:23-31. [CrossRef]

40. Yu YH, Zhao KS, Gong SP. Effect of limited volume resuscitation on hemodynamic changes in pregnant rabbit with hemorrhagic shock. [Article in Chinese] Zhonghua Fu Chan Ke Za Zhi 2008;43:50-3. [Abstract]
41. Ciesla DJ, Moore EE, Biffl WL, Gonzalez RJ, Silliman CC. Hypertonic saline attenuation of the neutrophil cytotoxic response is reversed upon restoration of normotonicity and reestablished by repeated hypertonic challenge. Surgery 2001;129:567-75. [CrossRef]
42. Watters JM, Tieu BH, Todd SR, Jackson T, Muller PJ, Malinoski D, et al. Fluid resuscitation increases inflammatory gene transcription after traumatic injury. J Trauma 2006;61:300-89. [CrossRef]

DENEYSEL ÇALIŞMA - *ÖZET*

Hipertonik salin, normal salin veya hiçbiri: Kontrol altına alınamayan hemorajik şok için en iyisi hangisi? Keçilerde deneysel çalışma

Dr. Morteza Saeedi,[1] Dr. Houman HajiseyedJavadi,[2] Dr. Samad Shams Vahdati,[2] Dr. Vahid Eslami,[1] Dr. Mohamad Mokhtarpour,[3] Dr. Mehdi Momeni,[1] Dr. Mohammad Reza Farnia,[1] Dr. Nima Hafezi Nejad[1]

[1]Tahran Üniversitesi Tıp Bilimleri, Acil Tıp Bölümü, Tahran, İran
[2]Tebriz Üniversitesi Tıp Bilimleri, Acil Tıp Bölümü, Tebriz, İran
[3]AJA Üniversitesi Tıp Bilimleri, Acil Tıp Bölümü, Tahran, İran

AMAÇ: Kontrol altına alınamayan hemorajik şokta değişik sıvıların etkileri değerlendirildi. Kontrol altına alınamayan hemorajik şokun en iyi tedavisinde uygun dozlar ve sıvı tiplerine ilişkin anlaşmazlıklar vardır. Bu çalışma sıvıyla resüsitasyon yapılmaksızın (NFR) kontrol altına alınamayan hemorajik şokta hipertonik (HTS) ve normal salinin (NS) etkilerini değerlendirmektedir.
GEREÇ VE YÖNTEM: Otuz keçiye anestezi verilip sağ bacakları cerrahi yolla çıkartıldı. Hayvanlar eşit sayılarda NFR, HTS ve NS gruplarına randomize edildi. Kontrol altına alınmamış hemorajik şoktaki hayvanlarda hemoglobin, kalp hızı, kan kaybı, ortalama arteriyel basınç, kanama zamanı ve pH analiz edildi ve hayvanlar ablasyondan iki saat sonra öldürüldü.
BULGULAR: HTS verilen keçilerin tümü 60 dakika, NS grubunda dört ve NFR grubunda ise bir keçi 120 dakika içinde öldü. NFR grubunda hemoglobin değerleri denemenin sonunda NS ve HTS grubuna göre anlamlı derecede daha yüksekti. HTS grubunda kan kaybı diğer iki gruba göre daha yüksekti ($p<0.05$). NS grubunda NFR grubuna göre kan kaybı daha fazlaydı ($p<0.05$). HTS grubunda ortalama arteriyel basınç ilk 60 dakika içinde hızla sıfıra doğru düştü. NFR ve NS gruplarında ortalama arteriyel basınç HTS grubuna göre daha yüksek olup ($p<0.05$), 35 dakika sonra 60 mmHg'de sabitlenmişti. Diğer iki gruba göre NFR grubunda pH değerleri daha yüksekti ($p<0.05$).
TARTIŞMA: Çalışmamız NFR ve NS ile karşılaştırıldığında kontrol altına alınamayan hemorajik şok tedavisinde HTS'nin uygun olmadığını göstermiştir. HTS ve NS ile tedavi edilenlerle karşılaştırıldığında NFR ile tedavi edilen keçilerin hemoglobin, pH, kan basıncı ve kanama zamanı gibi tüm kontrol altına alınamayan hemorajik şok parametreleri daha iyi idi. Hastane öncesi dönemde NS veya HTS ile tedavi cerrahi onarım gerçekleşene kadar durumu kötüleştirebilmektedir.
Anahtar sözcükler: Kontrol altına alınamayan hemorajik şok; sıvı; hipertonik salin; resüsitasyon; keçi.

Ulus Travma Acil Cerr Derg 2013;19(6):500-506 doi: 10.5505/tjtes.2013.31799