23.4% Hypertonic Saline

A Tactical Option for the Management of Severe Traumatic Brain Injury With Impending or Ongoing Herniation

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ABSTRACT

There are limited options available to the combat medic for management of traumatic brain injury (TBI) with impending or ongoing herniation. Current pararescue and Tactical Combat Casualty Care (TCCC) guidelines prescribe a bolus of 3% or 5% hypertonic saline. However, this fluid bears a tactical burden of weight (~570g) and pack volume (~500cm^3). Thus, 23.4% hypertonic saline is an attractive option, because it has a lighter weight (80g) and pack volume (55cm^3), and it provides a similar osmotic load per dose. Current literature supports the use of 23.4% hypertonic saline in the management of acute TBI, and evidence indicates that it is safe to administer via peripheral and intraosseous cannulas. Current combat medic TBI treatment algorithms should be updated to include the use of 23.4% hypertonic saline as an alternative to 3% and 5% solutions, given its effectiveness and tactical advantages.

Keywords: *traumatic brain injury; TBI; military medicine; hypertonic saline; Tactical Combat Casualty Care; TCCC*

Introduction

TBI is the most pervasive injury in modern conflicts with a wide range of sequelae from mild to life threatening.[1] Second only to uncontrolled hemorrhage, TBI accounts for 9% of deaths in casualties with potentially survivable injuries.[2] TBI grade is based on presenting neurologic function as measured on the Glasgow Coma Scale (GCS) – mild (13–15), moderate (9–12), and severe (3–8).[3] From 2000 to 2019, the Defense and Veterans Brain Injury Center reported 415,858 Servicemembers diagnosed with TBI, with 12% classified as moderate, severe, or penetrating TBI.[4] Blast, blunt, and penetrating mechanisms can cause TBI; blast is the most common in the combat environment (46–56%).[5,6]

The damage to neuronal tissue from the primary TBI cannot be treated by the combat medic. In the prehospital setting, the treatment focus for patients with moderate and severe TBI is on limiting the deleterious effects of secondary injury. This is defined as the compounding of parenchyma damage by physiologic, molecular, and biomechanical mechanisms that persist for hours to days following the initial injury. Collectively, these increase neuronal cell death, exacerbate the original brain injury, and in severe cases, lead to increased intracranial pressure (ICP) and herniation of brain tissue.[7–9]

While provision of adequate brain tissue oxygenation and perfusion are the primary goals to reduce secondary injury in the acute TBI patient, emergent strategies for acutely elevated ICP with signs of impending or ongoing herniation (IOH) are key to preventing irreversible injury and death.[10] Continued shift of brain parenchyma can compress the third cranial nerve leading to unilateral or bilateral mydriasis ("blown" pupil). Parenchymal shift can also damage the respiratory and cardiac automation centers in the medulla and pons.[11] Clinical signs of impending herniation include significant pupillary asymmetry, unilateral or bilateral fixed and dilated pupils, decorticate or decerebrate posturing, respiratory depression, and the "Cushing triad" of hypertension, bradycardia, and irregular respiration.[12]

Hyperosmolar Therapy

One of the primary treatments of acute posttraumatic elevated ICP and IOH is administration of intravenous (IV) hyperosmolar agents. Boluses of hyperosmotic agents are effective in lowering ICP on a short-term, emergent basis, primarily through the creation of an osmotic gradient that reduces cerebral swelling by moving fluid out of brain tissue and into the vasculature.[13,14] Hyperosmolar therapy has been in use since 1919 with a wide variety of agents proffered: glucose, urea, mannitol, and sodium chloride.[15] In current literature, mannitol and hypertonic saline (HTS) have been established as effective for the management of elevated ICP.[16]

Clinically, mannitol and HTS have limited evidence to suggest superiority of one over the other.[17,18] However, there are multiple reasons HTS is favored over mannitol in the combat environment. First, mannitol is a potent osmotic diuretic and causes intravascular depletion, which is detrimental in polytrauma patients with hemorrhagic shock.[19] Second, mannitol crystallizes when exposed to low temperatures, requiring the use of filters and rewarming to 70°C if crystals form.[20] Finally, mannitol use is cumbersome, with the typical dosing

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(0.5–1.0g/kg) of a 25% solution (12.5g/50mL) requiring up to seven vials to treat an 80kg patient. Because of these therapeutic and logistical limitations, the *Pararescue Medical Operations Handbook* (PJHB) and the Tactical Combat Casualty Care (TCCC) guidelines recommend HTS as the preferred agent for management of IOH.[21,22]

Current Practice and Tactical Considerations

The current TCCC guidelines for TBI management do not include HTS during tactical field care. However, during tactical evacuation care, the guidelines recommend a 250mL 3% or 5% HTS IV bolus for suspected herniation (indicated by unilateral dilated pupil with decreased level of consciousness).[22] Current Joint Trauma System Clinical Practice Guidelines for the management of elevated ICP in severe TBI also include the initial 3% HTS bolus followed by an infusion at 50–100mL/h with provision for serum sodium level monitoring.[23] Despite the current TCCC and PJHB treatment recommendations for the use of 3% or 5% HTS in the combat setting, the added weight and bulk in the medic's limited rucksack make carrying these solutions inefficient.

Hypertonic saline packaging varies depending on concentration. The 3%, 5%, and 7.5% concentrations come in 500mL polyvinyl chloride plastic bags identical to traditional IV crystalloid solutions, such as 0.9% sodium chloride (NaCl) and lactated Ringer's. The solution is accessed by inserting a sterile intravenous set directly into the bag spike port, and a 250mL bolus is administered over 10–30 minutes. The 23.4% HTS comes as a 30mL solution in a borosilicate glass vial sealed with a rubber stopper and plastic cap to maintain sterility. This formulation is administered as a slow push over 10 minutes to avoid transient hypotension.

The NaCl concentration, milliequivalents per container, container weight, and pack volume of the most common available hypertonic saline preparations are presented (Table 1). When compared with 3% or 5% solutions in 500mL bags, 30mL 23.4% HTS vials represent an advantage in terms of weight, pack volume, and shelf-life (36 versus 30 months).[24] These vials also deliver a similar sodium load to the TCCC recommended 250mL dose of 3% solution at a higher osmolarity (8,008 versus 1,026 mOsm/L). The 30mL 23.4% HTS vials are small enough to fit inside the hard, plastic cases that combat medics use to protect prefilled syringes and small medication vials. Glass vials and plastic infusion bags appear to be equally durable, although this characteristic of the respective containers has not been formally evaluated.

Clinical Support for 23.4% Hypertonic Saline

While there have been no randomized controlled studies of 23.4% HTS in the prehospital setting, in-hospital data support its efficacy. In a retrospective analysis, intermittent bolus doses of 23.4% HTS alone were shown to significantly reduce ICP without significant changes to hemodynamics.[25] In a study of patients with suspected herniation treated with 23.4% HTS, 75% had clinical reversal of transtentorial herniation with an accompanying decrease in ICP without significant changes in hemodynamic parameters. Among the patients who had ICP monitors, ICP decreased from 23.3 ± 16.2 mmHg to 13.8 ± 10.3 mmHg at 1 hour and to 11 ± 12 mmHg at 24 hours after 23.4% HTS administration.[26] A retrospective comparison of 5% or 23.4% HTS for sustained ICP > 20 mmHg found both solutions reduced ICP, without a statistically significant difference in percentage of responders or rate of adverse reactions.[27] In a pilot trial, 23.4% HTS was superior to mannitol in lowering ICP, suggesting it is at least as effective as lower concentrations of HTS, extrapolating from prior studies.[17,18,28]

Administration of Hypertonic Saline

Traditionally, HTS solutions greater than 2–3% NaCl are given via central venous catheter due to concern for extravasation injury and vein sclerosis. The administration of 23.4% HTS via intraosseous (IO) needle was reported in two small case series of neurological emergencies and noted to be a feasible route for drug delivery without any apparent injection site complications.[29,30] Animal research has demonstrated that peripheral vein phlebitis after IV administration of hyperosmolar agents is a function of agent weight-based osmolarity (mOsm/kg) and duration of infusion.[31] In an emergency without central venous or IO access, 23.4% HTS (8,008 mOsm/L) can be safely administered into a correctly placed and patent large vein IV as a bolus followed by a 0.9% saline flush. For comparison, phenytoin sodium (6,175 to 9,740 mOsm/L) is routinely given in a similar volume via large peripheral vein access for the emergent treatment of status epilepticus.[32,33]

In a series of pediatric neurological emergencies, four patients received 23.4% HTS via peripheral IV without access-site complications.[34] Some academic institutional protocols recommend 23.4% HTS by peripheral IV for emergent management of IOH, and analysis of quality assurance data suggests this is a safe practice.[12,35]

Regardless of which access is used, free withdrawal of blood and unrestricted flow of a 0.9% saline flush without local

TABLE 1 *Comparison of Available Hypertonic Sodium Chloride (NaCl) Solutions for Use in Management of Acutely Elevated Intracranial Pressure With Impending or Ongoing Herniation*

Solution	Volume (mL)	Sodium concentration (mEq/L)	Sodium content (mEq/container)	Osmolarity (mOsm/L)	Weight (g)	Pack volume (cm^3)	Container type
3% NaCl[1]	500	513	256.5	1,026	571*	500‡	Plastic bag
5% NaCl	500	856	428	1,712	571†	500‡	Plastic bag
7.5% NaCl	500	1,283	641.5	2,566	571†	500‡	Plastic bag
23.4% NaCl[2]	30	4,004	120.1	8,008	80	55	Glass vial

[1]B. Braun Medical Inc. (Bethlehem, PA), NDC# 0264-7805-10.
[2]Fresenius Kabi USA (Lake Zurich, IL), NDC# 63323-187-30.
*Weight including solution, bag, and outer protective wrap.
†Weight assumed to be equivalent to 500mL 3% NaCl bag.
‡Assumes 1mL saline in a flexible plastic bag to be $1cm^3$ pack volume.

swelling must be confirmed to prevent extravasation of the HTS dose. This is particularly important when an IO needle is used, considering the reported 89% and 74% first-time successful insertion rates in tibial and humeral sites respectively.[36] It should be noted that in a single study, rapid bolus of 23.4% HTS was associated with transient hypotension in up to 17% of patients; all cases were transient, rarely resulting in a sustained compromised cerebral perfusion pressure and were fluid or vasopressor responsive.[26] This response has been previously described in animal studies without TBI and may be due to vasodilatation in skeletal muscle.[37,38] It is recommended that the bolus be administered as a slow IV or IO push over 10 minutes to reduce the potential for transient hypotension.[12]

Conclusions

While the current TCCC and PJ treatment approach for IOH includes a 250mL bolus of 3% or 5% HTS, these concentrations are only available in 500mL bags. This presents a significant tactical disadvantage in additional ruck weight and bulk compared to using 30mL of 23.4% HTS. The use of 23.4% HTS given via IV or IO should be considered as an option for combat medic treatment of suspected herniation. From a tactical perspective, the smaller volume, lighter weight, and longer shelf-life make the loadout and use of 23.4% HTS vials an attractive option in the management of severe TBI with IOH (Table 2).

TABLE 2 *Take-Home Points*

Hyperosmotic fluids are an important adjunct in the management of elevated intracranial pressure and impending herniation.[12–14]
HTS is the ideal hyperosmotic fluid for field administration in polytrauma patients with TBI.[10]
23.4% HTS in 30mL vials has a space and weight advantage over 3% HTS in 500mL bags.
Adult dosing of 23.4% HTS: 30mL slow IV or IO push over 10 minutes to avoid hypotension.[12]

Disclaimer

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Author Contributions

SR conceived of the manuscript and use of 23.4% saline in the prehospital environment for military medics. ED, KC, BS, and CP performed research. ED performed data collection. ED and KC drafted the manuscript. DV, VR, and JD are subject matter experts who contributed to the rationale and strategy. All authors were involved in revisions and approved the final manuscript.

References

1. **Schmid KE, Tortella FC.** The diagnosis of traumatic brain injury on the battlefield. *Front Neurol*. 2012;3:90.
2. **Eastridge BJ, Hardin M, Cantrell J, et al.** Died of wounds on the battlefield: causation and implications for improving combat casualty care. *J Trauma*. 2011;71(1 Suppl):S4–S8.
3. **Mena JH, Sanchez AI, Rubiano AM, et al.** Effect of the modified Glasgow Coma Scale score criteria for mild traumatic brain injury on mortality prediction: comparing classic and modified Glasgow Coma Scale score model scores of 13. *J Trauma*. 2011; 71(5):1185–1192; discussion 1193.
4. Defense and Veterans Brain Injury Center. DoD Numbers for Traumatic Brain Injury. Department of Defense. 2020.
5. **Wojcik BE, Stein CR, Bagg K, et al.** Traumatic brain injury hospitalizations of U.S. army soldiers deployed to Afghanistan and Iraq. *Am J Prev Med*. 2010;38(1 Suppl):S108–S116.
6. **Bell RS, Vo AH, Neal CJ, et al.** Military traumatic brain and spinal column injury: a 5-year study of the impact blast and other military grade weaponry on the central nervous system. *J Trauma*. 2009;66(4 Suppl):S104–S111.
7. **Diringer MN, Videen TO, Yundt K, et al.** Regional cerebrovascular and metabolic effects of hyperventilation after severe traumatic brain injury. *J Neurosurg*. 2002;96(1):103–108.
8. **Morganti-Kossmann MC, Rancan M, et al.** Inflammatory response in acute traumatic brain injury: a double-edged sword. *Curr Opin Crit Care*. 2002;8(2):101–105.
9. **Kroemer G, Galluzzi L, Brenner C.** Mitochondrial membrane permeabilization in cell death. *Physiol Rev*. 2007;87(1):99–163. doi:10.1152/physrev.00013.2006
10. **Gurney JM, Loos PE, Prins M, et al.** The prehospital evaluation and care of moderate/severe TBI in the austere environment. *Mil Med*. 2020;185(Suppl 1):148–153. doi:10.1093/milmed/usz361
11. **Munakomi S, M Das J.** Brain Herniation. [Updated 2021 Feb 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK542246/
12. **Rajajee, V.** Management of acute moderate and severe traumatic brain injury. UpToDate. 2019. https://www.uptodate.com/contents/management-of-acute-moderate-and-severe-traumatic-brain-injury. Accessed 22 April 2021.
13. **Carney N, Totten AM, O'Reilly C, et al.** Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery*. 2017;80(1):6–15.
14. **Surani S, Lockwood G, Macias MY, et al.** Hypertonic saline in elevated intracranial pressure: past, present, and future. *J Intensive Care Med*. 2015;30(1):8–12.
15. **Todd MM.** Some historical notes on hyperosmolar therapy. *J Neurosurg Anesthesiol*. 2013;25(1):86.
16. **Farrokh S, Cho SM, Suarez JI.** Fluids and hyperosmolar agents in neurocritical care: an update. *Curr Opin Crit Care*. 2019;25 (2):105–109.
17. **Mangat HS, Chiu YL, Gerber LM, et al.** Hypertonic saline reduces cumulative and daily intracranial pressure burdens after severe traumatic brain injury. *J Neurosurg*. 2015;122(1):202–210.
18. **Cottenceau V, Masson F, Mahamid E, et al.** Comparison of effects of equiosmolar doses of mannitol and hypertonic saline on cerebral blood flow and metabolism in traumatic brain injury. *J Neurotrauma*. 2011;28(10):2003–2012.
19. **Van Wyck D, Loos P, Friedline N et al.** Joint Trauma System clinical practice guideline: traumatic brain injury management in prolonged field care (CPG ID: 63). https://jts.amedd.army.mil/assets/docs/cpgs/Prehospital_En_Route_CPGs/Traumatic_Brain_Injury_Management_PFC_6_Dec_2017_ID63.pdf. Accessed 22 April 2021.
20. **US Food & Drug Administration.** Mannitol intravenous prescribing insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/016269s055lbl.pdf. Accessed 22 April 2021.
21. **Pararescue Medical Operations Handbook**. 7th edition, Breakaway Media, LLC.
22. **TCCC Guidelines for Medical Personnel.** 5 November 2020. https://learning-media.allogy.com/api/v1/pdf/9e7beef5-e713-472f-9eb3-1f7f0fdf33a3/contents. Accessed 22 April 2021.
23. **McCafferty R, Neal C, Marshall S, et al.** Joint Trauma System clinical practice guideline: neurosurgery and severe head injury (CPG ID:30). https://jts.amedd.army.mil/assets/docs/cpgs/Neurosurgery_and_Severe_Head_Injury_02_Mar_2017_ID30.pdf. Accessed 22 April 2021.
24. Personal correspondence
25. **Bryant J, Rocker J, Robinson T, et al.** Evaluation of 23.4% hypertonic saline for the management of elevated intracranial pressure. *Crit Care Med*. 2013;41(12):A113.

26. **Koenig MA, Bryan M, Lewin JL 3rd, et al.** Reversal of transtentorial herniation with hypertonic saline. *Neurology*. 2008;70(13):1023–1029.
27. **Carter C, Human T.** Efficacy, safety, and timing of 5% sodium chloride compared with 23.4% sodium chloride for osmotic therapy. *Ann Pharmacother*. 2017;51(8):625–629.
28. **Kerwin AJ, Schinco MA, Tepas JJ 3rd, Renfro WH, Vitarbo EA, Muehlberger M.** The use of 23.4% hypertonic saline for the management of elevated intracranial pressure in patients with severe traumatic brain injury: a pilot study. *J Trauma*. 2009;67(2):277–282. doi:10.1097/TA.0b013e3181acc726
29. **Wang J, Fang Y, Ramesh S, et al.** Intraosseous administration of 23.4% NaCl for treatment of intracranial hypertension. *Neurocrit Care*. 2019;30(2):364–371.
30. **Farrokh S, Cho SM, Lefebvre AT, et al.** Use of intraosseous hypertonic saline in critically ill patients. *J Vasc Access*. 2019;20(4):427–432.
31. **Kuwahara T, Asanami S, Kubo S.** Experimental infusion phlebitis: tolerance osmolality of peripheral venous endothelial cells. *Nutrition*. 1998;14(6):496–501.
32. **Trissel LA.** Handbook on Injectable Drugs, American Society of Health-System Pharmacists, Bethesda, MD 2002.
33. **US Food & Drug Administration.** NDA 010151 Dilantin (phenytoin sodium) injection. https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/010151s036lbl.pdf. Accessed 22 April 2021.
34. **Cummings BM, Fernandes ND, Parker LF, et al.** Standardized volume dosing protocol of 23.4% hypertonic saline for pediatric critical care: initial experience. *Ann Pharmacother*. 2020;54(9):866–871.
35. **Personal correspondence**. Manuscript under preparation.
36. **Szarpak L, Truszewski Z, Smereka J, et al.** A randomized cadaver study comparing first-attempt success between tibial and humeral intraosseous insertions using NIO device by paramedics: a preliminary investigation. *Medicine (Baltimore)*. 2016;95(20):e3724.
37. **Coté CJ, Greenhow DE, Marshall BE.** The hypotensive response to rapid intravenous administration of hypertonic solutions in man and in the rabbit. *Anesthesiology*. 1979;50(1):30–35.
38. **Kien ND, Kramer GC, White DA.** Acute hypotension caused by rapid hypertonic saline infusion in anesthetized dogs. *Anesth Analg*. 1991;73(5):597–602.

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