

Study Title: Safety & Tolerability of Intraosseous Access for Hypertonic Saline Administration:  
A Pilot Study

NCT number: 03276494

Document last updated June 11, 2019

# Safety & Tolerability of Intraosseous Access for Hypertonic Saline Administration: A Pilot Study

## I. Objectives:

Question: Is it safe and tolerable to utilize intraosseous (IO) access in the ICU for hypertonic saline (HTS) administration?

Hypothesis: Utilizing the IO route for vascular access will be safe and tolerable for administration of hypertonic saline (3%) administration.

Operational definitions. Safety will be evaluated based on absence of extravasation of the infusion into the surrounding tissue and absence of tissue damage proximate to the IO infusion. Tolerability will be evaluated based on absence of pain severe enough that the patient requests the infusion be stopped or nonverbal indicators of pain such as agitation or pulling at the site.

## II. Background and rationale:

HTS is used to mitigate and temporize intracranial pressure (ICP) elevations and cerebral edema by creating an osmotic gradient across the cell wall. HTS is part of the elevated ICP algorithm in the emergency neurologic life support protocols (NCS, 2014). HTS is superior to mannitol which is the alternate osmotherapy agent (Kamel et al., 2011 & Ricard, et al., 2014). HTS is typically administered via central vascular access due to the concern that if extravasation of the infusion occurs, tissue damage from cell implosion can occur (Goutos, et al., 2014)

The IO route is generally accepted in resuscitation environments including the emergency department, EMS, and military settings with some authors recommending the IO as a primary method of obtaining emergency vascular access (Lewis & Wright, 2014). The adult advanced cardiac life support (ACLS) guidelines recommend either intravenous or IO access (Link, et al, 2015).

A number of studies have established the safety of IO administration of hypertonic solutions. Beberta, et al. (2014) randomized adult pigs to IO 7.5% HTS, IO 3% HTS, and 0.9% isotonic saline and found regular tissue morphology, no necrosis or microscopic ischemic changes in the HTS groups. Several studies conducted to evaluate the efficacy of hypertonic solutions on resuscitation for hemorrhagic shock used the IO route and did not make note of problems arising from the administration of IO HTS (Dubick, et al, 1992; Runyon et al., 1994). Another study using a canine model of hemorrhagic shock briefly mentioned transient lameness in the IO HTS group, but this resolved by 48 hours (Orasinski, Krahwinkel, & Sanders, 1992). While the majority of studies using hypertonic saline solutions did not make note of complications, one study induced hemorrhagic shock in dehydrated swine and resuscitated one group with 7.5% HTS and noted a high rate of local complications from soft tissue and bone marrow necrosis (Alam et al., 2002).

One study noted a subgroup of patients in which IO access was obtained on conscious patients (Schalk, et al., 2011). None of the patients received local anesthetic and none reported pain during insertion. Eighteen of the 22 conscious patients reported pain during fluid administration. Gazin, et al., reported all 5 conscious patients in their study reported pain with fluid administration (2001). Central venous catheter (CVC) placement is the current standard of care; even with

local anesthesia it can be painful. Most of the potential subjects, due to the nature of their severe neurologic injury, may not be affected by the pain associated with IO fluid administration. Manufacturer literature suggests the use of lidocaine to anesthetize the bone before infusing if possible (Teleflex).

It is expected that utilizing IO for vascular access in the ICU will be safe and tolerable. If this study confirms the anticipated results, there are numerous implications. First, neurologically injured patients requiring emergent HTS may have faster access to this therapy. A study comparing IO to CVC access undergoing resuscitation in the emergency department found IO to be faster to insert (2.3 vs. 9.9 minutes) and had fewer failures to access on the first attempt (Leidel, et al., 2009). Second, serious complications from IO were absent (Lewis & Wright, 2014) compared with severe to life-threatening mechanical complications from CVC including pneumothorax, damage to the carotid artery, and bleeding which were cited at 0.7%-2.1% depending on site (Parienti, et al., 2015). And thirdly, central line associated blood stream infections (CLABSI) are a leading cause of hospital acquired infections in the ICU and are associated with higher mortality (Lin, et al., 2015). CLABSI rates are measured by number of infections per 1,000 catheter days and shorter CVC dwell time is prudent. If a reliable and rapid source of vascular access could postpone or eliminate CVC insertion, risk of CLABSI may be reduced. These potential benefits outweigh the minimal expected risk.

### III. Procedures.

#### A. Research Design.

Prospective case series

#### B. Sample.

Potential subjects will be recruited when the determination by the neuroscience critical care unit (NCCU) care team is made to initiate HTS on a patient without a CVC/PICC. This pilot study will include 5 subjects. Potential subjects or their surrogate decision-makers will be approached by an investigator or assistant to request consent. Recruitment will be open to all NCCU patients fitting the above criteria regardless of primary diagnosis.

#### C. Measurements.

Outcomes

Primary outcome: safety

Secondary outcomes: tolerability

Data points

Absence of extravasation of the infusion into the surrounding tissue and absence of tissue damage proximate to the IO infusion

Pain scale (critical care pain observation scale) during insertion

Able to complete infusion without stopping for pain

Absence of nonverbal indicators of pain (CPOT)

Sodium:

Baseline serum sodium

2 & 6-hour post infusion serum sodium

Timing:

- Time of order for HTS
- Time of affirmative consent
- Time of start of IO procedure
- Time of successful IO placement (or failure to achieve access)
- Time until IO removed

#### D. Detailed study procedures

Pre-study Training. Use of the EZ-IO device is already established at OSUWMC & The James. Key NCCU nurse practitioners and physicians will receive a standard one-hour hands-on training session from the device manufacturer. Potential subjects will be identified by the NCCU physicians and nurse practitioners based on the below inclusion and exclusion criteria.

The NCCU team will identify potential subjects:

##### Inclusion criteria:

- NCCU patients in which osmotherapy with HTS is planned (standard of care)
- Does not already have a CVC or PICC.

##### Exclusion criteria:

- <18 years old
- Known pregnancy
- Long bone fracture in the targeted site
- Proximity to prosthetic joint
- Excessive tissue/absence of anatomical landmarks
- Cellulitis over potential insertion site
- History of osteopetrosis

Investigators or assistants will request written or verbal telephone consent from the patient or surrogate decision maker if the patient is unable to consent. An IO will be inserted and placement confirmed by an inability to tilt the hub of the needle and the ease of flushing through the needle. 40 mg lidocaine will be slowly infused into the IO over 120 seconds, and then allowed to dwell for 60 seconds before infusing HTS. Repeat doses of 20 mg dose of lidocaine may be used as needed for pain to a cumulative maximum dose of 1mg/kg over the 24 hour study period. 3% HTS will be bolused through the IO in doses as prescribed per the NCCU team. Serum sodium level will be sent at 2 and 6 hours following the HTS bolus and every 6 hours. Repeat HTS boluses and/or continuous infusion may ordered per the NCCU team. Placement will be confirmed before and at the end of each bolus as above.

If at any time during the study period the patient has intolerable pain, a CVC or PICC will be placed and the infusion moved to the CVC/PICC. The IO will be removed.

If serum sodium is not appropriately rising following IO boluses, a CVC or PICC will be placed and further infusions will be moved to the CVC/PICC.

If extravasation occurs, a new IO will be placed at an alternate site and further monitoring and treatment will be determined.

The IO will be removed at or before 24 hours. If continued vascular access is required, a CVC or PICC will be placed.

#### Data collection and storage procedure

This study will utilize REDCap (Research Electronic Data Capture), a software toolset and workflow methodology for electronic collection and management of clinical and research data, to collect and store data. The OSU Center for Clinical and Translational Science (CCTS) Research Informatics Services will be used as a central location for data processing and management. REDCap provides a secure, web-based application that provides an intuitive data manipulation interface, custom reporting capabilities, audit trail functionality, real-time data monitoring/querying of participant records, and variations of data exporting/importing. REDCap is hosted by OSUWMC IT in the Ackerman Datacenter (640 Ackerman Road; Room 345)

## Bibliography

Alam, HB., Punzalan, CM., Koustova, E., Bowyer, MW., Rhee, P. (2002). Hypertonic saline: intraosseous infusion causes myonecrosis in a dehydrated swine model of uncontrolled hemorrhagic shock. *J Trauma*. 2002 Jan;52(1):18-25.

Bebarta, VS., Vargas, TE., Castaneda, M., Boudreaux, S. (2014). Evaluation of extremity tissue and bone injury after intraosseous hypertonic saline infusion in proximal tibia and proximal humerus in adult swine. *Prehosp Emerg Care*. 2014 Oct-Dec;18(4):505-10. doi: 10.3109/10903127.2014.912704.

Dubick, MA., Pfeiffer, JW., Clifford, CB., Runyon, DE., Kramer, GC. (1992). Comparison of intraosseous and intravenous delivery of hypertonic saline/dextran in anesthetized, euvolemic pigs. *Ann Emerg Med*. 1992 May; 21(5):498-503.

Goutos, I., Cogswell, LK., & Giele, H. (2014). Extravasation injuries: a review. *The Journal of Hand Surgery (European Volume)*. 39E(8) 808–818.

Kamel, H., Navi, BB., Nakagawa, K., Hemphill, JC, & Ko, NU. (2011). Hypertonic saline versus mannitol for the treatment of elevated intracranial pressure: A meta-analysis of randomized clinical trials. *Crit Care Med*, 39(3).

Lin, K., Chen, A., Chen, Y., Hung, M., Wang, J., Sheng, W., et al. (2015). Central line-associated bloodstream infections among critically-ill patients in the era of bundle care. *Journal of Microbiology, Immunology and Infection*, 1-10. <http://dx.doi.org/10.1016/j.jmii.2015.07.001>

Leidel, BA., Kirchhoff, C., Bogner, V., Stegmaier, J., Mutschler, W., Kanz, KG., & Braunstein, V. (2009). Is the intraosseous access route fast and efficacious compared to conventional central venous catheterization in adult patients under resuscitation in the emergency department? A prospective observational pilot study. *Patient Safety in Surgery* 2009, 3:24 doi:10.1186/1754-9493-3-24

Lewis P, Wright C. Saving the critically injured trauma patient: a retrospective analysis of 1000 uses of intraosseous access. *Emerg Med J* 2014;31(9):784. doi:10.1136/emermed-2014-203588

Link, MS., Beskow, LC, Kudenchuk, PJ., Halperin, HR., Hess, EP., Moitra VK., et al. (2015). Part 7: Adult Advanced Cardiovascular Life Support 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2015;132[suppl 2]:S444–S464. DOI: 10.1161/CIR.0000000000000261.

NCS. (2014). Emergency Neurological Life Support Elevated ICP or Herniation, version 1.0. Accessed at <http://enlprotocols.org/files/ICP.pdf>

Parienti, JJ., Mongardon, N., Megarbane, B., Mira, JP., Kalfon, P., Gros, A., et al. (2015). Intravascular complications of central venous catheter by insertion site. *NEJM* 373(13), 1220-1229.

Rickard AC, Smith JE, Newell P, et al. (2014). Salt or sugar for your injured brain? A meta-analysis of randomised controlled trials of mannitol versus hypertonic sodium solutions to manage raised intracranial pressure in traumatic brain injury. *Emerg Med J*, 31, 679–683.

Runyon, DE., Bruiting, SP., Dubick, MA., Clifford, CB., Kramer, GC. (1994). Resuscitation from hypovolemia in swine with intraosseous infusion of a saturated salt-dextran solution. *J Trauma*. 1994 Jan;36(1):11-9.

Schalk, R., Schweigkofler, U., Lotz, G., Zacharowski, K., Latasch, L., Byhahn, C. (2011). Efficacy of the EZ-IO® needle driver for out-of hospital intraosseous access - a preliminary, observational, multicenter study. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine* 2011, 19:65

Teleflex. Consider using anesthetic for adult patients responsive to pain. Accessed online July 20, 2016 at <http://www.eziocomfort.com/ezio-comfort.html#dosing-&-administration>