Title: Study Protocol with Statistical Analysis Plan

NCT number: Pending

Document date: 11/15/2023

GENERAL STUDY INFORMATION

Study Title

Include the study title below.

Efficacy of Hypertonic Saline as a Treatment for Mild Traumatic Brain Injury in Pediatric Patients

1 Review Type (Choose one)

Please choose which level of review best fits your research. This is an investigator's assessment of review and does not preclude the IRB from alternate determinations. In cases where the investigator and the IRB's determination of review conflict, the IRB's determination will be considered the official determination.
***Note**: Expedited review does not refer to the timeliness of the review of your protocol, but specific categories of research defined by OHRP. If you would like help determining which type of review best fits your research study, please contact the IRB staff in the Office of Research Support & Compliance:*
https://research.utexas.edu/ors/human-subjects/get-help/

a ☐ **Full Board Review – Greater than Minimal Risk Research**
b ☒ **Expedited Review – Minimal Risk Research**

2 Research Hypotheses

Please describe the research aims and hypotheses in the box below. Note: Procedures will be explained in a separate section below.

We hypothesize that administering 3% hypertonic saline in the pediatric emergency department for mild traumatic brain injuries can result in immediate symptomatic relief and prevent long-term sequelae and persistent post-concussive syndrome. Secondarily, treatment with 3% hypertonic saline may reduce return visits to the emergency department, thus directly reducing the time and economic burden on patients and their families.

3 Study Background

Provide the rationale and the scientific or scholarly background for the proposed activity, based on existing literature (or clinical knowledge). Describe the gaps in current knowledge that the project is intended to address.

Annually in the United States, it is approximated that 1.7 million people suffer a TBI, also known as a concussion. Most of these incidences occur in young and healthy populations, including athletes in contact sports and military personnel. Over the past decade, there has been an increased motivation to study the neuropsychological effects of TBI. However, there has not been much advancement in acute treatment methods to prevent long-term effects. TBI symptoms, including persistent headache, irritability, and dizziness, are theorized to stem from brain contusion and swelling and can result in increased intracranial pressures (ICP). For over a century, 3% hypertonic saline has been used to combat elevated ICP in severely injured patients but has been minimally studied to treat acute mild TBI

symptoms and to prevent long-term sequelae, but its use has not been examined extensively in pediatric populations.

All patients presenting with a TBI at Dell Children's Medical Center (DCMC) Emergency Department (ED) receive routine symptomatic care with analgesics (Acetaminophen), and anti-emetics (Ondansetron) as clinically indicated. From here, standard of care varies with patient presentation and is up to the physician's discretion. Some patients are discharged home without fluids, some receive normal saline, and some receive hypertonic saline but it is left to the physician's discretion depending on the severity of symptoms.

4 Design and Methodology

Provide a brief description of the study design or data collection methodologies. Details regarding protocol specific research procedures will be discussed in a later section.

This randomized, double-blinded prospective study aims to determine the utility and efficacy of 3% hypertonic saline (HTS) to combat acute and long-term sequelae of TBI. We plan to enroll 74 participants, ages 8-17, who present to the Dell Children's Medical Center Emergency Department with a mild TBI. The intervention group (n=37) will receive 5ml/kg of 3% hypertonic saline, and the control group (n=37) will receive 5ml/kg of 0.9% normal saline. There is a maximum volume of 500ml for both fluids. A standardized concussion inventory score will be used to assess the severity of symptoms pre-infusion, and post-infusion. Participants (or their parent/guardian) will be asked to complete two additional inventory scores one week and one month after the injury, of which they will be reimbursed for successful completion. Primary outcomes will be the efficacy of HTS in treating acute and chronic concussion symptomatology, and secondary outcomes will include unscheduled revisits to the ED.

5 Data Analysis

Describe the data analysis plan, including any statistical procedures or power analysis.

Data collection and analysis will be performed by the study physicians with the support from research personnel and faculty at DCMC. Summary statistics of patient variables will be performed using means with standard deviations (normally distributed data), and medians with interquartile ranges (non-normal data). Categorical data will be presented as percentages. Chi-squared and t-test statistical analysis (or nonparametric equivalent) will be utilized as well where appropriate. Multivariate logistic regression modeling of the data will be utilized to identify and adjust for confounders.

STUDY ELEMENT IDENTIFICATION

6 Study Elements

Check each research procedure included in your study.
A full description of all study procedures should be provided in the Procedures (Details) section below.
Procedures denoted with "" below have supplemental forms. Navigate to the UTRMS-IRB Library, Templates tab to download the applicable supplemental form.*

☐	Bio-specimens*	☐	Biometrics	☐	Registry or Repository*
☐	Focus Group	☐	Genetic Analysis	☐	Genomic Data Sharing
☐	International Research*	☒	Interview/Survey	☐	MRI
☒	Protected Health Information*	☐	Observation	☐	Radioactive Material/PET/Nuc. Med
☒	Record Review	☐	Sensors (Externally Placed)	☐	Sensors (Inserted)
☐	Audio (only) Recording	☐	Video Recording	☐	X-Ray/CT/DEXA

7 Study Intervention

Click on the check box (or double click and type an "X" if using Google Docs) if you will implement any of the following interventions.
A full description of all study interventions should be provided in the Procedures (Details) section below.
** Interventions denoted with "*" below have supplemental forms. Navigate to the UTRMS-IRB Library, Templates tab to download the applicable supplemental form.*

☐	Behavioral	☐	Device*	☒	Drug/Biologic*

8 Clinical Trial

Click on the following check box (or double click and type an "X" if using Google Docs) if the research meets the below definition of a clinical trial.

☒ **This study meets the definition of a clinical trial according to clinical trials.gov in that it involves one or more human subjects who are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.**

9 Additional Oversight

Check the box(es) below if you are implementing research procedures that require oversight from additional UT committees.

☐	Energy introduced to the subject (electrical, magnetic, light)	☐	Human embryonic, human induced pluripotent, or human totipotent stem cells; or human gametes or embryos	☐	Radiation exposure without direct clinical benefit

☐ **Biological Samples, Biohazards, Recombinant DNA, or Gene Transfer**

If biological samples are used and stored on UT campus UT IBC approval is needed.

a ☐ **UT IBC has (or will have) oversight.**

Provide UT IBC Number:

b ☐ **Biological samples collected will not be stored at UT Austin and another agency has responsibility for biospecimen safety.**

10 Alternatives to Participation in This Study

Provide a description of alternatives to participation in this study, as applicable.

All patients will be treated for their presentation. Patients who are eligible for the study but choose to not participate will be treated with routine symptomatic treatment of mild traumatic brain injury to include analgesics and anti-emetics.

STUDY PROCEDURE DESCRIPTION

11 Procedure Description

Describe all study procedures, including a step-by-step outline of what participants will be asked to do or how data will be used. Be sure to describe all of the following in detail, as applicable:

- *Description of all research procedures being performed and when they are performed, in sequential order.*
- *Describe/list all research measures/tests that will be used [**NOTE: upload copies of all measures, surveys, scripts, data collection forms, etc., in "Other Attachments" in UTRMS-IRB**].*
- *Secondary data or specimens that will be obtained, how they are collected, how are they used.*
- *Where research activities will take place and duration (include expected time commitment of participants).*
- *Study elements checked in #6 above should be described here.*

Note: if this is a multi-site or collaborative study include the following:

- *This is a "Multi-site Study that involves more than one site performing ALL aspects of the research procedures as outlined above." OR "This is a collaborative study that involves UT Austin researchers working with external researchers who are engaged in performing the following study activities (list activities)."*
- *For assistance with multi-site/collaborative research, download HRP-UT932 Request to Rely Assessment Form from the UTRMS-IRB Library and email irbreliance@austin.utexas.edu.*

1. All patients presenting with a TBI will receive routine symptomatic care with analgesics (Acetaminophen), and anti-emetics (Ondansetron) as clinically indicated.
2. The study will be presented to potential participants and their parent/guardian by research personnel. Parents will have as much time as they want to make the decision to participate and ask questions unless the clinical condition makes the child ineligible at some point, e.g., a child who is very symptomatic or worsening and requiring some intervention by the provider.
3. Patients who participate in the study will be randomized and blinded to 5ml/kg of either 0.9% normal saline, or 3.0% hypertonic saline over one hour, with a maximum volume of 500ml. The surveying physician will also be blinded to the intervention. A separate provider will place the order for the intervention. The nurse will place an opaque covering over the fluids to blind the patient and guardian to the intervention. Although it is sometimes recommended to be administered via central line, hypertonic saline has proven to be safely administered through a peripheral IV, and it is standard policy here at Dell Children's Medical Center.

4. Patients will complete the concussion inventory to indicate current symptom severity after concussion, and fifteen minutes after fluid administration. Guardians may assist patients with completing the inventory.
5. Patients/guardians will be contacted to complete the online inventory at one week and at four weeks post intervention. Three attempts (per inventory) will be made to contact the parent/guardian to complete the inventories. Those that complete both inventories will receive a $20 ClinCard for their participation. Qualtrics will be used to complete the inventories.

   Expected research participation time during initial visit: 90 minutes – 15 minutes explaining the study and obtaining permission/assent, 45-60 minutes for fluid administration, 10-15 minutes for inventory completion. These are approximate times as the research personnel will work around clinical procedures being conducted during the visit. IV placement is completed with the patient by nursing staff as part of usual care and is not taken into account for research study time.

   Expected time during follow-up period: 10-15 minutes to complete each of the two follow-up inventory surveys. Total time for participants: 110-120 minutes

6. 3 months after the initial visit, study personnel will review the patient's electronic medical chart to determine if there have been additional visits by the patient to the ED (specifically to an ED, not an appointment for usual care or follow-up visits). If there are additional visits, we will review whether the visit was related to TBI or if the patient exhibited TBI symptoms.

SUBJECT POPULATION

12 Protected Subject Populations

Click on the check box (or double click and type an "X" if using Google Docs) each population, if they are specifically studied for this research.

☐ Active Military Personnel	☒ Children/Minors	☐ Decisionally Impaired Adults
☐ Emancipated Minors	☐ Fetuses	☒ Individuals with Limited English Proficiency
☐ Neonates (Uncertain Viability)	☐ Neonates (Non-Viable)	☐ Prisoners
☐ Pregnant Women	☐ UT Staff/Employees	☐ UT Students

13 Research Participant Information

Describe the general characteristics of the subject populations or groups including gender, health status, and any other relevant characteristics. ***If you have multiple research populations (e.g., teachers and students), clearly outline characteristics for each group.***

Patients that are candidates for this study are those that have incurred blunt head injuries within the past five days with any associated symptoms as outlined in the concussion inventory.

Patients that are excluded from this study are those in which administration of hypertonic saline or fluid administration may potentially be harmful. This will be left up to physician discretion, and to include cases where there is a chronic neurologic disorder, cardiac disease, pulmonary disease, or renal disease. Patients who also have an identified significant intracranial injury to include hemorrhage or skull fracture are excluded from this study.

b Minimum Age

*Include the minimum age range for target population. If you have multiple research populations **(e.g., teachers and students), clearly state the minimum age for each group.***

8 years old (the concussion inventory scale has been validated for a minimum age of 7 years old).

c Maximum Age

*Include the maximum age range for target population. If you have multiple research populations **(e.g., teachers and students), clearly state maximum age for each group.***

17 years old

d Inclusion Criteria

Describe the specific criteria that will be used to decide who will be INCLUDED in the research from interested or potential subjects. Define technical terms in lay language, as applicable.

1. Age 8-17
2. Blunt head injury within the past five days with any associated symptoms as outlined in the concussion inventory.
3. English or Spanish speaking.
4. Glasgow Coma Scale score of 13-15
5. Treating provider plans to use saline administration as part of patient's treatment plan

e Exclusion Criteria

Describe the specific criteria that will be used to decide who will be EXCLUDED from the research. Define technical terms in lay language, as applicable.

1. Intracranial injury diagnosed by CT / MR Brain, though imaging is not a requirement for this study.
2. Possible or witnessed posttraumatic seizure
3. Developmental delay / intellectual disability
4. Underlying cardiac, pulmonary, and renal pathology in which fluid administration or hypertonic saline may potentially be harmful, based on attending provider judgement.
5. Suspected use of alcohol or illicit substances
6. Associated injuries requiring the use of narcotics for analgesia

14 Total Sample Size

Enter the total target sample size below.

Sample size = 74 (37 each in the intervention group and control group).

15 Sample size rationale

Describe your sample size rational below.

A prior interventional study using the PCSS to assess response to a rehabilitation program found an effect size of approximately 10 and a standard deviation (SD) of 15 for the change in PCSS. Using the same effect size and SD for this project, with an α of 0.05 and β of 0.2, we anticipate needing to enroll 37 subjects per group (n=74 total).

SCREENING AND RECRUITMENT

16 Identification and Screening

*Check the box below if this study involves a screening process **prior** to the informed consent process.*

☐ **This study involves obtaining information or biospecimens for the purpose of screening, recruiting or determining eligibility of prospective subjects prior to informed consent by either:**
1. Oral or written communication with the prospective subject or LAR
2. By accessing records containing identifiable private information or stored identifiable biospecimens.

17 Identification and/or Screening Procedures

Describe the identification and/or screening procedures below.

Providers (MDs and DOs) who are part of the Pediatric Emergency Medicine Fellowship at DCMC will be trained on eligibility criteria for the study and asked to identify potential study candidates who are under their care. Patients are triaged upon arrival at the ED by nursing staff and a preliminary diagnosis and acuity level is assigned to the patient before they are seen by the ED provider. This triage information is available to all providers on call in the ED and patients are assigned to a provider based on acuity level of the patient. If they are not part of the research team, ED providers will reach out to research personnel to approach the patient about the study if, in the provider's clinical judgment, saline administration would be part of the patient's treatment plan. A trained enrolling researcher will approach patients and their parent/guardian to introduce the study. If a patient agrees to participate, the enrolling researcher will communicate this to the patient's designated provider. Research studies are common in the DCMC ED, and this process has been used for other studies, as well.

18 Recruitment Overview

Check box indicating all recruitment methods utilized for this research.

☐	**E-mail**	☐	**Flyer**
☒	**In-Person**	☐	**Letter**
☐	**Social Media**	☐	**Research Pool**
☐	**Telephone/Text**	☐	**Snowball Sampling**
☐	**Web-post**	☐	**Word of Mouth**

19 Describe the recruitment process, including where recruitment will take place.

Describe recruitment procedures in the box below. Describe all elements checked above to provide a complete understanding of the recruitment strategies/methods.

NOTE: Upload copies of all recruitment materials to UTRMS-IRB in the "Recruitment Materials" section.

Recruitment will take place at the DCMC ED. All patients with an emergency department intake diagnosis of mild TBI will be evaluated for study enrollment prior to being approached. If meeting inclusion and exclusion criteria, the patient and caregiver will be approached in their hospital room by an enrolling researcher. The enrolling researcher will inform the family about the study. Refusal to participate will not affect the quality of care they will receive.

OBTAINING INFORMED CONSENT

20 Consent Overview

Check the box(es) for consenting procedures that will be used.

☒	Obtaining Written Informed Consent/Parental Permission	☒	Requesting a Waiver of Documentation of Informed Consent
☐	Requesting a Waiver of Informed Consent	☐	Requesting an Alteration of the Required Elements of Informed Consent
☒	Obtaining Child Assent	☐	Obtain Consent Using a Short Form with a Witness

21 Consent and Assent Processes

Provide a detailed description of consent/assent procedures in the box below. Include: who will obtain consent, where will consent be obtained, how is consent obtained, how consent/assent is documented, and when the consent process will occur in such a manner that participants will have sufficient time for adequate consideration.

NOTE: Upload copies of all consent/assent/permission forms/scripts to UTRMS-IRB in the "Consent Forms" section. This is required for UTRMS-IRB to appropriately stamp consent forms for approval.

Enrollment will take place in the patient's room at the DCMC ED. An enrolling researcher will explain the study objectives, risks, benefits, and alternatives to families in person. If the patient is Spanish speaking, a HIPPA-certified video or telephonic translator may be used if the bilingual study coordinator is not available. Families will be provided a written consent form, with similar explanation and be given time to review prior to being given the opportunity for questions. If families agree to participation, signed consent will be obtained by research personnel. Signed assent will be obtained from the minor participant, as well.

For patients who turn 18 years old during the study period: Patients who are recruited at age 17 and turn 18 during the study period will be re-consented via telephone using an adult informed consent

form. Re-consent procedures will be completed by the bilingual research coordinator and phone calls will be made from a private office at Dell Children's Medical Center.

22 Electronic Consent

Check the box below if this study involves obtaining consent with an electronic signature. Be sure the section above is consistent.
NOTE: This box should NOT be checked participants are responding "yes" or clicking "I Agree" on a consent form. ***This section should only be completed if an electronic signature is being obtained.***

☐ **This study involves documenting informed consent/parental permission using an electronic signature.**

If true, specify method for obtaining e-consent below (e.g., DocuSign):

N/A.

23 Consent and Translation

Check the box below to indicate that consent documents/scripts will be translated to a language other than English.

☒ **The study population will likely include participants whose limited English speaking status requires translation of the consent form.**

Translation Process

If above is checked, complete the below information describing the translation process. Either A or B must be checked.

A ☐ **The consent documents will be translated by a certified translator.**

B ☒ **A non-certified translator will translate the consent documents.**

If selected, complete the next two items below. Section describing qualifications must be completed and backtranslation (ii) must be true.

i **Describe the translator's qualifications**

To input text, click in the light grey area below.

The consent form has been translated by the study coordinator Lina Palomares, LMSW. Ms. Palomares is fluent in Spanish and has 20 years of experience in survey design and translation.

ii ☒ **Another individual will confirm that the translation is accurate and appropriate**

26 Waiver of Documentation of Informed Consent

Only complete this section if a waiver of documentation of consent is requested (checked above in #21). To approve a waiver of documentation of consent, one of the following options must be appropriate and justified by the researcher. Please choose ***one*** *waiver option and provide additional information as prompted.* ***Waiver option 2 is most common.***

A **Waiver Option 1**

Check the box below for each item (all required – #1-4) and provide protocol-specific information as to how the criteria below are met.
NOTE: This is the only applicable waiver of documentation option for greater than minimal risk research. If your study is greater than minimal risk and does not meet Option 1 criteria, you will need to obtain written consent.

1 ☐ **The only record linking the subject and the research would be the consent document.**

i **Provide protocol specific information as to how this criterion is met.**

2 ☐ **The principal risk would be potential harm resulting from a breach of confidentiality.**

i **Provide protocol specific information as to how this criterion is met.**

3 ☐ **Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.**

i **Provide protocol specific information as to how this criterion is met.**

4 ☐ **Describe the mechanism for documenting that informed consent was obtained**

Briefly explain how the researcher will document that consent was obtained from participants.

B Waiver Option 2

Check the box below for each item (all required – 1-3) and provide protocol-specific information as to how the criteria below are met.

1 ☒ **The study is minimal risk.**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below

Waiver requested for patients who turn 18 years old during the study period: As the study procedures are those used in standard of care for mild TBI, the probability and magnitude of harm and/or discomfort anticipated in the research study are not greater than those ordinarily encountered during the performance of routine care for mild TBI.

2 ☒ **Written consent would not be required outside the research context.**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below

In the clinical context, documented written consent for treatment is obtained at the time of the initial visit but is not obtained to collect follow-up information from the patient or their parent/guardian.

3 ☒ **Describe the mechanism for documenting that informed consent was obtained**

Briefly explain how the researcher will document that consent was obtained from participants. To input text, click in the light grey area below.

i For patients who turn 18 years old during the study period, the research coordinator will reach out to the participant via telephone to obtain informed consent verbally. This will be documented in a new consent form for the now legally authorized participant.

C Waiver Option 3

Check the box below for each item (all required – 1-4) and provide protocol-specific information as to how the criteria below are met.

1 ☐ **The subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm**

i **Describe the cultural group or community.**

2 ☐ **The research presents no more than minimal risk of harm to subjects.**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below

3 ☐ **There is an appropriate alternative mechanism for documenting that informed consent was obtained.**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below

4 **Describe mechanism for documenting that informed consent was obtained**

To input text, click in the light grey area below

27 Waiver or Alteration of Informed Consent

Only complete this section if a waiver or alteration of consent is requested. To approve a waiver or alteration of consent, all of the following criteria must be appropriate and justified by the researcher. All boxes must be checked. SKIP THIS SECTION IF NOT REQUESTING A WAIVER/ALTERATION OF CONSENT

A ☐ **The research involves no more than minimal risk to the subjects.**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below

B ☐ **The waiver or alteration will not adversely affect the rights and welfare of the subjects.**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below.

C ☐ **The research could not practicably be carried out without the waiver or alteration (it is impracticable to perform the research if obtaining consent is required and not just impracticable to obtain consent).**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below.

D ☐ **If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.**

i **Provide protocol specific information as to how this criterion is met.**

To input text, click in the light grey area below.

28 Deception/Incomplete Disclosure and Debriefing

Only complete the sections below if requesting an alteration of informed consent for research that involves deception/incomplete disclosure.

Deception (as applies to research) means intentionally giving research subjects false information in order to establish false beliefs during the course of a research study.

Incomplete disclosure means that the principal investigator withholds some information about the real purpose of the study or the nature of the research procedures.
See IRB Policies and Procedures Section 15 for a description of deception.
If this study does not involve deception/incomplete disclosure, skip this section.

A ☐ **It is appropriate to provide additional pertinent information to the subject after research activities are complete (e.g., the researcher needed to deceive the subject to the nature of the study).**

B ☐ **Research participants will have the opportunity to withdrawal their data during the debriefing.**

C **Describe the nature of deception/incomplete disclosure and why it is necessary to conduct the research.**

To input text, click in the light grey area below.

D **Describe debriefing procedures.**

To input text, click in the light grey area below. ***NOTE: Upload the debriefing form to UTRMS-IRB in the "Consent Forms" section.***

BENEFITS

29 **Benefits to Society**

Describe the scientific and societal benefit(s) below.

The potential benefit of this research would be the identification of a superior treatment for acute symptomatic treatment of mild TBI, and potential prevention of long-term sequelae.

30 **Potential Direct Benefits to Participants**

Click on the applicable check box. A or B must be checked.

A ☐ **There is no anticipated direct benefit to participants.**

B ☒ **There are anticipated benefits to participants.**

i **If applicable, describe the potential direct benefits to participants.**

Describe potential direct benefits to participants below.

If use of hypertonic saline is a superior method of care, its use may prevent unscheduled revisits to the emergency department, or primary care physician offices. This will save unnecessary cost and time for families. It may also lead to fewer or less severe acute and long-term symptoms for patients.

RISKS

31 Describe the risks associated with each activity in this research

To input text, click in the light grey area below. Note: Risks should also be outlined in the consent form(s).

Prior review of the use of hypertonic saline at the proposed volume and rate of infusion has not shown to have additional risks compared to normal saline. The risk of hypernatremia (excessive sodium levels in the blood) is low with the proposed intervention. Per saline labeling: Plasma electrolyte concentrations should be closely monitored in the pediatric population as this population may have impaired ability to regulate fluids and electrolytes. With all saline administration, there is a possibility of the patient feeling chest tightness, wheezing, cough, or sore throat.

Fluid administration through an intravenous (IV) line has its inherent but uncommon risks to include pain or tenderness at the IV site, infection at the IV site, thrombophlebitis, extravasation, and hypervolemia.

There is also a potential for loss of confidentiality.

32 Describe how each risk is mitigated/minimized.

To input text, click in the light grey area below. Note: Risks mitigation should be outlined in the consent form(s), as applicable.

Trained nurses place the IV line and follow routine protocols for all patients in the ED. This will prevent risks of pain/tenderness, infection, thrombophlebitis, and extravasation. For all patients, services from Child Life are available when placing the IV to make the child more comfortable and explain the process in a manner that is understandable to them.

The risk of hypernatremia is low with the proposed intervention. Prior literature review of a similar study that provided 10ml/kg of hypertonic saline with a maximum of 1L reported no adverse effects. Patients who are at risk for electrolyte abnormalities will be excluded from the study and will not be approached. The risk of hypervolemia is low due to appropriate screening of candidates that will receive the fluid. Patients at high risk for volume overload will be excluded. All patients are monitored for adverse reactions in the ED and appropriately treated.

In regard to risk to plasma electrolyte imbalance, we understand the risks of the pediatric population to potentially have impaired ability to regulate fluids and electrolytes and mitigate this risk by excluding any child with any cardiac, pulmonary, or renal medical problems that would suggest potential impairment. Per the ED protocol for all patients, study participants will have continuous monitoring clinically with repeated vital signs measurements, and physical monitoring.

To minimize loss of confidentiality, all study procedures done at the initial visit will occur in the patient's private room in the ED. All participants will be assigned a unique study ID; identifiable information will only be accessible to the study PI and study coordinator for the purpose of ensuring that the data collected is correct for the enrolled patient and to conduct follow up.

33 Data Safety Monitoring

For additional information regarding data safety monitoring boards and data safety monitoring plans, please see Section 21 of our Policies and Procedures. One of the following must be checked (A, B, or C).

A ☒ **In the investigator's opinion, this study is minimal risk and does not require a Data Safety Monitoring Plan (DSMP) or a Data Safety Monitoring Board (DMSB).**

PLEASE NOTE: The IRB may determine minimal risk studies do require data safety monitoring under certain circumstances (e.g., if there is a known risk with an expected frequency).

B ☐ **This study does not have a Data Safety Monitoring Board, but researchers have an internal plan to monitor for safety (Data Safety Monitoring Plan (DSMP)).**

Complete Data Safety Monitoring Details

C ☐ **This study has a Data Safety Monitoring Board (DSMB).**

*Complete Data Safety Monitoring Details section below **or** upload this study's Data Safety Monitoring Board's charter that contains the information below.*

34 Data Safety Monitoring (Details)

*Complete this section if the study has a Data Safety Monitoring Plan. **SKIP this section there is not a DSMP/DSMB.** If the study has a DSMB, ensure all items below are addressed in the charter (and charted uploaded to UTRMS-IRB) or provide additional information below, as needed.*

A **How is safety information collected?**

B **When will safety data collection start (for each participant or for the whole study, as applicable)?**

C **How frequently will safety data be collected?**

D **Who will review the data for safety?**

E **How frequently will data be monitored for safety concerns?**

F **What data will be reviewed?**

G **State the frequency or periodicity of the review of cumulative data.**

H **State any conditions that would trigger an immediate suspension of the research.**

35 Early Withdrawal

Only complete this section if there are planned conditions under which a participant will be withdrawn from the study. *If not applicable, skip to next section. Include this information in your consent form.*

A **List the criteria for withdrawing individual participants from the study (e.g., safety or toxicity concerns, emotional distress, inability to comply with the protocol, or requirements from study sponsor).**

Children may be withdrawn at the discretion of the treating physician if he/she feels it is in the child's best interest.

B **Describe any necessary procedures for ensuring the safety of a participant who has withdrawn early.**

Children who are withdrawn will be under the care of a provider who will ensure their safety not just for the purposes of the study but as part of their care in the ED.

36 Describe any pre-specified criteria for stopping or changing the study protocol due to safety concerns.

Not applicable. The study interventions are both part of standard of care at DCMC.

REQUIRED DISCLOSURES

37 Required Consent Disclosures

Identify each element below that may require additional information to be disclosed in the consent form.

A ☐ **It is reasonable that researchers could discover or suspect child or elder abuse.**

Add appropriate disclosure in consent form(s).

B ☐ **It is reasonable that researchers could learn of an incident that could require reporting under Title IX.**

Add appropriate disclosure in consent form(s). See Title IX and Research Guidance for information and download the Title IX Reporting Form on the Special Topics page.

C ☐ **It is reasonable that researchers could discover incidental findings or other information of medical interest about a participant's previously unknown condition.**

Add appropriate language to consent form(s).

i **Articulate methods for addressing and reporting incidental findings, if applicable.**

Ensure appropriate information is in consent form(s), as applicable.

N/A.

PRIVACY AND CONFIDENTIALITY

38 **Privacy**

Describe how you will protect the identity and privacy of study participants during each phase of research. Privacy focuses on the individual participants rather than data. In this section, researchers should focus on issues such as where research activities take place and how participant involvement is protected from non-participants. Describe methods to ensure participants' privacy during identification, recruitment, screening, the consent process, the conduct of the study, and dissemination of data.

All initial research interactions with the patient will take place in a private room within the DCMC ED. Patients will only be approached once triaged, placed in a room in the ED, and examined by an ED provider who has confirmed the patient's eligibility for research personnel to approach. We will collect private information (e.g., name, phone number, email, medical record number) to be able to conduct follow-up interactions with the patient and/or their guardian and review the patient's visit history after discharge from the ED.

All follow up interactions, including chart review, phone follow-up (as needed), and data analysis will occur in a confidential location, specifically the PEM Fellows offices at Dell Children's Medical Center. The suite has individual offices, including a private office for the study coordinator, that ensures that phone conversations cannot be overheard, and data being assessed on a computer monitor cannot be seen by others.

39 **Confidentiality and Data Security Plan**

Provide general information below regarding confidentiality and data security plan. Provide additional details regarding how you will protect the confidentiality of data or address confidentiality concerns.
Include the following, as applicable:

- *If identifiers will be coded to protect confidentiality describe how and where identifiers are stored.*
- *Describe where and how data is stored and maintained.*
- *Include details regarding storage of consent forms, if applicable.*

Data will be stored in secure electronic databases. The survey database will be password protected and stored on a secure network. Data will be de-identified after the data preparation and collection stage. A unique ID number will be assigned to each subject included in the study. The PI will maintain a list correlating patient medical record numbers to the unique ID numbers in order to assist in quality control of the data. This file will be stored separately from any identifiable information. All data will be analyzed in a de-identified format. Upon study closure, identifiers will be destroyed. The data from this study may be published, but the subject identities will not be disclosed.

40 **Research Data/Records Destruction Details**

Confirm general research data/information (including consent forms, as applicable) destruction timeline. ***One of the following must be checked.***

☒ **Research Data/Records will be retained for 3 years after study completion per UT record retention policy.**

☐ **Research Data/Records will be retained for longer than 3 years and retention information is provided below.**

Describe data retention timeline below. To input text, click in the light grey area below.

41 Confirm identifiable data destruction details

One of the following must be checked.

☒ **Identifiable data will be destroyed.**

If checked, ensure the below section describes identifiable data destruction plan and timeline.

All identifiable data will be destroyed upon completion of the study. Consent forms will be retained according to federal law and University of Texas policy.

☐ **Identifiable data will not be destroyed.**

If checked, explain below the rationale for retaining identifiable data indefinitely.

42 Data Access

If you plan on creating a repository, complete the repository form as well.

☒ **Study Team Members** ☐ **External Collaborators** ☐ **Data coordinating center**

☐ **Sponsor** ☐ **Future Sharing with other researchers**

☐ **Others**

43 Describe data sharing plan for each group checked above and state whether researchers plan on sharing identifiable, coded, or de-identified data.

To input text, click in the light grey area below. Ensure that data sharing and future use is addressed in the consent form(s).

Only the PI and study coordinator will have access to identifiable information. The faculty advisor (also listed as study personnel) will assist with data analysis. Data will not be shared outside the study team.

44 Certificate of Confidentiality

Click on the check box (or double click and type an "X" if using Google Docs) to identify each element below that may require additional information to be disclosed in the consent form.

If a Certificate of Confidentiality is not applicable for this study, skip this section.

A ☐ **NIH has issued a Certificate of Confidentiality for this study.**

Ensure CoC language is included in the consent form(s).

B ☐ **A Certificate of Confidentiality has not been obtained, but there are plans to apply for one.**

Ensure appropriate CoC language is included in consent form(s). Apply for a CoC for non-NIH funded research here: NIH Certificate of Confidentiality System. Once CoC is granted by NIH, you must update the consent form language and ensure a copy of the CoC approval (only for non-NIH funded research) is uploaded to UTRMS-IRB.

COMPENSATION AND COSTS

45 **Compensation**

Click on the check box (or double click and type an "X" if using Google Docs). A or B must be checked.

A ☒ **Subjects receive compensation.**

i ☒ **Confirm: Amount of compensation and its form is reasonable for this population for the activities requested of them.**

ii **Total Amount of Compensation**

Include the total amount of compensation below.

$20

iii **Type of Compensation**

☐ **Cash** ☐ **Check** ☐ **Gift Card**

☐ **Course Credit** ☒ **ClinCard** ☐ **Tango Card**

☐ **Other**

Describe other form of compensation below.

N/A.

iv **Proration Schedule**

Describe the proration schedule for multi-visit/session studies. Skip if not applicable.

ClinCards will be mailed to the participant upon completion of post-study phone interview and receipt of post-study questionnaire.

B ☐ **Subjects will not receive compensation.**

46 **Costs**

A or B must be checked.

A ☐ **Participants will have no costs associated with this study**

B ☒ **Participants will have the following costs associated with this study.**

☒ **Standard of care procedures contributing to study data**

☐ **Research procedures not associated with standard of care**

☐ **Administration of drugs / devices**

☒ **Study drugs or devices**

☐ **Transportation and parking**

i **Describe all costs below.**

To input text, click in the light grey area below.

Patients or their insurance will be required to cover the cost of the visit as part of usual care. Uninsured patients will be given the option to enroll in Medicaid prior to discharge to minimize this cost. The cost of saline (normal or hypertonic) is included in the cost of usual care.