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Pilot Study to Identify the Feasibility of Measuring Hydration Status Utilizing Bioelectrical Impedance Analysis in Children with Sickle Cell Anemia

Teresa Anne Shurley

PILOT STUDY TO IDENTIFY THE FEASIBILITY OF MEASURING HYDRATION STATUS UTILIZING BIOELECTRICAL IMPEDANCE ANALYSIS IN CHILDREN WITH SICKLE CELL ANEMIA

by

Teresa Anne Shurley

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ABSTRACT

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Vaso-occlusive pain crisis is the hallmark complication of sickle cell anemia and may be precipitated by low hydration status. The purpose of this pilot study was to 1) identify the feasibility of measuring hydration status utilizing bioelectrical impedance analysis in children with SCA and 2) determine if sodium and fluid intake can be assessed in patients with SCA utilizing a 24 hour food recall. Ten children between the ages of 5 and 17 who have sickle cell anemia were evaluated to determine total body water, fluid intake, sodium intake and impact of temperature and humidity on pain crisis, hospitalization and use of pain medication. Despite lower than average total body water, low fluid intake, high sodium intake and temperatures above 80 degrees, participants did not present with pain crisis; therefore, temperature, humidity, total body water, fluid intake and sodium intake had no effect. Bioelectrical impedance analysis does seem to be a viable measure of total body water, however 3 day food records may be better suited to assess sodium and fluid intake in place of 24 hour recall.

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CHAPTER 1

REVIEW OF LITERATURE

Introduction

Sickle cell disease is an inherited condition of chronic hemolytic anemia that includes several hemoglobin (Hb) variants. HbSS is an autosomal recessive genetic disorder characterized by the predominance of hemoglobin S rather that the normal hemoglobin A in red blood cells (1). The change from hemoglobin A to hemoglobin S results in sickle-shaped red blood cells in place of the usual donut-shaped bi-concave disks which are commonly identified as HbSS. Other forms of sickle cell disease are named according to the specific type of hemoglobin by which they are characterized; Sickle cell hemoglobin C disease SC (SCD-SC), sickle cell B thalassemia zero (SCD-SB^0thal), and sickle cell B+ thalassemia (SCD-SB^+thal) (2). HbSS is the most common and severe form of sickle cell disease, affecting 1 in 600 African Americans in the United States (3).

Individuals with sickle cell disease suffer many complications; two primary manifestations are chronic hemolytic anemia and vaso-occlusion (1). Hemolytic manifestations of the disease include chronic anemia, jaundice, aplastic crisis and gallstones. Vaso-occlusion manifestations include recurrent acute pain or vaso-occlusive pain crisis (VOC), the absence of normal spleen function, acute chest syndrome, stroke, hyposthenuria and enuresis, chronic nephropathy, priapism, avascular necrosis, proliferative retinopathy and leg ulcers (3). Vaso-occlusion pain crisis is the most common reason for hospitalization in sickle cell

patients. Management of vaso-occlusive pain is largely supportive including providing fluid and analgesics and encouraging patients to rest (1).

Vaso-occlusion Pain Crisis

The hallmark complication of sickle cell disease is vaso-occlusive pain crisis. VOC develops when sickled red blood cells are inflexible becoming lodged in the vessel, resulting in obstruction of blood and damage to surrounding tissues and organs. Complexity of a vaso-occlusion pain crisis varies from patient to patient and in degrees of pain, crisis duration can last for 5 minutes, to several hours to several days or months (4). Pain sites vary for each patient, although, it tends to recur at the same location for a particular patient (5). In general, the lower back is the most common pain site and long bones and joints are also frequently affected (6). In children under the age of 2, swelling of the hands and feet (dactylitis) is very common, as opposed to the classic VOC episodes of pain (7). Reports indicate that some 34% of patients experiencing one or fewer VOC's per year and another 5% experiencing multiple events, accounting for 30% of SCD hospitalizations. In a prospective longitudinal and observation cohort study of adult patients, Ballas et al (6) determined the average length of stay for a pain episode to be 7.5 days and 50% of hospital admissions required readmission within 1 month after discharge. In this study the causes of hospital readmission included premature discharge, withdrawal syndrome, and recurrence of new acute episodes. For children the average length of stay was 4.4 days. Age was found to greatly influence the length of stay. In a single-center study by Frei-Jones et al. approximately 30% of pediatric

pain admissions resulted in readmission with the greatest risk factor for readmission being no outpatient hematology follow-up within 30 days of discharge. A small minority of patients have severe pain almost chronically (8).

Several types of pain crisis episodes have been noted; pain from an area of occlusion with no hematological changes, pain associated with bone marrow hypoplasia, high fever resulting in red blood cell count destruction, sudden and massive red cell blockage in the visceral organs especially the spleen, or manifestations of one or more crisis at one time (4).

Pain crisis episodes have been classified into four definable phases. Prodromal phase can last 1 to 3 days involving no pain but a combination of fatigue, jaundice, weakness, nausea, change of appetite and paresthesias. The beginning or evolving phase can last 1 to 2 days with pain at a mild to moderate level. The accelerated or peak phase can last 3 to 7 days with severe pain described as unrelenting and unbearable. The resolving phase can last 1 to 3 days and results in a gradual decrease in pain (9).

Although vaso-occlusion pain crisis is not fatal, it can lead to unnecessary suffering and potentially life threatening complications (10). Patients are often counseled to avoid certain factors that may lead to vaso-occlusion pain crisis including cold, infections, physical exertion or tiredness, stress and worry, dehydration, pregnancy, alcohol consumption (4). A 1980 study by Vichinsky and Lubin found low hydration status, weather changes, and low body temperature to be the most common factors leading to pain crisis (11).

Variables that Impact VOC and Pain Crisis

Weather

Chronic pain sufferers frequently report pain is affected by changes in the weather. Jamison, Anderson and Slater found 68% of chronic pain patients believed pain increased with weather changes (12). Cold and damp conditions were ranked as the highest influence of pain crisis. A possible theory for the influence of weather is the equilibrium the body establishes in relation to climate. Any change in the climate upsets the equilibrium and increases the incidence of pain (12). Another study found the body adjusts to decreases in ambient temperatures by increasing thermogenic factors suggesting an association between pediatric pain crisis and weather conditions. Researchers found a significant correlation between colder temperatures and humidity with the number of pain crises reported (13).

Although very few studies have addressed the effects of weather on VOC pain crisis it is another aspect which is worth reviewing. Weather can contribute to hydration status which can possibly affect pain crisis. In a study addressing temperature changes and extremes related to emergency visits and hospitalizations for sickle cell crisis done by Smith et al. (1) it was determined that temperatures <32º F and >80º F had positive correlations with hospital admissions that were statistically and clinically significant. Another study which looked at weather and hospital admissions for pain crisis conducted by Jones and colleagues concluded that high wind speeds and low humidity contribute to an increased number of pain crisis hospital admissions. High wind speed and

low humidity may also be associated with increased fluid loss through sweating (14).

Hydration, Oral Fluid and Sodium Intake

Proper hydration is an important factor in maintaining homeostasis in the body, it is necessary to regulate body temperature, maintain energy levels, aid digestion and eliminate toxins. In an adequately hydrated person, overall total body water accounts for 55-65% of overall body weight (15). Poor hydration increases the thickness or viscosity of blood. Even mild dehydration can have an impact on hemoconcentration (16). In sickle cell disease dehydration can occur for a number of reasons, including but not limited to diarrhea, severe vomiting, excessive sweating or inadequate fluid intake.

Hydration status can also be linked to dietary intake of fluids and sodium. Sodium regulates both intracellular and extracellular fluid levels impacting hydration. High sodium intake results in the movement of water across the cell membranes, causing cellular dehydration. Therefore, a moderate intake of dietary sodium in sickle cell patients may prove beneficial in preventing intracellular fluid deficits. An additional benefit of hydration was noted in a study by Beyer and Simmons who found when sickle cell patients increased fluid intake as a comfort measure, vaso-occlusion pain was decreased (17).

A study conducted at St. Jude Children's Research Hospital looked at a relationship between dietary intake of water and sodium in patients with sickle cell disease. Researchers found water intake was significantly lower than

adequate while sodium intake was significantly higher than sodium upper limit (18).

There is a deficit in the amount of information on hydration status and the role both dietary water and sodium play in the incidence of VOC and pain crisis in children with SCD or SCA. Studies have suggested that proper hydration can aid in the prevention and treatment of sickle cell pain crisis. This information could help determine if proper hydration may prove to be a simple treatment option, or an adjuvant of other anti-sickling therapies. Diet plans including proper energy, protein, and fluid needs can be created to minimize the risk of pain crisis. The purpose of this pilot study is to: 1) identify the feasibility of measuring hydration status utilizing bioelectrical impedance analysis in children with SCA and 2) determine if sodium and fluid intake can be assessed in patients with SCA utilizing a 24 hour food recall. The results will be used to help determine if further research is warranted.

CHAPTER II

METHODS

Subjects

Ten children between the ages of 5 and 17 who have sickle cell anemia (Hgb SS or Hb Sβ^0-thalassemia) and being treated and/or followed by St. Jude Children's Research Hospital were recruited from St. Jude Children's Research Hospital Sickle Cell clinics. The subject's physician or designee reviewed the study with the subject and caregiver to determine if the subject and caregiver or legal guardian were interested. Subjects and/or caregivers interested in participating in the study contacted the study investigator at The University of Memphis to set up an appointment.

The study was approved by the Institutional Review Board of the University of Memphis and review was waived by St. Jude Children's Research Hospital. Review was waived since St. Jude Children's Research Hospital was only recruiting. Informed consent was obtained. All research was conducted at The University of Memphis Human Performance Lab.

Inclusion Criteria

Inclusion criteria consisted of the ability to lie still for up to five minutes, as well as the ability to fast for 12 hours prior to the completion of bioelectrical impedance analysis (BIA). Subjects were asked to provide details of food and fluid intake for the past 24 hours, and details on pain crisis, hospitalizations or use of pain medicine 2 weeks prior to the BIA and 2 weeks after the BIA.

Exclusion Criteria

Subjects excluded from analysis were those who were using diuretics or other medications that can alter hydration status. Any subject or caregiver who was unwilling or unable to sign consent was also excluded.

Total Body Water Analysis

BIA was performed on all subjects to access total body water. Subjects were asked to remove their right shoe and sock then lie supine with both arms 30 degrees from the body and legs not touching. Jewelry was also removed. The right hand and foot were both cleaned with alcohol before electrodes were positioned. Subjects were asked to lie still while the analyzer was turned on and the test was conducted. After completion, the electrodes were removed and disposed. Data was entered into RJL Systems Body Composition Program, Version 2.1.

Nutrient Analysis

A 24 hour food and fluid recall was obtained by the study investigator to assess sodium and fluid intake. The quantity and time of day the food was consumed, and the name brand of the food if convenience or processed was obtained. Fluid and sodium amounts were analyzed using ESHA Food Processor Diet Analyzer and compared to the United States Department of Agriculture (USDA) Dietary Reference Intake (DRI) for children ages 5 to 17. Not included in the analysis was sodium added to the food by the subject before consumption.

Weather Analysis

All studies were performed before 10 am in an effort to not prolong the fasting period. At the time BIA was conducted, the temperature and humidity was obtained and recorded from the National Weather Service website (weather.gov) specific for the zip code at The University of Memphis.

Pain Crisis Analysis

Subjects and legal guardians were asked to recall and report all painful events, hospitalizations and use of any pain medication by the subject within 2 weeks prior of the BIA examination. A follow-up phone call was made to subjects and/or legal guardians to access any painful events, hospitalization and use of pain medication by the subjects 2 weeks after the BIA examination.

Data Analyses

Statistical analyses were performed using SPSS version 20 for Windows (SPSS Inc., Chicago, IL, USA). The *t* test for independent variables was used to compare the single measurements between genders. The independent variables were subject total body water, total body water average for children 5 to 17, subject sodium intake, RDI for sodium intake, subject fluid intake, and fluid requirements per the Holliday Segar equation. The significance testing and reported *p* values were two-sided for all variables. *P* less than 0.05 were considered statistically significant.

Compensation

After completion of the BIA, subjects received a snack. The caregiver or legal guardian received travel compensation of $50.00.

CHAPTER III

RESULTS

Patient Demographics

Ten subjects between the ages of 5 and 17 who have sickle cell anemia (Hgb SS or Hb Sβ^0-thalassemia) were enrolled in the study. Seven females and three males with a mean age of 11.3 completed the study. None of the subjects reported painful events, hospitalizations nor use of any pain medication within 2 weeks prior of the BIA examination or 2 weeks after the BIA examination. No subjects were excluded from the study.

Total Body Water (TBW)

The mean total body water for males without sickle cell anemia between the ages of 5 to 17 is 38.1 liters. The mean total body water for females without sickle cell anemia between the ages of 5 to 17 is 30 liters (19). In this study, the total body water (Table 1) mean was 21.82 liters $\pm$ 5.6 liters, with a minimum of 14.4 liters and a maximum of 28.7 liters TBW. The mean total body water for males in this study was 24.73 liters. A 13.4 liter TBW deficit or 65 % of the mean TBW of same age male children without sickle cell anemia. The mean total body water for females in this study was 20.57 liters. A 9.4 liter TBW deficit or 69% of the mean TBW of same age female children without sickle cell anemia.

Table 1. Total body water (TBW) of pediatric sickle cell anemia subjects versus pediatric non-sickle cell anemia of same age group.

Subject	Gender	Age	TBW SCA Subjects (L)	Mean TBW non-SCA (L) *	Difference (L)	Std Dev
1001	M	9	22.6	38.1	15.5	10.96
1002	F	6	14.4	30.0	15.6	11.03
1003	F	7	15.9	30.0	14.1	9.97
1004	F	17	28.7	30.0	1.3	.919
1005	M	13	26.0	38.1	12.1	8.56
1006	F	12	24.7	30.0	5.3	3.75
1007	F	10	15.0	30.0	15.0	10.6
1008	M	13	25.6	38.1	12.5	8.84
1009	F	17	28.0	30.0	2.0	1.41
1010	F	9	17.6	30.0	12.4	8.77

*RJL Systems BIA analysis

Fluid Intake

Fluid intake (Table 2) mean was 51.1 ounces $\pm$ 23.3 ounces, with a minimum intake of 24 ounces and a maximum intake of 90 ounces fluid. Males consumed a mean of 54.33 ounces fluid while females consumed 49.71 ounces of fluid, a non-significant difference of $P = 0.792$.

Baseline fluid requirements in children is 1500 ml for the first 20kg plus 20ml/kg for each kg over 20 kg (20). The average weight in the male group was 40.5 kg and the average weight in the female group was 39 kg. Using the average weight, baseline fluid requirement for the male group is 1910 ml or 64.6 ounces and the baseline fluid requirement for the female group is 1880 ml or 63.6 ounces. The mean fluid intake of the male group was 54.33 ounces fluid

while females consumed 49.71 ounces of fluid, considerably lower than baseline fluid requirements.

Table 2. Fluid intake of pediatric sickle cell anemia subjects versus pediatric recommendations using the Holliday-Segar method.

Subject	Gender	Age	Fluid Intake (oz)	Recommended Fluid Intake (oz)*	Difference (oz)	Std Dev
1001	M	9	90	61	29 (over)	20.5
1002	F	6	38	51	13	9.19
1003	F	7	88	53	35 (over)	24.7
1004	F	17	24	74	50	35.4
1005	M	13	31	68	37	26.1
1006	F	12	60	66	6	4.24
1007	F	10	44	60	16	11.3
1008	M	13	42	75	33	23.3
1009	F	17	32	72	40	28.3
1010	F	9	62	57	5 (over)	3.54

*First 20kg = 1500ml + 20ml per kg over first 20kg

Sodium Intake

Sodium intake (Table 3) mean was 2.4 grams $\pm$ 0.9 grams, with a minimum intake of 1 gram and a maximum intake of 3.9 grams sodium. This recorded sodium intake does not account for sodium added while cooking or before consumption.

Mean sodium intake in the male group was 2.7 grams. The mean sodium intake in the female group was 2.3 grams with non significance of $P = 0.511$.

The USDA dietary reference intake of sodium for children between the ages of 5 and 17 is 1.2 to 1.5 grams a day. The mean average of sodium intake for the male group was 2.7 grams. The mean sodium intake in the female group

was 2.3 grams. Both groups consumed a considerably larger amount of sodium than recommended.

Table 3. Sodium intake of pediatric sickle cell anemia subjects versus pediatric dietary reference intake.

Subject	Gender	Age	Sodium Intake (gm)	DRI Sodium (gm)+	Difference (gm)	Std Dev
1001	M	9	3.9	1.5	2.4	1.70
1002	F	6	2.5	1.2	1.3	0.92
1003	F	7	1.1	1.2	- 0.1	0.07
1004	F	17	1.3	1.5	- 0.2	0.14
1005	M	13	1.9	1.5	0.4	0.28
1006	F	12	3.3	1.5	1.8	1.27
1007	F	10	3.3	1.5	1.8	1.27
1008	M	13	2.3	1.5	0.8	0.57
1009	F	17	1.9	1.5	0.4	0.28
1010	F	9	2.4	1.2	1.2	0.85

+USDA Dietary Reference Intake

Temperature and Humidity

BIA was performed before 10 AM in the months of July and August. The mean temperature at the time of the study was 84.7 degrees $\pm$ 3.9 degrees. The mean humidity was 62.8% $\pm$ 10.8 percentage points.

CHAPTER IV

DISCUSSION

Review of the literature has shown that VOC in children with SCA is largely controlled by fluid and analgesics. Pain crisis can be triggered by low hydration status and weather changes (11). The purpose of this pilot study was to: 1) identify the feasibility of measuring hydration status utilizing bioelectrical impedance analysis in children with SCA and 2) determine if sodium and fluid intake can be assessed in patients with SCA utilizing a 24 hour food recall.

There are several ways to test total body water, including laboratory based tests and predication equations. Predication equations are based on various calculations taking into consideration maturation, ethnic background or specific medical conditions (19). BIA is inexpensive, rapid, can be conducted in various locations including hospital bedside or in a clinic and noninvasive (16). In a population, where hydration status may have an impact on pain crisis, BIA may be a viable way to access fluid. Subjects were able to lie still and follow all necessary procedures to complete BIA.

BIA results show the study population has a deficit of total body water by a mean of 10.6 liters when compared to non-SCA children in the same age group. Poor hydration increases the viscosity of the blood and can impact hemoconcentration resulting in VOC pain crisis (16).

It is well documented that hydration status is linked to dietary intake of fluids and sodium. Dietary intervention to limit sodium and increase fluid intake may be necessary in pediatric sickle cell patients. Dietary recall in this study

showed not only was fluid intake below recommended levels and sodium levels were above dietary recommendations, but the fluid becoming consumed was high in sodium content (sodas, and electrolyte-containing beverages). A study conducted by St. Jude Children's Research Hospital looking at the relationship between dietary intake and sodium in patients with SCA also found water intake to be significantly lower than adequate while sodium intake was significantly higher than sodium upper limits (18).

A study conducted by The University of Minnesota, found 24 hour recall to be a valid method for assessing dietary recall in children as young as 8 years of age (21). The 24 hour recall conducted in this study could not account for sodium added during cooking or added before consumption.

Contrary to lower than average total body water, high sodium intake and low fluid intake, none of the subjects presented with pain crisis, hospitalizations or use of medications 2 weeks prior and 2 weeks after the BIA. This result is confounding based on information found by Vichinsky and Lubin that low hydration status is a common factor leading to pain crisis in SCA (11).

Limitations

Limitations include having a limited sample size, using 24 hour recall to assess dietary intake, and the short study period. Having a limited sample size may not have given enough data to accurately assess pain crisis, hospitalization and use of pain medication in relation to low total body water, fluid intake, sodium intake and weather changes. Using 24 hour food recall may not accurately represent actual dietary intake since it is based on a person's recollection of what

food and beverage was consumed, not taking into account preparation or items that may be forgotten during the recall. As stated earlier, recorded sodium intake is lower than actual based on inability to account for added sodium during cooking or before consumption. A study period of 2 summer months could not account for humidity or temperature changes below 32 degrees or higher than the recorded mean of 84.7 degrees. Future studies may benefit from a higher number of participants, a longer research/study period, and monitoring sodium and fluid intake in both a control and test group while also using a 3 day food record completed by the participants.

Conclusion

The hallmark complication of sickle cell disease is vaso-occlusion pain crisis associated with hematological changes. Maintaining adequate fluid status may aid in the prevention of blood viscosity increases which precipitates the obstruction of blood flow leading to pain crisis (17). In this study, participants did not present with pain crisis, therefore, temperature, humidity, total body water, fluid intake and sodium intake had no effect. Additional research still needs to be done to determine whether total body water, sodium and fluid intake, and humidity and temperature changes are associated with increased VOC pain crisis in children with SCA. Bioelectrical impedance analysis does seem to be a viable measure of total body water, however 3 day food records may be better suited to assess sodium and fluid intake in place of 24 hour recall.

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APPENDIX A

Data Collection Form

Study ID_____

Phone_____

BIA_____

Pain Crisis (two weeks before accessed in person):_____

Pain Crisis (two weeks after accessed via phone): _____

Taken any of the following medications within those weeks:

- ☐ Motrin (other names, ibuprofen, advil, etc)
- ☐ Tylenol #3
- ☐ Percocet
- ☐ Morphine
- ☐ Oxycodone
- ☐ Lortab

Other_____

24 Hour Recall: Fluid:_____

Sodium:_____

Temperature (at time of BIA):_____

Humidity (at time of BIA):_____

APPENDIX B

SICKLE CELL DEHYDRATION STUDY

Dehydration in patients with sickle cell anemia can lead to pain crisis. Dehydration can be caused by not drinking enough fluids or by sweating a lot. Researchers from The University of Memphis would like to do a research study that will look at the amount of fluids children with sickle cell anemia drink every day and how it relates to the amount of fluid in the body.

Who can be on the study?

- Children between 5-17 years old who have sickle cell anemia being treated at St. Jude Hospital.
- English speaking
- Willing to participate and come to the University of Memphis one time to do the tests.

What will I have to do?

- Using bioelectrical impedance, a body analysis test will be done. This will take less than 5 minutes. You will not feel any pain or have any strange skin sensation. You will be lying down for the test.
- Record pain crisis for 2 weeks before and 2 weeks after the test.
- Describe what you ate and drank on the day before the test.

What are the risks?

- There are no risks related to the bioelectrical impedance body analysis test.

What are the benefits?

- You will help us learn about dehydration in patients with sickle cell anemia.

How do I participate?

- Contact Ruth Williams at 901-734-8132 or Teresa Shurley at 818-414-5915 to set up an appointment.

You will receive a snack bag and $50 for your time and travel expenses.

APPENDIX C

Consent to Act as a Human Subject

Title of Investigation: Pilot Study to Identify the Feasibility of Measuring Hydration Status Utilizing Bioelectrical Impedance Analysis in Children with Sickle Cell Anemia

Principal Investigator: Teresa Shurley 818-414-5915

Co-Investigators: Ruth Williams, MS, RD, EdD 901-734-8132

University of Memphis Institutional Review Board 901-678-2533

A. Purpose

The purpose of this study is to conduct a pilot study to 1) identify the feasibility of measuring hydration status utilizing Bioelectrical Impedance Analysis in children with SCA and 2) determine if patients with SCA will be able to keep a food log to assess sodium and fluid intake.

B. Study Design/Method

Once you agree to participate and sign the consent/assent forms, the researcher will conduct the following tests:

1. BIA (Bioelectrical Impedance Analysis) will be done once to look at body composition including fluid.

2. Subjects and legal guardian will be asked to recall and report all painful events, hospitalizations and use of any pain medication within 4 weeks (2 weeks prior and 2 weeks after the BIA examination.

3. Subjects of if the subject is limited by age the legal guardian will be asked to give a 24 hour food and fluid recall to assess sodium and fluid intake on the day BIA is obtained. Data will be entered into a nutrition software system.

4. Record high and low temperature and humidity at time of BIA.

C. Inclusion Criteria

1. All children between the ages of 5 and 17 who have sickle cell anemia Hgb SS or Hb Sβ°-thalassemia and being treated/followed by SJCRH.

2. All subjects must be able to lie still for 4-5 minutes.

3. Subjects must be able to fast for 12 hours before BIA is completed.

4. English – speaking and able to understand English items on the study instruments as these are only available in English.

5. Subjects willing to give assent to participate in the study and whose legal guardians are willing to give consent according to institutional guidelines for their child to participate.

6. Subjects willing to complete the study at the University of Memphis.

7. Subjects/legal guardians willing to provide transportation to the University of Memphis.

D. Exclusion Criteria

1. Inability or unwillingness of subject or legal guardian/representative to give written informed consent.

E. Off Study Criteria

1. Completed study.

2. Subject requests.

3. Subject does not return for appointment.

Patient Compensation

After completion of the study, subjects will receive a snack and the legal guardian will receive travel compensation of $50.00.

F. Alternative Procedures or Treatment

If any abnormal signs or symptoms are present during your child's participation, the testing will be terminated and you will receive immediate attention. Otherwise, no treatment will be provided.

G. Confidentiality

Your child's privacy will be protected during all aspects of data collection within the limits allowed by law. Your child will not be identified by name as a participant in any written materials. All materials will be kept in a file cabinet in a locked office when not being used by investigators. Following all analyses, all materials associated with individual subjects will be shredded.

H. Questions Regarding Research

Questions regarding the research itself or research-related injuries can be directed to Ruth Williams. You and your child are encouraged to ask questions not only at the time of signing the informed consent form, but throughout your child's participation as a research subject. Any new information that develops during the research will be provided to you if the information might affect your child's willingness to continue participating.

I. Voluntary Participation

Your child is free to refuse to participate or to withdraw consent to participate in this research at any time without prejudice. Participation is entirely voluntary.

J. Questions Regarding Subjects' Rights

Questions regarding research subjects' rights can be directed to the University of Memphis Institutional Review Board Administrator by email irb@memphis.edu and/or phone 901-678-2533.

You and your child have been given the opportunity to ask questions regarding participation, and all questions have been answered to your satisfaction. By signing this form, you are agreeing your child will participate in the research as described to you.

Subject Signature	Date
Subject Printed Name	
Legal Guardian Signature	Date
Legal Guardian Printed Name	
Phone	
Email	
Witness to Signature	Date

APPENDIX D

24-Hour Food Collection Form

Time Consumed	Food Item	Quantity (oz, cups)

APPENDIX E

Bioelectrical Impedance Analysis Informational Handout

- BIA is a safe and fast method to measure how much water is in your body.
- The entire process takes less than 5 minutes and completely painless.
- Your child will be asked his/her height and weight.
- Your child will need to remove his/her right shoe and sock.
- Your child will be asked to lay flat on his/her back on a flat surface for approximately 1 minute.
- Small items called electrodes will be put on one hand and one foot.

APPENDIX F

Assent Form

Your parent knows we are going to ask you to participate in this study. We want to know about pain crisis and the amount of fluid in your body. It will take 5 minutes to complete the task. Your name will not be written anywhere on the project paperwork. No one will know you are part of the study. If you do not want to participate, you can stop at any time. There will be no bad feelings if you do not want to do this. You can ask questions if you do not understand any part of the study.

Do you understand? yes or no

Is this OK? yes or no

Name (Please print): _____

Signature: _____

Date: _____

Investigator's Signature: _____

Date:_____