A Randomized Trial of Targeted Temperature Management with Whole Body Hypothermia for Moderate and Severe Neonatal Encephalopathy in Premature Infants 33-35 Weeks Gestational Age - A Bayesian Study

NCT01793129

Informed Consent Form

October 19, 2016

Informed Consent Statement for:

Preemie Hypothermia

Your baby is invited to participate in a research study of the possible benefits of whole body cooling. Your baby was selected as a possible subject because he or she was born prematurely at 33 to 35 weeks gestational age (GA), and has been evaluated and diagnosed with a condition called Neonatal Encephalopathy (NE).

Before you decide whether or not to allow your baby to participate, it is important for you to understand why this research is being done and what participation in the study involves. Please take time to read the following information carefully, and discuss it with relatives, friends and others if you wish, but please understand that the research procedures must begin before your baby is 6 hours old. If you have any questions at all about this research, please do not hesitate to ask us.

Investigator

Location

Telephone

Protocol Title
A Randomized Trial of Targeted Temperature Management with Whole Body Hypothermia for Moderate and Severe Neonatal Encephalopathy in Premature Infants 33-35 Weeks Gestational Age – A Bayesian Study

This study is sponsored by the *Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)*, which is part of the National Institutes of Health (NIH), and is being conducted at XXXXX by XXXXX (name of site and PI).

What is Neonatal Encephalopathy?

Neonatal Encephalopathy is a serious condition which usually occurs when too little blood flows to the brain and too little oxygen is provided to the brain, and is usually caused by problems around birth. Infants with NE have a high chance of brain injury and long term developmental problems, and death. Unfortunately, for premature babies who develop NE, there currently is no treatment to prevent or reduce the severity of brain injury.

How cooling is used:

In many hospitals, body cooling (hypothermia) is used as standard therapy for full-term babies born near their due date (at least 36 weeks GA) who are diagnosed with NE when less than 6 hours old. These full-term babies are cooled by using a special blanket to decrease their body temperature to 33-34°C (91.4-93.2°F) for 72 hours. Mildly decreasing the body's temperature (body cooling) has been shown to be an effective way to prevent and reduce the severity of brain damage in full-term babies with NE. In these babies, body cooling has reduced the number of deaths and the amount of serious disabilities when the babies are evaluated at the age of 18-22 months and at 6-7 years.

While this treatment has been shown to be effective in full-term babies, it is currently experimental in premature babies, like yours, born at 33 to 35 weeks GA.

WHY IS THIS STUDY BEING DONE?

The benefits and risks of using this cooling treatment on premature babies born at 33 to 35 weeks GA are not understood. We are doing this research study to learn whether cooling treatment for 72 hours is helpful in reducing death and improving outcomes for premature babies like yours born at 33-35 weeks and diagnosed with NE before being 6 hours old.

There are two main purposes for this study:

1) To determine whether body cooling is an effective treatment for reducing the risk of death or disability in premature babies who develop NE compared to similar babies who are treated using normal body temperature.

2) To monitor the safety of body cooling when given for 72 hours compared to infants maintained at a normal temperature.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

If your baby is eligible and you agree for them to participate they will be one of approximately XXX babies enrolled nationally. This site plans to enroll XX subjects.

WHAT WILL HAPPEN IF MY BABY TAKES PART IN THIS RESEARCH?

If you choose to allow your baby to participate in this research, they will be randomly assigned to one of two groups, with an equal chance of being assigned to either group.

Group 1	Body Cooling	33-34°C (91.4-93.2°F) for 72 hours
Group 2	Control Group (No Cooling)	Normal temp of 36.5-37.3°C (97.7 - 99.1°F)

Cooling Group

If your baby is assigned to the body cooling group, they will be placed on a blanket designed to gradually lower their body temperature. This blanket is currently used in children's hospitals as a way to cool babies and children during some types of surgery and, as described previously, is also used to provide cooling for full-term babies diagnosed with NE. Your baby's temperature will be kept at or around 33.5°C (92.3° F) for 72 hours. The temperature will be measured by inserting a narrow tube through your baby's nose or mouth into the esophagus (the part of the body that connects the mouth to the stomach) and placed just above the stomach. Your baby's skin temperature will also be checked regularly, and they will continue to receive all other standard NICU care during the study. If any problems occur, standard treatments will be given. At the end of the 72 hours of cooling, your baby will be slowly re-warmed until a normal body temperature is reached. Body cooling will be stopped if anything unexpected happens related to the low temperature. It will also be stopped if your baby needs ECMO (extracorporeal membrane oxygenation – which is a machine that provides oxygen to the blood when the lungs and heart are not working properly), or if your baby's neonatologist determines that they should no longer participate for any other reason.

Control Group

Infants who have been assigned to normal body temperature (control group) will be cared for according to their clinical condition and will receive all standard NICU care. If any problems occur, standard treatments will be given just as they would if your baby were not in the study. Infants in this group will also have their temperature measured with the goal of keeping a normal temperature of 36.5-37.3°C (97.7 -99.1°F). Temperatures of the skin and esophagus will be measured like the cooling group, until the temperature is in the normal range for 4 hours.

Both Groups

Infants in both groups will undergo a head ultrasound (which uses sound waves to create an image of the brain, similar to the ultrasounds you received of your baby during pregnancy) at their bedside within 24 hours of enrolling in this study. No special medications are required for this procedure. A brain MRI (which uses magnetic waves to create an image of the brain) will also be performed between 10-17 days after birth. Based on previous experience, we expect that no more than 10% of infants undergoing brain MRI may require sedation (drugs to make them fall asleep). The MRI studies may be sent to experts outside this institution to be read, but steps will be taken so that these experts will not know the identity of your baby.

While the initial research procedures for this study will only last for 72 hours, we will continue to collect data about your baby throughout their stay in this hospital and at any other hospital that the infant is transferred to from this hospital before being discharged home. Some information about the pregnancy will also be collected.

Once your baby has been discharged, they will be scheduled for follow up (FU) exams in our neonatal follow-up clinic. These exams will take place when your baby is between 18-22 months old and will include neurologic, developmental, vision and hearing tests. This follow-up testing is a very important part of the study because it helps us understand how your baby is developing. If you are unable to have the study FU visit at our institution, we can arrange for the visit to be conducted at another center in the Research Network. We may contact you in the future if further FU after 18-22 months is needed.

WHAT ARE THE RISKS AND POSSIBLE DISCOMFORTS FROM BEING IN THIS RESEARCH STUDY?

Your baby is eligible for this study because she/he has NE and therefore is at high risk of death, brain injury (including bleeding in the brain), intestinal injury and harm to many other organs whether or not they participate in this study. However, there may be some additional risks that result from participation in this study.

Cooling Group

There are potential risks to your baby if they receive body cooling through participation in this study. These potential risks include problems with irregular heart rhythm; the formation of blood clots; acidosis (blood has too much acid); too low or too high blood sugar which can cause brain injury; pulmonary hypertension (too high a blood pressure between the heart and lungs) which can cause breathing problems; bleeding in the brain (particularly a form called intraventricular hemorrhage [IVH, for short]); intestinal injury (particularly a form called necrotizing enterocolitis [NEC, for short]) that sometimes requires surgery; blood clots; bleeding or skin breakdown; and death. These same problems may also occur without cooling because of lack of blood supply or oxygen to the body. It is also unknown if cooling might decrease some of these risks.

Although some studies have shown the potential risks of cooling are acceptable in relation to the benefits for full-term infants with NE, we do not know for sure if these risks and benefits are the same for premature babies like yours. There is a possibility that body cooling in premature infants may have more complications than when performed in term newborns.

Control Group

Some babies with NE may develop an elevated temperature in the first days of life. If this happens, treatment will be given which may include lukewarm sponge baths or placing your baby on a cooling blanket to keep his/her temperature within the normal range. Babies in this group will not be cooled below the normal temperature range.

Both Groups

In both groups, there is a small chance that placement of the temperature-monitoring tube into the esophagus could result in bleeding, a tear in the esophagus, the tube entering the windpipe, or infection. However, similar tubes are used frequently in sick premature infants and generally do not cause complications. Both the cooling and non-cooling groups are at risk for abnormally low or high blood sugar. Your baby will be watched closely and treated for any side effects that may occur.

As noted above, your baby will undergo an MRI by participating in this research. Some babies require medicines to make them sleepy (sedation) when having an MRI so we can make sure they are still enough during the procedure to get good images. Sedation may last for a number of hours after the MRI, and sometimes can cause pauses in breathing or very shallow breathing. Your baby will be carefully monitored during and after their MRI. If any problems arise as a result of the sedation, the medical team will correct them as soon as possible. MRI and ultrasounds are used frequently in babies with and without NE and are not known to have any negative effects on them.

Unknown Risks

There may be risks involved in taking part in this study that are not known to the researchers at this time. Some unknown risks may be learned during this study. If any new risks arise during your baby's participation in this study, you will be informed of them by the study personnel.

Confidentiality

Another risk of this study is loss of confidentiality or privacy. Every effort will be made to keep your child's medical record confidential. There will be no names or other identifiable information about you or your baby in any study report that may be published after the study is complete. Measures taken to protect your and your

baby's identity are described in the confidentiality section of this form.

WHAT ARE THE BENEFITS OF TAKING PART IN THIS STUDY?

Cooling Group

If your baby is assigned to the body cooling group of this research study, he or she may benefit from the cooling procedure. Body cooling has been found to reduce death, brain injury and disability resulting from NE in full-term babies when they were cooled within 6 hours of birth. We do not currently know if babies born earlier than 36 weeks, such as your baby, benefit from the cooling procedure. This study is being done for the purpose of determining whether babies born earlier than 36 weeks receive similar benefit. We cannot promise any benefits to your child.

Control Group

If your baby is assigned to the normal temperature group (control), they will not receive the cooling procedure, but the special blanket used for cooling may be used to prevent their temperature from getting too high above what is normal. There may be benefit to your baby by preventing an abnormally high body temperature from occurring.

Follow-up

Participating in the follow-up part of this study, when your baby is 18-22 months old, may benefit you and your baby by detecting potential developmental problems early so that treatment for them can be started as soon as possible. Information from this study may benefit other babies with NE in the future.

It is possible that your baby will not experience any of these benefits from participating in this study.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT ALLOW MY BABY TO TAKE PART IN THIS STUDY?

Rather than being in this study, you have the option to not allow your baby to participate and instead receive standard NICU care as determined by your baby's neonatologist. If you choose not to enroll your infant in this study, they will continue to receive the usual NICU care that your baby's doctor determines is needed.

WILL MY BABY'S MEDICAL INFORMATION BE KEPT PRIVATE/CONFIDENTIAL?

Efforts are made to protect all research subjects from the inappropriate use of their personal information. We will do everything we can to keep your and your baby's records confidential, but we cannot guarantee absolute confidentiality. Your or your baby's personal information may be disclosed if required by law. Your and your baby's identity will not be disclosed in reports in which this study may be published.

Access to information about you and your baby is restricted to the XXXXX (University Division of Neonatology) clinical research staff that is involved in this study. Clinical and research information is maintained in a locked filing cabinet in our clinical research office, and on secure computer hard drives. This office is protected by on-site security staff 24 hours a day, 7 days a week. Clinical information collected from your baby's chart for this study will be labeled with a coded study identification (ID) number. The key linking the code number with your baby's identity will be kept locked in a filing cabinet in our clinical research office, accessible only to appropriate research staff.

Coded information is maintained in password-protected computers in the same office, also accessible only to research staff. Coded information will be sent to the NICHD Neonatal Research Network's Data Coordinating Center at Research Triangle Institute (RTI) in Research Triangle Park, North Carolina. We will keep all research records that identify your baby confidential to the extent allowed by the law. The University Institutional Review Board (IRB), Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) may access these records.

A description of this clinical trial will be available on ClinicalTrials.gov, ID number NCT 01793129, as required by U.S. Law. This website will not include information that can identify you or your baby. At most, the website will include a summary of the results of this study. You can search this website at any time.

WHAT ARE THE COSTS OF TAKING PART IN THIS RESEARCH STUDY?

You will not be charged, nor will your insurance company be charged, for any test, treatment or visit that is done

solely for the purpose of this study. The parts of your baby's care that would normally be done as standard treatment, including (but not limited to) treatment with a mechanical ventilator, antibiotics, feeding by vein, or blood pressure medications, will be billed to you or your insurance company. The study will pay for all parts of your baby's care that are required only for the study.

WILL I BE PAID FOR TAKING PART IN THIS RESEARCH STUDY?

You will not be paid for your baby's participation in this study.

The cost of the neonatal follow-up clinic visit at 18 – 22 months of age will be covered by the study. If you live more than 50 miles from the neonatal follow-up clinic you may be compensated for the cost of travel expenses for the study follow-up visit. For patients living out of state, or at a distance where it's not feasible for return travel in one day, we will arrange for an overnight stay at XXXXX (the University Guest House or a comparable facility).

WHAT HAPPENS IF MY CHILD IS INJURED AS A RESULT OF TAKING PART IN THIS RESEARCH STUDY?

In the event of physical injury to your baby resulting from their participation in this research, necessary medical treatment will be provided to your baby and billed as part of their medical expenses. Costs not covered by their health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your baby's health care coverage. There is no program in place for other monetary compensation for such injuries. However, you and your baby are not giving up any legal rights or benefits to which you are otherwise entitled.

IS PARTICIPATION IN THIS STUDY VOLUNTARY?

Yes, taking part in this study is voluntary. If you decide to allow your baby to take part you are still free to withdraw them at any time and without giving a reason. Refusal to allow your baby to participate or the decision to withdraw them from this study will involve no penalty or loss of benefits to which they are otherwise entitled. If your baby doesn't take part, they can still receive all standard care that is available to them. This will not affect the relationship you or your baby has with their doctor or other staff, nor decrease the standard of care that your baby receives as a patient. If you decide to withdraw your baby from the study and they are in the cooling arm, they will be slowly re-warmed until a normal body temperature is reached.

New Information

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your baby's research doctor or other research personnel will tell you about it and discuss with you whether you want your baby to continue in the study. If you decide to withdraw your baby at that time, the research doctor will make arrangements for your baby's medical care to continue. If you decide to allow your baby to continue in the study, you will be asked to sign an updated consent form.

Right of Investigator to Withdraw Participants

The investigator can withdraw your baby from the study without your approval. Possible reasons for withdrawal include the availability of new information that indicates the risks of the study are greater than the benefits or if your baby develops a severe problem that requires the study procedures to be stopped.

IF I HAVE QUESTIONS OR CONCERNS ABOUT THIS RESEARCH, WHOM CAN I CONTACT?

If you have any questions about the study or complaints or concerns during the study, you can contact the investigator (Dr. ___), the co-investigators (Drs. ___ or ___) or their designees via the University Paging Operator: (xxx) xxx-xxxx, the University NICU (xxx-xxx-xxxx or the ____ NICU (xxx) xxx-xxxx 24 hours a day. If you think your baby may have been injured from being in this study, you can contact the same individuals.

Institutional Review Board

Contact the Institutional Review Board (IRB) if you have questions regarding your baby's rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University IRB may be

reached by phone at (xxx) xxx-xxxx or by e-mail at irb@xxxxx.edu.

We are always available to answer your questions. If you have any questions that come during this study, please be sure to ask us.

STATEMENT OF CONSENT

I confirm that I have read this parental Informed Consent document and have had the opportunity to ask questions. I will be given a signed copy of this form to keep.

I agree to allow my child to participate in this research study and authorize you to use and disclose health information about my child for this study, as you have explained in this document.

_____
Child's Name

_____
1st Parent/Guardian's Name

_____ _____
1st Parent/Guardian's Signature Date

_____
Relationship to Child for 1st Parent/Guardian

_____
Name of Person Obtaining Authorization and Consent

_____ _____
Signature of Person Obtaining Authorization and Consent Date