Intermittent Hypoxia and Caffeine in Infants Born Premature (ICAF)

CONSENT TO PARTICIPATE IN A RESEARCH PROTOCOL AND AUTHORIZATION TO USE PROTECTED HEALTH INFORMATION

NCT03321734

November 16, 2017

CHILDREN'S NATIONAL MEDICAL CENTER

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TITLE OF STUDY: INTERMITTENT HYPOXIA AND CAFFEINE IN INFANTS BORN PRETERM (ICAF Study)

PRINCIPAL INVESTIGATOR: Mary Revenis, MD. Department of Neonatology

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"You" refers to "You" or "Your child" throughout this document

INTRODUCTION: We would like to invite you to consider a research study at Children's National Medical Center. Before you decide if you would like to participate, we want you to know why we are offering this research study.

You are being asked to allow your baby to be in this research study because your premature baby was given the medication caffeine as treatment for his/her immature breathing in the neonatal intensive care unit (NICU). Participation in this study is voluntary. Refusal to participate will not result in any penalty or loss of benefits to which you are otherwise entitled. Please read the information below, and ask questions about anything you do not understand, before deciding whether to take part in this study.

This form gives you information about the study. A doctor will talk to you about the study and answer any questions you have. We encourage you to discuss this study with your family and anyone else you trust before making your decision. We will ask you to sign this form to show that you understand the study. We will give you a copy of this form to keep. It is important that you know:

- You do not have to join the study;
- You may change your mind and stop being in the study any time you want.
- If we make any important change to the study we will tell you about it and make sure you still want to be in the study.

Your child's doctor may also be an investigator in this research study. Being an investigator means your doctor is interested in both your child and the study. You may want to get a second opinion about your child being in the study. You can do so now or at any time during the study. Another doctor who is not an

investigator can give you a second opinion about your child being in the study. You do not have to agree to have your child be in this study even though it is offered by your child's doctor.

Children's National has a bilingual (English/Spanish) research participant and family advocate. The advocate, Dr. Tomas Silber, is here to answer your questions or concerns about taking part in this research. Dr. Silber does not work for the doctors who are doing this research and they do not pay him. He is here only to help and protect you during any research. You may contact Dr. Silber at any time. This can be done before you decide to take part in the research, during the study, or even after you finish the study. You can call Dr. Silber at 202-476-3066 or reach him by e-mail at tsilber@childrensnational.org.

PURPOSE OF THE STUDY

The purpose of the study is to learn whether longer treatment with caffeine, the medicine your baby is receiving to treat his/her immature breathing, is helpful to premature babies. Caffeine treatment is usually stopped before a premature baby goes home. We know that early caffeine treatment is safe, and studies have shown that early caffeine improves later lung and brain health.

We know that many babies born very early may continue to have immature breathing for several weeks after routine treatment with caffeine has ended. This immature breathing may cause brief drops in the oxygen levels in the blood. These drops in oxygen are usually too brief and too mild to be seen by your doctors or you. However, some studies suggest that these brief drips in oxygen may affect baby's later brain health. Continuing caffeine longer than it is usually used may decrease these episodes and might protect a baby's brain.

You are being asked to allow your baby to be in this study because your baby's doctors decided earlier in his/her NICU stay that he/she had immature breathing that needed to be treated with caffeine. Since your baby is now more mature, your baby's doctors plan to stop routine caffeine treatment in the next few days, as is usual practice. We want to find out if longer treatment with caffeine has additional benefits. For this study, we plan to record his/her oxygen levels continuously for 7 to 10 weeks (depending on age started) and continue caffeine for 7 to 10 weeks after it would have been ordinarily stopped.

WHAT WILL HAPPEN IN THIS RESEARCH STUDY?

If you agree to allow your baby to be in this study, we will do the following:

- When your infant has reached 33-36 weeks postmenstrual age (4-7 weeks before your due date) and the NICU physicians plan to stop caffeine in the next week, your baby will be connected to a machine (recorder) which will continuously record oxygen levels. This recorder will be very similar to the monitor you have already seen used for your baby in the NICU, except there will be no active alarms and no number displayed. An elastic band with a red light is placed around a finger, toe, or foot to connect your baby to the recorder. The location of the band connecting your infant to the recorder will be rotated at least every 12 hours to avoid pressure injury to the skin. Any other treatment or monitoring prescribed by your baby's doctor will continue as ordered. Your baby will remain connected to the recorder for 7 to 10 weeks, until he/she reaches 3 weeks past your due date. If your baby is sent home from the hospital before this age, you will be sent home with the recorder to continue recording of your baby's oxygen level until that date.

- The day after your baby's doctors decide to stop caffeine therapy, he/she will assigned by chance (like flipping a coin) to receive "study drug", which will be either continued caffeine at 10 mg/kg/day by mouth once per day, or an equal volume of placebo (a salt water solution which does not have any effect

on the body). There is an equal chance (fifty-fifty) of your baby being in either one of the two groups (caffeine or placebo). The decision about whether your baby will be assigned to the continued caffeine or placebo group will be made by a computer by a randomization program. Neither you nor your baby's doctors, nurses, or research staff will know which group your baby is in. However, if there is a medical emergency, the researchers and your doctors may be told which group your baby is in. When your baby reaches an age of 4 weeks before your due date, the same dose of study drug will be given twice per day rather than once because babies "use up" caffeine faster as they get older.

- After starting the study, we will collect 1 ml of blood (1/5 of a teaspoon) to measure chemicals in the blood that are seen with increased inflammation. When possible, this blood sample will be collected at the same time as other blood tests ordered by your baby's doctor to avoid needing an extra needle stick.

- We will also obtain a magnetic resonance imaging (MRI) test of your baby's brain, soon after the study begins. The MRI will be done while your baby is naturally sleeping and swaddled after a feeding.

- At 2 to 3 weeks before your due date or when your baby is being sent home from the hospital (whichever comes first) we will collect a second sample of the same volume of blood to measure the same chemicals, also typically done at the same time as any blood tests ordered by your baby's doctor when possible. Prior to your baby going home you will be taught how to use the recorder and how to five the study medication (caffeine or placebo).

- At this same time, we will also collect a small sample of saliva (spit) to measure the level of caffeine in your baby's body. This will not cause any discomfort. A second salivary sample for a caffeine level will be done at about 1-2 weeks after your due date (this can easily be collected at home if your baby has been discharged from the hospital).

- We will continue the study medicine (caffeine or placebo) until 2 weeks after your due date, and the recorder for one additional week (till 3 weeks after your due date).

- We will schedule a follow up visit for your baby within 2 weeks of stopping the study medication and the recordings. At that time, we will have you return the recorder, measure your baby's growth, and do another MRI exam of the brain, again while your baby is normally sleeping and swaddled.

After your one-time follow-up visit, we ask that we be allowed to continue to be in contact with you after the conclusion of the study by phone and/or mail so we may request additional follow-up in the future (this would be optional; please see Future Contact section below).

AMOUNT OF TIME TO COMPLETE THE STUDY

Your baby will be part of this study until reaching about 5 weeks after your due date. At study end, you will be asked to bring your baby back to the hospital one time.

NUMBER OF PEOPLE WHO WILL TAKE PART IN THE STUDY

We plan to study a total of 220 babies in 5 different hospitals across the country. We will enroll up to 88 subjects at Children's National Medical Center.

POSSIBLE RISKS AND DISCOMFORTS

If your baby is already on an oxygen recording monitor in the NICU, an additional recorder probe (band with red light) will need to be placed. If the band is not rotated every 12 hours, there is a risk of skin injury at the site of placement. When your baby is sent home with the recorder, you will be asked to keep

the recorder going for as much of the day and night as possible and to rotate the probe site every twelve hours.

Caffeine is a commonly used drug in the NICU and has very little side effects. Possible side effects (occurring in 1-5% of all infants taking caffeine) include increased heart rate, upset stomach, and restlessness. These effects are all temporary and resolve shortly after caffeine is stopped. Your baby has already received caffeine in the NICU and did not have any problems with side effects. There are no additional side effects expected from continuing caffeine longer.

The placebo has no effect on the body and no risks or benefits.

The blood draws can cause discomfort but participation in this research study may not cause your baby any additional discomfort. To minimize pain from blood draws, whenever possible, the blood draw for the study will be done at the same time your baby's doctor has ordered blood to be drawn. The blood draw will usually be done by heel stick. All interventions normally used in the NICU to minimize pain during blood draws (such as warming the heel before the blood draw, swaddling the infant prior to the blood draw, etc.) will be followed.

MRI exams of the brain are safe, and your baby will be monitored continuously during the test. Your baby will be naturally sleeping and swaddled to prevent movement, but no sedative medicines will be given. If your baby is unable to sleep during the exam, we will stop.

While all risks that we know about have been listed above, other risks about which we do not know may occur or be discovered during future studies. If we find that there was a risk to your infant that was not known at the time of your participation in the study, and the risk might have some effect on your infant's health, you will be informed.

POSSIBLE BENEFITS

All babies enrolled in the study will benefit from closer monitoring since a physician, or research nurse not involved in their care, will be in frequent contact with their families.

It has been shown that premature babies have an improvement in brain development when caffeine is used in the NICU. Continuing caffeine longer may add additional benefits to brain development; no benefit is certain.

As part of the study, we will perform 2 brain MRIs on your baby. The MRIs will be read by the hospital radiologists. Any important findings will be communicated to your doctors and to you.

New information gained from this study may help us to manage premature infants like your child better so that they have better long-term outcomes.

VOLUNTARY PARTICIPATION

There will be no penalty or loss of benefits to which you are otherwise entitled if you decide to withdraw from the study.

ALTERNATIVES

The alternative to being enrolled in this proposed study would be to continue with usual or routine care in the NICU after routine caffeine treatment has been stopped by your doctors, which typically occurs about 5-7 weeks before your due date.

WILL I BE PAID FOR MY BABY'S PARTICIPATION IN THIS STUDY?

As a thank you for participating, you will receive a gift card when you return for the one-time follow-up visit at study end.

WILL I HAVE TO PAY FOR ANYTHING?

There is no extra charge to you or your baby for participating in this study. You and/or your baby's health insurance will be billed only for the costs of medical care your baby would get even if he/she were not in this study.

CONFIDENTIALITY

We will keep your baby's medical records and treatment records of this study confidential. The federal government can review the study records and medical records to make sure we are following the law and protecting the children. Your medical record is confidential, but just like any medical record there are some exceptions under state and federal law.

Federal and state agencies, if they are required by law or are involved in research oversight, may access information about your child from this study including your child's health information. Such agencies may include the U.S. Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and the State Department of Public Health. Information collected about your child will remain in the study record even if your child later withdraws.

We understand that your baby's health information is personal. We are committed to protecting the privacy of that information. If you decide to be in this study, the researcher will get information that identifies your baby and your baby's personal health information. We will remove identifying information as soon as possible after we receive it by using a code number. The code number does not directly identify your baby. The main researchers will keep a link between your baby and the coded information. We will keep this link secure and in a locked location. Only the main researchers or selected members of the research team will have access to it.

Any information that can identify you or your baby will remain confidential. The research team will only give this coded information to others to carry out this research study. We will keep the link to your baby's personal information for the duration of the study, or about 5 years, unless you consent to future contact (see Future Contact below). After that, code numbers will be destroyed and the research data can never be traced to a patient (anonymous). We will keep the anonymous data indefinitely.

A description of this clinical research will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify your baby. At most, the Web site will include a summary of the results. You can search this Web site at any time.

We might use our research data and your child's blood or saliva (spit) samples in future studies. These future studies might be done by us or by other investigators. Before we use your child's data or samples, we will remove any information that shows you or your child's identity.

HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY

In 1996 the government passed a law known as The Health Insurance Portability and Accountability Act (HIPAA). This privacy law protects your individually identifiable health information (Protected Health Information or **PHI**). The privacy law requires you to sign an agreement so researchers can use or share your PHI for research purposes. This describes to you how information about you may be used or shared

if you are in a research study. It is important that you read this carefully and ask a member of the research team to explain anything you do not understand.

I authorize Dr. Mary Revenis and her research staff to use and disclose my PHI for the purposes described below. This authorization does not expire.

Protected Health Information that may be used and shared includes:

1. Information from the medical record that identifies your baby such as name, address, telephone number, date of birth, and other details about your baby
2. Information that relates to your baby's health or medical condition from the medical records
3. Information obtained from the study procedures outlined in this consent form, for example: things done to see if your baby can join the study such as physical exams, blood and urine tests, x-rays and other tests, and any other medical information we learn from you about your health history and family history
4. Laboratory results obtained on specimens collected from you (blood, saliva)

The Researchers may use and share my Protected Health Information with:

- The Principal Investigator, other Investigators, Study coordinators, and all administrative staff in change of doing work for the study;
- Government agencies that have the right to see or review your PHI, including but not limited to the Office of Human Research Protections and the Food and Drug Administration;
- Children's National Medical Center Institutional Review Board;
- Audit Committee (review committee) of the Children's National Medical Center Institutional Review Board;
- Quality Improvement Program Coordinator and other staff in the Office for the Protection of Human subjects at Children's National Medical Center.

In addition to the above people and organizations, the researchers may also use and share my Protected Health Information with:

1. Doctors and staff at other places that are participating in your medical care, such as medical facilities where you may be transferred after discharge from Children's.
2. Laboratories with other people or organizations that look at your health information in connection with this study.
3. The Data Safety Monitoring Board (a person who reviews medical information during the study)
4. Other: Data Coordinating Center: Sloan Epidemiology Center, Boston University Medical Campus

Also, your primary physician and you will be contacted if during the course of the study the researcher learns of a medical condition that needs immediate attention.

Should your health information be disclosed to anyone outside the study, your information may no longer be protected by HIPAA and this Authorization. However, the use of your health information will still be regulated by applicable federal and state laws.

Storage of PHI in a Database:

We would like to store personal health information collected from you in this study in a database for future research. The database is maintained by the Data Center at Boston University Medical Campus.

Please indicate your approval of any or all of the following by initialing next to the statement:

My personal health information collected in this study may be stored in the above named database for future analysis related to this study. ___Yes ___No _____Initials

My personal health information may be stored in the above named database for future analysis related to immature breathing and caffeine use in preterm infants. ___Yes ___No _____Initials

My personal health information may be stored in the above named database. Researchers may contact me to request my authorization for future studies that are not related to this study or the disease named above.

___Yes ___No _____Initials

My personal health information may be stored without any of my identifying information for use in other studies of other diseases. ___Yes ___No _____Initials

If you agree to participate in this research study, the research team, the research sponsor (when this applies) and the sponsor's representatives, may use Personally Unidentified Study Data. Personally Unidentified Study Data may include your date of birth, initials, and dates you received medical care. Personally Unidentified Study Data may also include the health information used, created, or collected in the research study. The research team or the research sponsor may share the Personally Unidentified Study Data with others to perform additional research, place it into research databases, share it with researchers in the U.S. or other countries, or use it to improve the design of future studies. They may also publish it in scientific journals, or share it with business partners of the sponsor and to file applications with U.S. or foreign government agencies to get approval for new drugs or health care products.

The time period for using or giving out your child's health information:

- Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your child's health information.

You do not have to sign this Consent/Authorization. If you decide not to sign the Authorization, you will not be allowed to participate in the research study.

After signing the Consent/Authorization, you can change your mind and:

- Revoke (cancel) this authorization. If you revoke the Authorization, you will send a written letter to Dr. Mary Revenis, Dept. of Neonatology, 3rd floor west wing, Children's National Medical Center, 111 Michigan Ave. NW, Washington, DC 20010, to inform her of your decision.
- If you revoke (cancel) this Authorization, researchers may only use and disclose the PHI that was collected for this research study before you canceled the Authorization.
- If you revoke (cancel) this Authorization your PHI may still be used and disclosed if you should have an adverse event (unexpected side effect).

- If you change your mind and withdraw the Authorization, you will not be allowed to participate in the study.

If you have not already received a Notice of Privacy Practices from Children's Notional Medical Center, you may request a copy and will be given one. If you have any questions or concerns about your privacy rights, you may contact the Children's Hospital Privacy Officer at 202-476-4550.

Payment for Medical Care for Research-related Injury:

Children's National Medical Center cannot promise that the risks we have told you about or other unknown problems will not happen. If you think that something unexpected happened because your were in the study, please call the Principal Investigator, Dr. Mary Revenis at (202) 476-3396 or the Chief Academic Officer of the Children's National Medical Center at (202) 476-5000. If something unexpected happened resulting directly from your participation in this research study, we will give your child any urgent medical emergency treatment needed if the injury is reported in a timely manner. The Hospital will seek payment from your health insurance company or other third-party payor for any medical care or services you receive. The Hospital has no program to provide you with any additional payments as a result of any injuries.

FUTURE CONTACT

We would like to ask your permission to contact you and your child again in the future. This contact would be after the study has ended. Please initial your choice below:

____Yes ____No You may contact me again to ask for additional information related to this study

____Yes ____No You may contact me again to ask for additional biological samples (such as blood) related to this study

____Yes ____No You may contact me again to let us know about a different research study

CONSENT/AUTHORIZATION:

I am authorized to act on behalf of the participant (baby). I have read this information and will receive a copy of this form after it is signed.

By signing this form, you agree that you have talked to your doctor about the study and understand it, and you want to be in the study. You agree that we have talked to you about the risks and benefits of the study, and about other choices. You may decide to stop being in this study at any time and no one will mind and nothing will change about your medical care other than not being in the study. Copies of this form will be:

1) Kept in the study file by the Principal Investigator of the study,
2) Put in your medical record; and
3) Given to you to keep.

Please call the Principal Investigator, Dr. Mary Revenis, at 202-476-3396 if you have any questions.

Printed Name of Participant:_____

Medial Record Number:_____

Printed Name of Parent(s)/Guardian(s): _____

Signature of Participant:_____ Date:_____

Signature of Parent(s)/Guardian: _____ Date:_____

Signature of 2nd Parent/Guardian: _____Date: _____

(ONLY when applicable)

Witness (to signatures): _____Date:_____

(may be investigator)

Translator's Signature (if applicable):_____

Language:_____

AFFIDAVIT OF PERSON OBTAINING CONSENT: I certify that I have explained to the above individual(s) the nature and purpose of the study, potential benefits, and possible risks associated with participation in this study. I have answered any questions that have been raised.

Printed Name of Individual Obtaining Consent:_____

Title: _____Signature: _____Date:_____