Informed Consent

Red Blood Cell Survival Study: The Impact of Oxidative Stress on Erythrocyte

Biology

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University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

Consent Form Version Date: 01/12/2023
IRB Study # 21-0587
Title of Study: Red Blood Cell Survival Study: The Impact of Oxidative Stress on Erythrocyte Biology
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PURPOSE: To assess the impact of G6PD deficiency red cells have on RBCs in people with sickle cell disease.

STUDY LENGTH: About 6 months.

PROCEDURES: There will be a total of 18 study visits.

- Type and screen (x2) – 15 minutes
- Chromium infusion day (x2) – 8 hours
- 24 hour visit (x2) – 15 minutes
- 48 hour visit (x2) – 15 minutes
- 72 hour visit (x2) – 15 minutes
- Week 1 visit (x2) – 15 minutes
- Week 2 visit (x2) – 15 minutes
- Week 3 visit (x2) – 15 minutes
- Week 4 visit (x2) – 15 minutes

RISKS: May include pain, chills, fever, itching, hives, or decreased blood pressure.

INVASIVE PROCEDURES: Blood sample collection, blood transfusion, chromium-labeled red cell infusion

NON-INVASIVE PROCEDURES: Medical history, urine sample collection, physical exam, daily diary

BENEFITS: We do not know if this project will help you.

OTHER OPTIONS: Your options include-

- Joining a different project
- Routine care
- Getting no treatment

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary.

You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The desired impact of chronic red blood cell (RBC) transfusions in patients with sickle cell disease (SCD) is to reduce the associated risks, such as stroke or pain. How long these transfused red cells survive determines how helpful these red cells are. G6PD deficiency is a disease that some red cell donors have that may impact the survival of these red cells. Studies in healthy volunteers suggest G6PD deficient donors have red cells that survive after transfusion a shorter period of time. Given that up to 10% (1 in 10) of RBC donors for patients with SCD has G6PD deficiency, we need to know more regarding whether these units work as well as blood from donors without this disease. This study will attempt to correlate G6PD activity in a donor RBC unit with post-transfusion RBC survival in those with SCD.

You are being asked to be in the study because you are an adult aged 18-60, have been diagnosed with sickle cell disease, and receive red cell transfusion therapy for your routine care.

Are there any reasons you should not be in this study?
You should not be in this study if are pregnant or plan to be pregnant, have a history of severe transfusion reactions, have multiple red cell antibodies, have an enlarged liver or spleen, have known G6PD deficiency, or are participating in other clinical trials.

How many people will take part in this study?
Approximately 16 people at this institution will take part in this study.

How long will your part in this study last?
You are anticipated to be on this study for about 6 months.

What will happen if you take part in the study?
In this research study, you are being asked to participate in two red cell transfusions with single-blind chromium-labeled infusions. Chromium 51 is a compound commonly used in humans to label RBCs that help us to determine red cell survival. Chromium 51 is approved by the FDA and is being used within that approval for this study. To find out the impact that G6PD deficient donor RBCs has on individuals with SCD, you will be transfused one G6PD deficient unit and one G6PD normal unit throughout the study. Only the principal investigator and other study staff will know if the unit you are receiving is G6PD deficient or not. After the blood transfusion, you will be infused with a small amount of chromium-labeled RBCs and blood will be collected at certain time points to determine how long they survived after infusion. If you agree to take part in this study, there will be no change to your usual medical treatments and medications. Multiple visits are required to complete all study procedures.

Summary of Procedures:

24 – 72 hours prior to the 51Cr-labeled infusion:
- Read and sign informed consent (if not already done)
- Type & Cross sample collected

Day 1 - Prior to each chromium infusion:
- A physical exam will be performed by principal investigator or designee
- You will sign a blood transfusion consent
- Females will provide a urine sample
- Your vital signs will be checked
- We will collect pre-transfusion blood samples
- You will be given your blood transfusion/exchange over a 2-3 hour period
- You will be given a small infusion of chromium-51 labeled RBCs

Day 1 – Post infusion:
- Blood samples will be collected at 5, 7.5, 10, 12.5, 15, 30 minutes, and 1 hour

24 hour post infusion:
- You will return for a blood sample.
- You will be monitored for any side effects.
- You will bring in your daily diary for the staff to check.

48 hour post infusion:
- You will return for a blood sample.
- You will be monitored for any side effects.
- You will bring in your daily diary for the staff to check.

72 hour post infusion:
- You will return for a blood sample.
- You will be monitored for any side effects.
- You will bring in your daily diary for the staff to check.

1 week post infusion:
- You will return for a blood sample.
- You will be monitored for any side effects.
- You will bring in your daily diary for the staff to check.

2 weeks post infusion:
- You will return for a blood sample.
- You will be monitored for any side effects.
- You will bring in your daily diary for the staff to check.

3 weeks post infusion:
- You will return for a blood sample.
- You will be monitored for any side effects.
- You will bring in your daily diary for the staff to check.

4 weeks post infusion:
- You will return for a blood sample.
- You will be monitored for any side effects.
- You will bring in your daily diary for the staff to check.

After Day 35, you will be given a break (washout period) of about 3 months (120 days). After this break, you will be contacted to repeat the summary of procedures again.

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study. The use of your blood samples will not result in commercial profit, and you will not be compensated for the use of your samples other than what

is described in this consent form.

What are the possible risks or discomforts involved from being in this study?

There is a very small risk that blood not meant for you might be transfused to you if an error in identification is made. The laboratory confirmation of your blood type at the time of the infusion will help to minimize this risk. Infusion of any donor red cells, however, could cause an adverse reaction caused by pain, chills, fever, itching, hives, or could cause hepatitis or other transfusion transmitted diseases. There is also a risk of decreased blood pressure, clotting and/or bleeding, potential kidney damage, and death. However, these risks are no different than a regular transfusion of red cells.

The risks of a transfusion transmitted infectious disease is very unlikely as all red cells are tested for infectious disease markers on the day of the whole blood donation. There is a rare chance of bacterial contamination during the preparation and storage of the red cells; however, blood product quality control (sterility surveillance) will be performed on the red cells prior to the infusion.

There will be exposure to a small amount of radioactive Chromium-51 that will be used to label the red cells. Chromium 51 is approved by the FDA and is being used within that approval for this study. Only 1-3 tablespoons of red blood cells tagged with chromium will be infused into you. With such a small amount, the following risks are considered low. Use of radioactive tracers for labeling of red blood cells is a standard clinical and research procedure and the amount used is well within the safety limits of exposure to medical radioactive materials. Your radiation exposure during this study is not known to be associated with any biological hazard and is less than that you might receive from some types of other routine diagnostic radiology (X-ray) procedures (for example, computed tomography (CT) scan of the body).

In addition, if the red cells store poorly, they may hemolyze (break down) and produce symptoms, such as fever, chills, and red urine temporarily.

Blood Draw Risks

The side effects that you might experience as a consequence of the routine blood draws for this study include possible discomfort, pain, and bruising at the needle entry site. Rare complications of any venipuncture (drawing blood from a vein) include fainting, arterial puncture, peripheral nerve injury, local infection, and local blood clot. There may be other unanticipated risks, but every precaution will be taken to assure your personal safety and to minimize discomfort. The person drawing your blood will observe you for side effects, but please inform him or him if you experience any discomfort or feel faint.

Confidentiality Risks

There is a risk of loss of confidentiality. Every effort will be made to keep your study records confidential, but we cannot guarantee it. Depending on the kind of information being collected, if your study information were accidentally seen, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the study doctor director about whether this could apply to you.

Risks to women who could become pregnant
If you become pregnant during the project, you will be dropped from participation for safety reasons. If you become pregnant while you are participating in this study, we ask that you inform the research doctor immediately. The research doctor will ask you for written permission to obtain information from you or your obstetrician on your pregnancy and the health of the baby.

Pregnancy tests will be done on all females who might be able to get pregnant at the start of the study. We will pay for these tests as part of the study.

There may be uncommon or previously unknown risks. You should report any problems to the researcher.

Risks associated with radiation exposure
This research study involves exposure to radiation from Chromium 51 (infusion x2). Please note that this radiation exposure is not necessary for your medical care and is for research purposes only.

The average person in the United States receives a radiation exposure of 0.3 rem (or 300 mrem) per year from natural background sources, such as from the sun, outer space, and from radioactive materials that are found naturally in the earth's air and soil. The dose that you will receive from participation in this research study is less than amount you receive from these natural sources in one year.

The amount of radiation you will receive in this study has a minimal risk and is below the dose guideline established by The University of North Carolina Radiation Safety Committee for research subjects.

What is a Certificate of Confidentiality?
This research is covered by a Certificate of Confidentiality. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use.

The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research subjects or for any purpose you have consented to in this informed consent document.

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

What if we learn about new findings or information during the study?
You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will information about you be protected?

- Your data will be stored in locked and password protected files.
- Only the researchers and study staff who run the trial will have access to individually identifiable data.
- Your name or ID number will not be used to store study data. A number will be assigned for data collection purposes. The link between your identifiable information and the data collected for this study will be protected on a password protected file that will only be accessible to the PI and study staff involved in the data collection process.

Participants will not be identified in any report or publication about this study. We may use de-identified data and/or specimens from this study in future research without additional consent.

Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

By signing this informed consent document, you agree that some of the information generated by participating in this study and/or a copy of the consent form may be included in your medical record and that this information may be viewed by other physicians or caregivers who provide healthcare services to you. This will allow the doctors caring for you to know what study medications or tests you may be receiving as a part of the study and know how to take care of you if you have other health problems or needs during the study. Additionally, the information

may be shared with your medical insurance plan if the research services provided are billed to your insurance.

You will be asked to sign a separate form ("HIPAA Authorization") to allow researchers to review your medical records.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. If you are hurt, become sick, or develop a reaction from something that was done as part of this study, the researcher will help you get medical care, but the University of North Carolina at Chapel Hill has not set aside funds to pay you for any such injuries, illnesses or reactions, or for the related medical care. Any costs for medical expenses will be billed to you or your insurance company. You may be responsible for any co-payments and your insurance may not cover the costs of study related injuries.

If you think you have been injured from taking part in this study, call the Principal Investigator at the phone number provided on this consent form. They will let you know what you should do.

By signing this form, you do not give up your right to seek payment or other rights if you are harmed as a result of being in this study.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

If you withdraw or are withdrawn from this study all data collected up until the point of withdrawal will be retained, however no additional information will be collected unless you provide additional written permission for further data collection at the time of your withdrawal.

Will you receive anything for being in this study?

You will be paid $500 for each chromium infusion you complete. You will receive a total of $1,000 for completing both chromium infusions. Transportation to and from UNC for study-related activities will be covered by the study. You will also be provided with a $10 food voucher card on Day 1 chromium infusion days.

Your name, address, and U.S. tax payer identification number (SSN or ITIN) are required to process payments and/or to report taxable income to the IRS. You must complete a W-9 (for U.S. persons) or W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents (for non-resident aliens) in order to receive payment for participation.

U.S. person participants must complete Form W-9 in order to receive payment for participation. If payment by UNC equals or exceeds $600 per calendar year for U.S. persons,

UNC will report the amount to the Internal Revenue Service on Form 1099. Nonresident alien participants must complete Form W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents in order to receive payment for participation. Payments to nonresident alien participants may be subject to tax withholding and are generally reported to the Internal Revenue Service on Form 1042-S. This information will not be linked to any of the study data and will only be used for payment purposes.

If you do not provide your SSN or ITIN, or complete the appropriate documentation noted above, we cannot issue you a payment for participation. However, you may still choose to participate in this study.

Any payment provided for participation in this study may be subject to applicable tax withholding obligations

Will it cost you anything to be in this study?
It will not cost you anything to be in this study.

Who is sponsoring this study?
This research is funded by the National Institutes of Health. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____
Signature of Research Participant

_____
Date

_____
Printed Name of Research Participant

_____
Signature of Research Team Member Obtaining Consent

_____
Date

_____
Printed Name of Research Team Member Obtaining Consent

_____
Signature of Witness if applicable; e.g. literacy issues, visually impaired, physically unable to sign, witness/interpreter for non-English speaking participants using the short form)

_____
Date

_____
Printed Name of Witness