Washington University in St. Louis

INFORMED CONSENT DOCUMENT

Project Title: Postpartum depression after Cesarean delivery: Ketamine as a preventative intervention. A feasibility pilot-study

Principal Investigator: Dr. David Thomas Monks, MBChB FRCA MSc

Research Team Contact: Dr. David Thomas Monks, 314-273-2633
Benjamin Swan RN, 314-273-8257

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant. By signing this form you are agreeing to participate in this study.

- You should read and understand the information in this document including the procedures, risks and potential benefits.
- If you have questions about anything in this form, you should ask the research team for more information before you agree to participate.
- You may also wish to talk to your family or friends about your participation in this study.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you are a healthy woman having a planned cesarean delivery of your baby.

The purpose of this research study is to determine whether or not the drug ketamine (0.5 mg/kg), administered intravenously or injected under the skin, compared to a placebo, is an effective prevention against postpartum depression (PPD).

PPD is one of the most common medical complications surrounding pregnancy, with an estimated prevalence of 19.2% in the first 3 months following childbirth, and can have devastating effects on both mother and baby, including: maternal suffering, disruption of the parent-infant relationship, and in rare cases, suicide and/or infanticide (killing one's own child). PPD can also potentially impair the social, emotional, and cognitive development of a child. Unfortunately, the exact cause of PPD remains unknown.

Ketamine has shown some promise as a potential treatment to prevent PPD. Ketamine has been shown to be an effective pain killer during cesarean delivery and it is commonly used for this purpose; however, previous studies in non-pregnant populations have shown that ketamine also has an anti-depressant effect in treatment-resistant depression, and one study demonstrated a large reduction in the occurrence of PPD in women undergoing cesarean delivery. In that study the ketamine was given by an infusion over 2 days, but in this study the ketamine administration will be completed in the operating room within 40 minutes.

Ketamine is approved by the U.S. Food and Drug Administration (FDA) as an anesthetic (a drug that induces insensitivity to pain). However, the use of ketamine is considered investigational in this study.

WHAT WILL HAPPEN DURING THIS STUDY?

Should you decide to participate in this study, we will interview you and/or review your medical records to collect basic information about you (e.g. age, weight, height, ethnicity, etc.), your insurance status (i.e. insured/uninsured), your current and previous pregnancies and deliveries, and any current and/or previous physical and mental health problems, surgeries, and medications.

Prior to your surgery, you will be randomized (assigned by chance, like rolling dice) to one of the three treatments- this treatment will be given immediately following the delivery of your baby. An intravenous catheter (IV) will be placed in a vein in one of your arms in addition to the standard IV catheter required for the cesarean delivery. This IV will be used to collect blood from you during your procedure. Additionally, you will be asked to complete depression, anxiety, and psychosocial stress surveys (EPDS, GAD-7, and ANRQ, respectively) prior to being brought into the operating room (OR). You are free to skip any question you prefer not to answer on any survey.

Immediately following the delivery of your baby, you will receive the treatment you were randomized to. Regardless of treatment, you will receive 0.01 mL/kg of a drug or placebo injected under the skin and 0.01 mL/kg of an intravenous drug or placebo, infused over 40 minutes. You may receive placebo (salt water solution) in both the injection under the skin *and* the intravenous infusion or one of these routes may be 50 mg/mL of ketamine and the other route will be placebo (salt water solution).

During your surgery, we will collect blood from you at four time points before and after the delivery of your baby: Baseline and 20, 40, and 100 minutes after delivery. Following collection of the blood sample at the 100 minute time point, you will also be asked about your pain and any adverse effects you may or may not be experiencing. Additional information from your surgery (e.g. time of delivery, vital signs, medications given, APGAR scores, etc.) may be obtained from your medical records after the surgery is completed.

After your surgery, we will follow up with you at several time points while you are still in the hospital: 2, 6, 24, and 48 hours after surgery. At the 2 and 6 hour time points following surgery, you will be interviewed about your pain and any adverse effects (side effects) you may or may not be experiencing. At approximately 24 and 48 hours after surgery, you will again be asked about your pain level; however, at these times we will also follow up with you regarding your ability to breast feed (if applicable) and will ask you to complete the EPDS and GAD-7 surveys that you completed prior to your operation.

Two follow up telephone calls will be made at 21 and 42 days after you deliver your baby. During these telephone calls, you will again be asked about your pain level and will be asked the questions on the EPDS and GAD-7 surveys.

Will you save my research information and/or biospecimens to use in future research studies?

We would like to use the blood and data we are obtaining in this study for studies going on right now as well as studies that are conducted in the future. These studies may provide additional information that will be helpful in understanding the prevention of PPD, or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. By allowing us to use your blood and data you give up any property rights you may have in the blood and data.

We may share your blood and data with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at Washington University, at other research centers and institutions, or industry sponsors of research. We may also share your research data with large data repositories (a repository is a database of information) for broad sharing with the research community. If your individual research data is placed in one of these repositories only qualified researchers, who have received prior approval from individuals that monitor the use of the data, will be able to look at your information.

If you change your mind and do not want us to store and use your blood and data for future research you should contact the research team member identified at the top of this document. The blood and data will no longer be used for research purposes. However, if some research with your blood and data has already been completed, the information from that research may still be used. Also, if the blood and data has been shared with other researchers it might not be possible to withdraw the blood and data to the extent it has been shared.

Please place your initials in the blank next to Yes or No for each of the questions below:

My blood and data may be stored and used for future research as described above.

_____ Yes **_____ No**
Initials **Initials**

My blood and data may be shared with other researchers and used by these researchers for the future research as described above.

_____ Yes **_____ No**
Initials **Initials**

Identifiers may be removed from your private information, including blood and data, and used for future research or shared with others. If this occurs, we will not ask you for additional consent.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 60 people will take part in this study conducted by investigators at Washington University.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for approximately 6 weeks. You will initially be followed from the time of consent until discharge from the hospital or 48 hours following delivery, whichever comes first. You will be contacted via telephone at approximately 21 days and 42 days following delivery for additional follow up (e.g. pain assessment and depression survey).

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Some risks described in this consent document, if severe, may cause death.

Intravenous and Subcutaneous Ketamine:
Likely/Common: Dream-like feeling, euphoria (intense feeling of happiness), blurred vision, drowsiness, nausea, vomiting, loss of appetite, sleep problems
Less Likely/Less Common: Amnesia (loss of memory), rapid eye movement, double vision, dizziness, jerky muscle movements
Rare: Confusion, anxiety, hallucinations, unusual thoughts, fear

Intravenous Catheter
Likely/Common: Pain at insertion site, bruising and/or bleeding at insertion site
Less Likely/Less Common: Infection at insertion site
Rare: None

Questionnaires and Assessments
Completing the questionnaires or assessments may cause emotional discomfort; however, you have the right to refuse to answer any question for any reason.

Breach of Confidentiality
One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You may or may not benefit from being in this study.

However, we hope that in the future, other people might benefit from this study because the information provided may help us to reduce the prevalence of postpartum depression by using ketamine as a preventative intervention at cesarean delivery.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, your doctor will discuss the other options that are available to you. Instead of being in this study, you could choose to have your planned cesarean delivery without being in this study.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

As part of this study you will receive tests and procedures that are similar to what you would receive during routine clinical care of your condition. Your health plan/insurance company will be billed for some or all of these costs, and you will be responsible for any co-pays and deductibles that are normally required by your health plan/insurance. Not all insurance plans cover the costs associated with being in a study. Even if they do, you may be responsible for more out-of-pocket expenses, such as co-pays and deductibles, when there are more tests and procedures or more expensive tests and procedures involved in the study than if you were to receive routine clinical care outside the study.

If you wish to know whether there are more tests and procedures or more expensive tests and procedures in the study, you should ask your study doctor.

If you wish to know whether your insurance will pay, you should contact them directly, or speak with the study team about obtaining a financial pre-certification prior to enrolling in the study.

The study is providing the ketamine at no cost to you.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will need to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. You may also need to provide your address if a check will be mailed to you. Checks are mailed within approximately 2 weeks of each study milestone outlined below. If your social security number is obtained for payment purposes only, it will not be retained for research purposes.

In total, you will receive $50 for participating in this research study. You will receive one $25 check upon completion of the last in-hospital follow-up at approximately 48 hours following your surgery, and a second $25 check following completion of the final follow-up procedures at approximately 42 days following your surgery. If you do not complete all study follow ups you will be paid for those you do complete.

WHO IS FUNDING THIS STUDY?

The University and the research team are not receiving payment from other agencies, organizations, or companies to conduct this research study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator, Dr. David Monks, at 314-273-2633 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University. If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

Other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you. We will keep your participation in this research study confidential to the extent permitted by law.

- Government representatives (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- Hospital or University representatives to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and will be available to anyone with access to your health care record, including your health insurance company. This information may also be released as part of a release of information request.
- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures.
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.
- Any report or article that we write will not include information that can directly identify you. The journals that publish these reports or articles require that we share your information that was collected for this study with others to make sure the results of this study are correct and help develop new ideas for research. Your information will be shared in a way that cannot directly identify you.

To help protect your confidentiality, we will keep all study documents in a locked facility to which only study personnel will have access. The samples will be stored with your patient ID, in a secure laboratory to which only the study team will have access.

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

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- your treatment or the care given by your health provider.
- your insurance payment or enrollment in any health plans.
- any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
    - To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ or you may request that the investigator send you a copy of the letter.
        - **If you revoke your authorization:**
            - The research team may only use and share information already collected for the study.

- Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
- You will not be allowed to continue to participate in the study.

Can we contact you by email?

We would like to contact you by email for the purposes listed below. Some of these emails may contain health information that identifies you.

- Follow up communication regarding pain assessment, survey collection, and/or adverse effect monitoring.

Only the research team will have access to your email communications. We will only communicate by email to send you the information listed above. If you have any questions or need to contact us for an urgent or emergent situation, please contact the research team member identified at the top of this document.

You should be aware that there are risks associated with sending your health information via email.

- There is always a risk that the message could be intercepted or sent to the wrong email address. To avoid sending messages to the wrong email address, the first email we send you will be a test message to ensure we have the correct email address.
- When using any computer you should be careful to protect your username and password. Make sure you log-out before getting up from the computer.
- If you share a home computer with other family members, and do not want them to know you are participating in this study make sure you provide an email address that only you can access.
- Your employer will have access to any email communications sent or received on any electronic devices used for work or through a work server.

Do you agree to allow us to send your health information via email?

_____ Yes **_____ No**
Initials **Initials**

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ under Withdrawing from a Research Study.

If you withdraw from the study we will ask your permission to continue to follow up via telephone calls and/or electronic medical record review. Should this occur we will ask you to sign a separate consent form before collecting this information.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the investigator might decide to end your participation in this research study earlier than planned. This might happen for no reason or because in our judgement it would not be safe for you to continue, because your condition has changed, or because of delays in case start time due to the Labor & Delivery workload.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Benjamin Swan RN, 314-273-8257. If you experience a research-related injury, please contact: Dr. David Monks, 314-273-2633.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office web site, http://hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 11/25/20.

_____ _____
(Signature of Participant) (Date)

_____
(Participant's name – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)

_____
(Name of Person who Obtained Consent - printed)