A Randomized Controlled Trial to Assess the Effectiveness of Multimodal Prophylactic Uterotonics in Patients Undergoing Non-Elective Cesarean Sections after a Trial of Labor

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INFORMED CONSENT DOCUMENT

Project Title: **A Randomized Controlled Trial to Assess the Effectiveness of Multimodal Prophylactic Uterotonics** in **Patients Undergoing Non-Elective Cesarean Sections after a Trial of Labor**

Principal Investigator: Nicole Masse MD

Research Team Contact: [redacted]

This consent form describes the research study to help you decide if you want to participate. This form 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 as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- 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 are inviting you to participate in this research study because you are a candidate for a vaginal trial of labor.

Laboring patients who ultimately require a cesarean section are at increased risk of poor uterine contraction and postpartum hemorrhage (excess bleeding at delivery). The purpose of this research study is to assess whether laboring patients who ultimately require a cesarean section will benefit from prophylactic methylergonovine (a medication that may help poor uterine contraction and postpartum hemorrhage).

HOW MANY PEOPLE WILL PARTICIPATE?

Up to 160 patients who meet criteria for the study will take part in this study conducted by investigators at the University of Iowa.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for the duration of the cesarean delivery (~ 2 hours). No long -term follow-up is needed. We will continue to collect your medical data for several days after delivery.

WHAT WILL HAPPEN DURING THIS STUDY?

Participants undergoing a vaginal trial of labor who ultimately require a cesarean section will be randomly assigned to receive one of the two study treatments, either methylergonovine or placebo (normal saline). Methylergonovine is a drug commonly administered in the postpartum period to help control bleeding and poor uterine contraction after birth. As you will be randomized, this means that whichever study treatment you receive will be determined purely by chance, like flipping a coin. You will have a 50/50 chance of receiving any one of the study treatments. Enrollment in the study will have no impact on your chances of having a successful vaginal delivery .

At the time of cesarean section, following delivery of your baby, the standard dose of oxytocin infusion will be administered to you. Following administration of the standard oxytocin infusion, you will then receive either 200 micrograms of methylergonovine or placebo (1 ml of normal saline) as a shot in the muscle. This will be drawn up and administered by an anesthesiologist.

The obstetrical provider will be responsible for determining and relaying to the anesthesiologist whether additional uterotonics (medications for poor uterine contraction) are needed throughout the procedure. Additional uterotonics will be given in accordance to the current guidelines outlined by the American Congress of Obstetricians and Gynecologists (ACOG). We will evaluate the need for additional uterotonic medications at the time of cesarean delivery which include: methylergonovine, carboprost and misoprostol.

The obstetrical provider will assess the tone of your uterus 4 minutes following delivery of your baby and report whether uterine tone is satisfactory or unsatisfactory. As routinely done at the time of cesarean delivery, the registered nurse will be responsible for measuring and documenting the quantitative blood loss. As routinely performed on all are patients who undergo a vaginal or cesarean delivery, preoperative hemoglobin and postoperative day one hemoglobin levels will be collected. Other outcomes we will be assessing include: the need for a blood transfusion, endometritis, intensive care unit admission.

No additional long-term follow up will be needed.

We will collect information from your medical chart about: blood loss from your cesarean section, preoperative and postoperative hemoglobin levels, the need for additional uterotonic agents throughout the cesarean section, the need for a blood transfusion, the development of postpartum endometritis and the need for intensive care unit admission.

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. Rarely observed reactions have included: irritation at injection site, hypersensitivity (anaphylaxis), acute myocardial infarction, transient chest pains, vasoconstriction, vasospasm, coronary arterial spasm, bradycardia, tachycardia, dyspnea, hematuria, thrombophlebitis , water intoxication , seizures, hallucinations, leg cramps, dizziness, tinnitus, nasal congestion, nausea, vomiting, diarrhea, diaphoresis, palpitation, rash, and foul taste.

To avoid life threatening risks from the study drug, patients with contraindications to methylergonovine have been excluded from the study. Contraindications to methylergonovine include: hypersensitivity to the drug, chronic high blood pressure, gestational high blood pressure, preeclampsia and coronary artery disease. HIV/AIDS patients on protease inhibitors (Pls) will also be excluded as the use of methylergonovine with protease inhibitors has been associated with exaggerated vasoconstrictive responses.

You may receive a placebo (an inactive substance) during this study. This means that you would receive no active study treatment while participating, thus you may not receive the potential additive benefit of a prophylactic uterotonic. However, there is a risk of receiving methylergonovine when the drug itself is not necessary.

WHAT ARE THE BENEFITS OF THIS STUDY?

You may not directly benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because we hope to learn whether the administration of prophylactic uterotonic medications will serve to improve poor uterine contraction and decrease the incidence of postpartum hemorrhage.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any additional costs for being in this research study.

WILL I BE PAID FOR PARTICIPATING?

You will not be paid for being in this research study.

WHO IS FUNDING THIS STUDY?

The Department of Maternal Fetal Medicine is funding this study. The University and the research team are receiving no payments from other agencies, organizations, or companies to conduct this research study.

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

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- The University of Iowa does not plan to provide free medical care or payment for treatment of any illness or injury resulting from this study unless it is the direct result of proven negligence by a University employee.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.

WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that 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.

- federal government regulatory agencies,
- auditing departments of the University of Iowa, and
- the University of Iowa Institutional Review Board (a committee that reviews and approves research studies)

To help protect your confidentiality, we will be collecting the minimal amount of data needed to answer the research question. All records containing protected health information will be transported in a manner that no identifiable information is visible. All hard copy material will be kept in a secure office within a locked file cabinet. Electronica data will be collected by reviewing your medical chart through EPIC. All protected health information obtained will be stored through REDCap (research electric data capture) a secure web-based interface for storing study information. At the end of the study, all study maternal will be destroyed. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

The University of Iowa Hospitals and Clinics generally requires that we document your participation in research occurring in a University of Iowa Health Care facility. This documentation will be in either your medical record or a database maintained on behalf of the institution reflecting that you are participating in this study. The information included will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your medical record chart.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. A copy of the informed consent document will be available on this website. 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.

WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires the University of Iowa Health Care to obtain your permission for the research team to access or create " protected health information" about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study. Once the University of Iowa Health Care has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under "Confidentiality."

We may share your health information related to this study with other parties including federal government regulatory agencies, the University of Iowa Institutional Review Boards and support staff,

You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes to give us permission to use or create health information about you.

Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use our health information for this research study by sending a written notice to [redacted]. However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

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. 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 Drop Out of the Study?

Can Someone Else End my Participation in this Study?
Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned. This might happen in the event you develop medical condition s which would be contraindications to receiving the study drug. For example, in the event you develop gestational hypertension or preeclampsia during labor, this would make you ineligible for the study as the administration of methylergonovine may worsen hypertensive disorders.

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WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: [redacted]. If you experience a research-related injury, please contact: [redacted].

If you have questions, concerns, or complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Rd, The University of Iowa, Iowa City, IA 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking "Info for Public" on the Human Subjects Office web site, http://hso.research.uiowa.edu/. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

This Informed Consent Document 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 signing this Informed Consent Document. 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 copy of this form.

Subject's Name (printed): _

_____	_____
(Signature of Subject)	(Date)

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

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