STUDY TITLE:

Scheduled Ketorolac administration after cesarean section and its effect on opioid use: a randomized control trial

PRINCIPAL INVESTIGATOR

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TUFTS MEDICAL CENTER
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INFORMED CONSENT TO PARTICIPATE IN RESEARCH

Scheduled Ketorolac administration after cesarean section and its effect on opioid consumption: a randomized control trial

Principal Investigator: Mohak Mhatre, MD
Co-Investigators: Jean Hostage, MD
Study team telephone number: 617-636-4549

Key Information: The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?
We invite you to take part in a research study because it is a study involving the best way to control pain after a cesarean section while in the hospital, and you may have a cesarean delivery.

What should I know about a research study?

- Someone will explain this research study to you.
- Please also read all of the following information carefully.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can decide to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide. Do not sign unless you understand the information in it and have had your questions answered to your satisfaction.

PURPOSE OF STUDY

The purpose of this study is to determine if a pain medication plan can help reduce the amount of opiate medication needed to control pain after cesarean sections. Ketorolac is an FDA approved anti-inflammatory medication similar to Ibuprofen. It is already used commonly for standard of care to control pain after cesarean sections and many other types of surgeries on an "as needed" basis. Our goal is to see if scheduled doses of Ketorolac given every 6 hours for the first 24 hours after surgery will improve pain control and decrease the need for opiate medications. It is possible that the scheduled doses may decrease the need for opiate medications. But it is also possible that this new plan will have no effect or even increase the need for opiate medications.

The study will be conducted at Tufts Medical Center, 800 Washington Street, Boston MA 02111 on Labor and Delivery. 500 subjects will be enrolled however not all of these subjects will have

a cesarean delivery. We plan to randomly assign 148 subjects to either the standard plan for pain control or a study plan for pain control. If you participate in this study, you may have access to the study drug if you require it during future hospitalizations. However, this drug is not available as a home medication.

PROCEDURES TO BE FOLLOWED

If you have a cesarean delivery and decide to be part of this study, the pain medication plan you get will be chosen by chance. Neither you nor the study doctor will choose what plan you get. You will have a 50% chance of being part of the study plan and 50% chance of being part of the standard plan. The decision for standard or study plan will be made randomly like a coin flip. Neither you nor the study doctor will know which pain medication plan you are getting. Whether you are assigned to the study or standard plan, your pain will be assessed and treated appropriately as part of your regular standard of care. Standard of care includes using acetaminophen (Tylenol) or opioid medications to control pain.

All subjects regardless of which pain control plan they are assigned to, will receive one dose of Ketorolac before leaving the Operating Room.

If you are randomized to receive the standard plan you will receive up to two (2) doses of Ketorolac after your cesarean section. This is the current pain control plan at Tufts Medical Center. If you are part of the standard group, you will also receive four (4) doses of a placebo, or inactive drug. This will consist of only normal saline, or salt water.

If you are randomized to receive the study plan you will receive a scheduled five (5) doses of Ketorolac after your cesarean section. Regardless of which group you are assigned to, you will receive your first dost of pain medication (Ketorolac) before leaving the operating room.

For both plans, you will also need to have an intravenous catheter (an "IV") in place for the first 36 hours after leaving the operating room. Typically, the IV is removed about 12 hours after a patient leaves the operating room. For both plans, per standard of care, blood samples will be collected to measure your blood count on the days after the cesarean section. At this time, your kidney function will also be evaluated by evaluating that blood sample.

For both plans, you will also be evaluated throughout your time in the hospital as you normally would. To measure how well your pain is controlled and the amount of opiate medications you needed in the hospital, your medical records will be reviewed, as will notes from a follow up phone conversation after you leave the hospital. You will receive a phone call and be asked a series of 9 questions about your stay in the hospital at about 2 weeks after you are discharged from the hospital. The phone call should take less than 10 minutes of your time. If you do not answer, we will leave a voicemail and try to reach you a second time. The total time of participation in the study will be 2 weeks. Per normal obstetric care, you will have a 2 week wound check visit and a 6 week postpartum visit. For these visits you can follow up with an obstetrician at Tufts Medical Center or your primary obstetrician, and this may not be at Tufts Medical Center. Six weeks after delivery is the usual period of time that women are followed

after having a baby. None of the information gathered at the six week check-up will be used for research. If you have any additional concerns about your pain control outside of these outlined evaluations, you can call the Maternal Fetal Medicine clinic at Tufts Medical Center (617-636-4549) and an appointment will be arranged.

Your information that is collected as part of this research will not be used or distributed for future research studies, even if all of your identifiers are removed.

Even if you decide not to participate in the study, you could still receive either one of the pain control plans. Your regular doctor would decide what kind of pain medication plan you receive.

RISKS

Women undergoing cesarean section will have some degree of pain or discomfort. Other risks of the procedure include discomfort from placing or maintaining the IV catheter and any side effects from Ketorolac. Side effects may be more likely to occur in the repeated doses in the study plan. Side effects of ketorolac are rare, but can potentially include headache, upset stomach, nausea, vomiting, risk for bleeding stomach ulcers, kidney injury, excessive bleeding, blood clots in your legs, lungs brain or heart, including heart attack, heart failure, high blood pressure, skin reactions, effects on liver function, low blood count and serious allergic reactions. Extra precautions will be taken in patients who have a history of asthma, as Ketorolac can trigger an asthma attack. Available information has not shown any specific adverse events (side effects) in nursing infants; however, please contact the study doctor right away if you notice any.

Normally, the standard of care at Tufts Medical Center, for subjects like you who would benefit equally from both study plans, would involve a conversation between you and the doctor about the best pain medication plan. The decision to choose a pain medication plan may depend on your medical history]or the personal preference of the doctor. Participating in this study is different from the standard of care because neither the patient nor the doctor gets to choose the pain medication plan. You will be randomly assigned to the standard plan or the study plan.

Loss of confidentiality is a risk of study participation. However, data collected from this study will be stored on a locked spreadsheet on a computer in a locked office at Tufts Medical Center so the risk of loss of confidentiality is low. Paper records will be stored in a locked office at Tufts MC.

BENEFITS

There are no direct benefits to you from participating in this study if you are randomized to receive the standard plan. If you are randomized to the study group, there is a potential benefit of less narcotic use and better pain control after your delivery. Potential benefits of less narcotic use include; less constipation and sedation, leading to improved pain control and possibly shorter hospital stay.. However, data collected for this study may contribute to the knowledge of post-operative pain control and women in the future may benefit from what is learned.

ALTERNATIVES

The alternative is to NOT participate in the research study. Your medical care during your hospitalization will not change if you do not participate. If you chose not to participate, then you could receive either the standard plan or study plan depending on the preference of your attending surgeon.

Detailed Information: The following is more detailed information about this study in addition to the information listed above.

WITHDRAWAL

If you are eligible to participate and decide to be in the study, the Principal Investigator may still choose to stop your participation in this study if he thinks it is in your best medical interest. You will not be included in the study if you have a cesarean delivery but are not assigned to either study arm while in the operating room.

You can also leave the research at any time it will not be held against you. If you refuse to participate in the study or stop being in this study, it will not affect your care or treatment outside this study, payment for your health care, or your health care benefits.

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

If you withdraw or are withdrawn from the study, any data collected from you before your withdrawal will still be used for the study.

If you stop being in the research, already collected data may not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

RESEARCH RELATED INJURY

Emergency medical treatment will be given to you if you are hurt or get sick as a direct result of being in this research study. You or your insurance carrier will be required to pay for any such medical care. Any needed medical care is available at the usual cost. All needed facilities, emergency treatment, and professional services are available to you, just as they are to the general public. The institution will not pay for your treatment if you become ill or injured as part of this study.

COSTS

There are no additional costs associated with this study. The cost of your usual standard of care will continue to be your responsibility or that of your insurance. At this time, the hospital does not bill patients separately for the pain medications used after cesarean delivery.

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your condition. This includes:

- The costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- The costs of getting the ready Ketorolac and giving it to you.
- Your insurance co-pays and deductibles.

PAYMENT

You will not be paid for participating in this study.

PRIVACY AND CONFIDENTIALITY

Research data and medical information will be stored in password protected documents on a Tufts MC computer in a locked office. Paper records will also be stored in a locked office at Tufts MC. For analysis, your file will be assigned a code that is only accessible to members of the research team.

If you decide to take part in this research study, your personal information will not be given to anyone unless we receive your permission in writing. It will only be given if the law requires it. It will also only be given for regular hospital treatment, payment, and hospital management activities.

We will make every effort to keep your information private, but it cannot be completely guaranteed. The Institutional Review Board of Tufts Medical Center and Tufts University Health Sciences may check records that identify you. This might include your medical or research records and the informed consent form you signed. The records of this study might also be reviewed to make sure all rules and guidelines were followed.

We may publish the results of this research. However, we will keep your name and other identifying information confidential.

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.

AUTHORIZATION TO USE OR DISCLOSE YOUR IDENTIFIABLE HEALTH INFORMATION

If you sign this document, you give permission to the Principal Investigator named above and research staff at Tufts Medical Center as well as other individuals at Tufts Medical Center who may need to access your information to do their jobs (such as for treatment, payment (billing) or health care operations) to use or disclose (release) your health information that identifies you for the research study described above.

The parties listed in the preceding paragraph may disclose the health information described below to the following persons and organizations for their use in connection with the research study:

- Individuals or organizations working under the direction of the Principal Investigator(s) for the study,
- Outside individuals or entities that have a need to access this information to perform activities relating to the conduct of this research, such as analysis by outside laboratories on behalf of Tufts Medical Center,
- Other researchers and institutions that are conducting or participating in this study,
- The Office for Human Research Protections in the U.S. Department of Health and Human Services, the United States Food and Drug Administration (FDA) and other federal and state agencies that have the right to use the information as required by law, and
- The members and staff of any Institutional Review Board (IRB) that oversee this study.

The health information that we may use or disclose (release) for this research study includes all information in your medical record related to the diagnosis and management of your postoperative course, including the record of your care, as well as any information collected or created during the course of this study.

Tufts Medical Center is required by law to protect your health information. By signing this document, you authorize Tufts Medical Center to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them. You may not be allowed to see or copy the information described on this form as long as the research is in progress, but you have a right to see and copy the information upon completion of the research in accordance with hospital policies.

Tufts Medical Center may not withhold or refuse to provide you with clinical care based on whether or not you sign this form.

This authorization does not have an expiration date. You may change your mind and revoke (take back) this authorization at any time. Even if you revoke this authorization, this site's clinical, administrative and research staff may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this authorization, you must write to: HIPAA Privacy Officer for Research,

800 Washington Street, Box 5100, Boston, MA 02111. If you revoke this authorization, you may no longer be allowed to participate in the research described in this form.

WHOM TO CONTACT

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at:

> Mohak Mhatre, MD, mmhatre@tuftsmedicalcenter.org , 617-636-4549 (Day)
> Jean Hostage, MD jhostage@tuftsmedicalcenter.org, 617-636-4549 (Day) 617-636-4250 (evening)

If you have question about your rights as a research study subject, call the Tufts Medical Center and Tufts University Health Sciences Institutional Review Board (IRB) at (617) 636-7512. The IRB is a group of doctors, nurses, and non-medical people who review human research studies for safety and protection of people who take part in the studies. Federal law requires the IRB to review and approve any research study involving humans. This must be done before the study can begin. The study is also reviewed on a regular basis while it is in progress. This research study has been reviewed and approved by the IRB of Tufts Medical Center and Tufts University Health Sciences.

Documentation of Consent

I have been given a copy of this form. I have read it or it has been read to me. I understand the information and have had my questions answered to my satisfaction. I agree to take part in this study.

I understand that I will be informed of any new findings developed during the course of this research study that may affect my willingness to stay in this research study.

_____	_____	_____
Participant's Signature	Date	Time (required for all clinical trials at Tufts Medical Center)

I have fully explained to _____ the nature and purpose of the above-described study and the risks that are involved in its performance. I have answered all questions to the best of my ability.

_____	_____
Date	Principal Investigator or Representative's Signature

Witness Signature:

_____	_____	_____
Witness' Signature	Date	Time (required for all clinical trials at Tufts Medical Center)

_____
Witness Printed Name