Management of Pain After Cesarean: A Randomized Control (MOPAC) Trial

Clinical Trials Number: NCT0329640

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CONSENT FOR RESEARCH
Penn State College of Medicine
Penn State Health

Title of Project: Management Of Pain After Cesarean (MOPAC) Trial

Principal Investigator: Serdar Ural, MD

Address: Penn State Health, Department of Obstetrics and Gynecology
Division of Maternal Fetal Medicine
500 University Drive, Hershey, PA 17033

Telephone Numbers: Weekdays: 8:00 a.m. to 5:00 p.m. (717) 531-8142 opt 5. After hours call (717) 531-8521. Ask for the obstetrician doctor on 24-hour call.

Subject's Printed Name: _____

We are asking you to be in a research study.

Whether or not you take part is up to you. You can choose not to take part. You can agree to take part and later change your mind. Your decision will not be held against you, and there will be no penalty or loss of benefits to which you are entitled.

This form gives you information about the research. Please ask questions about anything that is unclear to you and take your time to make your choice.

KEY INFORMATION

The following is a short summary of this study to help you decide whether or not to be a part of this research. More detailed information is provided later in this form. If you have any questions, be sure to ask the study team.

Why am I being invited to take part in this research study?

We are asking you to take part in this voluntary research study because you are scheduled to have a Cesarean section (C-section), which is a surgical procedure in which babies are born through the abdomen (stomach).

What is the purpose of this research study?

The purpose of this voluntary research study is to see if a standardized pain regimen combining ibuprofen with acetaminophen on schedule is better at controlling pain than a regimen of ibuprofen with placebo, which is a tablet designed to look like the acetaminophen tablet but which has no therapeutic effect. We also wish to study how much opiate medication women consume in both groups.

How long will the research study last?

If you agree to take part in this research, you will participate for two weeks after your Cesarean section.

What will I need to do?

If you take part in this research, your major responsibilities will include:

- Allowing the study team to review your medical chart after you are discharged to record your pain scores and calculate how much opiate pain medication you received in the hospital
- Allowing the study team to review your operative report and all notes associated with your surgery to assess for rates of complications
- Completing a survey one week after surgery which asks questions regarding medication prescription, consumption, and your overall satisfaction with your pain control
- Completing two surveys two weeks after surgery: one which will ask additional questions regarding medication consumption and your overall satisfaction with your pain control, and another which will ask questions regarding your quality of life.
- Please note: you are free to skip any questions that you would prefer not to answer.

What are the main risks of taking part in the study?

For this study, the main risks to know about are: Risk of loss of confidentiality if your information or your identity is obtained by someone other than the investigators. There is a risk that the pain regimen that you receive will not be satisfactory to you. While acetaminophen is generally considered safe and can be purchased over-the-counter, it is metabolized by the liver and too much may lead to liver injury. This could be made worse if you have chronic liver disease or liver injury, which you may not be aware of. If you have a known history of chronic liver disease or other known reason why you should not take acetaminophen, you should not participate in this study. To minimize the risk, acetaminophen dosages have been calculated to be below the daily recommended total dosage.

What are the possible benefits to me that may reasonably be expected from being in the research?

We cannot promise any benefits to you from taking part in this study. However, possible benefits include perceived better pain control if you receive our experimental pain regimen and require less opiate pain medication for breakthrough pain. Results of the study may benefit other people in the future by helping us learn more about guidance and motivation for future studies to address post-operative pain control in women who have undergone Cesarean section.

What happens if I do not want to be in this research project?

If you do not wish to participate in this research project, you will receive standard pain medication as prescribed by the delivering obstetrical team.

DETAILED INFORMATION

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

1. Why is this research study being done?

This research is being done to see if a standardized pain regimen combining ibuprofen with acetaminophen on schedule is better at controlling pain than a regimen of ibuprofen with placebo. We also wish to study how much opiate medication women consume in both groups.

144 women will take part in this research study at the Penn State Health Hershey Medical Center.

2. What will happen in this research study?

Date of Patient Cesarean Section

You will be approached by a study team member to see if you are interested in participating in this research. The consent form will then be thoroughly explained to you and all your questions will be answered. If you agree to participate, we will proceed with signing the consent. Once signed by you and the study team member, a copy will be given to you and placed on your medical chart so that others caring for you will know that you are participating in this project.

We will then collect demographic and other information about your obstetric and medical history. You are free to skip any questions that you are not comfortable answering.

You will then be randomized (assigned by a computer program) to receive the pain regimen of ibuprofen plus acetaminophen or ibuprofen plus placebo. You have a 50% chance of being placed in either group, similar to the odds of flipping a coin and landing on "heads" or "tails." Neither you nor the research team will know which study treatment you are receiving, but the research team will be able to get this information quickly if it is needed to ensure your safety.

You will then undergo your Cesarean section by the obstetrical team per standard of care.

After Cesarean Section until Your Discharge

Before you are able to take medication by mouth, you may receive medication intravenously (through the IV) or intramuscularly (as an injection) for relief of pain as prescribed by the obstetric and/or anesthesia team, which would be beyond the control of this trial. Once able to take medication by mouth, you will be given pain medication as assigned by your grouping (randomization). You will either receive one regimen (ibuprofen 600mg and placebo scheduled every 6 hours), or the other regimen (ibuprofen 600mg and acetaminophen 650 mg every 6 hours). You will also have the option to ask for either one or two tablets of oxycodone 5mg every 4 hours if you have "breakthrough" pain. "Breakthrough" pain is defined as pain that is present at a time which no scheduled pain medication is due (in other words, the pain "broke through" the scheduled medication and additional medication may be needed). Scheduled medication, either ibuprofen + placebo or ibuprofen +acetaminophen, will be administered every 6 hours on schedule regardless of your reported pain on the pain scale without oxycodone. Oxycodone will be given if you have pain (4 or greater; 1 pill if pain 4-6 or 2 pills if pain 7-10) at a time when no scheduled medication is due. Here is a schedule to help you understand when you may receive pain medication, and what medication may be dispensed:

0000 - Pain assessed; scheduled medication given
0400 – Pain assessed; may receive oxycodone if pain score 4+
0600 – Pain assessed; Scheduled medication given
0800 – Pain assessed; may receive oxycodone if pain score 4+
1200 - Pain assessed; scheduled medication given
1600 – Pain assessed; may receive oxycodone if pain score 4+
1800 - Pain assessed; scheduled medication given
2000 - Pain assessed; may receive oxycodone if pain score 4+

Hospital Discharge

Pain scores and the drug amount that you have taken will be recorded based on review of your chart. You will receive a prescription for narcotic which is the standard for all women who have a C-section at the Penn State Hershey Medical Center: 20 tablets of oxycodone 5 mg of which you can take 1-2 tablets every 6-8 hours for breakthrough pain. You will be free to take additional over-the-counter pain medication if you would like.

One Week Post-Surgery

You will receive an invitation via electronic mail (email) to complete another survey online to assess opiate consumption. You will then receive a daily reminder for three days if the survey is not complete. If the survey remains incomplete after that time, the invitation link will expire and you will not be able to complete the survey.

Two Weeks Post-Surgery

You will again receive an invitation to complete another survey to assess opiate consumption, as well as a quality of life survey (called the WHOQOL-BREF). The invitations will be sent via email. You will then receive a daily reminder for three days if the surveys are not complete. If the surveys remain incomplete after that time, the invitation links will expire and you will not be able to complete the surveys.

What are my responsibilities if I take part in this research?

If you take part in this research, your major responsibilities will include:

- Allowing the study team to review your medical chart after you are discharged to record your pain scores and calculate how much opiate pain medication you received in the hospital
- Allowing the study team to review your operative report and all notes associated with your surgery to assess for rates of complications
- Completing a survey one week after surgery which asks questions regarding medication prescription, consumption, and your overall satisfaction with your pain control
- Completing two surveys two weeks after surgery: one which will ask additional questions regarding medication consumption and your overall satisfaction with your pain control, and another which will ask questions regarding your quality of life.
- Please note: you are free to skip any questions that you would prefer not to answer.

3. What are the risks and possible discomforts from being in this research study?

You will be assigned to a treatment program by chance. The treatment that you receive may prove to be less effective or to have more side effects than the other research treatment or other available treatment.

While acetaminophen is generally considered safe and can be purchased over-the-counter, it is metabolized by the liver and too much may lead to liver injury. This could be made worse if you have chronic liver disease or liver injury, which you may not be aware of. If you have a known history of chronic liver disease or other known reason why you should not take acetaminophen, you should not participate in this study. To minimize the risk, acetaminophen dosages have been calculated to be below the daily recommended total dosage.

There is also a risk that the pain regimen you receive will not be satisfactory to you. This risk is low because all medications used in the study have been extensively studied and found to be very good at

treating pain in the post-operative period. Additionally, these medications are already in use for treating post-operative pain at the Hershey Medical Center, and you will be allowed to request additional medication as needed. What makes this study unique is that our regimens will standardize the schedule of medication administration

There is a risk of loss of confidentiality if your information or your identity is obtained by someone other than the investigators, but precautions will be taken to prevent this from happening. The confidentiality of your electronic data created by you or by the researchers will be maintained as required by applicable law and to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

4. What are the possible benefits from being in this research study?

4a. What are the possible benefits to me?

There is no guarantee that you will benefit from this research. The possible benefit you may experience from this study is that you may require less opiate pain medication if you receive our experimental pain regimen.

4b. What are the possible benefits to others?

The results of this research may guide the future studies to address post-operative pain control in women who have undergone Cesarean section.

5. What other options are available instead of being in this research study?

You do not have to take part in this study to be treated for your condition. Instead of participating in this research, you could:

- Receive normal standard of care for your pain management from the caring obstetrical team.
- Be part of a different research study, if one is available.

Before you decide if you want to be in this research, we will discuss the other choices that are available to you. We will tell you about the possible benefits and risks of these choices.

6. How long will I take part in this research study?

Participation in this study will last approximately 2 weeks after your surgery. This time period will include one 10-15 minute survey 1 week after your surgery and 2 surveys at 2 weeks after your surgery that will take 30-45 minutes to complete.

7. How will you protect my privacy and confidentiality if I decide to take part in this research study?

7a. What happens to the information collected for the research?

Efforts will be made to limit the use and sharing of your personal research information to people who have a need to review this information. Reasonable efforts will be made to keep the personal information in your research record private. However, absolute confidentiality cannot be guaranteed, and there may be situations where disclosure is required by law.

In our research files at Penn State Health (PSH) and Penn State College of Medicine (PSU) we will include these identifiers: your name, address, phone number, date of birth, medical record number, email address, and a code number.

- A list that matches your name with your code number will be kept in a locked file in the Division of Maternal Fetal Medicine's research office and only the study team members will have access to it.
- Your research records will be labeled with: your code number and your initials and will be kept in a safe area in the Division of Maternal Fetal Medicine's research office.

- A copy of this signed consent form will be included in your PSH medical record. This means that other PSH healthcare providers will know you are in this study.

In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

7b. What will happen to my research information and/or samples after the study is completed?
We may use your research information in future studies with other investigators for future research without your additional informed consent. Before we use or share your information we will remove any information that shows your identity.

7c. How will my identifiable health information be used?
In general, under federal law (including the Health Insurance Portability and Accountability Act – HIPAA or privacy laws) your health information is private. By signing this form, you are authorizing us to collect, use, and disclose your identifiable health information, sometimes referred to as "Protected Health Information" or "PHI" under HIPAA, for the purposes of this research study. We will use and disclose your information only as described in this form, in the PSH Privacy Notice, and as may be required or allowed under the applicable privacy laws.

The research team may use the following health information:

- Past, present, and future medical records, including identifiable information
- New health information from tests, procedures, visits, interviews, or forms filled out as part of this research study.

The following people/groups may see, use, and share your identifiable health information:

- PSH/PSU research staff involved in this study
- The PSH/PSU Institutional Review Board (IRB), a group of people who review the research study to protect subjects' rights and welfare
- The PSH/PSU Human Subjects Protection Office
- The PSH/PSU Research Quality Assurance Office
- Non-research staff within PSH/PSU who need this information to do their jobs (such as for treatment, payment (billing), or health care operations)
- Federal and state agencies (such as the U.S. Food and Drug Administration, the Office for Human Research Protections, the Department of Health and Human Services, the National Institutes of Health, and other U.S. or foreign government bodies that oversee or review research)
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Organizations that provide independent accreditation and oversight of hospitals and research
- Public health and safety authorities (for example, if we learn information that could mean harm to you or others, we may need to report this, as required by law)
- The PSH/PSU pharmacy
- A group that oversees the data (study information) and safety of this research

These groups may also review and/or copy your original PSH/PSU records while looking at the results of the research study. It is possible that some of the other people/groups who receive your health information may not be required by Federal privacy laws to protect your information. We share your information only when we must, and we ask anyone who receives it from us to protect your privacy.

Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your identifiable health information and samples may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

We may remove identifying information from your protected health information. Once we do this, the remaining information will not be subject to the privacy laws. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Because research is an ongoing process, your permission for the use, storage and sharing of your health information will continue indefinitely.

Your privacy rights:

- You have the right to refuse to sign this form that allows us to use and share your health information for research; however, if you don't sign it, you will not be able to take part in this research study.
- You have the right to withdraw your permission for us to use or share your health information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing using the address on the front of this form. Once permission is withdrawn, you cannot continue to take part in the study.
- If you withdraw your permission, we will stop collecting health information about you for this study; we may continue to use and share your health information that we already have if it is necessary for safety and scientific soundness of the research study; and we will not be able to take back information that has already been used or shared with others.
- You have the right to see and get a copy of your health information that is used or shared for treatment or for payment. However, you may not be allowed to see or copy certain health information that is a part of this research study. This is only for the period of the study. You will be allowed to see that information when the entire research study is complete.

8. What are the costs of taking part in this research study?

8a. What will I have to pay for if I take part in this research study?

For costs of medical services for care you would receive even if you were not in this research study:

- You and/or your insurance company will be responsible for the cost of routine medications, tests and procedures that you would receive even if you were not in this research.
- You and/or your insurance company will be billed for the costs of these routine tests and procedures in the usual manner.
- You will be responsible for any co-payments, co-insurance and deductibles that are standard for your insurance coverage.
- You will be responsible for any charges not reimbursed by your insurance company.
- Some insurance companies may not pay for routine costs for people taking part in research studies. Before deciding to be in this research you should check with your insurance company to find out what they will pay for.
- You will not be required to pay for medication dispensed by the study (placebo or acetaminophen 650 mg tablets).

If you have any questions about costs and insurance, ask the research study doctor or a member of the research team.

8b. What happens if I am injured as a result of taking part in this research study?
It is possible that you could develop complications or injuries as a result of being in this research study. If you experience a side effect or injury and emergency medical treatment is required, seek treatment immediately at any medical facility. If you experience a side effect or injury and you believe that emergency treatment is not necessary, you should contact the principal investigator listed on the first page of this consent form as soon as possible and the principal investigator will arrange for medical treatment. You should also let any health care provider who treats you know that you are in a research study.

PSH/PSU compensation for injury

- There are no plans for PSH/PSU to provide financial compensation or free medical treatment for research-related injury.
- If an injury occurs, medical treatment is available at the usual charge.
- Costs will be charged to your insurance carrier or to you.
- Some insurance companies may not cover costs associated with research injuries.
- If these costs are not covered by your insurance, they will be your responsibility.

When you sign this form you are not giving up any legal right to seek compensation for injury.

9. Will I be paid to take part in this research study?
Reimbursement and payment must occur in accordance with PSU Research Protection Guidelines: RPG03, as outlined below.

Payment must be issued by Greenphire ClinCard

- *The subject must be paid by deposit onto the card, which may be used as a credit or debit card;*
- *Social security number must always be collected, but it will only be used to generate a 1099 form for tax reporting purposes for money offered as a stipend. Reimbursement dollars will not be counted towards tax reporting purposes.*
- *If you believe that you cannot use the Greenphire ClinCard, please contact the Controller's Office at* controller@pennstatehealth.psu.edu.

If you complete the one week opiate consumption/pain control survey, you will be receive $10. If you complete the two week opiate consumption/pain control survey, you will receive $10. If you complete the quality of life survey, you will receive $20. Therefore, the total compensation you could receive is $40. If you do not complete a survey for any reason, you will receive compensation only for the surveys you have completed. Payments will be provided by a Greeenphire ClinCard which will be mailed to your home address upon completion of your participation in the study.

This reimbursement will be issued by an external company called Greenphire, which will issue your reimbursement. You will be issued a ClinCard, which is a debit card that your funds are loaded onto and can be used at your discretion. The research team will give Greenphire some personal information about you, as described below. Greenphire will only use your personal information to process this reimbursement and will not share it with anyone for any other purpose. Details of the debit card system are explained on an additional sheet. If you lose the card, you may be responsible for the replacement fee.

When the survey(s) are completed, funds will be approved and loaded onto your card. The funds will be available within 2-3 business days. In order to assign a ClinCard to you and load funds onto the ClinCard, Greenphire will need your Study/Subject ID, Name, Address, and Social Security Number.

You will have the option to receive updates related to payment alerts via text message and/or email message. Standard text messaging rates will apply. In order to send you messages Greenphire will need your Mobile Phone Number and/or E-mail Address.

10. Who is paying for this research study?

Funds from the Department of Obstetrics and Gynecology, Penn State College of Medicine will be used to support this research. The Penn State Addiction Center is providing computer equipment.

11. What are my rights if I take part in this research study?

Taking part in this research study is voluntary.

- You do not have to be in this research.
- If you choose to be in this research, you have the right to stop at any time.
- If you decide not to be in this research or if you decide to stop at a later date, there will be no penalty or loss of benefits to which you are entitled.

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 medical information from your routine medical care. If you agree, this data will be handled the same as research data. If you withdraw completely from the research study, no further information will be collected and your participation will end. You may discontinue taking part at any time without penalty or loss of benefits to which you are otherwise entitled.

Your research doctor may take you out of the research study without your permission. Some possible reasons for this are: continuing the research would be harmful because of serious side effects, you cannot receive NSAIDs or you require acetaminophen for a reason other than pain.

During the course of the research you will be provided with any new information that may affect your health, welfare or your decision to continue participating in this research.

12. If I have questions or concerns about this research study, whom should I call?

Please call the head of the research study Dr. Serdar Ural at 717-531-8142, option #5 or the Obstetrics doctor on 24-hour call at (717) 531-8521 if you :

- Have questions, complaints or concerns about the research.
- Believe you may have been harmed by being in the research study.

You may also contact the research protection advocate in the PSH Human Subjects Protection Office (HSPO) at (717) 531-5687 if you:

- Have questions regarding your rights as a person in a research study.
- Have concerns, complaints or general questions about the research.
- Have questions about your privacy and the use of your personal health information.
- You may also call this number if you cannot reach the research team or wish to offer input or to talk to someone else about any concerns related to the research.

You may visit the Penn State College of Medicine's Clinical Research web site at http://med.psu.edu/clinical-research/faqs for:

- Information about your rights when you are in a research study;
- Information about the Institutional Review Board (IRB), a group of people who review the research to protect your rights; and
- Links to the federal regulations and information about the protection of people who are in research studies. If you do not have access to the internet, copies of these federal regulations are available by calling the HSPO at (717) 531-5687.

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.

INFORMED CONSENT AND AUTHORIZATION TO TAKE PART IN RESEARCH

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the research to the subject or subject representative, provided the subject or subject representative an opportunity to discuss and consider whether or not to participate in the research, and have answered any questions about the research.

_____	_____	_____	_____
Signature of person who explained this research	Date	Time	Printed Name

(Only approved investigators for this research may explain the research and obtain informed consent.)

Signature of Person Giving Informed Consent and Authorization

Before making the decision about being in this research you should have:

- Discussed this research study with an investigator,
- Read the information in this form, and
- Had the opportunity to ask any questions you may have.

Your signature below means that you have received this information, have asked the questions you currently have about the research and those questions have been answered. You will receive a copy of the signed and dated form to keep for future reference.

Signature of Subject

By signing this consent form, you indicate that you voluntarily choose to be in this research and authorize your information to be used and shared as described above.

_____	_____	_____	_____
Signature of Subject	Date	Time	Printed Name