COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

YALE-NEW HAVEN HOSPITAL

Study Title:
Dexamethasone on Post-Operative Pain after C-section in Patients using Medication Assisted Treatment (MAT) during Pregnancy

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Research Study Summary:

- We are asking you to join a research study.
- The purpose of this research study is to look at improving pain after c-section in individuals that are taking medication assisted treatment (methadone or suboxone for a history of substance abuse), as it is known that individuals with a history of opioid use disorder now utilizing medication assisted treatment often experience a more complicated pain management course and require more opioid pain medication after c-section than individuals without a history of opioid use disorder.

Study procedures will include:

- Receiving 100cc of fluids (< ½ cup) through the IV that will be placed for your c-section, which will either contain 0.1mg/kg of dexamethasone (a steroid, anti-inflammatory medication) or only plain fluid (a placebo), based on which group you are randomly assigned to.
- Only your c-section hospital visit is required. Information about your delivery will be collected on review of your medical record.
- Optional follow up survey administered via phone call at 6 months and 12 months postpartum
- The psychological, social, legal and financial risk associated with this protocol are low. There are some risks in participating in this study (reviewed on page 3), as well as possible risk of breach of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.
- The study may have no benefits to you. Subjects of this study may receive the benefit of improved pain and require a smaller amount of opioid pain medication following their cesarean section as a result of participation in this study. Further this research will help to improve the clinical understanding of pain management in women with medication assisted treatment who undergo surgery.
- There are other choices available to you outside of this research. You may undergo current standard of care which is to receive no additional medications in addition to routine pain medications offered to our post-partum individuals, as there are no proven alternative effective adjunctive treatments.
- Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You can also change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.
- If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Take as much time as you need before you make your decision. Ask the study staff questions about anything you do not understand.

APPROVED BY THE YALE UNIVERSITY IRB 10/23/2023

Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

Why is this study being offered to me?
We are asking you to take part in a research study because you have been identified as a individual who has a history of opioid use disorder now utilizing medication assisted treatment during pregnancy.

Who is paying for the study?
This study is being funded by Dr. Merriam's research account

Who is providing other support for the study?
No additional support at this time.

What is the study about?
The purpose of this study is to investigate possible benefit of using dexamethasone to improve post-cesarean pain in individuals using medication assisted treatment, as there currently are no proven methods to improve post-surgical pain in this individual population. Dexamethasone has been shown to reduce pain and decrease the amount of opioid medication needed to control post-operative pain in individuals without a history of opioid use disorder, and we are testing to see if there are similar benefits in the chronic opioid using population. We plan to enroll 40 subjects.

What are you asking me to do and how long will it take?
If you agree to take part in this study, this is what will happen:

- Shortly after leaving the operating room from your c-section, you will be brought to the post-anesthesia care unit (PACU) for close monitoring, as is routine following surgery.
- At that time, based on which study group you would be randomly assigned to, you would receive 100cc of IV fluids (< ½ cup) through the IV that was placed for your procedure. The IV fluid will either contain a dose of dexamethasone (a steroid medication) or only plain fluid (a placebo).
- After that, nurses will be assessing your pain level as is routine care following surgery using standard pain scales (1-10).
- Randomization of subjects into one of the two groups will be done by assigning you a computer-generated number. There is a 50% chance of being assigned to either group, similar to a flip of a coin.
- Use of a 'placebo' through your pre-placed IV allows us to be sure that it is the dexamethasone medication itself and not the experience of receiving IV fluid that would affect your pain following your c-section.
- We will also be looking at several things about you including: your age, prior pregnancy and delivery history, BMI, admission toxicology screen, gestational age, singleton vs. multiple gestation, and neonatal weight at birth.
- At 6 and 12 months following delivery you have the option of being contacted via phone call for a short 5 question survey

What are the risks and discomforts of participating?

This is a widely used and well understood medication that is safe and can be taken without side effects in most individuals.

Risks with one time dosing of dexamethasone apply primarily to individuals with pre-existing health conditions that are not participating in this study, including:

Heart disease: Heart failure and/or high blood pressure; use has been associated with water retention, changes in lab values for electrolytes, and high blood pressure. Use with caution following heart attack; corticosteroids, such as dexamethasone, have been associated with damage to the muscle of the heart.

Diabetes: may alter blood sugar control leading to elevated blood sugar levels.

Intestinal disease: (diverticulitis, recent bowel surgery, stomach ulcers, ulcerative colitis, infection) due to risk of a hole forming in the wall of the intestines or stomach

For subjects who plan to breastfeed following delivery:

Although the risk to newborns is unknown for any corticosteroid, use of dexamethasone (a corticosteroid) is supported by ACOG (the ObGyn national society), and found to be safe in pregnancy, especially for short term use. It is regularly given to mothers for benefits to unborn babies, mainly lung development for pregnancies at risk of preterm delivery. If you plan to breastfeed your baby, this drug likely does appear in small quantities in breast milk and there is a very small risk the drug will have the potential to cause negative side effects in a breastfed baby (eg, problems with growth, problems with hormone creation in the baby) if there were to be long term use, which there is not part of this study. Information related to long term use is not available. One time doses of dexamethasone are considered safe with breastfeeding.

While data on the use of dexamethasone during lactation are not available, the American Academy of Pediatrics lists the corticosteroids prednisone and prednisolone (similar drugs to dexamethasone) as safe when breastfeeding. At 1 to 5 hours after a single dose of corticosteroids, there is no drug found at high enough levels to be found in breast milk after one day. Breastfeeding while taking corticosteroids carries very low risk of exposure to the baby, which may be lowered even more by breast feeding right before or more than 4 hours after taking the medication. Further, although no data are available on the if dexamethasone enters human breast milk, it is likely the same as prednisone which enters breast milk in very low amounts. Doses of prednisone as high as 120 mg do not cause the drug to be found in breast milk (similar to a dose of 18mg of Dexamethasone which is significantly more than the dose given in this study). This drug is commonly used in pediatrics for treating immune diseases such as joint problems and, asthma or other lung diseases. It is not likely that the amount of dexamethasone in breast milk would cause an effect on the baby unless used in high doses over long periods of time.

More detailed information can be given to you about the possible risks of the medication (dexamethasone) if you would like.

Lastly, the psychological, social, legal and financial risk associated with this protocol are low

How will I know about new risks or important information about the study?

- We will tell you if we learn any new information that could change your mind about taking part in this study.

How can the study possibly benefit me?

- Subjects of this study who receive the study medication may receive the benefit of decreased pain and require a smaller amount of opioid pain medication following their cesarean section as a result of participation in this study. Participants who receive the placebo are not expected to have any benefits.

- It is possible that this improvement in pain and decrease in opioid requirement may decrease the risk of the poor maternal outcome associated with untreated pain and stresses incurred on individuals with a history of opioid use disorder including those that lead to increased rates of relapse and overdose.

How can the study possibly benefit other people?

The benefits to science and other people may include a better understanding of how to better reduce post-cesarean pain in individuals with a history of opioid use disorder utilizing medication assisted treatment during pregnancy.

Are there any costs to participation?

If you take part in this study, you will not have to pay for any services, supplies, study procedures, or care that are provided for this research only (they are NOT part of your routine medical care). You or your health insurance must pay for services, supplies, procedures, and care that are part of your routine medical care. You will be responsible for any co-payments required by your insurance.

Will I be paid for participation?

You will not be paid for participating in this study.

What are my choices if I decide not to take part in this study?

The alternative is not to participate in the study and continue c-section pain management as is currently done at our hospital. Your decision to participate or not will not affect your care in anyway.

Of note there are no established or evidence-based methods of improving post-cesarean pain in individuals with a history of opioid use disorder currently using medication assisted treatment. All currently used adjunctive opioid sparing strategies are used inconsistently and are not medically recognized as standard of care in this population.

How will you keep my data safe and private?

We will keep information we collect about you confidential. We will share it with others if you agree to it or when we have to do it because U.S. or State law requires it. For example, we will tell somebody if you we learn that you are hurting a child or an older person.

When we publish the results of the research or talk about it in conferences, we will not use your name. If we want to use your name, we would ask you for your permission.

We will also share information about you with other researchers for future research but we will not use your name or other identifiers. We will not ask you for any additional permission.

What Information Will You Collect About Me in this Study?

The information we are asking to use and share is called “Protected Health Information.” It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, we cannot use or share your health information for

research without your permission. If you want, we can give you more information about the Privacy Rule. Also, if you have any questions about the Privacy Rule and your rights, you can speak to Yale Privacy Officer at 203-432-5919.

We will look at information including your age, prior pregnancy and delivery history, BMI, admission toxicology screen, what pain medications are given during delivery hospitalization, gestational age, singleton vs. multiple gestation, and neonatal weight at birth.

The follow up survey after delivery will include questions related to if you are still currently taking your medication assisted therapy and if you have used any non-prescribed opiates in the last 6 months. The information collected in this survey will not be shared with anyone in healthcare or law enforcement. Your answers will not be able to be traced back to you when the study results are published.

Information from in your medical record from YNHH that we will collect, use, and share includes:

- Research study records
- Medical and laboratory records of only those services provided in connection with this study including the entire research record and any medical records held by ***YNHH*** created from the start to end of your admission for your c-section
- Information obtained during this research regarding
    - HIV / AIDS test results
    - Hepatitis infection
    - Sexually transmitted diseases
    - Other reportable infectious diseases
    - Physical exams
    - Pain scale responses
    - The diagnosis and treatment of a mental health condition
    - Use of illegal drugs or the study of illegal behavior
    - Records about any study drug you received

How will you use and share my information?

We will use your information to conduct the study described in this consent form.
We may share your information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- The U.S. Food and Drug Administration (FDA) This is done so that the FDA can review information about dexamethasone involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies.
  Drug regulatory agencies in other countries
- Governmental agencies to whom certain diseases (reportable diseases) must be reported
- Health care providers who provide services to you in connection with this study.
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.
- Co-Investigators and other investigators
- Study Coordinator and Members of the Research Team

We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this.

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.
All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine and Yale-New Haven are required to comply with HIPAA and to ensure the confidentiality of your information. Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Why must I sign this document?
By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes. You always have the right to review and copy your health information in your medical record.

However, this is a double blinded treatment study and if you sign this permission form, you will not be allowed to look at or copy your study related information until after the research is completed.

What if I change my mind?
The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to *Victoria Wesevich* at the Yale University, New Haven, CT 06520.

If you withdraw your permission, you will not be able to stay in this study but the care you get from your doctor outside this study will not change. No new health information identifying you or your newborn will be gathered after the date you withdraw. Information that has already been collected may still be used and given to others until the end of the research study to insure the integrity of the study and/or study oversight.

Who will pay for treatment if I am injured or become ill due to participation in the study?

If you are injured while participating in this study, you will receive treatment as appropriate given your clinical condition by the medical team providing your care during your admission for your c-section. You will not receive any other kind of payment. There are no plans to pay you for such things as lost wages, disability, or discomfort as part of this study.
Yale School of Medicine and Yale-New Haven Hospital do not provide funds for the treatment of research-related injury. You or your insurance carrier will be expected to pay the costs of this

treatment. No additional financial compensation for injury or lost wages is available. You will still be responsible for any co-pays required by your
insurance company for standard treatment. You do not give up any of your legal rights by signing this form

What if I want to refuse or end participation before the study is over?

Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

We would still treat you with standard therapy or, at your request, refer you to a clinic or doctor who can offer this treatment. Not participating or withdrawing later will not harm your relationship with your own doctors or with this institution.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part.

The researchers may withdraw you from participating in the research if necessary. If the subject has a major complication during her c-section, it may be deemed that it is no longer medically safe and appropriate for her to possibly receive Dexamethasone following her surgery. The decision is determined by her obstetrician and anesthesia team present at the time of her surgery. If the subject has additional medical needs at the time of withdrawal from the study whether determined by the medical team or subject, she will continue to receive necessary care as is routine. The subject should know that once the Dexamethasone is administered, it cannot be reversed.

What will happen with my data if I stop participating?

If you wish, you may withdraw your data from this study at any time.
When you withdraw from the study, no new health information identifying you will be gathered from your electronic medical record after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight. The information collected will only remain in your electronic medical record as the post-partum pain scores and medications given are to remain, as they are part of your health records during your post-partum period.

Who should I contact if I have questions?

Please feel free to ask about anything you don't understand.
If you have questions later or if you have a research-related problem, you can call the Principal Investigator at: **475-298-6149**

If you have questions about your rights as a research participant, or you have complaints about this research, you call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

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 and Permission

Your signature below indicates that you have read this consent document and that you agree to be in this study.

We will give you a copy of this form.

Participant Printed Name	Participant Signature	Date
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date
Person Witnessing Phone Consent	Person Witnessing Phone Consent Signature	Date

Your signature below indicates that you have read this consent document and that you agree to the follow up phone surveys at 6 and 12 months postpartum

Participant Printed Name	Participant Signature	Date
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date
Person Witnessing Phone Consent	Person Witnessing Phone Consent Signature	Date