The Efficacy and Cost-Effectiveness of a 24-hour course of Methenamine Hippurate For Preventing Post-Operative Urinary Tract Infection

NCT02358993

April 18, 2017

UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title:	**The Efficacy and Cost-Effectiveness of a 24-hour course of Methenamine Hippurate for Preventing Post-Operative Urinary Tract Infection**
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You are being invited to participate in a research study. Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you decide to participate, you will be asked to sign this form.

Why am I being asked to volunteer?
You are being asked to volunteer because you have decided to undergo surgical repair of pelvic organ prolapse, incontinence, or both, and may potentially require a short-term catheter – a drainage tube in your bladder, also known as an indwelling catheter – for a few days after your surgery. Catheterization may put you at higher risk of urinary tract infections. You are being asked to participate in a research study to determine if a short course of methenamine hippurate is effective in decreasing the risk of urinary tract infection after short-term indwelling catheterization for pelvic reconstructive surgery.

What is the purpose of this research study?
Patients who undergo pelvic reconstructive surgery (that is, surgery for pelvic organ prolapse, incontinence, or both) may require short-term indwelling catheterization after surgery because of urinary retention. Urinary retention occurs when patients are unable to empty their bladders completely or properly. Catheterization puts patients at higher risk of urinary tract infections. The purpose of this study is to determine whether using a medication called methenamine hippurate will prevent urinary tract infections in patients requiring a short-term catheter after pelvic reconstructive surgery.

Methenamine hippurate is FDA-approved and has few, mild side effects. This medication has been shown to be effective in 5-13 day courses in studies for prevention of urinary tract infection after short-term indwelling catheterization for gynecologic surgical procedures. This study will examine the effectiveness of a short course (a 2 dose course) of methenamine hippurate for prevention of urinary tract infection after short-term indwelling catheterization for pelvic reconstructive surgeries. The use of two doses of methenamine hippurate for the prevention of

IRB Approval From: 04/18/2017 to: 04/17/2018

urinary tract infections associated with catheter use after pelvic reconstructive surgery IS INVESTIGATIONAL. This means that the treatment may not necessarily provide any benefits.

How long will I be in the study?

You will be part of the study until 6 weeks after your surgery.

A total of 230 subjects will be involved in this study, which will only be conducted at sites affiliated with Penn.

What am I being asked to do?

If you choose to participate in this study, you will be randomly assigned (like flipping a coin) to take either two doses of methenamine hippurate or two doses of a placebo medication, which is a medication that has no medical effect. You will be randomly assigned at the time of this consent, which will be prior to your surgery. This study is double-blinded, meaning that neither you nor the investigators and physicians involved in your care will know which medications (methenamine or placebo) you have been assigned to take.

After your surgery, your bladder function will be tested. If you are able to urinate, you will not be eligible to be part of this study. If you are unable to urinate completely and require a urinary catheter, you will be randomly assigned to receive either methenamine hippurate or placebo. The day that you are scheduled to return to the office for catheter removal, you will take the first dose of medication two hours before catheter removal. The second dose you will take about 12 hours after your catheter is removed.

Your bladder function will again be tested at the time of the catheter removal. If you are unable to urinate completely and require a second urinary catheter, you will again be assigned two doses of the same medication for the time of the second catheter removal. However, if you are able to urinate or if you are taught self-catheterization instead, you will not be given any additional doses of medication.

Afterwards, you will be asked to call the office or come to the office at any time if you think you may have any symptoms of a urinary tract infection or any side effects from the medication. Just as you would for any urinary tract infection outside of the study, you will be asked to submit a urine sample for testing for possible infection. Physicians will help to determine whether this is a true urinary tract infection, and treat you with the usual antibiotic treatment if needed.

Otherwise, you will participate in weekly phone calls after surgery for three weeks, as well as a post-surgery office visit scheduled at 6 weeks. This visit is routinely scheduled for all patients undergoing surgery regardless of participation in the study.

During the three weekly phone calls, nurses or investigators will ask you whether you have experienced any symptoms of urinary tract infection, whether you were treated for any urinary tract infections at our office or by any other medical providers, whether you have had any complications because of any urinary tract infection you had (such as infection of the kidneys or hospital re-admission), and whether you have experienced any side effects from the medication. During your usual post-surgical office visit, physicians will ask you the same questions in addition to the routine physical examination.

What are the possible risks or discomforts?

The risks from methenamine hippurate are generally rare and mild, but exist. The most common side effects are rash, nausea, upset stomach, and pain with urination. All of these side effects happened in less than 4% (or 4 out of every 100) of people who used the drug. The most serious side effects of methenamine hippurate include allergic reactions and infection of the lungs (pneumonia).

Additionally there is the potential loss of confidentiality; that is, someone could find out that you have participated in this study, and potentially any data on you that has been collected during the

study. This could potentially lead to embarrassment and loss of personal health information. However, we will decrease this risk through the following: all data needed for the study will be stripped of any identifiers (such as name and medical record number) and associated with an assigned subject identification number only, so that it cannot be directly linked to you. Also, all files, forms, and any consent forms or any other documents that could link to you will be locked in a secure area at all times. Only investigators involved in this study will have access to these files

At any time in this study you are injured or harmed and require medical attention, you should inform your treating physician that you are in a research study.

Research may involve risks that are currently unforeseeable.

Reproductive risks: Because of the effects of this drug, there could be serious harm to unborn children or children who are breast-feeding. These effects could also harm the mother. It is also possible that harmful side effects that are not yet known could happen to both the mother and unborn or breast-feeding child. If you are currently pregnant or if you are currently breast-feeding, it is important that you inform the investigator because you will not be able participate in the study. If you are able to become pregnant, you will be given a serum pregnancy test or a urine pregnancy test before entry into the study, which is routinely performed prior to scheduled surgeries. You should not become pregnant while you are taking this drug. If you do become pregnant, you must tell the investigator and consult an obstetrician or maternal-fetal specialist. If you are breast-feeding, you must tell the investigator and consult an obstetrician or a pediatrician.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?

This study may benefit you by decreasing your risk of urinary tract infection after short-term catheterization. However, you may not get any benefit from being in this research study.

Additionally, this study may benefit society by providing an alternative medication besides antibiotics to prevent urinary tract infection after short-term catheterization, which could decrease healthcare costs because of hospital-associated infections and decrease antibiotic resistance in hospitals.

What other choices do I have if I do not participate?

If you choose not to participate, and require short-term catheterization after pelvic reconstructive surgery, you may or may not be given medication (such as an antibiotic) to prevent urinary tract infections based on your physician's routine practice.

Will I be paid for being in this study?

You will not be paid for being in this study.

Will I have to pay for anything?

The medications (methenamine hippurate or placebo) will be provided without cost. However, you are still responsible for any deductibles or applicable co-pays for routine office visits (such as the post-surgical visit 6 weeks after your surgery), routine urinary tests in case of suspected urinary tract infection, and any necessary routine imaging and blood work. Please talk to your doctor and study team about putting you in touch with a financial counselor to determine exactly what the deductible and co-pay will be for you; this is highly variable depending on your type of insurance.

What happens if I am injured from being in the study?

Potential injuries include side effects from the medication. Although, as noted before, the risk of major side effects is minimal, if you experience harm from the side effects, you should contact your on-call physician and seek care immediately from your primary care physician or from the emergency room, if your situation is emergent.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in the consent form. Additionally, please contact the on-call physician for the physician who performed your surgery, who you can contact through the hospital operator at 215 662 4000.

When is the study over? Can I leave the study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This is expected to be approximately 1 to 1.5 years after the study starts. This study may also be stopped at any time by your physician or the study Sponsor without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Sponsor or the study's Principal Investigator has decided to stop the study.

If you decide to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care.

Who can see or use my information? How will my personal information be protected?

We will do our best to make sure that the personal information obtained during the course of this research study will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. Otherwise, only investigators and other personnel involved in the study and in routine patient care will be able to see or use your information. The Institutional Review Board (IRB) at the University of Pennsylvania will also have access to the records. Any information disclosed outside of the covered entity may not be protected.

Extensive efforts will be made to ensure and maintain security of PHI and maintain participant confidentiality.

During the study, any interactions with you will take place in a private room at your physician's office. Post-operative telephone calls will be performed in a private manner in the office setting.

Data will be recorded on data collection forms, which will be associated with an assigned Subject ID number only. Your name, medical record number, or other identifiers will not be present on the data collection forms themselves. Any consent forms, record logs, data collection forms, or other information will be stored in a secure and locked filing system at all times. Data will be entered electronically onto spreadsheets using assigned Subject ID numbers only. This Excel spreadsheet form will be stored in a password-secured file and a physical backup copy of this file will be made at the end of every other week and the copy stored in a separate, secure area/filing system.

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.

Electronic Medical Records and Research Results

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.
If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

What information about me may be collected, used or shared with others?

- Name, address, telephone number, date of birth
- Email addresses
- Personal and family medical history
- Results from a physical examinations, tests or procedures
- Records of office visits and telephone calls conducted for routine care
- Records of your operation
- Medical records related to illnesses or medical events that happen to you while you are in the study, if applicable

Why is my information being used?

Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right.

Who may use and share information about me?

The following individuals may use or share your information for this research study:
The investigator for the study and the study team
Clinical personnel who are part of your physician's office and part of routine care
IRB at the University of Pennsylvania

Who, outside of the School of Medicine, might receive my information?

IRB at the University of Pennsylvania
FDA

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may the School of Medicine use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?

Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

By signing this document you are permitting the School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent and HIPAA authorization form will be given to you.

Name of Subject (Please Print)	Signature of Subject	Date
Name of Person Obtaining Consent (Please Print)	Signature	Date