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CONSENT FOR RESEARCH

Penn State College of Medicine
The Milton S. Hershey Medical Center

Comparison of Methohexital with Propofol for Anesthetic induction in patients treated with an Antagonist of the Renin-Angiotensin System.

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Telephone Numbers: Weekdays: 8:00 a.m. to 5:00 p.m. Please call (717) 531-6597
After hours call (717) 531-8521. Ask for the Anesthesiology 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.

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.

1. Why is this research study being done?

We are asking you to be in this research because you are taking a medication called an angiotensin receptor blocker or angiotensin converting enzyme inhibitor and you will be undergoing surgery at Penn State Milton S Hershey Medical Center.

This research is being done to find out if certain medications used to put you to sleep and under anesthesia cause more changes in blood pressure than other medications. The 2 medications that might be used to put you to sleep are both FDA-approved and have a long track record of safety as anesthetics. One is called propofol and the other is called methohexital. Both medications can cause a decrease in blood pressure after they have been given, especially if you are taking angiotensin receptor blockers or angiotensive converting enzyme inhibitors on a regular basis. We would like to investigate whether one causes more of a decrease in blood pressure than the other, so that we could recommend the use of one over the other in patients taking the blood pressure medications that you are taking at home.

Approximately 120 people will take part in this research study at Hershey Medical Center.

2. What will happen in this research study?

On the day of your surgery, the anesthesiologist will place two IV (intravenous) lines using numbing medication (lidocaine) in the same day unit. This is standard of care for the type of surgery that you will be undergoing, and enables the anesthesiologist to give you medications to put you to sleep in the operating room. When this IV line is placed, we will take approximately 15 milliliters (3 teaspoons) of blood from that IV. This will be used to test your blood for any chemicals that may predict low blood pressure after you are put to sleep for your surgery. This is not standard of care, and will be used for the purposes of research only. It will not affect your anesthetic care in the operating room.

You will then be transported to the operating room to get your surgery. The anesthesiologist will use one of two medications to put you to sleep. Both of these medications are FDA-approved and safe medications. The medication you will receive will be determined randomly, which means that whichever study treatment you receive will be determined purely by chance. You will have an equal chance of receiving either of the 2 medications. You will not be told which treatment you are getting, however your study doctor will know and will be familiar with each of the 2 medications.

After you are asleep, the anesthesiologist will draw 4 more blood samples (each of which is 15 milliliters, or approximately 3 teaspoons) to test for chemicals that may predict low blood pressure. Again, these samples will be used purely for research purposes and will not affect your anesthetic care in the operating room. The study lasts a total of 15 minutes after you go off to sleep.

You will be kept safe at all times, and an anesthesiologist will be present in the operating room for the duration of the study. You will receive standard anesthetic care for the surgery, and no follow-up is necessary after the study. You will not be contacted by any study staff after you participate in the study.

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

You will be randomly assigned to receive one of the two study treatments, either propofol or methohexital. This means that whichever study treatment you receive will be determined purely by chance, like flipping a coin. You will have an equal chance of receiving any one of the study treatments.

There is a risk of your blood pressure becoming low when you are being put to sleep for surgery. This is a risk you would have **with or without** the research study. The risk of your blood pressure becoming low is **not** increased with the research study. Rather, it is a risk that is well-known with the blood pressure medication that you are taking at home (known as angiotensin receptor blocker or angiotensin converting enzyme inhibitor) and with either of the 2 medications that you will receive to put you to sleep. Propofol is by far the most commonly used medication used to put patients under anesthesia. However, it may cause burning or itching at the injection site (incidence in adults is approximately 18%). Methohexital may also cause injection site pain, although less commonly so. A more comprehensive list of all the possible side effects of each drugs is included below.

Risks of propofol:

>10% incidence: low blood pressure (3%-26%), Injection site burning, stinging, or pain (18%),

stop breathing for 30-60 seconds (adults 24%)

1% to 10% incidence: abnormal heart rhythm (1% to 3%), slow or fast heart rate (1% to 3%), cardiac output (volume of blood pumped by the heart per minute) decreased (1% to 3%;)

Risks of methohexital (frequency not defined but these complications are considered very rare since methohexital is considered standard of care):

Sudden stop in blood circulation due to the failure of the heart, low blood pressure, shutdown of arteries and veins in the arms and legs, fast heart rate, agitation coming out of general anesthesia, headache, anxiety, restlessness, seizures, convulsion, injection site pain, abdominal pain, nausea or vomiting, blood clot in your leg that blocks one or more of your veins, breathing problems (stop breathing, bronchospasm, cough, labored breathing, hiccups, spasm of the vocal cords making it difficult to speak or breath, inadequate breathing).

The discomfort associated with removing blood by venipuncture (by needle from a vein) is a slight pinch or pin prick when the sterile needle enters the skin. We will be using numbing medication to numb up the skin prior to venipuncture. The risks include mild discomfort and/or a black and blue mark at the site of puncture. Less common risks include a small blood clot, infection or bleeding at the puncture site, and on rare occasions fainting during the procedure.

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 to the degree permitted by the technology used. Absolute confidentiality cannot be guaranteed.

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

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

4a. What are the possible benefits to me?

You will not benefit from this research study.

4b. What are the possible benefits to others?

The results of this study may guide the future selection of medication used to put people to sleep if they are taking blood pressure medications similar to the one you are currently taking.

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

You may choose not to be in this research study.

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

Being in this research study does not require any time on your part.

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. In our research files at The Milton S. Hershey Medical Center (HMC) and Penn State College of Medicine (PSU) we will include these identifiers: your name, medical record number, date of birth and a code number to identify the blood samples.

- A list that matches your name with your code number will be kept in a locked file in the Anesthesia research office.
- Your research records will be labeled with your name, medical record number, date of birth and a code number and will be kept in a safe area in the Anesthesia research office.
- Your research samples will be labeled with: a code number and will be stored in the locked Anesthesia laboratory.
- A copy of this signed consent form will be included in your HMC medical record. This means that other HMC 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. How will my identifiable health information be used?

If you give your consent, health information that can be traced to you will be collected for this research study. In general, under federal law, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use, and share your health information for research and why they may need to do so. We will use and disclose your information only as described in this form and in the HMC Privacy Notice.

The research team may use the following health information:

- Past, present, and future medical records
- 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:

- HMC/PSU research staff involved in this study
- The HMC/PSU Institutional Review Board (IRB), a group of people who review the research study to protect subjects' rights and welfare
- The HMC/PSU Human Subjects Protection Office
- The HMC/PSU Research Quality Assurance Office

- Non-research staff within HMC/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)
- The HMC/PSU pharmacy
- 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

These groups may also review and/or copy your original PSU/HMC 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.

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 tests and procedures that are <u>only</u> being done for the research study:

- You and/or your insurance company will not be charged for the cost of any tests or procedures that are required as part of the research and are outside the standard of care (what is normally done) for your condition.

- The research-related tests and procedures that will be provided at no cost to you include: blood collection for research laboratory testing (norepinephrine, epinephrine, arginine vasopressin and angiotensin II).

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. This includes the cost of the induction drug used as part of the study (propofol or methohexital). An induction drug is always necessary to put you to sleep for surgery, whether you are included in this research study or not. However, the out-of-pocket cost for different drugs may vary depending on which drug you are randomized to receive and what insurance program you have. 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.

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.

<u>HMC/PSU compensation for injury</u>

- There are no plans for HMC/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.

9. Will I be paid to take part in this research study?

You will not receive any payment or compensation for being in this research study.

10. Who is paying for this research study?

The institution and investigators are receiving a grant from Penn State Department of Anesthesiology to support this research.

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 or an unexpected anesthetic complication occurs during the study
- Also, the sponsor of the research may end the research study early.

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 (principal investigator), Anthony Bonavia at 717-531-0003 (extension 311247), or the Anesthesiology 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 HMC 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 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 HSPO's web site at http://pennstatehershey.org/irb under research subject information 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 and have answered any questions he/she has 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 agree to allow your information to be used and shared as described above.

_____ _____ _____ _____
Signature of Subject Date Time Printed Name

Optional part(s) of the study
In addition to the main part of the research study, there is another part of the research. You can be in the main part of the research without agreeing to be in this optional part.

Optional Storage of Tissue for Future Research
In the main part of this study, we are collecting blood samples from you. If you agree, the researchers would like to store leftover sample(s) and health information for future research.

- These future studies may be helpful in understanding the effects of anesthetics on blood pressure.
- It is unlikely that these studies will have a direct benefit to you.
- The results of these tests will not have an effect on your care.

- Neither your doctor nor you will receive results of these future research tests, nor will the results be put in your health record.

Your leftover samples will be labeled a code number

- These samples will be stored in a freezer in a locked research laboratory
- The length of time they will be used is unknown.
- You will be free to change your mind at any time.
- You should contact the research coordinator and let them know you wish to withdraw your permission for your blood to be used for future research. Any unused blood will be destroyed and not used for future research studies.

You should initial below to indicate what you want regarding the storage of your leftover blood for future research studies.

a. Your sample*[s]* and related health information may be stored and used for future research studies to learn about the effects of anesthetics on blood pressure.

_____ Yes _____ No

b. Your sample[s] and related health information may be stored and used for research about other health problems.

_____ Yes _____ No

c. Your sample*[s]* and related health information may be shared with other investigators/groups without any identifying information.

_____ Yes _____ No

Signature of Person Obtaining Informed Consent

Your signature below means that you have explained the optional part(s) to the research to the subject or subject representative and have answered any questions he/she has about the research.

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

Signature of Person Giving Informed Consent

Signature of Subject

By signing below, you indicate that you have read the information written above and have indicated your choices for the optional part(s) of the research study.

_____	_____	_____	_____
Signature of Subject	Date	Time	Printed Name