UNIVERSITY OF CALIFORNIA, IRVINE
CONSENT TO ACT AS A HUMAN RESEARCH SUBJECT

Dexmedetomidine for Acute Pain Control in Patients with Multiple Rib Fractures: A Randomized Controlled Trial

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STUDY LOCATION(S):
University of California, Irvine Medical Center
Departments of Trauma and Critical Care

SUMMARY OF KEY INFORMATION:

The information provided in this box includes a brief yet complete summary of key information about the research, presented first as required by the federal regulations. Some sections that require additional information may be repeated later in this document.

Participation is Voluntary
You are being asked to participate in a research study. Participation is completely voluntary. Please read the information below and ask questions about anything that you do not understand. A researcher listed above will be available to answer your questions.

Study Purpose
The purpose of this research study is to evaluate the effectiveness of dexmedetomidine (precedex) in the treatment of acute pain related to rib fractures.

Study Procedures
You will be randomized (such as randomization is assigning patients by chance to groups that receive different treatments) to either the experimental or the placebo arms. Patients within the placebo arm will receive standard of care multi-modal pain management and saline infusion. Patients in the experimental arm will receive standard of care multi-modal pain management and an infusion of dexmedetomidine for 24 to 48 hours.

Expected Duration
Participation will last approximately two days for the administration of the study medication. After which data will be collected for up to one year after your discharge from the hospital. There will be no additional study visits.

Risks of Participation
There is a theoretical minimal risk of a breach in confidentiality due to a compromise of your protected personal information. Additionally, dexmedetomidine has associated side effects including slow breathing rate, low blood pressure, slow heart rate, abnormal fast irregular heart rate, nausea, and confusion.

Benefits to Participants
Taking part in this study may or may not make your health better. If you are in the group that receives dexmedetomidine and it proves to treat your condition more effectively and with fewer side effects than standard therapy, you may benefit from participating in the study, but this cannot be guaranteed.

Benefits to Others or Society
This study will help researchers learn more about dexmedetomidine, and it is hoped that this information will help in the treatment of future patients with multiple rib fractures.

Alternative Procedures or Treatments
If you decide not to participate, or if you withdraw from this study before it is completed, your other choices may include:
- Getting no treatment
- Getting standard treatment for your condition without being in a study

WHY IS THIS RESEARCH STUDY BEING DONE?
The purpose of this research study is to evaluate the effectiveness of dexmedetomidine (precedex) in the treatment of acute pain related to rib fractures and compare it to the current standard of care.

Rib fractures cause a significant amount of pain and are associated with an increased risk of lung infections, long hospitalization, and increased cost. Effective pain control is the cornerstone of management to improve lung function and minimize complications. Most often this is done with a multimodal pain routine consisting of: acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), topical lidocaine, muscle relaxants, and opioids. However, dexmedetomidine is a promising alternative to treat acute pain associated with rib fractures. We think the addition of dexmedetomidine to a multimodal pain regimen will improve pain and decrease opioid use.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Approximately 40 participants will take part in the research at UCI.

AM I ELIGIBLE TO PARTICIPATE IN THIS STUDY?
Please note this may not be a complete list of eligibility criteria. We have included a few examples of study criteria to help you better understand how your eligibility in the study will be determined; your study team will go through the study eligibility criteria with you to verify if you qualify for participation in this study.

Inclusion Requirements
You can participate in this study if you are at least 18 years of age and have sustained blunt chest trauma with 3 or more rib fractures that requires you to be admitted to the intensive care unit (ICU).

Exclusion Requirements
You cannot participate in this study if you:
- Pregnant
- Prisoner
- Have a history of adverse reaction or allergy to dexmedetomidine
- Are unable to communicate with staff because of come, dementia, psychiatric illness, or language barrier

- Have pre-existing heart condition such as; severe congestive heart failure, severe sinus bradycardia, or second/third degree heart block without a pacemaker
- Have symptomatic low blood pressure
- Currently take chronic opioids for pain control
- Have a history of cirrhosis (liver disease)

HOW LONG WILL THE STUDY GO ON?
You will take dexmedetomidine for up to 24 hours or until the medication is stopped due to safety concerns. This study will continue during the duration of your hospitalization, the length of your hospitalization may vary on the severity of any additional injuries. We ask for your participation for up to one year after your discharged for additional data collection. The researchers do not plan for any additional follow-up exams or office visits.

WHAT PROCEDURES ARE INVOLVED WITH THIS STUDY?
Before you can participate in the main part of the study...
The research staff will identify patients that you meet eligibility criteria and screen your medical records. If you meet criteria for inclusion, you or your LAR (legal authorized representative) will be approached for informed consent.

During the main part of the study...
If you agree to take part in the study, then you will have the following procedures and tests done. The main study tests and procedures include…
Randomization – you will be randomized into one of two groups

- Group 1 will receive standard of care pain medications (acetaminophen, NSAIDs, lidocaine patch, muscle relaxants, and opioids) plus a dexmedetomidine infusion
- Group 2 will receive standard of care pain medications with an infusion of normal saline (placebo)

The procedures for both groups are the same.

You will receive an infusion of either dexmedetomidine (precedex) or normal saline starting within 12 hours of admission. The starting infusion rate will be set at 0.4 mcg/kg/h. Infusion will continue for up to 24 hours. The transfusion will be stopped if transferred out of the ICU or held due to safety concerns. Nurses will evaluate your pain every 2 to 4 hours which is standard of care. If pain is uncontrolled after 2 consecutive evaluations your doctor will have the option to increase the infusion to 0.6 mcg/kg/h.

Medical record review – your medical record will be reviewed and relevant data will be extracted. There is a theoretical minimal risk of a breach in confidentiality due to a compromise of your protected personal information

After you complete the main part of the study
You will be followed for your injuries as per standard of care. You will continue to receive pain medication as needed and have your pain assessed approximately every 4 to 8 hours. Once discharged from the hospital you will only have your standard of care follow up appointments.

No additional tests, procedures, or exams are needed.

RETURN OF RESULTS
You will be provided any clinically relevant information that may pertain to your health.

WHAT ARE THE POSSIBLE SIDE EFFECTS OR RISKS RELATED TO THE STUDY?
You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. Side effects may be mild or very serious. The researchers may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking dexmedetomidine. In some cases, side effects can be serious, long lasting, or may never go away.

You should talk to the research team about any side effects you experience while taking part in the study.

Other adverse events with a causal relationship to dexmedetomidine include:

Likely (>2%)

- Hypotension (Low blood pressure)
- Hypertension (High blood pressure)
- Bradycardia (Slow heart rate)
- Nausea and vomiting
- Dry mouth
- Atrial Fibrillation (irregular heart rate)
- Fever/Chills

Less Likely (<2%)

- Tachycardia (Fast heart rate)
- Agitation
- Atelectasis or Pleural effusion (Fluid in the lungs)
- Hyperglycemia (High blood sugar)
- Hypoxia (Low oxygen levels)
- Hypocalcemia (Low calcium in the blood)
- Low urine output
- Wheezing
- Edema (Swelling of the legs)

Rare but serious

- Hypotension, bradycardia, and sinus arrest (low blood pressure and slow heart rate causing the heart to stop)
- Transient hypertension (temporary high blood pressure)

Randomization: You will be assigned to a study group by chance (like a coin flip) rather than by a medical decision made by the researchers. The treatment you receive may prove to be less effective or to have more side effects than the other study group(s), or than standard treatments available for your condition.

Placebo: During this study there is a 50% chance that you will receive a placebo. During this time, you may experience worsening of your condition, including increased symptoms such as pain. The researchers will carefully monitor your condition. If your symptoms worsen and make you uncomfortable, you can withdraw from the study.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

You will not be compensated for your participation in this research study.

Reimbursement

You will not be reimbursed for any out-of-pocket expenses, such as parking or transportation fees.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

There is no cost to you or your insurer for your participation in this study. However, there may be out-of-pocket expenses such as parking and transportation fees. You and /or your health plan/insurance will be billed for the costs of any standard medical care you receive to diagnose and/or treat any medical condition(s) outside of this study. You will also be responsible for any deductibles or co-payments that would normally be associated with these standard medical costs.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?
It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study. You can tell the researcher in person or call him/her at the number listed at the top of this form.

If you are injured as a result of being in this study, UCI will provide necessary medical treatment. The costs of the treatment may be covered by the University of California, the study sponsor, or billed to you or your insurer just like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about this, you may call UCI Human Research Protections (949) 824-6068 or (949) 824-2125 or by e-mail at IRB@research.uci.edu

WHAT HAPPENS IF I WANT TO STOP TAKING PART IN THIS STUDY?
You are free to withdraw from this study at any time. **If you decide to withdraw from this study, you should notify the research team immediately**. The research team may also end your participation in this study if you do not follow instructions, miss scheduled visits, the study sponsor decides to stop the study or your safety and welfare are at risk.

If you experience any of the side effects listed above, if your health worsens, or if you are injured during the research, you may need to be withdrawn from the study, even if you would like to continue. The research team will make this decision and let you know if it is not possible for you to continue. The decision may be made to protect your safety and welfare, or because the research plan does not allow people who develop certain conditions to continue to participate.

If you withdraw or are removed from the study, no further action is required

If you elect to withdraw or are withdrawn from this FDA-regulated research study, the data collected from your participation in this study must remain in the trial database in order for the study to be scientifically valid.

HOW WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT?
Subject Identifiable Data
Identifiable information collected about you will be removed at the end of data collection.

Data Storage
Research data will be maintained in paper format in a secure location at UCI.

Research data will be stored electronically on a secure electronic REDCap database in an encrypted file with password protection

Only authorized individuals will have access to electronic or paper research information.

Data Retention
In accordance with UC Office of the President policy, information will be retained for 10 years after the end of the calendar year in which the research is completed.

WHO WILL HAVE ACCESS TO MY STUDY DATA?
The research team, authorized UCI personnel, and regulatory entities such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP), may have access to your study records to protect your safety and welfare.

While the research team will make every effort to keep your personal information confidential, it is possible that an unauthorized person might see it. We cannot guarantee total privacy.

Future Research Use
Researchers will use your information to conduct this study. Once the study is done using your information, we may share them with other researchers so they can use them for other studies in the future. We will not share your name or any other private identifiable information that would let the researchers know who you are. We will not ask you for additional permission to share this de-identified information.

ClinicalTrials.gov
ClinicalTrials.gov is a Web site that provides information about clinical trials. 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.

Medical Care
If you agree to participate in this research study, a signed copy of this consent document and the privacy authorization form may be filed in your electronic medical record (EMR) and your study participation may be added to your EMR. This information will be used for your care and treatment and for healthcare operations, which may include billing and payment.

Investigator Financial Conflict of Interest

No one on the study team has a disclosable financial interest related to this research project.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?
If you have any comments, concerns, or questions regarding the conduct of this research, please contact the research team listed at the top of this form.

A 24-hour number is also listed on the top of this form to report any health concerns or unanticipated problems you may experience after normal hours or on weekends.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any suggestions, problems or concerns you may have about the study, please contact the UCI Institutional Review Board by phone, (949) 824-6068 or (949) 824-2125, by e-mail at IRB@research.uci.edu or at 160 Aldrich Hall, Irvine, CA 92697.

What is an IRB? An Institutional Review Board (IRB) is a committee made up of scientists and non-scientists. The IRB's role is to protect the rights and welfare of human subjects involved in research. The IRB also assures that the research complies with applicable regulations, laws, and institutional policies.

HOW DO I AGREE TO PARTICIPATE IN THIS STUDY?
You should not sign and date this consent form until all of your questions about this study have been answered by a member of the research team listed at the top of this form. You will be given a copy of this signed and dated consent form, and the attached "Experimental Subject's Bill of Rights" to keep.
Participation in this study is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your future relationship with UCI or your quality of care at the UCI Medical Center.

If, during the course of this study, significant new information becomes available that may relate to your willingness to continue to participate, this information will be provided to you by the research team listed at the top of the form.

Your signature below indicates you have read the information in this consent form and have had a chance to ask any questions you have about this study.

Note: If the research described in this form involves your protected health information (PHI), you will be asked to sign separate UC HIPAA Research Authorization form for the use of your PHI.

I agree to participate in the study.

_____ _____
Subject Signature **Date**

_____
Printed Name of Subject

_____ _____
Legally Authorized Representative/Guardian Signature ***Date***

_____ _____
Printed Name of Legally Authorized Representative/Guardian ***Relationship to Subject***

_____ _____
Signature of Person Obtaining Informed Consent **Date**
(For research that is greater than minimal risk, this individual must be listed on Page 1 of this consent)

_____
Printed Name of Person Obtaining Informed Consent

A witness signature is required on this consent form only if: (Researchers: check which one applies)

IMPORTANT! If no witness signature is required, this witness signature section of the consent form may be left blank.

☐ Consent is obtained from the subject via the Short Form process, as approved by the IRB.
☐ The subject has decision-making capacity, but cannot read, write, talk or is blind.
☐ The subject's guardian/legally authorized representative (LAR) cannot read, write, talk or is blind.
☐ The IRB specifically mandated a witness signature for this study (e.g., high risk and/or invasive research procedures).

For the witness:
I confirm that the information in this consent form was accurately explained to and understood by the subject or legally authorized representative and that informed consent was given freely.

_____ _____
Witness Signature **Date**
Note: The witness must be impartial (i.e. not a member of the subject's family, not a member of the study team).

_____
Printed Name of Witness

UNIVERSITY OF CALIFORNIA, IRVINE
Experimental Subject's Bill of Rights

The rights listed below are the right of every individual asked to participate in a research study. You have the right:

1. To be told about the nature and purpose of the study.

2. To be told about the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.

3. To receive a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.

4. To be told of any benefits that you may reasonably expect from the participation in the study, if applicable.

5. To receive a description of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.

6. To be told of what sort of medical treatment, if any, will be available if any complications should arise.

7. To be given a chance to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.

8. To refuse to participate in the research study. Participation is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your right to receive the care you would receive if you were not in the experiment.

9. To receive a copy of the signed and dated written consent form and a copy of this form.

10. To be given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

If you have any concerns or questions regarding the research study you should contact the research team listed at the top of the consent form.

If you are unable to reach a member of the research team and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research subject, please contact the UCI's Human Research Protections unit in the Office of Research by calling (949) 824-6068 or (949) 824-2125 Monday – Friday, 8 am – 5 pm; or by e-mail at IRB@research.uci.edu; or by writing us at 160 Aldrich Hall, Irvine, CA 92697.