

Cover Page

Title: Comparison of Intramuscular Ketorolac at Two Single-Dose Regimens for Treatment of Acute Musculoskeletal Pain in a Military Emergency Department: A Randomized Controlled Non-Inferiority Trial

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**WILLIAM BEAUMONT ARMY MEDICAL CENTER
CONSENT TO PARTICIPATE IN RESEARCH**

Principal Investigator: Nathaniel J. Turner, Captain, SP, MPAS

Protocol Title: Comparison of Intramuscular Ketorolac at Two Single-Dose Regimens for Treatment of Acute Musculoskeletal Pain in a Military Emergency Department: A Randomized Controlled Non-Inferiority Trial

Key Information: This section provides a one-page summary of the information outlined in this consent form. More information will be provided to you on the pages that follow.

Voluntary Participation	You do not have to take part in this research. It is your decision. You can also choose to stop participating at any time during the study.
Purpose	The purpose of this research study is to learn whether lower doses of ketorolac, a common non-steroidal anti-inflammatory medication used to treat pain, can provide equal pain relief when compared to higher doses in an emergency room setting.
Duration	You will be in this study for about 70 minutes.
Procedures	While you are in the study, you will be randomly assigned to one of two ketorolac doses. You will be asked to complete a pain scale and provide additional information about your pain before and after the dose is administered.
Drugs/Devices	The drug(s) used in this study is/are: ketorolac
Why might you want to participate in this research (benefits)?	Prior studies show that lower ketorolac dosing is related to fewer side effects. By demonstrating equal pain relief across doses, future patients may benefit by using the lower dose.
Why might you choose not to participate in this research (risks)?	The main risks from being in this study are: <ul style="list-style-type: none"> Side effects and adverse reactions that may occur with ketorolac. Risk of breach of confidentiality of your information. You may or may not benefit as a result of your participation in this study.
What are the alternatives to participating?	Your participation in this study is completely voluntary. You have several alternative options, including not participating in this study.



Payment	You <u>will not</u> be paid for your participation in this study.
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Contact the Principal Investigator with any questions: Nathaniel J. Turner, Captain, SP, MPAS; Phone (210) 289-4156. Address 5005 N. Piedras Street, El Paso, TX 79920

- PROTOCOL TITLE:** Comparison of Intramuscular Ketorolac at Two Single-Dose Regimens for Treatment of Acute Musculoskeletal Pain in a Military Emergency Department: A Randomized Controlled Non-Inferiority Trial

You may be eligible to take part in this research study. This form gives you important information about the study.

Please take time to review this information carefully. You should talk to the researchers about the research study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or your personal physician) about your participation in this study. If you decide to take part in this research study, you will be asked to sign this document. Before you sign this document, be sure you understand what the research study is about, including the risks and possible benefits to you.

Please tell these researchers if you are taking part in another research study.

You do not have to take part if you do not want to. You may also leave the research study at any time. If you choose not to take part in this research study or if you leave the study before it is finished, there will be no penalty.

Your decision will not affect your future care at William Beaumont Army Medical Center (WBAMC).

- WHAT IS THE PURPOSE AND DURATION OF THIS RESEARCH AND WHO WILL TAKE PART?**

You are being asked to take part in this research study because you are between 18 and 55 years of age, your Emergency Severity Index (ESI) is 4 or 5 (triage category indicating non-life threatening injury), you have a chief and sole complaint of musculoskeletal pain (i.e., general muscular, neck, back, shoulder, elbow, wrist, finger, hip, knee, ankle, foot, and toe), and your reported pain is 2 or greater out of 10 on the pain scale.

The purpose of this research study is to learn about whether lower doses of ketorolac, a common non-steroidal anti-inflammatory medication used to treat acute pain, can provide equal analgesia (i.e., pain relief) when compared to higher doses in an emergency room setting. Ketorolac tromethamine is a prescription only, FDA-approved, non-steroidal anti-inflammatory drug (NSAID). It is indicated for the short-term management of moderate to severe acute pain that requires analgesia at the opioid level. It is regularly used in the clinics and emergency room at WBAMC. What is not fully understood is the role lower doses of ketorolac, injected



intramuscularly, play in emergency medicine pain management. Recent research has supported the use of lower doses, showing an analgesic ceiling of 10mg. An analgesic ceiling refers to the dose beyond which there is no additional analgesic effect (pain relief). However, doses of 60mg intramuscularly in patients less than 65 years old remains the standard.

The intent of this study is to see if lower doses of ketorolac provide equal analgesia when compared to higher, standard doses in an emergency room setting. By using lower doses of ketorolac, it is anticipated that there will be a lower rate of adverse outcomes.

The duration of participation per visit is approximately 70 minutes. There is no separate research-specific visit to the hospital associated with this study; all study data collection will take place during your visit to the WBAMC Emergency Department today. You will not be required to come back for any follow-up visits associated with this research study.

There will be up to 122 people recruited to take part in the study at WBAMC over the course of one year of data collection.

At the end of this research study, the clinical results, including research results about you, will not be shared with you. This is because all data collected about you will be de-identified during the data collection process. This means that the research team will not be able to identify any results specifically about you after your data collection is complete.

3. SCREENING PROCESS TO QUALIFY FOR PARTICIPATION IN THIS STUDY

Before you can take part in this study, you will need to provide some information so that the Investigator can confirm that you qualify for the study. This is called the “Screening Process”. Part of this process will include the investigator verifying that you meet all of the inclusion criteria and do not meet any exclusion criteria. This set of criteria has been created to ensure that your safety and protection are upheld throughout your participation in this study. Furthermore, part of the validation of your eligibility is your provider agreeing with you receiving the randomized dosage of ketorolac for your presenting medical concern. Additionally, if you are a female and able to become pregnant, you will be required to provide a urine sample for a pregnancy test.

4. WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH?

You will undergo the following procedures if you choose to participate in this research study:

- Upon completion of this consent form, your current pain level will be assessed and documented on a specified pain scale, called the Visual Analog Scale. You will be asked about your current pain level, the duration of the pain, and if any medications were taken to relieve the pain within 12-hours of your initial triage in the WBAMC Emergency Room. This pain scale and questionnaire are specific to the research study and will take approximately 5 minutes to complete.
- If you are a female of child bearing age and have the ability to become pregnant, you will be required to provide a urine sample for urine pregnancy testing. This test is used to



ensure that you are not currently pregnant. If you are pregnant, you cannot be in the study.

- After you complete the pain scale, you will be randomly assigned to one of two ketorolac doses. Randomization is a process like flipping a coin and means you will have the same chance of being assigned to the high dose or low dose. The randomization will be done via computer-generated calculator to ensure proper randomization. This process is specific to the research study and will take approximately 5 minutes to complete. The two study-specific treatment conditions are:
 - o Group A: 60 mg dose of ketorolac (standard “higher” dose)
 - o Group B: 15 mg dose of ketorolac (experimental “lower” dose)
- You will receive a dose of ketorolac administered by a member of your healthcare team, who is licensed and credentialed to administer medications. The dose you receive is dependent on which group you are randomized to. This study is a single-blind study, which means that you will not know which dose of the ketorolac you are receiving, but the investigator will know which dose you received. The injection will be given intramuscularly, either into the deltoid (shoulder) muscle in the upper arm or in to the gluteus maximus (buttocks) muscle. The administration will take place in a private room. The injection site will be cleansed with an alcohol pad and allowed to dry prior to administration. This process will take approximately 10 minutes and as noted above, the randomization to a certain dosage is specific to the study. If you choose not to participate in the study, you may still receive a dose of ketorolac if your provider determines that it is appropriate for your care.
- After administration of the medication, you will wait for 30 minutes to allow the medication to work. At the end of the 30 minute period you will be evaluated for pain level and adverse events related to the medication. Then you will be asked to wait another 30 minutes, for a total of 60 minutes post medication administration. You will be re-assessed at the end of the 60 minute period for pain level and adverse events related to the medication.
 - o The 60 minute study period will coincide with your ED encounter. Your participation in this study will not expedite, or delay your evaluation in ED; however, it may be possible that your encounter will be extended to meet the 60-minute requirement.

5. **WHAT ARE THE RISKS OR DISCOMFORTS FROM BEING IN THIS RESEARCH?**

If you choose to take part in this study, there is a risk of:

As with any medication, side effects and adverse reactions may occur with ketorolac. While we anticipate a low likelihood of side effects and adverse reactions, according to the medication manufacturer, these risks include, but are not limited to:



- Headache
- Abdominal pain
- Indigestion
- Nausea
- Swelling
- High blood pressure
- Dizziness
- Drowsiness
- Sweating
- Itching
- Rash
- Diarrhea
- Constipation
- Flatulence
- Bloating
- Gastrointestinal bleeding or perforation
- Ulcer
- Heartburn
- Mouth sores
- Vomiting
- Anemia
- Prolonged bleeding
- Liver irritation
- Pain at injection site
- Ringing in ears
- Kidney dysfunction

Although efforts are made to protect your research study records, there is always a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.

You may have a bruise or be sore at the site where the medication is administered. There is also a slight possibility of infection at the site of medication administration.

Ketorolac has been shown to cause birth defects. For this reason, women of child bearing potential will be required to provide a urine sample for pregnancy testing.

Ketorolac belongs to the class of medications known as non-steroidal anti-inflammatory drugs (NSAIDs). This class of medications act in varying ways within the body to either decrease inflammation or relieve pain. The chronic use of NSAIDs in women of reproductive age may be associated with infertility that is reversible upon discontinuation of the medication. Consider discontinuing use in women having difficulty conceiving or those undergoing investigation of fertility. The use of NSAIDs close to conception may be associated with an increased risk of miscarriage (Bermas 2014; Bloor 2013). If you are a FEMALE ABLE TO BECOME PREGNANT and you want to take part in this study, you should know that ketorolac might be harmful to (1) an unborn child if you are pregnant; or (2) an infant if you are breast-feeding.



You will take a pregnancy test before you can participate in this study. You should not get pregnant or breastfeed while in this study. The only completely reliable methods of birth control are not having sex or surgical removal of the uterus. Other methods, such as the use of condoms, a diaphragm or cervical cap, birth control pills, IUD, or sperm killing products are not totally effective in preventing pregnancy.

If you are pregnant or feel you might be pregnant, let your doctor or the study investigators know immediately.

There is the potential for inadequate pain control while participating in this study. You are entitled to additional pain control medications at any time, as appropriately determined by your provider.

There may also be other risks of taking part in this study that we do not yet know about.

6. WHAT ARE THE POSSIBLE BENEFITS FROM THIS RESEARCH?

There may be no direct benefits to you for taking part in the study. Study subjects receiving the lower dose may experience fewer adverse effects. However, no benefit can be guaranteed. Others may benefit in the future from the information learned during this study. The possible benefits to others are demonstrating equal pain relief across doses to decrease post-administration side effects and adverse reactions by using the lower dose.

7. WHAT ARE THE ALTERNATIVES TO TAKING PART IN THIS RESEARCH?

There may be other options for pain relief during your time at the Emergency Department. Alternative treatments and/or procedures that may be available to you include oral or intravenous analgesics (pain relievers) to reduce symptoms of pain. Supportive care, such as a heating pad or ice pack. You should talk with your personal physician about these options. The medication involved in this research study may also be available to you without taking part of this study.

Choosing not to take part in this research study is also an option.

8. IS THERE COMPENSATION FOR YOUR PARTICIPATION IN THIS RESEARCH?

No, you will not receive any compensation for participating in this study.

9. ARE THERE COSTS FOR PARTICIPATING IN THIS RESEARCH?

No, there are no costs to you for taking part in this research study.

10. WHO IS CONDUCTING THIS RESEARCH?

This research is being conducted by the WBAMC Emergency Department.



11. STUDY SPONSOR (the organizations or persons who oversee the study and are responsible for analyzing the study data):

Not applicable

As the sponsor of this research, the Department of Defense may have access to your research data in accordance with DoDI 3216.02.

12. SOURCE OF FUNDING:

Not applicable

13. PRINCIPAL INVESTIGATOR (the person(s) responsible for the scientific and technical direction of the study):

Principal Investigator: CPT Nathaniel J. Turner, PA-C, EMPA Resident, Department of Emergency Medicine, William Beaumont Army Medical Center.

Phone: (210) 289-4156

Email: nathaniel.j.turner3.mil@mail.mil

14. LOCATION OF THE RESEARCH:

William Beaumont Army Medical Center
Department of Emergency Medicine
5005 N. Piedras St.
El Paso, TX 79920

15. DISCLOSURE OF FINANCIAL INTERESTS AND OTHER PERSONAL ARRANGEMENTS:

There are no financial interests or other personal arrangements to disclose.

16. WHO WILL SEE MY INFORMATION (PRIVACY) AND HOW WILL IT BE PROTECTED (CONFIDENTIALITY)?

Records of your participation in this research study may only be disclosed in accordance with state and federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing regulations. DD Form 2005, Privacy Act Statement - Military Health Records, contains the Privacy Act Statement for the records. A copy of DD Form 2005 can be given to you upon request, or you can read on-line at:

<http://www.dtic.mil/whs/directives/infomgt/forms/eforms/dd2005.pdf>.

The research team will keep your research records. These records may be looked at by staff from the William Beaumont Department of Emergency Medicine, the Institutional Review Board (IRB) (a committee responsible for protecting research participants), and the DoD Higher Level Review as part of their duties. These duties include making sure that the research participants are



protected. Confidentiality of your records will be protected to the extent possible under existing regulations and laws but cannot be guaranteed.

Procedures to protect the confidentiality of the data in this study include but are not limited to:

- There will be no identifiers on the hard copy data collection forms used during the data collection period. This is to better ensure patient confidentiality.
- When the data are entered into a computer, an encrypted Microsoft Excel file will be maintained on a government access computer accessible only with dual identification via Common Access Card (CAC) and Personal Identification Number (PIN).
- When in use, the computer will be in the possession of the principal investigator at all times. Otherwise, it will be stored in a locked cabinet.
- Paper copies will be maintained in a locked filing cabinet in the principal investigator's locked office.

Researchers will make every effort to protect your privacy and confidentiality; however, there are risks of breach of information security and information loss.

If applicable, 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 results. You can search this Web site at any time.

By signing this document, you give your permission for information gained from your participation in this research study to be published in literature, discussed for educational purposes, and used generally to further science. You will not be personally identified; all information will be presented as anonymous data.

Complete confidentiality cannot be promised for military personnel, because information regarding your health may be required to be reported to appropriate medical or command authorities to ensure the proper execution of the military mission, including evaluation of fitness for duty.

The following individuals will have access to your records and agree to safeguard your protected health information by using and disclosing it only as permitted by you in this consent or as directed by state and federal law.

- The study team with oversight from the Emergency Department
- The WBAMC Human Research Protections Office
- The Regional Health Command – Central IRB
- Other Department of Defense or Federal Agencies as part of their oversight role

17. WHAT HAPPENS IF YOU ARE INJURED AS A RESULT OF THIS RESEARCH?

If you think that you have a research-related injury, notify your Principal Investigator immediately at (915) 742-1928. You may also contact the WBAMC Human Protections Office at (915) 742-9502, the Regional Health Command-Central IRB Office at (210) 916-2598, or the WBAMC Judge Advocate General at (915) 742-2280.



If you are injured because of your participation in this research and you are a DoD healthcare beneficiary (e.g., active duty military, dependent of active duty military, retiree), you are authorized space-available medical care for your injury within the DoD healthcare system, as long as you remain a DoD healthcare beneficiary. This care includes, but is not limited to, free medical care at DoD hospitals or DoD clinics.

If you are injured because of your participation in this research and you are not a DoD healthcare beneficiary, you are authorized space-available medical care for your injury at a DoD hospital or an DoD clinic; medical care charges for care at a DoD hospital or a DoD clinic will be waived for your research-related injury. If you obtain care for research-related injuries outside of a DoD or DoD hospital or clinic, you will not be reimbursed for those medical expenses.

For DoD healthcare beneficiaries and non-DoD healthcare beneficiaries: Transportation to and from hospitals or clinics will not be provided or paid for by DoD. Unless you are covered by TRICARE, no DoD reimbursement is available if you incur medical expenses to treat research-related injuries. No compensation is available for research-related injuries. You are not waiving any legal rights.

18. WHAT WILL HAPPEN TO YOUR SAMPLES AFTER THIS RESEARCH HAS ENDED?

During this research study, you could be asked to provide the following types of samples (biological specimens): urine. This sample will only be collected from females for the purpose to test for pregnancy. The sample will be handled then destroyed in accordance with WBAMC laboratory and Emergency Department policies and procedures. Additionally, in accordance with policies, your sample will not be de-identified however, it will not be stored or used for future research

19. WHAT HAPPENS IF I WITHDRAW FROM THIS RESEARCH?

You may withdraw your consent at any time and stop participating in this research study without affecting your eligibility for care or any other benefits to which you are entitled. Should you choose to withdraw, you must inform the investigator then will be officially withdrawn. Your information will no longer be collected. Upon confirmation of your desire to withdraw from the study, further pain relief may be provided in the WBAMC Emergency Department in accordance with treatment plan from your provider if pain persists or worsens. Additionally, if an alternate diagnosis is suspected, appropriate triage, evaluation, and treatment will take place in accordance with standard of care in the WBAMC Emergency Department.

Please note that withdrawing your consent to participate in this research does not fully revoke your HIPAA Authorization Form to use/disclose your protected health information. To make that revocation, please send a letter to the principal investigator as discussed in the HIPAA Authorization Form.



The principal investigator of this research study may terminate your participation in this research study at any time if he determines this to be in your best interest, if you are unable to comply with the procedures required, or if you no longer meet eligibility criteria.

Furthermore, if your provider determines that your participation in this study must be stopped so as to not interfere with medical treatment, the study may be stopped at their request. Your data will not be used for study purposes in this instance.

20. VOLUNTARY PARTICIPATION:

The decision to take part in this research study is completely voluntary on your part. You will be informed if significant new findings develop during the course of this research study that may relate to your decision to continue participation.

21. INCIDENTAL FINDINGS

There is a possibility that while reviewing your test results we may see an abnormality that we did not expect to see in this study. This is what is called an "incidental finding." An incidental finding may cause you to feel anxious. Since an incidental finding will be part of your medical record, you could face greater difficulty in getting health or life insurance.

We will let you know if we see such an incidental finding. Depending on the type of incidental finding, we may contact you by phone. In the case of a potential serious emergency, the researcher will inform you right away.

You do not have an option to decline receiving information about an incidental finding. A qualified person (usually a member of the research team) will talk to you if there is an incidental finding.

We will also give information about this incidental finding to your primary doctor or we will refer you to an appropriate doctor for further evaluation.

The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility. If you are a DoD beneficiary, you will have access to care through standard Military Health System and TRICARE procedures.

22. CONTACT INFORMATION:

Principal Investigator (PI)

The Principal Investigator or a member of the research staff will be available to answer any questions throughout this study.

Principal Investigator: Nathaniel J. Turner, Captain, SP, MPAS
Phone: (210) 289-4156
Mailing Address: 5005 N. Piedras Street, El Paso, TX 79920



Institutional Review Board (IRB) Office

If you have any questions about your rights as a research participant or if you have concerns or complaints about the research study, please contact the IRB Office at:

Mailing Address:

RHC-C IRB Office, Brooke Army Medical Center
ATTN: MCHE-ZQ, Department of Quality and Safety
3551 Roger Brooke Drive
Fort Sam Houston, Texas 78234-6315
Phone: 210-916-2598

IF THERE IS ANY PORTION OF THIS DOCUMENT THAT YOU DO NOT UNDERSTAND, ASK THE INVESTIGATOR BEFORE SIGNING. YOU MAY CONSULT WITH YOUR PERSONAL PHYSICIAN OR LEGAL ADVISOR, IF YOU WISH.

A signed and dated copy of this document will be given to you.

23. LONG TERM USE OF DATA

Your data and specimen collected as part of this research will not be used for future research studies or given to anyone else for future research studies, even if all information that personally identifies you is removed.

SIGNATURE OF PARTICIPANT

Printed Name of Participant

Signature of Participant

Date



SIGNATURE OF WITNESS TO CONSENT/CONSENT PROCESS

(This individual can be a relative of the participant, but cannot be an individual involved with the research study.)

Printed Name of Witness

Signature of Witness

Date

SIGNATURE OF INDIVIDUAL ADMINISTERING CONSENT

(Can only be signed by an investigator or staff approved to administer consent)

Printed Name of Administering Individual

Signature of Administering Individual

Date

