

**A prospective, double-blind, randomized pilot study evaluating the effects of Toradol and Lyrica verses placebo for pain control after donor nephrectomy**

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## Background and Introduction

Perioperative pain management is a significant challenge following surgery. Many pathways contribute to perioperative pain, including nociceptive, inflammatory, and neuropathic sources. Although opioids have long been a mainstay for perioperative analgesia, other non-opioid therapies have been increasingly used as part of a multimodal analgesic regimen to provide improved pain control while minimizing opioid-related side effects

TORADOL (ketorolac tromethamine), is a nonsteroidal anti-inflammatory drug (NSAID), is indicated for the short-term (up to 5 days in adults), management of moderately severe acute pain that requires analgesia at the opioid level.

Anecdotal evidence has shown that the use of Toradol (Ketorolac) is safe in renal surgery patients (Grimsby, 2012). We aim to further evaluate this in a pilot study specifically in the population of patient who have donated their kidney in live kidney transplants. We will assess how the use of toradol affects return to bowel function and see if there is a difference in length of hospital stay. Narcotic use can affect bowel function so we hypothesize that use of Toradol will decrease delayed bowel function and aid in a patients discharge and reduction of hospital stay. We will assess differences in visual analog pain scores and total narcotic consumption, whereas secondary endpoints of urine output, serum creatinine and hemoglobin levels to assess for efficacy and safety.

Pregabalin is prescribed for neuropathic pain. In many studies, preoperative administration of pregabalin reduced postoperative morphine consumption and early postoperative pain.

There will be two arms of the study including:

- Arm 1 (pure placebo group): Placebo oral preop then Saline placebo IV x 1 in the OR, then saline placebo IV every 6 hours for 7 doses.
- Arm 2: Pregabalin 75mg oral preop, then Ketorolac 30 mg IV x 1 in the OR, then ketorolac 15 mg IV every 6 hours for 7 doses.

Toradol and Lyrica will be used consistent with its FDA approval in terms of dosing, route of administration, etc.

## Purpose and Objectives

The study is seeking to understand how the use of Toradol/ Lyrica in live donor nephrectomies affects:

- 1) Reduce/ minimize narcotic use
- 2) Return to bowel function
- 3) Shortened hospital stay
- 4) Ensure proper kidney function

## Study Population

**Age of Participants:** 18+

**Sample Size:**

At Utah: 62

All Centers: n/a

**Inclusion Criteria:**

Patients who are 18 years or older and able to provide informed consent and who are anticipated donating a kidney in a live donor kidney transplant. Both male and female patients will be included.

**Exclusion Criteria:**

Patients who are not able to provide informed consent, younger than 18, not receiving a donor nephrectomy, pregnant, lactating or nursing mothers, medical allergies or history that would otherwise be contraindicated for use of a nonsteroidal anti-inflammatory drug.

## Design

Prospective Clinical Research

Double Blind

Placebo Controlled

Randomized

## Study Procedures

### Recruitment/Participant Identification Process:

Study team will identify patients who are scheduled for live donor kidney transplant- donor nephrectomies. A review of their medical record will be performed to look for inclusion/exclusion criteria. Patient will then be approached and have the study explained to them through the informed consent process. No study procedures will be initiated until informed consent is obtained.

### Informed Consent:

#### Description of location(s) where consent will be obtained:

Transplant clinic and pre-operative suite.

#### Description of the consent processes(es), including the timing of consent:

Patients will be approached before their donor nephrectomy about the study. They will have sufficient time to understand study and procedures as well as risks and benefits. Time for questioning will be available. They will be allowed as much time as needed for the decision process. A return visit before the operation can be held if necessary.

### Procedures:

Study team will identify patients who are scheduled for live donor kidney transplant- donor nephrectomies. A review of their medical record will be performed to look for inclusion/exclusion criteria. A pregnancy test will be performed on eligible females. Patient will then be approached and have the study explained to them through the informed consent process. No study procedures will be initiated until informed consent is obtained.

Once consented, patients will be randomized in a 1:1 manner by investigational drug pharmacy and assigned to a study arm.

- Arm 1 (pure placebo group): Placebo oral preop then Saline placebo IV x 1 in the OR, then saline placebo IV every 6 hours for 7 doses.
- Arm 2: Pregabalin 75mg oral preop, then Ketorolac 30 mg IV x 1 in the OR, then ketorolac 15 mg IV every 6 hours for 7 doses.

Patients will be followed by study staff for 30 days to determine narcotic use, length of hospital stay, and return of bowel function (which is obtained by review of daily progress reports).

This study will be conducted in addition to standard pain protocols for patients ie: no patients will be deprived of pain medication following surgery. The Transplant team develops the pain med protocol for each individual patients needs based on allergy history, former narcotic tolerance/preference due to side effects, etc. and in conjunction with the pain management team recommendations. Therefore, it is possible that Toradol could be given as part of a patients personalized pain management regime and Toradol is approved by the FDA for this group, but this study is standardizing it for all donor nephrectomy patients. Lyrica is typically used during a patient's anesthesia course in the operative period. However, there is no standardized protocol for anesthesia for a patient, it is left up to the individual anesthesiologist, so again this study would just standardize its use in this particular group.

### Procedures performed for research purposes only:

Only administration of Toradol/ Lyrica vs. placebo will be non-standard of care procedures. The donor nephrectomy and subsequent care will be standard of care.

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## Statistical Methods, Data Analysis and Interpretation

Randomization will be stratified based on whether receiving a left or right kidney during their standard of care.

Study team is working with SDBC biostatistician for data analysis.

Simple t-statistics and chi-squared data analysis will be performed for primary and secondary endpoints.

Power calculation is based off of the average number of donors per year and the endpoints of kidney function and narcotic use.