# Intravenous Dexamethasone for Prolongation of Analgesia Following Supraclavicular Brachial Plexus Block for Shoulder Arthroscopy: A Randomized, Controlled, Phase IV Dose Response

FUNDER: Anesthesia Research Fund

PROTOCOL NO.: 2015-853

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# PROTOCOL SYNOPSIS

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|---|---|
| **Protocol Title:** | Intravenous Dexamethasone for Prolongation of Analgesia Following Supraclavicular Brachial Plexus Block for Shoulder Arthroscopy: A Randomized, Controlled, Phase IV Dose Response Study |
| **Protocol Number:** | 2015-853 |
| **Protocol Date:** | 9/29/2016 |
| **Sponsor:** | Anesthesia Research Fund |
| **Principal Investigator:** | Meghan Kirksey |
| **Products:** | IV Dexamethasone (Fresenius Kabi USA, LLC) |
| **Objective:** | The study is looking for findings that may allow clinicians to use lower doses of IV dexamethasone to maximize improve patient satisfaction, and minimize side effects. |
| **Study Design:** | Randomized Control Trial |
| **Enrollment:** | 140 |
| **Subject Criteria:** | 1. Patients undergoing shoulder arthroscopy under regional anesthesia<br>2. Ages 18-80 |
| **Study Duration:** | • 5/23/16-10/20/2017 |
| **Data Collection:** | Name, ID, age, ethnicity, race, gender, height, weight, BMI, ASA, time of IV Dexamethasone administration, block injection time, Midazolam dose, Midazolam time administration, Fentanyl time administration, Fentanyl dose, deviation from protocol, fingerstick blood glucose, NRS Score, NRS (average, worst, best), hand grip, motor exam, sensory exam, time of motor block resolution wrist, motor block resolution elbow, pain relief from block, time to first pain, time of normal sensation, total daily amount of opioid taken, total daily amount of antiemetic taken, nausea, vomiting, pruritis, satisfaction with post op analgesia, Postop complications nerve injury, wound healing, infection, reason for dissatisfaction with postop analgesia, dose of IV dexamethasone. |
| **Outcome Parameters:** | Duration of motor block from the supraclavicular block will be defined as the time from block placement to restoration of normal strength at both the wrist and elbow. Strength will be assessed before discharge from PACU, on POD#1 and POD#2, and on POD#3 (if the block persists). A hand grip strength test will also be performed preoperatively in the holding area and postoperatively in the PACU. |

| | |
|---|---|
| | Blood glucose levels, which will be checked by fingerstick (1) in the operating room after sedation and prior to nerve block and IV dexamethasone, (2) in the OR or PACU 1 hour after administration of dexamethasone, and (3) in the OR or PACU 2 hours after administration of dexamethasone. |
| **Statistical Analysis:** | Dunnett's test (three pairwise comparisons, one between each of the three IV dexamethasone groups and control) |

## 1.0 INTRODUCTION:

In order to determine the effects of IV dexamethasone on block duration and blood glucose levels, it is necessary to know the duration of such blocks in the absence of IV dexamethasone and the impact of surgery and anesthesia on blood glucose in the absence of IV dexamethasone. Should any patient develop postoperative nausea refractory to zofran, other standard antiemetics can be administered, such as scopolamine, Trimethobenzamide, and reglan. IV dexamethasone can be administered for nausea in the PACU at the discretion of the prescriber, however this will be considered a deviation from protocol and data from these patients will be analyzed as part of an intention to treat analysis.

## 2.0 PRODUCT DESCRIPTION:

Numerous studies have confirmed that perineural dexamethasone prolongs bupivacaine and ropivacaine brachial plexus blocks by approximately 10 hours (from approx. 12 to 22 hours)(1) without clinical evidence of toxicity. However, perineural toxicity in an animal model has raised concern about its use as a peripheral nerve block adjuvant (2). Moreover, recent studies suggest that high dose IV dexamethasone (810mg) prolongs analgesia to a similar degree as perineural dexamethasone for interscalene (3), supraclavicular (4) and sciatic nerve (5) blocks performed with ropivacaine and bupivacaine. However these studies only utilized fixed, high level doses of IV dexamethasone. Moreover, there remains a concern that high dose IV dexamethasone may lead to postoperative hyperglycemia and could possibly increase the risk of postoperative wound infection (6,8). Open surgery under general anesthesia has been shown to increase blood glucose levels with a peak at approximately 2 hours postinduction and results have been conflicting regarding whether or not IV dexamethasone causes greater increase (9,10). To our knowledge, it is not yet known if arthroscopic surgery under regional anesthesia triggers a similar increase in blood glucose levels and if this is impacted by administration of IV dexamethasone.

## 3.0 OBJECTIVE OF CLINICAL STUDY

A supraclavicular nerve block is an injection of numbing medication (local anesthetic) near nerves that supply your shoulder that is often used to provide numbness both during and after surgery. The purpose of this study is to determine the effect of a medication called dexamethasone on the duration of the supraclavicular nerve block that you will receive for your surgery today. Advantages of prolonging the duration of a nerve block include lower pain levels and less of a need to use pain-killers, postoperatively.

## 4.0 STUDY HYPOTHESES

IV dexamethasone prolongs analgesia after supraclavicular nerve blocks performed for shoulder arthroscopy and the effect is dose dependent.

## 5.0 STUDY DESIGN

This is the “gold standard” for clinical research. These prospective studies have at least two groups. Patients meeting strict inclusion/exclusion criteria are enrolled and randomly assigned to receive either an experimental intervention or to receive what is considered to be an acceptable alternative – usually the current standard of care or a placebo (e.g., study of hylauronic acid injection versus cortisone for arthritis).

### 5.1 Study Duration

There will be follow ups for the following days:

POD0, POD1, POD2, POD3, POD 21.

### 5.2 Endpoints

#### 5.2.1 Primary Endpoint

- Participation will involve, at most, 5 study contacts – which will include one preoperative contact and up to four following surgery. Follow up will be by phone on the first and second day after surgery to ask questions about pain, sensation, use of pain medication, and any problems after surgery. If there are still numb from the block on the second day after surgery (this is unlikely), we will follow up with a call on the third day.

**Secondary Endpoints**

- Three weeks after surgery (day 21), we will place a call for a final time to ask about subject's experience and satisfaction with subject's care. Each contact is expected to average about 15 minutes.

#### 5.2.2 Safety Evaluations:

- Glucose test, surveys/questionnaires, randomization, surgery.

### 5.3 Study Sites

The study will be performed at the main hospital.

## 6.0 STUDY POPULATION

### 6.1 Number of Subjects

140

### 6.2 Inclusion Criteria

Subjects of either gender will be included if they:

1. Patients undergoing shoulder arthroscopy under regional anesthesia
2. Ages 18-80

### 6.3 Exclusion Criteria

Subjects will be excluded from the study if they:

1. General anesthesia
2. Contraindication to regional anesthesia
3. Pre-existing neuropathy in the surgical limb
4. Intraarticular injections for postoperative pain control
5. Diabetes Mellitus
6. History of postoperative nausea and vomiting and/or motion sickness
7. Open surgical procedures
8. Patients on systemic oral or IV steroid therapy within 6 months
9. Patients who received Cortisone injection(s) within 1 month

10. Chronic opioid usage (defined as daily opioid and/or gabapentinoid consumption for 6 weeks)
11. Non English speaking

### 6.4 Randomization

Randomizer an Excel compatible randomizing program will be used by non-study research personnel to assign the dose of IV dexamethasone that will be administered for each study case. The designated dose of IV dexamethasone (either 0mg, 4mg, 6mg, or 8mg) will be prepared by someone other than the anesthesia provider within a blinded syringe.

## PROCEDURES

### 6.5 Surgical Procedure

Shoulder arthroscopy

#### 6.5.1 Investigational Product Application

N/A

### 6.6 Imaging Procedure

N/A

### 6.7 Medical Record Requirements

N/A

### 6.8 Data Collection

The following data will be collected:

**Pre-operative/Baseline**

- basic demographic data
- patient weight & height, BMI

**Surgical procedure**

- date of surgery
- type of surgery

**Follow-up visits (6 weeks, 12 weeks, 6 months, 1 year, 2 years)**

- There will be no extra visits. A phone call will be performed on POD21.

### 6.9 Schedule of Assessments

| STUDY VISIT # | FINGER STICK BLOOD GLUCOSE TEST | SURVEYS / QUESTIONNAIRES | RANDOMIZATION | SURGERY |
|---|---|---|---|---|
| #1: Holding Area (Before Surgery) | | X | X | SOC |
| #2: Operating Room (During Surgery) | X | | | |
| #3: Recovery Room | X | X | | |
| #4: Postoperative Day 1 | | X (via phone) | | |
| #5: Postoperative Day 2 | | X (via phone) | | |
| #6: Postoperative Day 3 (if necessary) | | X (via phone) | | |
| #7: Postoperative Day 21 | | X (via phone) | | |

### 6.10 Radiological Evaluations

N/A

### 6.11 Clinical Evaluations

N/A

#### 6.11.1 Revision Surgery

N/A

## 7.0 STATISTICAL ANALYSIS

1. Proposed analysis (e.g., student's t-test, ANOVA, chi square, regression, etc.): Dunnett's test (three pairwise comparisons, one between each of the three IV dexamethasone groups and control)
2. Alpha level: Family wise type I error rate = 0.05 (two sided)
3. Beta or power level: 80% power to detect all pairs of groups that actually differ in duration of analgesia
4. Primary outcome variable estimate (mean +/s.d. for continuous outcome, frequency/percentage for categorical variable): Mean ± SD duration of analgesia in control group = 13.7 ± 8.5 hours (Desmet 2013)
5. Number of groups being compared (use 1 for paired analysis within the same subjects): 4
6. Effect size or change expected between groups: Investigators defined 8 hours as a clinically meaningful difference in duration of analgesia
7. Resulting number per group: 31
8. Total sample size required: 124 + 10% to account for attrition = 138 (round up to 140)

## 8.0 ADVERSE EVENT ASSESSMENT

All Adverse Events (AEs) will be reported in the final study report. Definitions for Adverse Event (AE) used in this study are listed below and are based on FDA and international guidelines:

### 8.1 Adverse Event (AE)

### 8.2 Serious Adverse Events (SAE)

### 8.3 Subsequent Surgical Interventions Definitions

### 8.4 Adverse Event Relationship

Participation in this research involves the potential risk of a breach of confidentiality to your stored health information. HSS tries to minimize those risks by (i) removing some direct identifiers from stored information (i.e., names, social security numbers, medical record numbers); (ii) securing, in a separate location, and limiting access to information that would identify you; and (iii) limiting access to information stored to HSS investigators.

There may be risks or side effects that are unknown at this time. If we learn about new risks that may affect your willingness to continue your participation, we will make you aware of them and you will be asked to re-consent to continue your participate in the study.

### 8.5 Adverse Event Recording

### 8.6 Adverse Event Reporting

## 9.0 INVESTIGATOR RESPONSIBILITIES, RECORD AND REPORTS

### 9.1 Subject Consent and Information

Patients will be identified from the OR schedule on the day before surgery. On the day of surgery, the RA or anesthesiologists will approach and consent eligible patients in the holding area.

### 9.2 Subject Data Protection

Any information collected electronically will be stored on the REDCap server. The REDCap server and data are hosted by Weill Cornell Medical College CTSC, with the servers physically located in the Payson building of Weill Cornell New York Presbyterian Hospital. Access to this space is limited to members of the Hospital's informatics department. Electronically, several intrusion protection mechanisms, including firewalls and encryption, are in place to protect the server and its data. Any paper based data sheets utilized for the study will be stripped of all personal identifiers whenever possible and stored the department's locked office.

### 9.3 Staff Information

Eugene Kremer
Meghan Kirksey, MD, Ph.D.
Jacques YaDeau, MD, PhD IRB Vice Chair
Carrie Guheen, MD
Angie Zhang, Research Assistant
Stephen Caleb Haskins, MD
Isabel Armendi, Research Assistant
Thuyvan Luu, Research Assistant
Swetha Pakala, MD
Ajay Dharmappa, MD
Jodie Curren, RN
Candace Gopaul
Denesy Mancenido
Mark Jensen
Pamela Wendel, MD
Aaron Schweitzer, Research Assistant
Jennifer Cheng Research Associate
Valeria Buschiazzo
Phuong Dinh Mac, Research Assistant
Kanupriya Kumar, M.D.
Katherine Lee, Research Assistant

Richard Kahn, MD

### 9.4 Protocol Reviews

Literature searches will be conducted on a routine basis to search for latest news concerning dexamethasone and patient safety. If the drug is deemed unsafe at any point, or if significant development arise, immediate changes will be made to the study protocol and informed consent form.

## 10.0 REFERENCES

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