



Interscalene Block versus Superior Trunk Block: A Randomized Controlled Clinical Trial

FUNDER: Research & Education Fund, Department of
Anesthesiology, Critical Care & Pain
Management

PROTOCOL NO.: IRB#2017-0979

VERSION & DATE: 12/3/19

PROTOCOL SYNOPSIS

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| Protocol Title: | Interscalene Block versus Superior Trunk Block: A Randomized Controlled Clinical Trial |
| Protocol Number: | 2017-0979 |
| Protocol Date: | 7/3/2019 |
| Sponsor: | N/A |
| Principal Investigator: | David Kim, MD |
| Products: | N/A |
| Objective: | Sparing the phrenic nerve by administering ultrasound-guided low volume superior trunk block (STB) and interscalene block (ISB) for arthroscopic shoulder surgery. |
| Study Design: | Randomized Controlled Trial |
| Enrollment: | 126 total |
| Subject Criteria: | <ul style="list-style-type: none"> • Patients who will be undergoing arthroscopic primary unilateral labral repair/stabilization of the shoulder, arthroscopic shoulder rotator cuff repair, and arthroscopic shoulder • capsular release, labral debridement, and bankart repair • Age 18 to 80 years • Planned use of general anesthesia and interscalene or superior trunk block • Ability to follow study protocol • English speaking • ASA I - III |
| Study Duration: | <ul style="list-style-type: none"> • 9/2017- 8/2018 |
| Data Collection: | <ul style="list-style-type: none"> • Demographics • Respiratory Parameters (MV, RR, TV) • Diaphragm Analysis • Patient Satisfaction • Incidence of Adverse Effects (horner's/hoarseness, dyspnea, hiccups, coughing) • Pulm Function (NIF, FEV1, FVC) • Sensory Exam • Handgrip • NRS pain scores at rest, at movement • Opioid Consumption • Neuropraxia |

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| | <ul style="list-style-type: none"> • Nerve Block Success • Length of PACU stay • Blinding assessment • Time to meet discharge criteria |
| <p>Outcome Parameters:</p> | <ol style="list-style-type: none"> 1. Our primary outcome will be the incidence of hemidiaphragmatic paralysis (HDP) with superior trunk block and interscalene blocks as measured by ultrasound before and after the surgery as well as NRS Pain scores at rest in the PACU measured after the surgery every 30 minutes where worst pain in PACU will be the highest recorded number during PACU stay. 2. Full resolution of the block will be reported by the patient on POD 1 via RA phone call 3. Handgrip as measured by dynamometer. Maximum grip strength will be assessed pre op and upon 60 min after PACU arrival (2 measurements will be done per time point and the average will be recorded) 4. Change in respiratory function as measured by changes in average minute ventilation, respiratory rate and tidal volume from preoperative baseline using a non-invasive monitoring device, and by changes in forced maneuvers: NIF, FEV1 and FVC measured preoperatively in holding area and 60 minutes postoperatively in the PACU. 5. incidence of ISB related side effects: horner's syndrome, hoarseness, hiccups, coughing, dyspnea in PACU 6. Time to readiness for PACU discharge (time of PACU admission to time of readiness to discharge, measured by Post Anesthetic Discharge Scoring System) evaluated every 15 minutes. 7. Block duration 8. Incidence of paresthesia / neuropraxia (POD1, POD 2): persistent tingling, numbness in POD1, if patient reports persistent neuropraxia after POD2, will follow up on POD7. If persists, will notify attending anesthesiologist and continue to follow until postoperative neurologic symptoms (PONS) resolves. 9. NRS Pain Scores at rest and with movement (PACU, POD 1, POD2) 10. Opioid consumption (PACU, POD1, POD2) |
| <p>Statistical Analysis:</p> | <p>Proposed analysis (e.g., student's t-test, ANOVA, chi-square, regression, etc.): Non-inferiority and superiority tests</p> <ol style="list-style-type: none"> 2. Alpha level: 0.025 3. Beta or power level: 80% |

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| | <p>4. Primary outcome variable estimate (mean +/- s.d. for continuous outcome, frequency/percentage for categorical variable): Two primary outcomes for join hypothesis:</p> <p>1 – Incidence of HDP: 76% vs. 40.6%; appx. 35% clinically meaningful difference (Dimeo, unpublished) – used for superiority hypothesis</p> <p>2 – NRS worst pain in PACU: 1.6 points non-inferiority margin (Kim (2014) citing Ilfeld (2011)), 2.9 within-group SD (Kahn, unpublished) – used for non-inferiority hypothesis(See below)</p> <p>5. Number of groups being compared (use 1 for paired analysis within the same subjects): 2</p> <p>6. Effect size or change expected between groups: See below</p> <p>7. Resulting number per group: 52</p> <p>8. Total sample size required: 104 + 20% to account for attrition/withdrawal -->126</p> <p>9. Who conducted your sample size calculation? Sarah Weinstein and Yan Ma (Conducted prior analysis for Dr. Stavros Memtsoudis ISB vs SCP study)</p> <p>Primary outcomes: The incidence of HDP between two groups will be compared using chi-square/Fisher's exact test. Logistic regression analysis may be performed to compare the incidence of HDP between the two blocks while adjusting potential confounders. NRS worst pain scores in PACU will be compared between the two groups using the Mann-Whitney-Wilcoxon U test or two-sample t-tests (depending on the distribution of the data).</p> <p>Secondary outcomes: Continuous secondary outcomes measured at one time point (e.g., PACU length of stay, etc.) will be compared between the STB and ISB groups using t-test / Mann Whitney Wilcoxon rank test (depending on data distribution) Categorical secondary outcomes measured at one time point will be compared between the STB and ISB groups using chi-square/Fisher's exact test (depending on data distribution). Continuous and categorical outcomes measured at multiple time points (e.g., opioid consumption, change in respiratory consumption, patient satisfaction, etc.) will be analyzed using a generalized estimating equations (GEE) approach.</p> <p>Baseline characteristics:</p> |
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| | <p>Demographics and other baseline characteristics will be compared between the STB and ISB groups. Balance diagnostics, such as described in Austin 2009 [1] may be used for assessing similarity of baseline characteristics between the two study groups.</p> |
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1.0 INTRODUCTION

Peripheral nerve blocks (PNBs) have been the mainstay analgesic for ambulatory shoulder arthroscopies. PNB's provide both surgical anesthesia and postoperative analgesia.

The interscalene block (ISB) remains the gold standard for shoulder arthroscopic surgeries. However, it is not without untoward effects, mainly the blockade of the phrenic nerve (diaphragmatic hemiparesis), sympathetic nerves (horner's syndrome), and recurrent laryngeal nerve (hoarseness). A study done at HSS has revealed the incidence of phrenic nerve paresis to be 76% with an ISB in comparison to 40.6% with a supraclavicular block using 45 ml of 0.5% bupivacaine (Dimeo et.al. not published).

Ultrasound has allowed for the refinement of peripheral nerve blocks. Under ultrasound guidance, regional blocks can be performed with pinpoint accuracy, enabling the practitioner to target only the nerves that supply the area needed for the surgery and sparing nerves that would normally be blocked. The adductor canal block is an example of such refinement, where the femoral nerve and its motor blockade of the quadriceps are spared with the ACB. Another such refinement of the interscalene block is the superior trunk block (STB), isolating the bundle of nerves that would provide anesthesia and analgesia for the shoulder joint, sparing the phrenic nerve, recurrent laryngeal nerve and a portion of brachial plexus enabling patient to hand grip.

Low-volume targeted PNB's like the superior trunk block theoretically should lead to a lower incidence of phrenic nerve paresis but the literature is lacking in examining this and also its implication of sparing respiratory function. This study would help elucidate the question of whether the STB spares the phrenic nerve, and provide adequate analgesia.

2.0 PRODUCT DESCRIPTION

N/A

3.0 OBJECTIVE OF CLINICAL STUDY

1. Does the Superior trunk block spare the phrenic nerve more often than the ISB?
2. Does the Superior trunk block provide as adequate analgesia as an ISB for shoulder arthroscopy?
3. Does the Superior trunk block spare motor blockade of the hand?
4. Does the Superior trunk block spare the recurrent laryngeal nerve, preventing hoarseness more often than the ISB?

4.0 STUDY HYPOTHESES

1. The superior trunk block spares the phrenic nerve more often than the ISB.
2. Forced respiratory maneuvers (negative inspiratory force (NIF), FEV1, and FVC) will be spared with the STB in comparison to the ISB.
3. STB will be noninferior to the ISB with respect to worst NRS pain score at rest in the PACU

5.0 STUDY DESIGN

5.1 Study Duration

9/2017 – 8/2018

5.2 Endpoints

5.2.1 Primary Endpoint

- Our primary outcome will be the incidence of hemidiaphragmatic paralysis (HDP) with superior trunk block and interscalene blocks as measured by ultrasound before and after the surgery as well as NRS Pain scores at rest in the PACU measured after the surgery every 30 minutes where worst pain in PACU will be the highest recorded number during PACU stay.

5.2.2 Secondary Endpoints

- Full resolution of the block will be reported by the patient on POD 1 via RA phone call
- Handgrip as measured by dynamometer. Maximum grip strength will be assessed pre op and upon 60 min after PACU arrival (2 measurements will be done per time point and the average will be recorded)
- Change in respiratory function as measured by changes in average minute ventilation, respiratory rate and tidal volume from preoperative baseline using a non-invasive monitoring device, and by changes in forced maneuvers: NIF, FEV1 and FVC measured preoperatively in holding area and 60 minutes postoperatively in the PACU.
- incidence of ISB related side effects: horner's syndrome, hoarseness, hiccups, coughing, dyspnea in PACU
- Time to readiness for PACU discharge (time of PACU admission to time of readiness to discharge, measured by Post Anesthetic Discharge Scoring System) evaluated every 15 minutes.
- Block duration
- Incidence of paresthesia / neuropraxia (POD1, POD): persistent tingling, numbness in POD1, if patient reports persistent neuropraxia after POD2, will follow up on POD7. If persists, will notify attending anesthesiologist and continue to follow until postoperative neurologic symptoms (PONS) resolves.
- NRS Pain Scores at rest and with movement (PACU, POD 1, POD2)
- Opioid consumption (PACU, POD1, POD2)

5.3 Study Sites

Hospital for Special Surgery Main Hospital – Ambulatory Surgery

6.0 STUDY POPULATION

6.1 Number of Subjects

126 subjects

6.2 Inclusion Criteria

Subjects of either gender will be included if they:

1. Patients who will be undergoing arthroscopic primary unilateral labral repair/stabilization of the shoulder, arthroscopic shoulder rotator cuff repair, and arthroscopic shoulder
2. capsular release, labral debridement, and bankart repair
3. Age 18 to 80 years
4. Planned use of general anesthesia and interscalene or superior trunk block
5. Ability to follow study protocol
6. English speaking
7. ASA I - III

6.3 Exclusion Criteria

Subjects will be excluded from the study if they:

1. Pre-existing neuropathy of the operative limb
2. Younger than 18 years old and older than 80
3. Patients with severe respiratory disease
4. Allergy to one of the study medications
5. Chronic gabapentin/pregabalin use (regular use for longer than 3 months)
6. Chronic opioid use (taking opioids for longer than 3 months)
7. Contraindication to general anesthesia, interscalene or superior trunk block
8. Herniated Cervical Disk, Cervical Myelopathy
9. BMI >35
10. Non English speakers

6.4 Randomization

The randomization will occur upon IRB approval and prior to start of study enrollment. Randomization will be revealed to the anesthesiologist after the patient gives consent in the holding area prior to surgery. After consent is obtained, the anesthesiologist will be given a sealed opaque envelope corresponding to the patients study ID number and randomization to either treatment or control. The envelope will be opened in the operating room, not in the presence of the investigators that assess the patients post-operatively

7.0 PROCEDURES

7.1 Surgical Procedure

Arthroscopic shoulder surgery

7.2 Data Collection

- Our primary outcome will be the incidence of hemidiaphragmatic paralysis (HDP) with superior trunk block and interscalene blocks as measured by ultrasound before and after the surgery as well as NRS Pain scores at rest in the PACU measured after the surgery every 30 minutes where worst pain in PACU will be the highest recorded number during PACU stay.
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- NRS Pain Scores at rest and with movement (PACU, POD 1, POD2)
- Opioid consumption (PACU, POD1, POD2)

7.3 Schedule of Assessments

| Study Visit # | Surveys / Questionnaires | Randomization | Arthroscopic Shoulder Surgery | Ultrasound/Handgrip measurement/ Pulmonary Function Assessment |
|---------------------------|--------------------------|---------------|-------------------------------|---|
| Pre-op Holding Area | X | X | | X |
| Surgery | | | SOC | X |
| Post Anesthesia Care Unit | X | | | X |
| POD 1 | X | | | |
| POD 2 | X | | | |

X= Research procedures

SOC= Standard of care (care you would receive if you were not participating in this study)

8.0 STATISTICAL ANALYSIS

1. Proposed analysis (e.g., student's t-test, ANOVA, chi-square, regression, etc.): Non-inferiority and superiority tests
2. Alpha level: 0.025
3. Beta or power level: 80%
4. Primary outcome variable estimate (mean +/- s.d. for continuous outcome, frequency/percentage for categorical variable): Two primary outcomes for joint hypothesis:
 - 1 – Incidence of HDP: 76% vs. 40.6%; appx. 35% clinically meaningful difference (Dimeo, unpublished) – used for superiority hypothesis
 - 2 – NRS worst pain in PACU: 1.6 points non-inferiority margin (Kim (2014) citing Ilfeld (2011)), 2.9 within-group SD (Kahn, unpublished) – used for non-inferiority hypothesis (See below)
5. Number of groups being compared (use 1 for paired analysis within the same subjects): 2
6. Effect size or change expected between groups:
See below
7. Resulting number per group: 52
8. Total sample size required: 104 + 20% to account for attrition/withdrawal -->126
9. Who conducted your sample size calculation? Sarah Weinstein and Yan Ma (Conducted prior analysis for Dr. Stavros Memtsoudis ISB vs SCP study)

Primary outcomes:

The incidence of HDP between two groups will be compared using chi-square/Fisher's exact test. Logistic regression analysis may be performed to compare the incidence of HDP between the two blocks while adjusting potential confounders.

NRS worst pain scores in PACU will be compared between the two groups using the Mann-Whitney-Wilcoxon U test or two-sample t-tests (depending on the distribution of the data).

Secondary outcomes:

Continuous secondary outcomes measured at one time point (e.g., PACU length of stay, etc.) will be compared between the STB and ISB groups using t-test / Mann Whitney Wilcoxon rank test (depending on data distribution)

Categorical secondary outcomes measured at one time point will be compared between the STB and ISB groups using chi-square/Fisher's exact test (depending on data distribution). Continuous and categorical outcomes measured at multiple time points (e.g., opioid consumption, change in respiratory consumption, patient satisfaction, etc.) will be analyzed using a generalized estimating equations (GEE) approach.

Baseline characteristics:

Demographics and other baseline characteristics will be compared between the STB and ISB groups. Balance diagnostics, such as described in Austin 2009 [1] may be used for assessing similarity of baseline characteristics between the two study groups.

9.0 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:

9.1 Adverse Event (AE)

Patients will be made aware of the potential risks and study medications before enrollment. We will not enroll any patients with a history of adverse reactions to any of the study medications or are uncomfortable with study procedures. Once enrolled, if there is a physical risk, therapy will be initiated in the hospital, and patients will be monitored per standard of care by the hospital staff.

The anesthetic and surgical methods applied in the study are well documented and practiced for Shoulder Arthroscopy. The combination of these methods may increase the anticipated benefits by lowering patients' chances of hemidiaphragmatic paralysis and its side effects. Further, it may also spare hand grip. As a result, this may increase patient satisfaction post surgery.

9.2 Serious Adverse Events (SAE)

If a patient experiences complications, they will be kept at HSS for observation and withdrawn from the study. Such complications that would cause safety and toxicity concerns include local anesthetic toxicity, cardiac toxicity, and central nervous toxicity.

9.3 Subsequent Surgical Interventions Definitions

N/A

9.4 Adverse Event Reporting

The study will be monitored by the study investigators for adverse events. Any adverse events will be reported to the Institutional Review Board.

10.0 INVESTIGATOR RESPONSIBILITIES, RECORD AND REPORTS

10.1 Subject Consent and Information

Written/signed consent will be collected from participants in the holding area before surgery.

10.2 Subject Data Protection

- HSS tries to minimize those risks by (i) removing some direct identifiers from information stored [(i.e., names, social security numbers, medical record numbers)]; (ii) securing, in a

separate location, and limiting access to information linking codes (i.e., linkage codes) assigned to the registry information with direct participant identifiers; and (iii) limiting access to information stored to HSS investigators.

- Access to the REDCap program is password-protected, and access to a specific study's information within the program is limited to the research assistant and other IRB-approved study personnel who have been given permission to view and/or enter study data. REDCap program access is authorized by the CTSC; particular study access is granted by the research assistant. For data exports, fields marked as protected health information (PHI) in REDCap will be de-identified, if feasible.
- All transmission of data will occur via encrypted networks in password-protected files. Any paper-based data sheets utilized for the study will have personal identifiers removed whenever possible and will be stored in the department's locked office. Each subject will be assigned a unique study number for identification, and that number will not be derived from or related to information about the individual. Presentations and publications that result from this study will not contain any individual identifiers (at most the unique study numbers may be referred to). Thus our research presents a minimal risk of harm to subjects' privacy.