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Testing the feasibility of a clinical trial comparing a pre-surgery medication cocktail and nerve-numbing injections for pain management after minimally invasive shoulder surgery

Submission date
18/12/2018

Recruitment status
Recruiting

Registration date
03/01/2019

Overall study status
Ongoing

Last Edited
02/07/2026

Condition category
Musculoskeletal Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Pain after surgery occurs in four out of every five patients and is a major public health concern. The goal of this pilot study is to evaluate if a larger randomized controlled trial (RCT) addressing pain management after surgery is possible. Other objectives are to: 1) identify solutions to challenges that may arise in conducting the study, and 2) obtain some data to determine how many patients will be needed for the larger RCT. We chose to study patients undergoing shoulder surgery since it is a common surgery associated with fairly severe pain that is poorly controlled with current opioid-based regimens.

Who can participate?
Adults who are 18 years or older and having shoulder surgery for rotator cuff injury or shoulder instability.

What does the study involve?
The study involves receiving one of two treatments that are routinely used at the participating hospitals. Patients will be randomized to receive: 1) a nerve block, or 2) a combination of pain medications before surgery plus the nerve block.

What are the possible benefits and risks of participating?
We cannot guarantee that there is any personal benefit to participating in the study, i.e. that one treatment is better than the other. However, participants will have the opportunity to contribute to research in pain management. As all the study interventions are routinely used at the participating sites, the risks of this study are the same as the risks assumed when undergoing this surgery without participating in the study. We have reduced some risk by excluding people who are unlikely to benefit or at high risk of certain adverse events.

Where is the study run from?
Patients will be recruited from St. Mary's Hospital.

When is the study starting and how long is it expected to run for?
April 2018 to September 2030.

Who is funding the study?
This study is funded by the Canadian Institutes of Health Research.

Who is the main contact?
Dr Ana Velly
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
PJT-156259

Study information

Scientific Title
Optimizing pain management: a pilot randomized trial in patients undergoing arthroscopic shoulder surgery

Study objectives
Current study hypothesis as of 09/01/2025:
This trial is an exploratory pilot study to test the feasibility for a future pragmatic trial – this is the primary outcome. We are collecting pilot data on the interventions on post-operative pain only as a secondary outcome, and preliminary data suggests that PMC may reduce pain intensity at 24 hours post-surgery, and possibly reduce routine opioid use as compared to PMC+Block. Therefore, the hypotheses are:

Primary hypothesis: The future pragmatic RCT is feasible.

Primary hypothesis for the future definitive RCT: PMC+Block will reduce pain intensity at 24 hours post-surgery compared to Block alone; and will reduce the need for rescue opioid medication.

Previous study hypothesis:
This trial is an exploratory pilot study to test the feasibility for a future pragmatic trial – this is the primary outcome. We are collecting pilot data on the interventions on post-operative pain only as a secondary outcome, and preliminary data suggests that PMC may reduce pain intensity at 24 hours post-surgery, and possibly reduce routine opioid use as compared to PMC+Block. Therefore, the hypotheses are:

Primary hypothesis: The future pragmatic RCT is feasible.

Primary hypothesis for the future definitive RCT: PMC will reduce pain intensity at 24 hours post-surgery compared to either PMC+Block or Block alone; and will reduce the need for rescue opioid medication.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 25/02/2020, Health Canada, ref: HC6-24-c235630
2. Approved 18/08/2020, St. Mary's Hospital ERB, ref: SMHC-19-03

Primary study design
Interventional

Study design
Pilot randomized parallel trial

Study type(s)
Other

Health condition(s) or problem(s) studied
Rotator cuff pathology or shoulder instability

Interventions
Current interventions as of 04/07/2025:

Consenting patients will be randomly assigned to receive one of two study interventions: Block, or PMC+Block.

PMC Group:
Pregabalin: 25mg at night on the 5th day prior to surgery, 25mg BID on the 4th day prior to surgery, 50 mg BID on the 3rd day prior to surgery, 75 mg BID on the 2nd and 1st day prior to surgery. In our pilot data (Section 3.5), 75 mg BID appeared effective and it is less likely to create adverse events. If patients do not tolerate the 75mg dose (e.g. sedation), we will use the greatest tolerable dose.

Non-steroidal anti-inflammatory drugs: Celecoxib 100 mg PO BID starting 5 days prior to surgery. In case of contra-indication or intolerance, Naproxen EC 500 mg PO BID for 5 days will be used.

Block Group:
Interscalene Block. An anesthesiologist experienced in providing nerve blocks will administer a preoperative single-shot interscalene block, approximately 1 hour prior to the start of surgery. Either ropivacaine or bupivacaine in a volume of 5-15 ml, and a concentration of 0.5%, with no adjuvants, will be used. We will not use continuous interscalene block due to logistical challenges.

Duration of the treatment.
For the PMC and PMC+Block groupsgroup, they will receive the PMC 5 days prior to their surgery date. The duration of treatment for these groups is thus 5 days. The Block group will receive their treatment right before their surgery – the duration of treatment is therefore 1 day. Following that, all groups will receive the same, standard postoperative treatment. All participants will have their last follow-up assessment performed at 6 months post-surgery. The time points for follow-ups are at 6 hours, 24 hours, 7 days, 2 and 6 months post-surgery.

Randomization.
We will apply stratified randomization of patients by surgeon using random number generation by an independent third party. To improve blinding, distinct evaluators will be making assessments. A research assistant will assess POP intensity and research nurses will assess pain medication and adverse events. Further, we will ask patients not to disclose their treatment. However, we recognize that the evaluators may be unblinded if patients disclose their treatment (see Section 7.1). We will also blind the supervising statistician to prevent biases during the analysis (e.g., model selection, and handling of missing data).

Wash-out period.
There is no wash-out period in this parallel RCT, and there are 3 treatment groups.

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Consenting patients will be randomly assigned to receive one of two study interventions: Block, or PMC+Block.

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Non-steroidal anti-inflammatory drugs: Celecoxib 100 mg PO BID starting 5 days prior to surgery. In case of contra-indication or intolerance, Naproxen EC 500 mg PO BID for 5 days will be used.

Block Group:
Interscalene Block. An anesthesiologist experienced in providing nerve blocks will administer a preoperative single-shot interscalene block, approximately 1 hour prior to the start of surgery. Either ropivacaine or bupivacaine in a volume of 5-15 ml, and a concentration of 0.5%, with no

adjuvants, will be used. We will not use continuous interscalene block due to logistical challenges.

Duration of the treatment.
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Wash-out period.
There is no wash-out period in this parallel RCT, and there are 3 treatment groups.

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Previous interventions:

Consenting patients will be randomly assigned to receive one of three study interventions: PMC, Block, or PMC+Block.

PMC Group:
Pregabalin: 25mg at night on the 5th day prior to surgery, 25mg BID on the 4th day prior to surgery, 50 mg BID on the 3rd day prior to surgery, 75 mg BID on 2nd and 1st day prior to surgery. In our pilot data (Section 3.5), 75 mg BID appeared effective and it is less likely to create adverse events. If patients do not tolerate the 75mg dose (e.g. sedation), we will use the greatest tolerable dose.
Non-steroidal anti-inflammatory drugs: Celecoxib 100 mg PO BID starting 5 days prior to surgery. In case of contra-indication or intolerance, Naproxen EC 500 mg PO BID for 5 days will be used.

Block Group:
Interscalene Block. An anesthesiologist experienced in providing nerve blocks will administer a preoperative single shot interscalene block, approximately 1 hour prior to the start of surgery. Either ropivacaine or bupivacaine in a volume of 5-15 ml, and a concentration of 0.5%, with no adjuvants will be used. We will not use continuous interscalene block due to logistical challenges.

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Wash-out period.
There is no wash-out period in this parallel RCT, and there are 3 treatment groups.

Intervention Type
Mixed

Primary outcome(s)
Current primary outcome measure as of 09/01/2025:
1. Recruitment and consent: Recruitment rate will be assessed as the number of eligible participants who consent to participate in the study, by month, every month. If patient recruitment is below 25% early in the process, we will develop methods to improve recruitment decreasing the barriers to recruitment.
2. Treatment allocation randomization, blinding: Problems will be summarized through internal communications. We will assess evaluator unblinding after the trial, and whether it was caused by study processes (solutions would be implemented during the pilot trial), active treatment efficacy, or adverse events.
3. Adherence: We will document challenges and the proposed solutions with all participating surgeons through internal communications. Adherence rate will be calculated by number of participants who adhered at least 50% of the medication as prescribed 5 days before surgery divided by the total of participants who received the prescribed medication (PMC+Block groups). If we cannot increase adherence (defined as taking at least 50% of the medication as prescribed 5 days before surgery) to occur in at least 75% of participants, we will consider the definitive trial to be non-feasible.
4. Attrition: Attrition rates will be assessed by the number of patients who consent to participate who remain in the study until the end of the follow-up period. We will assess dropout during the study. We will document challenges and the proposed solutions with all dropouts through internal communications. We consider a dropout rate of ≤ 20% to be the threshold for a feasible future definitive RCT.
5. Response rates to questionnaires and incomplete questionnaires: We will consider 80% as an acceptable threshold. We will ask all non-responders why they did not to respond the questionnaire or the question and use this information to decide how to improve response rates.
6. Time needed to collect data. We will record how long each set of questionnaires requires, and elicit feedback as to its acceptability. If more than 25% of patients consider the time unacceptable, the definitive RCT will focus on the most important data.

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1. Recruitment and consent: Recruitment rate will be assessed as the number of eligible participants who consent to participate in the study, by month, every month. If patient

recruitment is below 25% early in the process, we will develop methods to improve recruitment decreasing the barriers to recruitment.
2. Treatment allocation randomization, blinding: Problems will be summarized through internal communications. We will assess evaluator unblinding after the trial, and whether it was caused by study processes (solutions would be implemented during the pilot trial), active treatment efficacy, or adverse events.
3. Adherence: We will document challenges and the proposed solutions with all participating surgeons through internal communications. Adherence rate will be calculated by number of participants who adhered at least 50% of the medication as prescribed 5 days before surgery divided by the total of participants who received the prescribed medication (PMC and PMC+Block groups). If we cannot increase adherence (defined as taking at least 50% of the medication as prescribed 5 days before surgery) to occur in at least 75% of participants, we will consider the definitive trial to be non-feasible.
4. Attrition: Attrition rates will be assessed by the number of patients who consent to participate who remain in the study until the end of the follow-up period. We will assess dropout during the study. We will document challenges and the proposed solutions with all dropouts through internal communications. We consider a dropout rate of ≤ 20% to be the threshold for a feasible future definitive RCT.
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6. Time needed to collect data. We will record how long each set of questionnaires requires, and elicit feedback as to its acceptability. If more than 25% of patients consider the time unacceptable, the definitive RCT will focus on the most important data.

Key secondary outcome(s)
1. Cumulative consumption of opioids for pain management. The research nurse/assistant will assess if patients use opioids at 6 h, 1 day, and 1 week after surgery during their follow-ups at these time points.
2. Pain intensity at 1 day post-surgery. This is generally the primary outcome in trials assessing the effectiveness of POP management. We will measure POP intensity using the standardized, validated questionnaire recommended by the APS: “Patient Outcome questionnaire”(POQ).
3. Pain intensity. We will also assess pain intensity at 6 h, 1 week, 2 and 6 months post-surgery using the POQ as above.
4. Supplemental pain management. We will assess if patients received non-opioid supplemental pain management (rescue medication, other treatments) during follow-ups at 6 h, 1 day, 1 week, and 2 and 6 months after surgery, and identify the treatments received. The research nurse /assistant will be responsible for this.
5. Physical Activity. We will use the validated self-assessment portion of the POQ. This questionnaire will be used at 2 and 6 months post-surgery.
6. Frequency of adverse and serious adverse events: Adverse and serious adverse events will be recorded by the research nurse/assistant at 6h, 1 day, and 7 days post-surgery. In addition, the research nurse/assistant will contact the study surgeons weekly to assess any occurrence of serious adverse events.
7. Cost data. We will record the cost of the anesthesiologist’s time, miscellaneous items (e.g., syringes, gauze pads), and medications by region (Ontario and Quebec).

Completion date
01/09/2030

Eligibility

Key inclusion criteria
1. Aged 18 years or older
2. Understand English or French;
3. Undergoing arthroscopic surgery for shoulder rotator cuff pathology or shoulder instability with at least 6 months of symptoms.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
64 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current participant exclusion criteria as of 09/01/2025:
1. Allergies to any of the following drug combinations:
1.1. pregabalin, or
1.2. both celecoxib and naproxen EC; or
1.3. bupivacaine
2. Allergic-type to reactions to sulfonamides
3. History of asthma, urticaria, or allergic-type reactions after taking Acetylsalicylic Acid (ASA) or other NSAIDs (i.e. complete or partial syndrome of ASA-intolerance-rhinosinusitis, urticaria /angioedema, nasal polyps, asthma);
4. Angioedema
5. Bleeding disorders
6. History of ulcers
7. Inflammatory bowel disease
8. Cerebrovascular disease (including but NOT limited to stroke, cerebrovascular accident, transient ischemic attacks and/or amaurosis fugax)
9. Ischemic heart disease (including but NOT limited to acute myocardial infarction, history of myocardial infarction and/or angina)
10. Congestive heart failure (NYHA II-IV)
11. Liver impairment
12. Renal impairment (Renal impairment is identified by an estimated glomerular filtration rate (eGFR) of less than 60 mL/min per 1.73 m2. This valued is estimated from a calculator found at https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation)

13. Known hyperkalemia
14. Chronic pulmonary lung disease (COPD)
15. Contraindications to pregabalin, or both celecoxib and naproxen EC; or bupivacaine
16. Current use of high-dose opioids (>60 mg equivalents of morphine), gabapentinoids, antidepressants, antipsychotics, or cannabinoids
17. Cancer
18. Pregnancy or lactation. All females under age 55 get pregnancy tests prior to surgery. If they are pregnant, the surgery is cancelled. This procedure is not specific to this study, but a standard practice for all hospitals before surgery.
19. Frail or debilitated patients
20. Life expectancy of less than one year
21. Those without DSQ (Dossier Santé Québec) or ClinicalConnect (Ontario) access
22. Cannot be randomized to receive an interscalene block
23. Patients who refused to do a blood test.
24. Patients with BMI<19 will be excluded
25. Unable to communicate in English or French

Previous participant exclusion criteria as of 10/01/2022 to 09/01/2025:
A potential participant who meets any of the following criteria will be excluded from participation in this study:
1. Allergies to any of the following drug combinations:
1.1. Pregabalin
1.2. Both celecoxib and naproxen EC
1.3. Both ropivacaine and bupivacaine
2. Allergic-type reactions to sulfonamides
3. History of asthma, urticaria, or allergic-type reactions after taking Acetylsalicylic Acid (ASA) or other NSAIDs (i.e. complete or partial syndrome of ASA-intolerance-rhinosinusitis, urticaria /angioedema, nasal polyps, asthma)
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16. Current use of high-dose opioids (>60 mg equivalents of morphine), gabapentinoids, antidepressants, antipsychotics, or cannabinoids
17. Cancer
18. Pregnancy or lactation. All females under age 55 get pregnancy tests prior to surgery. If they are pregnant, the surgery is cancelled. This procedure is not specific to this study, but a standard practice for all hospitals before surgery.
19. Frail or debilitated patients

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21. Those without DSQ (Dossier Santé Québec) or ClinicalConnect (Ontario) access
22. Cannot be randomized to receive an interscalene block
23. Patients who refused to do a blood test.

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Previous exclusion criteria as of 12/05/2021:

1. Allergies to any of the following drug combinations:
o pregabalin, or
o both celecoxib and naproxen EC; or
o both ropivacaine and bupivacaine
2. Allergic-type reactions to sulfonamides
3. History of asthma, urticaria, or allergic-type reactions after taking Acetylsalicylic Acid (ASA) or other NSAIDs (i.e. complete or partial syndrome of ASA-intolerance-rhinosinusitis, urticaria /angioedema, nasal polyps, asthma);
4. Angioedema
5. Bleeding disorders
6. History of ulcers
7. Inflammatory bowel disease
8. Cerebrovascular disease (including but NOT limited to stroke, cerebrovascular accident, transient ischemic attacks and/or amaurosis fugax)
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13. Known hyperkalemia
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17. Frail or debilitated patients
18. Life expectancy of less than one year
19. Current use of high-dose opioids (>60 mg equivalents of morphine), gabapentinoids, antidepressants, antipsychotics, or cannabinoids
20. Cannot be randomized to receive an interscalene block
21. Contraindications to pregabalin, or both celecoxib and naproxen EC, or both ropivacaine and bupivacaine
22. Those without DSQ (Dossier Santé Québec) or ClinicalConnect (Ontario) access.
23. Patients who refused to do a blood test.

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Previous exclusion criteria:

1. True allergies or other contraindications to any of the medications used in the study
2. Bleeding disorders

3. History of ulcers
4. History of cancer
5. Life expectancy for less than one year
6. Current use of high-dose opioids (>60 mg equivalents of morphine), gabapentinoids, antidepressants, antipsychotics, or cannabinoids;
7. Patients with chronic pulmonary lung disease (COPD)

Date of first enrolment
01/09/2026

Date of final enrolment
28/09/2029

Locations

Countries of recruitment
Canada

Study participating centre
St. Mary's Hospital
3830 Lacombe Avenue
Montreal
Canada
H3T 1M5

Sponsor information

Organisation
Canadian Institutes of Health Research

ROR
https://ror.org/01gavpb45

Funder(s)

Funder type
Government

Funder Name
Canadian Institutes of Health Research

Alternative Name(s)

Instituts de Recherche en Santé du Canada, The Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research (CIHR), Canadian Institutes of Health Research | Ottawa ON, CIHR - Welcome to the Canadian Institutes of Health Research, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository. (REDCap; https://project-redcap.org/). Data will be collected only after consent from participants is obtained. Only key study staff will have direct access to REDCap and its data. The study staff is permitted access to only the minimum necessary data required to fulfill their role in the study.

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.11	11/03/2021	04/07/2025	No	No