Quadratus Lumborum Block After Cesarean Section: Analgesic Efficacy of Different Concentrations of Local Anesthetics. A Randomized Clinical Trial

Unique Protocol ID: RP DAE/2022/102

Date: August 2022

Danat Al Emarat Hospital for Women & Children
RESEARCH ETHICS COMMITTEE (REC)

APPLICATION FORM

DAE REC will review all applications to ensure that the proposed research meets acceptable standards with respect to scientific merit, design, ethical and United Arab Emirates cultural propriety, patient safety and convenience, and relevance. Proposals which meet these requirements will be approved. Advice will be provided for those projects for which the Committee feels there could be improvement.

Proposals should be submitted on an application form in an electronic form. The signed original form should be provided together with the support documents as detailed on the check list provided. Incomplete submissions will be returned to the applicant. Principle investigators may be called to the meeting to discuss their proposals. Applicants will be notified as early as possible of the Committee's decision with any appropriate explanations. Brief annual and final reports are required for approved proposals. All sections of the application must be completed. Enter "not applicable (N/A)" where appropriate.

All application forms should be submitted to
Ms. Sara Bachar
DAE Research and Ethics Committee Coordinator
at: research@danatalemarat.ae and sara.bachar@danatalemarat.ae

Title of the project

Quadratus lumborum block after cesarean section: analgesic efficacy of different concentrations of local anesthetics. A Randomized Clinical Trial

Abstract (100-150 words)

QLB is an injection of a local anesthetics around the quadratus lumborum muscle. It uses a fascial compartment path to extend the distribution of local anesthetics into the posterior abdominal wall and paravertebral space. Acute post C-section pain is a leading anesthetic concern for women; a key determinant of maternal satisfaction; may lead to persistent postoperative pain; is a predictor of postpartum depression; and can reduce early breastfeeding success. Effective postoperative analgesia should, therefore, be prioritized to improve outcomes following caesarean delivery. Our study is a Double-blinded, randomized and controlled trial.

A written, informed consent is discussed with and signed by all participants, and they are randomly assigned into one of two groups; (Group 1) to receive bilateral QLB with 0.125% bupivacaine 0.2 ml/kg, (Group 2) to receive bilateral QLB with 0.25% bupivacaine 0.2 ml/kg. For all patients, spinal anesthesia is performed with ultrasonography guidance in a standardized manner using hyperbaric bupivacaine 15mg and fentanyl 25 µg.

At the end of the procedure in the supine position, all participants receive bilateral QLBs performs under ultrasound guidance and aseptic technique. The internal oblique muscle is identified and followed laterally to the lateral interfacial triangle sitting above the quadratus lumborum muscle.

Results will be reported as

1. Total number of PCA morphine demands and the actual doses delivered at predetermined time intervals (1, 2, 4, 6, 12, 24 and 48 h) after surgery
2. Record of supplemental and regular analgesics.
3. Visual analogue score for pain at rest (Static) and with movement (dynamic) defined as the elevation of the head and shoulders off the pillow from the supine position), (0, no pain; 10, worst pain imaginable).
4. Opioids-related side effects i.e., sedation scores (Ramsay scale), itching (0, none; 1, mild; 2, moderate; 3, severe), nausea (0–3 scale: 0, none; 1, mild; 2, moderate; 3, severe or vomiting),
5. Block-related complications (i.e., hematoma, organ injury, local anesthetic systemic toxicity, sepsis, and block failure).

For Committee use only:

Research Proposal Number/ version	
Date received	
Reviewer 1	
Reviewer 2	
Review Deadline	
Committee Review Deadline	
Date of Committee Decision:	
Decision:	

PROJECT INVESTIGATORS

The purpose of this section is to document the person(s) responsible for the study.

Name, Affiliation, and Position of Principal Investigator	**Signature**
Jinan Jameel Al-Aloosi Danat Al Emarat Hospital Consultant Anesthesiologist	

Name and Signature of all investigators:

Name, Affiliation, and Position	**Signature**
Rabiah Noueihed, Danat Al Emarat Hospital Consultant Anesthesiologist	

Approval/Endorsement of Head of Department or Deputy	**Signature**

Name and contact address of Investigator to which correspondence should be sent:

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Rabiah Noueihed ; rabiah.noueihed@danatalemarat.ae
Mob. 0526925514

Study Timeframe

Estimated study commencement date	**Estimated study end date**
August 2022	February 2023

C. DETAILS OF PROPOSED RESEARCH

Please complete all sections succinctly and cite pertinent supportive references.

C1. Overall objective(s), specific aim(s) and hypotheses.

QLB is an injection of a local anesthetics around the quadratus lumborum muscle. It uses a fascial compartment path to extend the distribution of local anesthetics into the posterior abdominal wall and paravertebral space. This central effect can be of vital importance when managing the visceral pain after caesarean section.

Many studies have shown that the inclusion of quadratus lumborum block to a multimodal analgesic regimen would reduce pain scores, opioids consumption, and prolonging time to first rescue analgesic after cesarean delivery.

However, the dose and concentration of the local anesthetic used among the studies are varied, and literature search identified no randomized controlled trial which looked at the concentration -response of local anesthetic to optimize the concentration resulting in the best pain relief.

The aim.

To design a prospective randomized controlled trial to compare the analgesic efficacy of 2 different concentration of Bupivacaine to standardize postoperative analgesic protocol used for QLB after caesarean section.

The objective.

We hypothesized that using the higher concentration (0.25%) of local anesthetic (Bupivacaine) would increase the analgesic effect without increasing the side effects and complications.

C2. Rationale & Background (Please include a literature review).

Caesarean delivery is the most common inpatient surgical procedure performed worldwide; improving the perioperative care of parturient has significant global implications [1].

Acute postpartum pain is a leading anesthetic concern for women [2]; is a key determinant of maternal satisfaction [3]; may lead to persistent postoperative pain [4, 5]; is a predictor of postpartum depression [6]; and can reduce early breastfeeding success [7]. Effective postoperative analgesia should, therefore, be prioritized to improve outcomes following caesarean delivery. In an effort to apply the latest evidence-based practices towards improving maternal outcomes, Enhanced Recovery after Surgery (ERAS) protocols have been adapted for cesarean delivery, with one of its key components being the optimization of post-cesarean delivery analgesia via a multimodal, opioid-sparing approach [8,9]. While neuraxial administration of opioids has been shown to be a safe and effective means of managing post-cesarean delivery pain, however, they are commonly associated with adverse effects such as nausea, vomiting, sedation, pruritus and have the potential for misuse [10], which have prompted the search for alternative non-opioid analgesic adjuncts. Regional anesthetic techniques are commonly included in ERAS protocols due to their proven efficacy in improving postoperative analgesia and the consequent reduction in nausea and vomiting [8,9]. Truncal nerves block such as transversus abdominis plane (TAP) blocks and quadratus lumborum blocks (QLB), are increasingly being incorporated into obstetric anesthetic practice to improve analgesic outcomes [11–16]. QLB involves local anesthetic infiltration adjacent to the quadratus lumborum muscle, which may facilitate the spread of local anesthetic into the thoracic paravertebral space [17]. By blocking both somatic nerves and the lower thoracic sympathetic trunk, the QLB could theoretically relieve both somatic and visceral pain, providing superior analgesia compared to the TAP block, which mainly targets somatic pain [18]. Quadratus lumborum blocks have been studied in several obstetric randomized controlled trials, and advocates of this technique postulate that it is associated with superior analgesic outcomes when compared with either control or TAP blocks [18]. Several studies have used different doses and concentrations of local anesthetics for QLB. However, a literature search identified no randomized controlled trials that evaluated the optimal concentration of local anesthetics used for QLB after caesarean section (19,20). We designed a prospective randomized controlled trial to compare the analgesic efficacy of 2 different concentrations of Bupivacaine to standardize postoperative analgesic protocol used for

QLB after caesarean section. QLB aims to infiltrate local anesthetic into a fascial plane that can reach the paravertebral space by dissecting the space behind the quadratus lumborum muscle. Blanco et al. performed studies with contrast-enhanced MRI and examined the spread of contrast within the fascial plane. The MRI images showed that injection at the posterior border of the quadratus lumborum muscle, between the quadratus lumborum and the latissimus dorsi muscles (QLB 2), may provide a more predictable spread of local anesthetic into the paravertebral space. This method has the advantage of a more superficial point of injection with better ultrasonographic resolution. It is also potentially safer because the needle tip is separated from the peritoneum by the quadratus lumborum muscle, reducing the risk of intraperitoneal injection and bowel injury (18).
Blanco et al. in his study on 2015 used bupivacaine 0.2 ml/kg at a conc. of 0.125%.

References:

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4. Weibel S, Neubert K, Jelting Y, et al. Incidence and severity of chronic pain after caesarean section: a systematic review with meta-analysis. European Journal of Anaesthesiology 2016; 33: 853–65.
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18. Blanco R, Ansari T, Girgis E. Quadratus lumborum block for postoperative pain after cesarean section: a randomized controlled trial. Eur J Anaesthesiol 2015;32:812–8.
19. Quadratus lumborum block vs. transversus abdominis plane block for caesarean delivery: a systematic review and network meta-analysis* K. El-Boghdadly ,1,2 N. Desai,1,2 S. Halpern,3 L. Blake,4 P. M. Odor,5 S. Bampoe ,5 B. Carvalho 6 and P. Sultan7
20. Quadratus lumborum block for postoperative analgesia after cesarean delivery: A systematic review with meta-analysis and trial-sequential analysis Hon Sen Tan (MD, MMed)a, Cameron Taylor (MD)a, Dan Weikel (MSc)b, Karen Bartonc, Ashraf S. Habib (MBBCh, MSc, MHSc, FRCA).

C3. Study Procedures

a. Study design, including the sequence and timing of study procedures (Distinguish research procedures from routine care).

It is a Double-blinded, randomized and controlled clinical trial. The participants are the patients attend the pre-assessment anaesthesia clinic and are scheduled for elective caesarean section under spinal anesthesia. A written, informed consent is discussed with and signed by all participants. Participants are randomly assigned into one of two groups; (Group 1) to receive bilateral QLB with 0.125% bupivacaine 0.2 ml/kg, (Group 2) to receive bilateral QLB with 0.25% bupivacaine 0.2 ml/kg. For all participants, spinal anesthesia is performed with ultrasonography guidance in a standardized manner using hyperbaric bupivacaine 15mg and fentanyl 25 μg. Spinal anesthesia is considered successful when a bilateral block to T6, assessed by loss of cold (ice cube) and/or touch (blunt pin) are established 5 min after the spinal injection. Anesthetic and surgical treatment are performed in the usual manner. At the end of surgery, all participants receive paracetamol 1g IV and Dexketoprofen 50 mg IV. While in the supine position, all participants receive bilateral QLBs performs under ultrasound guidance and aseptic technique. All participants are continuously monitored throughout the performance of the block. The internal oblique muscle is identified and followed laterally to the lateral interfacial triangle sitting above the quadratus lumborum

muscle (Posterior approach of QLB). The optimal point of injection is determined using hydrodissection. In the recovery room, all participants are connected to a morphine PCA pump set to deliver 1mg intravenous bolus on demand, with a lockout interval of 5 min and no background infusion.

All participants receive regular intravenous paracetamol 1 g 6 hourly, and oral diclofenac 50 mg at 8-hourly intervals. Intravenous ondansetron 4 mg is used to treat nausea and vomiting. Participants with a score of 10 in the modified Aldrete scoring system are considered eligible for discharge to the surgical ward. Data collection is continued on the ward for 48 h.

b. Primary and Secondary Outcome Measures. What will be measured and how (describe tests that patients need to undergo?).

The primary outcome measure of the study is the total number of PCA morphine demands and the actual doses delivered at predetermined time intervals (1h, 2h, 4h, 6h, 12h, 24h and 48h) after surgery. The following variables are measured and documented: heart rate, respiratory rate, oxygen saturation and noninvasive blood pressure.

The secondary outcomes are the visual analogue score for pain at rest (static) and with movement (dynamic) defined as the elevation of the head and shoulders off the pillow from the supine position), (0, no pain; 10, worst pain imaginable). Residual nerve block (the time to mobilization), opioids-related side effects (sedation scores (Ramsay scale), itching (0, none; 1, mild; 2, moderate; 3, severe), nausea (0–3 scale: 0, none; 1, mild; 2, moderate; 3, severe or vomiting), block-related complications (i.e., hematoma, organ injury, local anesthetic systemic toxicity, sepsis and block failure). Record of supplemental and regular analgesics.

c. What data-collecting instruments will be used? (Measurements, questionnaires, interviews etc.). Please enclose a copy of these instruments.

d. Study duration and number of study visits required of research participants.

A single center between November 2022 and April 2023. No visits required after discharge.

e. Blinding, including justification for blinding or not blinding the trial, if applicable.

Double-blinded, randomized and controlled clinical trial

C4. Subjects

a. Study population with inclusion/exclusion Criteria

Inclusion criteria are American Society of Anesthesiologists physical status 1 or 2 and a normal singleton pregnancy with a gestation of at least 37 weeks who are scheduled for elective caesarean section under spinal anesthesia and consented to be enrolled into the study. We exclude.

a. Patient who has contraindications to spinal or regional anesthesia and patients who have Allergy/sensitivity/contraindication to study medications.
b. Patient who has congenital coagulopathy or who use anticoagulants.
c. Patients with anatomical abnormalities, localized infection
d. History of chronic pain or regular opioid use
e. Unable to comprehend or use the verbal rating pain scoring system
f. Requirement for conversion to general anesthesia after spinal anesthesia or failed spinal.

b. Subject Numbers.

98 patients each in group 1 and group 2

C5. Study Statistics

a. **Statistical plan including sample size justification and interim data analyses.**
Assuming the mean 48-hour morphine consumption in the group 1 (bilateral QLB with 0.125% bupivacaine 0.2 ml kg 1) to be 11 mg with standard deviation10 mg [18] and based on 33% difference in morphine consumption between the two groups, the sample size calculation indicated that 98 participants will be required in each group, with 80% power type I error associated with this test for null hypothesis is 5%.
Data will be collected and entered the computer as numerical or categorical data. Statistical analysis will be performed using SPSS for Windows with $P < 0.05$ set to be statistically significant. The values of continuous variables will be presented as mean ± standard deviation and the categorical data will be described as count and percentages. Comparisons will be performed between the two groups using independent t tests or Mann–Whitney tests, as appropriate. Categorical data will be compared through Pearson Chi-square test or Fisher exact test.

b. **Describe randomization and/or sampling procedures.**
Participants are allocated randomly by means of computer generation sequencing. The allocation sequence with unique study number for each participant will be concealed in sequentially numbered, opaque, sealed, and stapled envelopes. This envelope will be opened by an anesthetist who was not involved in the study. This Anesthetist prepares the study medication as per the allocation and labels the syringe with the unique study number; this number will be used to identify the study medication and will be revealed only on completion of data collection at the end of the study. The investigators, participants and other healthcare providers who are involved in postoperative care, are blinded to the patient group allocation.

c. **Early stopping rules.**
Not Applicable

D. ETHICAL CONSIDERATIONS

D1. Risks, discomforts, and safety.

a. **Describe risks to the participants, and steps taken to minimize these risks.**
Hypotension can be possibly related to spread of local anesthetic in the paravertebral spaces. Local anesthetic toxicity can be due to large volume used specially in cases of bilateral blocks. These two complications "Hypotension & Local anesthetic toxicity" can happen mainly during the first 30-60 min. after the block, and we are continuously monitoring the patient after the procedure in OT and in PACU. Search through systematic review and meta-analysis showed that QLB considered as a relatively safe technique as local anesthetic toxicity has not been reported and the complications related to technical challenges of the deeper block and inadequate visualization and hence injury to surrounding structures should be kept in mind. Retroperitoneal hematoma, injury to organs and nerve roots are potential complications, but systematic review and meta-analysis search demonstrate that no block-related complications occurred, especially with Posterior approach of QLB, and with experienced hands. Long experience in using ultrasound for nerves block for QLB and TAP block of the investigators. Infection at the site of injection; full aseptic precautions are used to avoid infection or abscess formation.

b. **What possible discomfort, inconvenience and possible side effects, costs may be experienced by the subjects?**

Lower extremity weakness has been reported with quadratus lumborum block leading to delay in mobilization. Local anesthetic distribution to the nerve roots or branches of lumbar plexus through spread in paravertebral spaces or via transversalis fascia is likely responsible for weakness of hip flexors (psoas and iliacus) and knee extensors (quadriceps). Quadriceps weakness was reported to be most associated with anterior quadratus lumborum block, but less by posterior and lateral approaches respectively.

c. Plans for reporting unanticipated problems or study deviations.

D2. Describe the probable benefits for:

a. The participant. Detail compensation for participants and any proposed reductions or penalties for not completing the protocol.

No additional risk or involvement required from the participant; hence no compensation is proposed.

b. **The institution(s). Hospital**.

Improve patient's satisfaction, and reduce postoperative opioids consumption, as well as postoperative chronic pain incidence.

Getting involved in research will benefit hospital's aim to become a center of excellence in research medicine

c. **Society, including the UAE as a country**.

Several studies have used different doses and concentrations of local anesthetics. However, a literature search identified no randomized controlled trials that evaluated the optimal concentration of local anesthetics used for QLB resulting in the best pain relief after caesarean section. This study will help to standardize postoperative analgesic protocol used for QLB after caesarean section.

D3. Informed Consent

a. What information will be given to subjects and how will it be given? Include copies of information letters.

b. From whom and how will informed consent be ensured and obtained?

The participant are the patients attend the pre-assessment anesthetic clinic and are scheduled for elective caesarean section under spinal anesthesia. Information sheet about the study (in Arabic and English languages) will be given to the patients who fulfill the inclusion criteria for the study, the procedure will be explained, and all the questions will be answered. The consent form then asked to be signed.

D4. Confidentiality

a. How and where will the data obtained from the study be stored and secured?

The study data will be collected and stored in one excel document that will be password encrypted. This document will be saved on the principle investigator's personal computer which is password protected. Patients' information such as MRN number and DOB, will be stored safely in the secured excel document. However, during statistical analysis, no identifying patient's information will be included, and the results will be completely anonymous. There will be no sharing of information via email or between other devices.

b. How will respect for the patient's rights (preservation of confidentiality, the possibility to withdraw without negative consequences etc.) be ensured?

The participants will sign a consent stating.

- The participation is voluntary, and participants are free to withdraw at any time of the study.
- Withdrawal from the study will not adversely affect their management plan.
- The study results will be completely anonymous, and all their information will be stored confidential and in a safe secured place.

D5. Has this proposal received ethical approval from any other institution(s)? If yes, please provide name of institution(s) and a copy of approval document(s).

No

D6. How will you report back to the involved departments/units and to the Research Ethics Committee and the Research Review Committee?

Study results will be documented in an evaluation report, and a summary presentation will be prepared by the research team.

E. BUDGET

E1. Describe the envisaged expenses for the study in terms of personnel, supplies/Equipment, services, etc.

We are performing QLB on most of our patients who are scheduled for caesarean section.

No additional expenses incurred for the study.

E2. How are the expenses covered? Describe the funding of the project, including possible contributions from industry. Please attach copies of agreements made with commercial institutions.

Not applicable as no additional cost involved.

No commercial funding, all extra time is volunteer by the study group.

F. ADDITIONAL COMMENTS AND INFORMATION

Support for this study was provided solely from institution and departmental resources.
Supports are provided from Research ethic committee and quality departments.

CHECK LIST FOR Submission of Application

Requirements for approval of a project by DAE Research Ethics Committee

- Documentation requirements for ethical application include:
  - Completed application form
  - Questionnaires
  - Consent form [sample enclosed]
  - Patient information sheets both in Arabic and English.
  - [Short CV relevant to the project (applicants outside DAE)

- Requirements for a favorable opinion
  - See attached document

GUIDELINES FOR PARTICIPANT REQUIREMENTS FOR A FAVORABLE OPINION[i]

Before giving a favorable opinion, Al Ain Medical District Human Research Ethics Committee should be adequately reassured about the following issues, as applicable:

1.1 *Scientific design and conduct of the study*:

a. The appropriateness of the study design in relation to the objectives of the study, the statistical methodology (including sample size calculation where appropriate) and the potential for reaching sound conclusions with the smallest number of research participants.

b. The justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants, other present and future patients, and the concerned communities.

c. The justification for use of control arms in trials, (whether placebo or active comparator), the randomization and binding process to be used as well as the methods used to provide allocation concealment, intention-to-treat analysis and sufficient follow up.

d. Criteria for prematurely withdrawing research participants in trials.

e. Criteria for suspending or terminating the research as a whole in trials.

f. The adequacy of provisions made for monitoring and auditing the conduct of the research in trials, including the constitution of a data safety monitoring committee (DSMC).

1.2 *Recruitment of research participants*

a. The characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status and ethnicity) and the justification for any decisions made in this respect.

b. The means by which initial contact and recruitment is to be conducted.

c. The means by which full information is to be conveyed to potential research participants or their representatives.

d. Inclusion criteria for research participants.

e. Exclusion criteria for research participants.

1.3 *Care and protection of research participants*

a. The safety of any intervention to be used in the proposed research.

b. The suitability of the investigator(s)'s qualifications and experience for ensuring good conduct of the proposed study.

c. Any plans to withdraw or withhold standard therapies or clinical management protocols for the purpose of the research, and the justification of such action.

d. The health and social care to be provided to research participants during and after the course of the research.

e. The adequacy of health care and social supervision and psychosocial support for the research participants.

f. Steps to be taken if research participants voluntarily withdraw during the course of the research.

g. The criteria for extended access to, the emergency use of, and/or the compassionate use of study products in trials.

h. The arrangements, if appropriate, for informing the research participant's general practitioner, including procedures for seeking the participant's consent to do so.

i. A description of any plans to make the study product available to the research participants following the research.

j. A description of any financial costs to research participants.

k. The rewards and compensations (if any) for research participants (including money, services and/or gifts).

l. Whether there is provision in proportion to the risk for compensation/treatment in the case of injury/disability/death of a research participant attributable to participation in the research; the insurance and indemnity arrangements.

m. The nature and size of any grants, payments or other reward to be made to any researchers or research hosts.

n. Circumstances that might be lead to conflicts of interest that may affect the independent judgement of the researcher(s).

1.4 *Protection of research participants' confidentiality*

a. A description of the persons who will have access to personal data of the research participants, including medical records and biological samples.

b. The measures taken to ensure the confidentiality and security of personal information concerning research participants.

c. The extent to which the information will be anonymised.

d. How the data/samples will be obtained, and the purposes for which they will be used.

e. How long the data/samples will be kept.

f. To which countries, if any, the data/samples will be sent.

g. The adequacy of the process for obtaining consent for the above.

1.5 *Informed consent process*

a. A full description of the process for obtaining informed consent, including the identification of those responsible for obtaining consent, the timeframe in which it will occur, and the process for ensuring consent has not been withdrawn.

b. The adequacy, completeness and understandability of written and oral information to be given to the research participants, and, when appropriate, their legally acceptable representatives.

c. Clear justification for the intention to include the research individuals who cannot consent, and a full account of the arrangements for obtaining consent or authorization for the participation of such individuals.

d. Assurances that research participants will receive information that becomes available during the course of the research relevant to their participation (including their rights, safety and well-being).

e. The provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project.