Sonographic Nerve-block for Laparoscopic Appendicectomy in Children - SNAP trial

STUDY PROTOCOL

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Scientific background

The laparoscopic approach to appendicectomy reduces pain and hospital stay in children and adolescents compared to the open approach[1] but post-operative pain remains significant. In a recent trial from our institution 65% of children required opiate analgesia.[2]
Local anaesthetic wound infiltration reduces post-operative pain in adult general and gynaecological surgery when compared to placebo.
Nerve blocks classically relied on landmark localization and physical clues such as 'pops', 'scratch' and 'loss of resistance'. The use of ultrasound guidance for nerve blocks is growing thanks to increasing availability of portable ultrasound machines. Ultrasound guidance may improve block quality, reduce time to onset and reduce complications.[7] The accuracy of needle placement within the rectus sheath was increased from 45% – 89% in one study.[8]
The rectus sheath nerve block places local anaesthetic anterior to the posterior rectus sheath to block segmental sensory nerves (T 9-11) to the umbilicus. The technique is reported to be 'safe and effective' in paediatric and neonatal surgery[11] although one small study which randomized children undergoing umbilical hernia repair to wound infiltration or a rectus sheath block found no analgesic advantage.[12]
Like the rectus sheath nerve block, the transverse abdominal plane (TAP) block anaesthetizes segmental sensory nerves to the abdomen. Recent systematic reviews suggest that TAP or rectus sheath blocks reduce opiate consumption and pain scores after abdominal surgery.[13] [14] The Cochrane systematic review by Charlton *et al* [13] included 8 randomized controlled trials, 5 TAP block (ultrasound guidance in three [15-17]) and 3 rectus sheath block, 2 in laparoscopic surgery, one in acute surgery (open appendicectomy),[17] and one in paediatric surgery (umbilical hernia repair).[12] There is thus a paucity of evidence for the efficacy of ultrasound guided in paediatric laparoscopic acute surgery.
At Starship Children's Hospital local anaesthetic infiltration by the operating surgeon prior to laparoscopic port placement is standard practice. First a 10mm diameter port is placed at the umbilicus by a cut-down technique, followed by two 5mm ports (left iliac fossa and suprapubic). Prior to placing the 5mm ports local anaesthetic is infiltrated at the site under laparoscopic visualization, thus accurate placement into abdominal wall musculature is likely. For the larger 10mm umbilical port local anaesthetic is infiltrated blindly prior to the skin incision.
We hypothesise that many children do not achieve good analgesia at this port site based on the fact that no visual guidance technique is employed, and that an ultrasound guided rectus sheath block would improve analgesia.

Study Population

Inclusion Criteria

All children presenting to Starship Children's Hospital, aged between 8 and 14 years, diagnosed with acute appendicitis requiring urgent laparoscopic appendectomy.

Exclusion Criteria

- Diagnosis of developmental delay, neuro-muscular impairment, attention-deficit disorder, chronic pain, or psychiatric illness.
- Unable to speak and read English
- Partially sighted or blind
- Previous open abdominal surgery
- Presence of any abdominal prostheses such as a gastrostomy or ventriculo-peritoneal shunt
- Immuno-suppression
- Allergy to morphine
- Consent not obtained from both the participating child and one parent or legal guardian

Consent

1. Written consent obtained from the participating child **and** an accompanying parent/ guardian.
2. Details of the study will be explained by the Principal Investigator or by operating surgical registrars or consultants. Participant Information Sheets are available for prospective participants and accompanying parent/ guardian. Adequate time will be given for answering questions and discussion with other family/whānau members.
3. Consent will be obtained as soon as possible (within 2 hours) in keeping with the acute nature of appendicitis and the need for early operative treatment.
4. If a parent/guardian is not present during the consent process, consent can be discussed and obtained by telephone. Written consent should be obtained as soon as possible thereafter.
5. Study Consent Forms will be kept in the Participant's clinical notes at all times.
6. When consent is not obtained from an eligible child and/or respective parent/caregiver for any reason, the circumstances will be documented by the Principal Investigator. This helps to ensure enrolled patients are representative of the entire study population and allows identification of problems arising during the recruitment process.

Pre-operative Management

Diagnostic workup of each participant will be at the discretion of surgical admitting team members. Normal resuscitation practices will be followed as clinically indicated. Pre-operative administration of antibiotics will be standardised according to **Starship Children's Health Clinical Guidelines for Treatment of Suspected Appendicitis**. This algorithm outlines the appropriate use of antibiotics before, during and after surgical treatment for simple and complicated appendicitis. It is available online: http://www.adhb.govt.nz/StarShipClinicalGuidelines/Appendicitis%20Suspected.htm

Intra-operative Intervention

After induction of anaesthesia an ultrasound-guided rectus sheath 'nerve-block' will be performed by the surgeon or anaesthetist.

Ultrasound equipment

The portable ultrasound machines available in Starship Operating Theatres are Sonosite®. The block operator will chose a suitable transducer, usually a linear array high frequency probe for thin children, or a lower frequency curved probe for larger individuals.

Ultrasound setup

One of the operating theatre portable ultrasound machines will be brought into theatre during set-up for the laparoscopic appendicectomy. The ultrasound machine will be situated on the patient's right side, the same side as, but cranial (towards the head) to the laparoscopic stack.

A pre-scan should be performed first using the "patient, preset, probe" approach. *Patient* details (name, NHI) are entered onto the patient page of the ultrasound machine. 'Vascular' or 'nerve' *presets* are often best for visualising needle insertion; depth and gain (near-gain & far-gain) are optimised. An appropriate *probe* is chosen (as above).

After preping and draping the abdomen, at the time the laparoscopic leads are being set up, the ultrasound probe will be draped with a sterile plastic cover in the standard manner using sterile transduction jelly.

Local anaesthetic and placebo preparation

After determining group allocation the unblinded circulating theatre nurse together with the scrub nurse will draw up in a **20ml syringe** either (according to allocation) 0.25% bupivacaine with 1:400,000 adrenaline (**Marcaine 0.25% with Adrenaline 1:400,000 Injection**) ***or*** 20ml of **0.9% sodium chloride** into a 20ml syringe. The syringe will be attached to a Sonoplex® needle and labelled "nerve block" and handed to the operator without divulging allocation.

Local anaesthetic dose

The volume of solution available for the nerve block will be calculated according to the patient's body weight up to a maximum of 20ml, to maintain a maximum dose of bupivacaine at or below 2.5mg/kg.

Volume (ml) = Weight (kg) – 6 (ml)

If >26kg, only 20ml is drawn up.
If <26kg, it is crucial to use the above formula to avoid overdose.

WEIGHT (kg)	**STUDY SOLUTION (20ml syringe)**	**LA (10ml syringe)**
20 kg	14ml	6ml
21 kg	15ml	6ml
22 kg	16ml	6ml
23 kg	17ml	6ml
24 kg	18ml	6ml
25 kg	19ml	6ml
26 kg	20ml	6ml
>26kg	20ml	6ml

In addition to the nerve block, 6ml 0.25% bupivacaine with 1:400,000 adrenaline will be available for the surgeon for local infiltration, 2ml for each port site, subcutaneous at the umbilical port and infiltrated into abdominal muscles under laparoscopic guidance for the 5mm ports.

Example: 24kg child: 18ml study solution for the nerve block, **+** 6ml bupivacaine for local infiltration.

Nerve block technique

Using sliding movements of the ultrasound transducer the lateral edge of the rectus muscle is identified, noting a point at the level of or slightly cranial to the umbilicus. The syringe containing the study solution is attached to a 45^0 bevelled needle or a standard 22 or 23 gauge needle. Guided by a transverse ultrasound image the needle is inserted in-plane to the ultrasound beam and its tip advanced stepwise (using the sequence, advance-visualise) to the junction of the posterior rectus sheath with the rectus muscle. Aim for a point 1-2cm medial to the lateral edge of the rectus sheath. On injecting a small amount of solution, a hypo-echogenic lentiform swelling will help confirm correct needle tip position. Half of the solution is injected at this point. The process is repeated on the contralateral side.

Standardised Anaesthesia

Intraoperative analgesia is standardised to:
Morphine up to 0.3ml/kg;
Fentanyl 2mcg/kg titrated as required;
Paracetamol 15mg/kg, if paracelamol has not been given pre-operatively;
Standardised prophylactic antiemetic is ondansetron 0.15mg/kg.
The anaesthetist is asked to avoid dexamethasone and other forms of intraoperative analgesia including non-steroidal anti-inflammatory drugs or alternative opioids.

Standardised Surgery

Laparoscopic access is by three ports: 5-10mm umbilical, 5mm left iliac fossa and 5mm suprapublic. Local anaesthetic (2ml 0.25% bupivacaine with 1:400,000 adrenaline) is infiltrated at each site prior to incision. At the umbilical site, local is infiltrated subcutaneously only. At the 5mm port sites local is instilled both subcutaneously and intramuscularly under laparoscopic guidance.
Wound closure is by absorbable sutures. Technical aspects of the appendicectomy are at the surgeon's discretion.

Intra-operative findings to be noted

1. Macroscopic state of the appendix:
    a. Uncomplicated
        i. Acute appendicitis
        ii. Normal appendix
    b. Complicated
        i. Perforated appendicitis (defined as a laparoscopically visible macroscopic perforation)
        ii. Free pus in the abdomen:
            1. Right iliac fossa;
            2. Pelvis;
            3. Generalised.
    c. Other cause for pain (eg Meckel's diverticulitis; torted ovarian cyst).

Post-Operative Pain Scores

Localised Pain Scores

Unless the patient is asleep, pain scores will be recorded using the Faces Pain Scale Revised (FPS-R) and the Pain Site Score diagram and recording chart at the following post-operative times: Post-Anaesthetic Care Unit (PACU), 4, 8, 12, 16, 20, 24 and (if still in hospital) 48 hours post-operatively.

General Pain Scores

Unless the patient is asleep, overall pain scores will be recorded using the visual analogue scale (VAS) at the following post-operative times: Post-Anaesthetic Care Unit (PACU), on arrival onto the ward, 2 hours, 4 hours, 6 hours, 8 hours, 10 hours, 12 hours, 16 hours, 20 hours and 24 hours.

Post-operative Pain Management

** Regular Analgesia for the first 24 hours**

1. ***Paracetamol***

Regular oral paracetamol 20mg/kg 6 hourly (maximum single dose 1000mg), up to a maximum of the lesser of 90mg/kg, or 4000mg in 24 hours.
Substitute with intravenous paracetamol 15mg/kg 6 hourly (maximum single dose 1000mg) up to the lesser of 60mg/kg, or 4000mg in 24 hours, if not able to tolerate oral intake.

2. ***NSAIDS*** – (if no contraindications)

One of the following:

Ibuprofen	Oral: 10mg/kg, Q8hours
Diclofenac	Oral: 1mg/kg, (50mg if over 50kg), Q8-12hours If vomiting – Suppository: 0.5-2mg/kg daily, max daily dose 150mg

3. ***Opiates***

a/ Tramadol
Oral: 2-3mg/kg stat, then 1-2mg/kg, Q4-6hours as required: Maximum dose 800mg/24h

b/ Morphine or Fentanyl
All Opiate analgesia required in the first 12 hours is given intravenously.

The Starship Children's Health Clinical Guideline for Morphine Administration, online at:
http://adhbintranet/ADHB_Policies_and_Procedures/Clinical/Starship_Children's/PainMgmtMorphineIntermittentIV.pdf

Patients who require more than 5 titrations of morphine within a 25 minute period will be provided with a patient controlled analgesia pump devices (PCA). Morphine or fentanyl are used for PCAs at the discretion of the Acute Pain Service.

The **Starship Children's Health Clinical Guideline for Morphine Administration** is included in Appendix 2 and also available online at:
http://www.starship.org.nz/Clinical%20Guideline%20PDFs/Morphine%20Administration.pdf

Post-operative Care

- Routine recordings of vital observations on the ward
- Anti-emetic medications as required
- Eating and drinking as soon as able to tolerate
- Early mobilisation
- Daily wound review

Discharged Criteria

- Afebrile
- Tolerating adequate oral intake
- Mobilising independently
- Free of nausea and vomiting
- Oral analgesia for pain relief

Follow-up

10-day postal (or phone) Recovery questionnaires

The Day 10 Post-operative Recovery Questionnaire is distributed to participants upon discharge from hospital. This is a 10 question report adapted from the PedsQL™ Pediatric Quality of Life Inventory, along with a general question on perceived quality of care. Participants are asked to complete this Questionnaire the morning of Day 10 after their surgery and return it to the Principle Investigator using a pre-paid postage envelope.

6-week follow-up phone call

At 6 weeks post-discharge participants will be phoned to determine any complications, representations to an emergency department or re-admission to any hospital.

Randomization

The generation of random numbers will be facilitated by an independent research assistant. The allocation sequence will be generated using an open source computer-based on-line random number generator, http://www.random.org. All numbers from 1 to 156 (to give 20% redundancy) will be generated in random sequence arranged in 2 columns. Study allocation will be based on these numbers.

Randomization implementation

Once recruited and consented, the allocation of each participant to the intervention or control group will be performed by an unblinded circulating theatre nurse just prior to the start of the procedure.

This nurse will receive written instructions not to disclose the participant's group allocation to anybody and will have no involvement in the post-operative care of the patient or in data collection, analysis or reporting.

Blinding

Patients, families, investigators, surgeons, anaesthetists, theatre personnel (except the unblinded circulating nurse and scrub nurse), ward nursing staff and pain team responsible for the intra- and post-operative care of participants will all remain blinded to group allocation.
The unblinded circulating nurse will open the allocation envelope and prepare the study solution. The unblinded scrub nurse will draw up the study solution. Prior to participants entering these two unblinded nurses will, away from the view of other theatre personnel, draw up either (according to allocation) 20ml of 0.25% bupivacaine with 1:400,000 or 20ml or 0.9% sodium chloride into a 20ml syringe. The syringe will be labelled "nerve block" and subsequently handed to the operator without divulging allocation.
Data collection will be carried out by blinded investigators. Blind statistical analysis will be facilitated by a research assistant with no involvement in the study who will prepare data spreadsheets with concealed study group allocations. Allocations will subsequently be revealed at the completion of data analysis.

Data Collection and Storage

The Principle Investigator is responsible for ensuring all sections of the Investigator's Checklist are completed and that the Day 10 Questionnaire is completed and returned.

Study data will be stored securely at Auckland District Health Board for the duration of study and for 10 years from the time each participant turns 16 years of age.

Summary of Study Outcome Measures (as per Investigator's Checklist)

1. Pain:
   Intraoperative opiate dose (Morphine Equivalent Daily Dosage, MEDD)
   Post-operative opiate analgesia consumption (MEDD)
   Post-operative umbilical pain site score (Lolipops score, umbilicus)
   Post-operative overall pain scores (VAS)

2. Post-operative Recovery:
   Day 10 Post-operative Recovery Questionnaire

3. Peri-operative Complications

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