LOCAL ANESTHETIC WOUND INFUSION VERSUS STANDARD ANALGESIA IN PAEDIATRIC POST-OPERATIVE PAIN CONTROL

A RANDOMISED CONTROL TRIAL

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DECLARATION

I, **Dr. Machoki, Mugambi Stanley** hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Date: **28th October 2014 (Revised January 2015)**

DEDICATION

To Mercy,

Amani & Zawadi

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ABSTRACT

Introduction:

Post-operative analgesia currently relies on multimodal therapy including epidural analgesia, intravenous morphine and/or paracetamol (Perfalgan®) infusion. Local wound infusion has been effectively utilized in adults with promising results but has not been prospectively tested in children undergoing different abdominal operations. The aim of this study was to compare continuous local anesthetic wound infusion to the current standard of care in post-operative pain control in children.

Methods: We conducted a prospective randomized, pain assessor blinded trial comparing Bupivacaine wound infusion (Continuous Local Anaesthetic Wound Infusion – CLAWI) in addition to intravenous paracetamol (Perfalgan®) and morphine for rescue analgesia. This was compared to: (a) epidural bupivacaine plus intravenous morphine and Perfalgan® [EPI] for children undergoing open abdominal surgery and (b) intravenous morphine and Perfalgan® infusion alone [standard post-operative analgesia - SAPA] in children undergoing Lanz incision laparotomy for complicated appendicitis.

Patients aged between 3 months and 12 years undergoing laparotomy or open appendectomy were randomly selected for local anesthetic wound infusion (CLAWI) versus EPI or CLAWI versus (SAPA) respectively. Exclusion criteria were neurological impairment, post-operative ventilation and history of adverse reaction to bupivacaine. Consent from the guardian, assent from patients above the age of 7 years and ethics approval from the University of Cape Town Human Ethics Research Committee was obtained. The wound infusion catheter ('InfiltralLong', PANJUNK®) was placed sub-fascially after suture of the peritoneum and 0.2 % bupivacaine 2mls/kg infused on anesthetic reversal followed by 0.2ml/kg/hour thereafter for 48 hours. Pain assessments were performed for each patient at regular intervals by a single assessor who had training in pediatric pain management and who was blinded to the group allocation. The duration of surgery, length of incision, perioperative antibiotics, wound class risk of surgical site infection, time to return to full feeds, drug reactions; hospital stay, surgical site infection and wound catheter and epidural catheter complications were recorded for each patient. Primary outcome measure was total morphine used in the appendectomy-SAPA vs appendectomy-CLAWI group and rescue morphine requirements in the laparotomy-EPI vs laparotomy-CLAWI group. The secondary outcomes were pain control as measured using the FLACC scale, time to full feeds, mobilization and requirement for urinary catheter.

Results: Sixty patients (18 Laparotomy-CLAWI (LAP-CLAWI), 17 Laparotomy-EPI (LAP-EPI) and 12 Appendectomy-CLAWI (APP-CLAWI), 13 Appendectomy-SAPA (APP-SAPA)) were analyzed.

Within these two main study groups, the subgroup demographic, clinical variables and secondary outcome variables were analyzed for frequencies/percentage, means and standard deviation as appropriate. The Student's t-test was used for continuous variables and Chi-square for categorical variables to assess for differences between subgroups. Total morphine requirement for the APP-SAPA vs APP-CLAWI groups were calculated for each patient and expressed as a mean and standard deviation for each subgroup. Total rescue morphine requirements were used in the LAP-EPI vs LAP-CLAWI groups. The Student's t-test was used to compare morphine requirements between subgroups. Pain scores were recorded at multiple regular intervals for each study participant. Each participant had a total of eight pain scores done by the blinded pain assessor. A time series of pain scores for each subgroup was created and used to compare pain control trends between groups. A mean and standard deviation of the pain scores was also calculated and the means compared between subgroups using the t-test. The average FLACC (Face, Legs, Activity, Cry & Consolability) pain score in the CLAWI groups was 2.5 [=minimal pain] (1-4) and 3.0 (1-5) in the EPI group and 3.5 (2-5) in the SAPA group. Mean morphine requirements were significantly higher in the control groups: Appendectomy-standard analgesia group had a mean of 490ug compared to 96 ug in the infusion group, p-value 0.016. Laparotomy-epidural group had a mean morphine requirement of 406ug compared to a mean of 230ug in the infusion group, p-value 0.052. The SAPA and EPI group had a longer duration to removal of urinary catheter and mobilization (average 4 days vs. 2 days in the CLAWI group). Time to full feeds was comparable in all groups. There were no wound infections and no bupivacaine related complications in the CLAWI group.

Conclusion: Continuous subfascial bupivacaine infusion is a reliable, safe and effective technique for post-operative pain control in children undergoing open abdominal surgery. It is comparable to current standard of care and has the benefit of a considerably reduced requirement for opioid analgesia in children undergoing various abdominal operations.

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LIST OF ABBREVIATIONS AND ACRONYMS

CLAWI: CONTINUOUS LOCAL ANESTHETIC WOUND INFUSION

EPI: EPIDURAL ANALGESIA

SAPA: STANDARD POST-OPERATIVE ANALGESIA

LAP: LAPAROTOMY

APP: APPENDECTOMY

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INTRODUCTION

Postoperative pain is a cause of morbidity and contributes indirectly to prolonged hospital stay and cost of care. For these reasons and to ensure quality patient care, the control of pain in the postoperative period is paramount for optimal outcomes in pediatric surgery.

The current methods of postoperative pain management are prone to complications and vary in their effectiveness. Furthermore the application of standardized tools of assessment of pain in the pediatric population is not widely utilized.

Local anesthetic as a continuous infusion in the subfascial space of the surgical wound for postoperative pain control has been used in adult patients with promising results. However, its application in pediatric patients (age more than 3 months to 12 years) has not been adopted in most centers. Controlled trials comparing standard postoperative analgesia to continuous subfascial bupivacaine infusion for children undergoing different abdominal operations are few.

There is also limited information on the physiological benefits of subfascial local anaesthetic wound infusion in pediatrics in terms of return to bowel function, need for urethral catheterization, hospital stay as well as rates of surgical site infection and short term wound complications.

We conducted a pain assessor blinded randomized control trial comparing subfascial bupivacaine wound infusion to the standard of care in post-operative analgesia to determine the morphine requirements among patients undergoing varied abdominal operations. The other endpoints were to determine the rates of surgical site infections, local wound infusion related complications, length of hospital stay, the time to resumption of full feeds, need for and duration of urethral catheterization and mortality.

CHAPTER 1: LITERATURE REVIEW

1.1 PAIN

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage". It is a combination of unpleasant sensory, emotional and mental experiences which are associated with autonomic, psychological, and behavioral responses[1].

Pain has plagued mankind since we can remember and has been described by some as "a problem of epidemic proportions"[2]. In the Montreal declaration of 2011, pain control was adopted as a human right(3-4).

1.2 POSTOPERATIVE PAIN

Although there is a degree of overlap, pain can be classified as inflammatory/acute or neuropathic/chronic. This classification is founded on the understanding of the pathways involved in the onset and evolution of pain in surgical practice. It informs to a large extent, the design and application of targeted therapies and monitoring tools(5-6). One of the factors associated with the transition from acute to chronic pain is inadequate postoperative analgesia[5].

Postoperative pain falls in the acute category. Surgery causes tissue damage including injury to the peripheral nerves. This leads to local and regional inflammatory reaction accompanied by a local, regional and systemic neural response. The local effects of these reactions include wound site tissue hypo-perfusion. The systemic effects include reduced general movement and respiratory effort as a result of skeletal and diaphragmatic splinting. Uncontrolled pain also has deleterious effects on gastrointestinal and bladder functions due to release of catecholamines and stress hormones. Therefore a patient with poor pain control is at risk of respiratory dysfunction and surgical site infections, poor venous return and ileus among other complications[6–9].

POSTOPERATIVE PAIN IN INFANTS AND CHILDREN

The impact of pain during and following surgical procedures in infants is now well recognised.This was not the case in the 19th and 20th centuries mainly due to the misconception that neonates did not experience pain due to what was thought to be underdeveloped nerual circuitry[10]. The fact that the manifestation of pain in neonates, infants and children is different from adults contributed to this notion and lead to a practice where children, especially neonates and infants, underwent painfull procedures with minimal or no analgesia[11].

Neonates, infants and children may in fact suffer more adverse consequences of inadequate pain control when compared to adults due to a robust generalised inflamatory response and lack of central neural inhibition reflex[12, 13]. The longterm effects of a previous painful experience may be evident on followup and include a lowered threshold to noxious stimuli[14].

Although the pain control and monitoring for pain in children has improved from the 19th and 20th century, different surveys show that Infants and children are still at a higher risk of suffering from pain and its consequences[9, 15]. They are more likely to suffer pain more frequently and more likely to have suboptimal postoperative analgesia. Some of the contributing factors include the fear of side effects, especially from opiates, a misconception that pediatric pain control is complex and time consuming, non-application of pain assessment tools and lack of dedicated pediatric pain services[16, 17][16–20].

Pain management services are critical in the delivery of surgical care for children. Furthermore regular audits on pain management in every unit and research in post-operative analgesia in paediatrics are important for the development and adoption of more effective modalities[21].

Research on the efficacy and safety of new post-operative analgesia modalities in children has lagged behind when compared to the adult population. Studies in paediatric postoperative pain control have not shown a significant difference in hospital stay and return to function. Studies aimed at showing physiological gains (bowel and bladder function and physical activities) are also lacking[22].

1.3 PAEDIATRIC POSTOPERATIVE ANALGESIA

The mainstay of current post-operative analgesia regimens is multi-modal therapy. This includes pre-emptive analgesia through local and regional nerve blockade peri-operatively and a combination of opioid and non-steroidal agents or paracetamol in the post-operative period [23]. The aim of multi-modal pain therapy is to achieve near total pain control from the synergistic and additive effects of the drugs while reducing their individual side effects and potential complications[24, 25].

1.4 CONTINOUS LOCAL ANESTHETIC WOUND INFUSION (CLAWI)

One of the modes of post-operative analgesia is the use of a multi-holed catheter placed in the wound to deliver a local anesthetic continuously. It allows continuous interruption of efferent nociception at the site of surgical trauma eliminating noxious stimulus sensation in the pain nerve circuitry[26].

The concept of local wound infusion is not new. Continuous local anesthetic wound infusion (CLAWI) has been used in obstetrics, gynecology, urology, thoracic surgery and colorectal surgery in adults with good efficacy and without increase in complications[27–29]. Although the safety and efficacy of CLAWI has been shown to a large extent, simple extrapolation of potential benefits of local wound infusion from the results involving adult populations cannot be made as the pharmacodynamics of the utilized agents is different in pediatrics[13, 30].

The results of studies on the efficacy of continuous local anesthetic wound infusion in children have been published recently. They include patients undergoing urologic[31], thoracic[32] and abdominal procedures[33] and show a similar trend towards better or equivalent pain control with reduction in morphine requirements. The site of multi-holed wound catheter placement is dependent on the type of operation and preference. Placement of the catheter on the pre-peritoneal area or within the muscle fascia is associated with better pain control compared to the subcutaneous layer[22, 34].

At the time of this study CLAWI was not an option for post-operative analgesia at our center and within the African continent as a whole partly due to unavailability of multi-holed catheters , the relative lack of robust evidence for its use in children undergoing different abdominal operations and the fear of increased risk of infections.

1.5 PAIN ASSESSMENT IN POST-OPERATIVE PEDIATRIC PATIENTS

There are several validated tools for pain assessment for non-verbal or neurologically impaired patients. There is a wide variety of pain assessment scales available to clinician. This allows one to choose the most appropriate means depending on the patient age, neurological status, and underlying disease. The ease of application and social/cultural factors that may influence the expression of pain are also important consideration in pain scale choice[35–37].

Pain assessment scales are useful in the monitoring and documenting pain scores in the postoperative period as well in research requiring pain measurement. Ideally all postoperative patients should have regular pain assessment as part of the vital sign measurements[38]. The best tool for assessment is the one that can be applied easily, has low inter-observer variability and is both sensitive and specific. In this study we used the Faces, Legs, Activity, Cry and Consolability (FLACC) scale[37], shown in

Figure **1** *& Appendix II.* It is applicable in both the communicating and non-communicating pediatric patients, is already use in our center, easy to apply and requires a short duration of observation to make an assessment. To reduce the degree of inter-observer variability, this study had one pain specialist doing all the pain scores.

FLACC Behavioral Pain Assessment Scale

CATEGORIES	SCORING		
	0	1	2
Face	No particular expression or smile	Occasional grimace or frown; withdrawn, disinterested	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid, or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs; frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or being talked to; distractable	Difficult to console or comfort

Figure 1: FLACC pain scale.

CHAPTER 2: THE STUDY

2.1 STUDY JUSTIFICATION

HYPOTHESES

Given the results from the adult patient studies on continuous local anesthetic wound infusion, we inferred that there would be difference in post-operative pain control between pediatric patients undergoing subfascial wound bupivacaine infusion and those who receive continuous epidural bupivacaine infusion or continuous intravenous morphine infusion with or without adjunctive oral or rectal paracetamol.

The use of an effective continuous local anesthetic wound infusion alone or in combination with other modalities is an attractive option for the following reasons:

- It will obviate the need for the more invasive, technically demanding and time consuming epidural analgesia[39, 40].
    - At our institution the placement of epidural catheters is done by an anesthesiologist who also follow-up its use and function. CLAWI will reduce the workload on anesthesiologists.
    - Patients on epidural analgesia are nursed at least in a high care ward for continuous monitoring. This is because epidural catheters are prone to malfunction (leak, blockage or kink) or get dislodged besides other complications. CLAWI will reduce demand on high care beds
    - Some patients are unable to have an epidural catheter due to coagulopathy, associated spinal abnormality or other disease processes that increase the risk of epidural catheter placement[41]. CLAWI is applicable to a broader spectrum of patients
- It will allow lower doses of opioid analgesia with a resultant decrease in the commonly associated side effects such as hypotension[36], nausea and vomiting, ileus, drowsiness and risk of apnea[42, 43].
- CLAWI requires less expertise for placement and does not require intensive post-operative monitoring[44].
- CLAWI is a more cost effective analgesia than epidural as the catheters are relatively cheaper
- CLAWI is more suitable to the African continent as less skills in both anaesthetic and nursing field are required

2.2 OBJECTIVES OF THE STUDY

PRIMARY OBJECTIVE:

- To determine the efficacy of post –operative analgesia through local wound infusion compared to current standard of care among patients undergoing various abdominal operations:
    - As a surrogate marker for efficacy, the total morphine dose required as rescue analgesia *was also recorded for each patient.*

SECONDARY OBJECTIVES:

- Efficacy was also determined by pain scores measured by a single pain specialist who was blinded to the patient treatment arm.
- To determine any associated complications with local wound infusion compared to standard post-operative pain management regimens. We recorded the following as complications:
    - Surgical site infections
    - *Infusion catheter and epidural catheter blockage, leak, dislodgment*
    - Bupivacaine adverse drug reactions
    - Morphine adverse drug reactions
- To determine the postoperative course between groups in terms of physiologic parameters:
    - Time taken to tolerate feeds
    - Time to mobilization
    - *The need for and duration of urethral catheterization*
    - Length of hospital stay

2.3 MATERIALS AND METHODS

SETTING

The study was carried out in a tertiary level children's hospital with a wide referral basin. The care of post-operative patients initially takes place in a high-care section of the surgical ward or in the shared intensive care unit. A pain management service is available and comprises anesthesiologists, nurses trained in pain assessment as well as a specialist in pediatric pain assessment and management. The nursing staffs in these areas are also trained on the use of the Faces, Legs, Activity, Cry and Consolability (FLACC) scale.

STUDY DESIGN

A pilot study using the same inclusion and exclusion criteria to select sequential study participants to undergo continuous local wound infusion post operatively was conducted. This was to determine the feasibility and local acceptance of the study and included 15 patients (5 open appendectomy patients and 10 laparotomy patients) to undergo continuous local anesthetic wound infusion. In this series, all five appendectomy patients had complicated appendicitis, had average pain scores of 2.5, and no wound complications or bupivacaine related complications. The patients undergoing laparotomy for various conditions (liver biopsy-1, open pyelolithotomy-1, Wilm's tumor-2, diaphragmatic hernia-2, intestinal obstruction-1, hydatid cyst-1, Takayasu's disease-1, bladder reconstruction-1) had mean pain scores of 2.3, no bupivacaine related complications with 4 wound infusion catheter leaks particularly in the beginning. There were no wound infections in this cohort as well.

Following the pilot study, a pain assessor-blinded randomized control trial was carried out in two parts running concurrently. The first part was to compare CLAWI to intravenous morphine and paracetamol in patients undergoing Lanz incision appendectomy. The second part was to compare continuous local anesthetic wound infusion to Epidural analgesia in patients undergoing laparotomy.

Part I:

This was a pain assessor-blinded randomized control trial involving pediatric patients undergoing open appendectomy via a Lanz incision for complicated appendicitis. Patients fitting the inclusion and exclusion criteria were randomly assigned to one of two arms once consent and assent was obtained. The intervention arm comprised those who would receive continuous local anesthetic wound infusion plus intravenous paracetamol with tapered intravenous morphine for rescue analgesia (CLAWI). The control arm comprised those who would receive tapered intravenous morphine plus intravenous paracetamol, that is, current standard post-operative analgesia (SAPA).

Part I study population:

Eligible patients comprised children between the age of 3 months and 12 years with a diagnosis of complicated appendicitis undergoing a Lanz incision open appendectomy. The diagnosis of appendicitis was based on clinical findings. Complicated appendicitis was determined by the attending clinician based on examination findings of a mass and/or peritonitis with a few patients requiring imaging for pre-operative confirmation. The decision for open appendectomy was made by the attending clinician without prior knowledge on study group assignment.

Part I patient selection:

Inclusion criteria:

- Age of 12 years and below
- Surgical intervention via open appendectomy
- Informed consent from legal guardian
- Assent for patients 7 years old and above

Exclusion criteria:

- Laparoscopic appendectomy
- Prolonged post-operative sedation and ventilation
- Lack of assent for patients 7 years and older
- Lack of informed consent from legal guardian

Part II:

This was a pain assessor-blinded randomized controlled trial involving pediatric patients undergoing various abdominal operations via laparotomy incisions for varied diagnoses. Eligible patients were assessed for inclusion and exclusion prior to random allocation to one of two groups once consent and assent was obtained. The intervention arm group comprised those who received continuous local wound infusion plus intravenous paracetamol and tapered intravenous morphine for rescue analgesia (CLAWI). The control group comprised those who received continuous epidural analgesia plus intravenous paracetamol and tapered intravenous morphine for rescue analgesia (EPI).

Part II study population:

Eligible patients comprised children between the age of 3 months and 12 years undergoing planned open abdominal surgery for various conditions. The type and length of abdominal incision was determined by the surgeon.

Part II patient selection:

Inclusion criteria:

- Age of 12 years and below
- Surgical intervention via laparotomy
- Patients eligible for epidural analgesia
- Informed consent from legal guardian
- Assent for patients 7 years and older

Exclusion criteria:

- Laparoscopic abdominal surgery
- Prolonged post-operative sedation and ventilation
- Lack of informed consent from a legal guardian
- Lack of assent for patients 7 years and older

2.4 PROCEDURES

SAMPLE SIZE CALCULATION

We estimated a 25% to 50% difference in morphine requirements between the control (SAPA/EPI) and intervention(CLAWI) arms.[44]. Using the O'Brien-Fleming Continuity correction[45, 46] we required 45 participants in each group within the SAPA vs CLAWI arms and 25 participants in each group within the EPI vs CLAWI arm. This would be able to detect a difference of 20% in morphine requirement between the groups in each arm with 80% power and at a significance level (p-value) of 0.05.

Part of the protocol, an ethics board requirement, was to perform an interim analysis at 50% recruitment. This was powered to detect marked differences between the two arms and allow justification for conclusion or continuation of the study should either technique of analgesia prove significantly superior or inferior.

RANDOMIZATION

The patients were assessed for eligibility sequentially. This was done after clinical assessment and decision for surgery. Study participants fulfilling the inclusion criteria were subsequently randomly allocated to a study group. An online computer random number generator, (http://www.randomizer.org), was used to create the random number sequences for the two parts of the study.

BLINDING

The pain assessor was blinded to the post-operative treatment allocation. Study participant group allocation was revealed only to the principal investigator, the operating surgeon, anesthesiologist and the data and safety management board.

To ensure blinding during pain assessment, the patient wound dressings were identical in all groups and left in place for the duration of the study. Infusion pumps and the connections to the pumps regulating delivery of morphine, epidural and local anesthetics were identical as equipment is standardized in the hospital.

2.5 POST-OPERATIVE ANALGESIA REGIMENS

CONTINOUS LOCAL WOUND INFUSION

Delivery of the local anesthetic to the wound was via a fenestrated (multi-holed) FG 2.5 inert tubing ('InfiltraLong', PANJUNK® catheter) (*Figure 2*). The fenestrations are designed to ensure equal outflow of fluid. The catheter was placed in the subfascial space at the time of wound closure. The subfascial layer is the potential space created at the time of wound closure between the sutured transversalis fascia and/or the posterior leaf of the rectus fascia as the floor with the overlying closed muscles and fasciae as the roof.

Wound closure began with closure of the peritoneum and transversalis or rectus fascia to create the floor of the potential space. The tip of the catheter was positioned at the most lateral or cranial end of the wound. All the fenestrations lay along this floor. The non-fenestrated part of the catheter would then exit via a separate skin puncture site away from the wound, *Figure 3*. The catheter was then connected to a filter provided in the set. A 5ml 0.9% saline bolus was then instilled through the filter to check for leaks and confirm appropriate placement of the fenestrated end of the catheter within the wound. The rest of the abdominal layers were then closed, the catheter exit site secured with adhesive dressing and the wound covered with opaque dressing. Before reversal from general anesthesia, a 0.1-0.2ml/kg bolus of 0.2% bupivacaine was administered through the filter connected to the wound infusion catheter and subsequently connected to a 50 ml syringe with 0.2% bupivacaine in 0.9% saline to run continuously using an electrical syringe driver set to run at 0.1-0.2 mls/kg/hr.

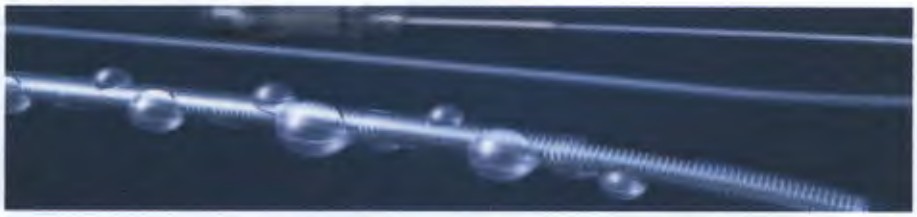

Figure 2: Multi-hole wound infusion catheter

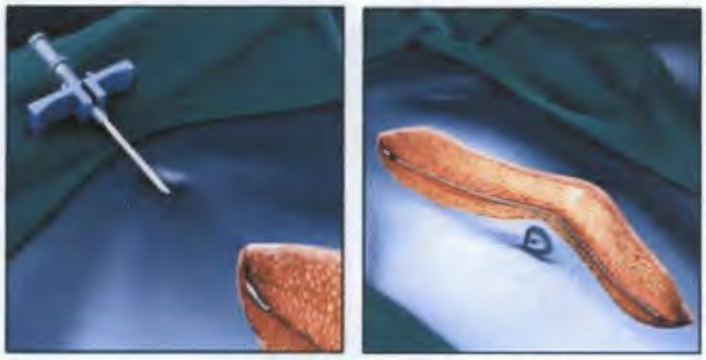

Figure 3: Wound infusion catheter placed within the fascia

EPIDURAL ANALGESIA

Epidural catheter placement was performed by the anesthesiologist whilst the patient was under general anesthesia and before the surgical incision. Once the catheter position was confirmed, a 0.1-0.2ml/kg bolus of 0.2% bupivacaine in 0.9% saline was administered. The catheter exit site was secured and trailed along the back of the patient with adhesive dressing. The epidural analgesia was run at 0.1-0.2ml/kg/hr during surgery.

Surgery proceeded as planned and at conclusion and wound closure, an opaque dressing was applied to the wound. The epidural site was checked for leak or dislodgement after anaesthetic reversal and the infusion continued at recovery and in the ward. The epidural infusion was to run for up to a maximum of 72 hours as per protocol as longer infusions are associated with a rise in septic complications.

2.6 POST-OPERATIVE ANALGESIA IN THE STUDY GROUPS

PART I

Control group- Standard Post-operative analgesia (SAPA):

The study participants received scaled intravenous morphine (0.5 mg per kilogram body weight mixed in 50 mls of 5% dextrose) at 1-2ml per hour (i.e. 5-10 ug/kg/hr) and intravenous paracetamol (20mg/kg stat at reversal, then 15mg/kg every 4hrs) then oral paracetamol at 15mg/kg every 4hours once oral intake was established.

Morphine infusion was started at 5ug/kg/hr. In case of pain as assessed by the attending staff, the rate was increased to 10ug/kg/hr as per standard of care. Scaling down of morphine was by decrements of 2.5ug/kg/hr after every pain assessment once both the attending staff and pain assessor were satisfied that the study participant was not in pain

Intervention group-Continuous local anesthetic wound infusion (CLAWI):

At wound closure the infusion catheter would be placed and managed as described above. 0.2% bupivacaine in 0.9% saline was infused continuously at a rate of 0.1-0.2ml/kg/hr using an infusion pump. The local wound infusion was to run for up to a maximum of 72 hours. The study participants also received scaled intravenous morphine (0.5 mg per kilogram body weight mixed in 50 mls of 5% dextrose) at 1-2ml per hour (i.e. 5-10 ug/kg/hr) and intravenous paracetamol (20mg/kg stat at reversal, then 15mg/kg every 4hrs) then oral paracetamol at 15mg/kg every 4hours once oral intake was established. Morphine infusion was started at 5ug/kg/hr. In case of pain as assessed by the attending staff, the rate was increased to 10ug/kg/hr as per standard of care. Scaling down of morphine was by decrements of 2.5ug/kg/hr after every pain assessment once both the attending staff and pain assessor were satisfied that the study participant was not in pain recurrence of pain.

PART II

Control group- Epidural analgesia (EPI):

The placement and peri-operative management of the epidural catheter has been described in the preceding paragraphs. 0.2% bupivacaine in 0.9% saline was infused at a rate of 0.1-0.2mls/kg/hr using an infusion pump. Epidural infusion was for up to a maximum of 72 hours.

The study participants assessed to be in pain at recovery also received scaled intravenous morphine (0.5 mg per kilogram body weight mixed in 50 mls of 5% dextrose) at 1-2ml per hour (i.e. 5-10ug/kg/hr) and intravenous paracetamol (20mg/kg stat at reversal, then 15mg/kg every 4hrs) then oral paracetamol at 15mg/kg every 4hours once oral intake was established.

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Scaling down of morphine was by decrements of 2.5ug/kg/hr after every pain assessment once both the attending staff and pain assessor were satisfied that the study participant was not in pain.

2.7 RESCUE ANALGESIA

For all study groups rescue analgesia was administered as intravenous morphine bolus at 5micrograms per kilogram body weight over 10 minutes. This would be administered by the in-house staff at any time as deemed necessary by the attending staff as per standard of care. The time and dose was recorded in the treatment chart. There was thus no analgesia restriction by study staff. All rescue analgesia was documented in the notes of the patient and transferred to the data sheet.

2.8 PAIN ASSESSMENT PROTOCOL

All patients in the study were assessed for pain by the same pediatric pain specialist, who was blinded to the treatment arms, using the same pain scale and at equal intervals of up to 6 hourly. The nursing staff are trained to do pain assessments using the FLACC scale, also assessed the patients for pain as per standard of care and the attending doctor was free to administer rescue morphine analgesia as required.

2.9 ASSESSMENT AND RECORDING OF OTHER OUTCOME MEASURES

Assessment for passage of stool/flatus per rectum or stoma was by the attending clinician as per standard of care for all patients.

Time to resumption of full feeds, episodes of vomiting, wound complications, sepsis, chest infection, time to mobilization out of bed, time to removal of urethral catheter, epidural catheter complications, peripheral line complications and time to discharge (duration of hospital stay) was recorded in the clinical notes by the attending surgeon.

2.10 PATIENT MONITORING:

All study participants were initially cared for in a high care setting with continuous pulse oximetery, regular blood pressure and temperature checks. The time spent in high care was determined by the attending clinician. The wound catheters and epidural catheters were checked daily for any signs of leak, kink, blockage or dislodgment by the anesthesia team and the investigator. Refilling of the bupivacaine syringe was by the investigator for wound infusion and by the anesthesia team for the epidural catheter as per the institutions epidural protocol.

CHAPTER 3: ETHICS OF THE STUDY:

The study was assessed and approved both by the Red Cross War Memorial Children's Hospital research ethics committee and the University of Cape Town Human Research and Ethics Committee (Appendix III).

All study participants were assessed for eligibility with strict inclusion and exclusion criteria. Informed consent was obtained for each participant. Assent was also obtained for participants older than 6 years. (Appendix IV)

An initial pilot study was conducted to assess for safety, feasibility and local acceptance.

Only the study number was used to identify each study participant on the database to avoid breach of confidentiality. Both the attending clinician and the study participant were free to withdraw consent for the study at any time during the study

CHAPTER 4: DATA MANAGEMENT

4.1 OUTCOMES OF INTEREST

- Primary outcome:
  - Total intravenous morphine dose in the control arms compared to the intervention arms.
- Secondary outcomes:
  - Post-operative pain scores in the control arms compared to the intervention arms
  - Time to full mobilization in days
  - *Time to resumption of full feeds in days*
  - Wound complications:
    - Superficial surgical site infection
    - Deep surgical site infection
    - Organ space infection
  - Epidural and subfascial Catheter complications:
    - Blockage
    - Dislodgement or migration
    - Leakage
    - Infection
  - Other complications:
    - Morphine drug adverse drug reactions:
      - Cardiovascular: hypotension, syncope, bradycardia, tachycardia
      - Central nervous system: CNS depression, seizure
      - Dermatologic: Pruritus
      - Gastrointestinal: Nausea, vomiting, constipation,
      - Genitourinary: Urinary retention requiring catheterization or re-catheterization
      - Respiratory: Respiratory depression
      - Other: Anaphylaxis
    - Bupivacaine drug adverse drug reactions:
      - Cardiovascular: Cardiac arrest, hypotension, bradycardia
      - Central nervous system: Headache, restlessness, anxiety, seizures
      - Dermatologic: Pruritus, angioneurotic edema
      - Gastrointestinal: Nausea, vomiting
      - Chest infections
      - Hypotension
      - Venous thrombosis or thromboembolism
      - 30 day mortality
      - Time from skin incision to wound dressing
      - Long term complications:
      - Delayed wound infections
      - Chronic pain
      - Incisional hernia

4.2 DATA COLLECTION

Data regarding all the outcomes of interest for all the study participants was collected through a data collection sheet using Microsoft, 2010 Excel® spread sheet which was predesigned for direct transfer onto a pre-coded database on Statistical Package for the Social Sciences (SPSS®) – IBM 2012, Version 21 for analysis.

After recruitment each study participant was assigned a study number and allocated to a study arm as per the randomization procedure. The study number, group allocation, date of birth, date of surgery, date of discharge, gender, body weight and diagnosis was recorded.

At the time of the surgery the data collection sheet was filled to indicate the type of incision, the length of incision (in centimeters) and wound class (0 to 3). All the surgical incisions were categorized based on the wound classification system by the Centers for Disease Control and Prevention (CDC) for risk of surgical site infection. (See appendix I It classifies surgical wounds as clean, clean contaminated, contaminated or dirty. The risk of surgical site infection increases with the degree of contamination[45]. The time of incision and wound closure were also recorded.

Pain assessment scores were charted by the pain specialist using the Faces, Legs, Activity, Cry and Consolability (FLACC) scale. The scale is from 0 to 10, where 0 is no pain at all, 1-3 is mild discomfort, 4-6 is moderate pain and 7-10 is severe pain (
Figure **1** *& Appendix II*). Each assessment session comprised two observations for 5 minutes each. The final score was then tabulated and the time recorded. The time of assessment and the pain score were then transferred onto the data collection sheet.

The start and end date & time for morphine infusions were recorded on the treatment chart for each participant. This also included any morphine doses administered as rescue analgesia. The total dose of morphine, in micrograms per kilogram, required for each participant was then calculated by adding the total dose infused to the rescue morphine analgesia and entered onto the database.

The date of surgery and dates when the participant tolerated enteral feeds, when the urine catheter was removed, when the participant was fully mobile and when the study participant was discharged from hospital were all entered onto separate columns on the data collection sheet. These dates were subsequently used to calculate the time intervals for the different secondary outcome measures.

Complications from epidural and wound catheters were assessed for daily by the anesthesia team and the investigator. These complications were coded for blockage, dislodgement or migration, leakage and infection and entered onto the data collection sheet.

Wound infections were determined by the attending clinician. Wound infections were categorized according to Centers for Disease Control and Prevention (CDC) as superficial, deep or organ space[46]. Data on wound infections was coded for from 0 to 3 (0= no infection, 1=superficial, 2=deep and 3=organ space) and entered onto the data collection sheet for each study participant.

Complications from morphine, paracetamol and bupivacaine were determined by the attending clinician and also looked for by the investigator in each study participant. This data was coded for and entered.

Data collection was by the principle investigator. All the data sheets were stored in a locked cabinet within the institution study center with access limited to the investigators. Transfer of data from the data collection sheet onto the computer Microsoft Excel® 2010 was done by three trained research assistant volunteers. Double entry for each variable was performed. That is for each study participant data set two volunteers would enter the data separately and the data sets compared for consistency. Consistency checks were performed by one of the research assistants and checked a second time by the primary investigator. This computer database was stored in a single computer and the folder encrypted with a password. A password protected removable software memory stick was used as back-up.

CHAPTER 5: ANALYSIS

Data was analyzed using IBM®SPSS® statistics Ver. 21 (2012).

The two parts of the study (Appendectomy group and laparotomy group) were assessed separately. Within these two main study groups, the subgroup demographic, clinical variables and secondary outcome variables were analyzed for frequencies/percentage, means and standard deviation as appropriate. The Student's t-test was used for continuous variables and Chi-square for categorical variables to assess for differences between subgroups. Total morphine requirement as the primary outcome calculated for each patient and expressed as a mean and standard deviation for each subgroup. The Students t-test was used to compare morphine requirements between subgroups.

Pain scores were recorded at multiple regular intervals for each study participant. A time series of pain scores for each subgroup was created and used to compare pain control trends between groups. A mean and standard deviation of the pain scores was also calculated and the means compared between subgroups using the t-test.

CHAPTER 6: RESULTS

71 study participants were recruited in the study after initial assessment for eligibility out of 88 potential study participants presenting for general surgery at Red Cross War Memorial Children's Hospital from January 2013 to January 2014. 34 potential study participants had a working diagnosis of complicated acute appendicitis and initially planned for open appendecectomy. Out of the 34, six were deemed not eligible (4 due to after-hours surgery and 2 due to change of diagnosis and management plan after further review and imaging. 54 potential study participants were planned for laparotomy for various diagnoses. Out of the 54, eleven were not eligible (6 due to after-hours surgery and 5 due to change of management plan with 3 having there elective surgery postponed after review of imaging post chemotherapy and 2 had planned post-operative ventilation). Out of the 71 study participants, 14 underwent open appendectomy and standard post-operative analgesia (APP-SAPA), 14 had open appendectomy and continuous local anesthetic wound infusion (APP-CLAWI), 19 had laparotomy and epidural analgesia (LAP-EPI) and 24 had laparotomy and continuous local anesthetic wound infusion (LAP-CLAWI). 11study participants were excluded from the final analysis; 1 in the APP-SAPA group, 2 in the APP-CLAWI group, 2 in the LAP-EPI group and 6 from the LAP-CLAWI group. The flow chart in *figure 4* shows the recruitment process and reasons for exclusion in each subgroup.

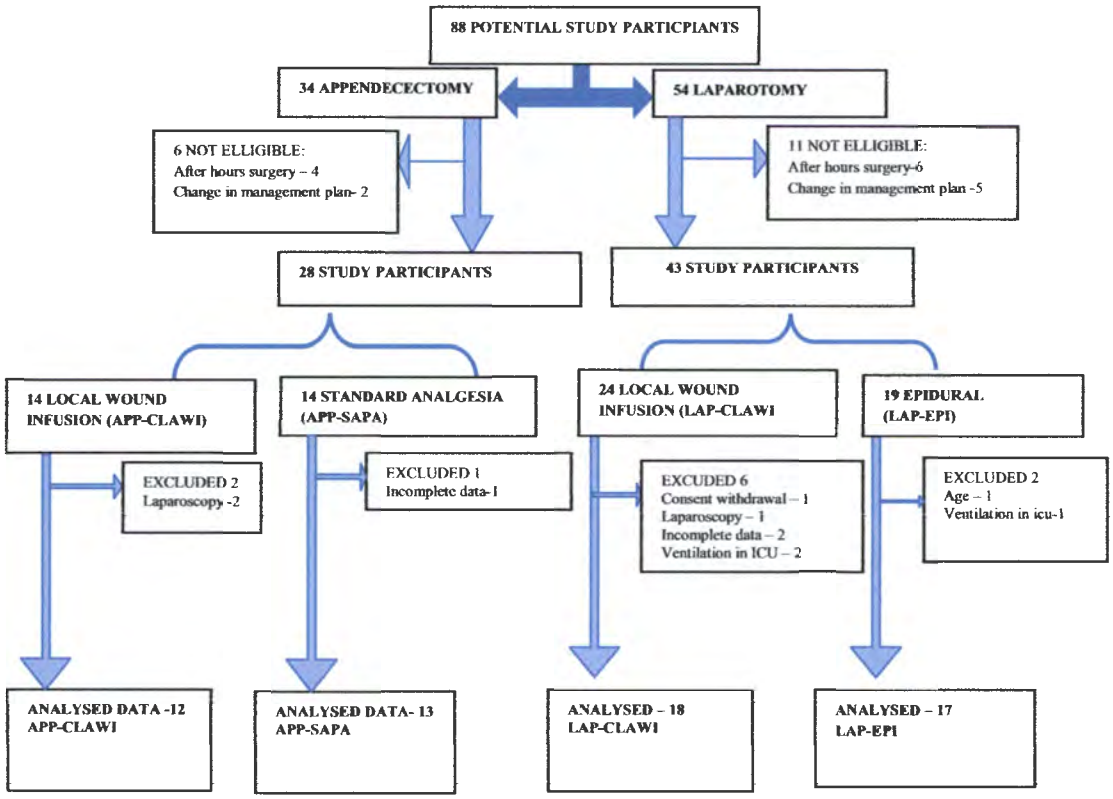

Figure 4: Flow chart of the study participant enrolment.

6.1 DEMOGRAPHICS

The APP-SAPA and APP-CLAWI subgroups (*Table 1*) were comparable in terms of age with a slightly higher female population in the control arm (62% vs 38%). All the study participants in the appendectomy group (APP-SAPA & APP-CLAWI) underwent a Lanz incision laparotomy. There was no difference in the length of incisions. All 12 participants in the APP-CLAWI subgroup had complicated appendicitis (perforated appendix, mass or collections) compared to 77% of the participants in the APP-SAPA subgroup.

		APP-SAPA (N=13)	APP-CLAWI (N=12)
AGE (years)	MEAN(STDEV)	8.8(2.3)	9.5 (2.2)
	P-VALUE	0.841	
GENDER	M	5(38%)	6(50%)
	F	8(62%)	6(50%)
SURGERY PLANNIG	URGENT	13(100%)	9(75%)
	EMERGENCY	0	3(25%)
WOUND CLASS	CLEAN	0	0
	CLEAN-CONTAMINATED	3(23%)	0
	CONTAMINATED/DIRTY	10 (77%)	12 (100%)
COMPLICATED APPENDICITIS	n (%)	10(77%)	12(100%)
NON-COMPLICATED APPENDICITIS	n (%)	3(23%)	0
INCISION LEGHTH (CM)	MEAN (STDEV)	7.5 (3.1)	9.36 (2.8)
	P-VALUE	0.816	
PAIN SCORE	MEAN(STDEV)	3.5(0.7)	2.5(0.8)
	P-VALUE	0.023	
TOTAL MORPHINE REQUIREMENTS(Ug/Kg)	MEAN(STDEV)	490(9.4)	96(50)
	P.VALUE	0.016	
SURGICAL SITE INFECTIONS	INCISION SITE INFECTION	2	0
	DEEP	1 (total 3(23%))	0
DAYS TO FEED	MEAN(STDEV)	3.6(1.7)	2.8(1.7)
	P-VALUE	0.25	
DAYS TO MOBILISE	MEAN(STDEV)	4.8(2.5)	2.6(1.7)
	P-VALUE	0.06	
LENGTH OF HOSPITAL STAY	MEAN(STDEV)	4.3(2)	4(0.98)
	P-VALUE	0.76	

Table 1: Part 1 Study group Demographics, wound class, incisions length, pain score, morphine requirements, surgical site infection, days to feed & mobilize and length of hospital stay for the APP-SAPA vs APP-CLAWI subgroups.

In the laparotomy subgroups (*Table 2* & *3*), majority of the operations were elective in both groups. There were a higher percentage of males in the wound infusion arm. Most of the operations were classed as clean-contaminated and the length of incision was comparable. The number of study participants in the laparotomy group for specific surgical indications were few as shown in table 3.

		LAP-EPI (N=17)	LAP-CLAWI (N=18)
AGE (years)	MEAN(STDEV)	4.4(4.1)	4.5(4)
	P-VALUE	0.398	
GENDER	M	10(59%)	13(72%)
	F	7(41%)	5(28%)
SURGERY PLANNIG	ELECTIVE	11(65%)	11(61%)
	URGENT	69(35%)	7(39%)
	EMERGENCY	0	0
WOUND CLASS	CLEAN	2(11%)	3(16%)
	CLEAN-CONTAMINATED	15(89%)	11(61%)
	CONTAMINATED/DIRTY	0	4(23%)
INCISIONS	UPPER TRANSVERSE	12(70%)	10(56%)
	SUBCOSTAL	2(11%)	2(11%)
	MIDLINE	1(6%)	4(22%)
	PFANNESTEIL	2(11%)	1(6%)
	FLANK	0	1(6%)
INCISION LENGTH (CM)	MEAN (STDEV)	16.2 (5.2)	12.8 (5.4)
	P-VALUE	0.55	
PAIN SCORE	MEAN(STDEV)	3.0(1.2)	2.4(1.2)
	P-VALUE	0.041	
TOTAL MORPHINE REQUIREMENTS(Ug/Kg)	MEAN(STDEV)	406(200)	230(100)
	P.VALUE	0.052	
SURGICAL SITE INFECTIONS	INCISION SITE INFECTION	0	0
	DEEP	0	0
DAYS TO FEED	MEAN(STDEV)	3.4(1.5)	2.2(1.8)
	P-VALUE	0.33	
DAYS TO MOBILISE	MEAN(STDEV)	5.1(1.8)	4(1.9)
	P-VALUE	0.13	
LENGTH OF HOSPITAL STAY	MEAN(STDEV)	7.2(3)	6(3)
	P-VALUE	0.6	

Table 2: Part 2 study group Demographics, wound class, incision types &length, pain score, morphine requirements, surgical site infection, days to feed & mobilize and length of hospital stay for the LAP-EPI vs LAP-CLAWI subgroups.

INDICATION FOR SURGERY/PROCEDURE	LAP-EPI	LAP-CLAWI
COLOSTOMY CLOSURE	1	1
LONGSTANDING CDH	1	1
OPEN NISSEN FUNDOPLICATION	2	2
LIVER BIOPSY	1	1
LIVER SEGMENTECTOMY	1	1
HYDATID CYST LIVER/EXCISION	1	1
INTESTINAL OBSTRUCTION	3	2
CHRONIC MALROTATION/LADD'S	1	1
MESENTERIC CYST/EXCISION	1	0
NEPHROLITHIASIS/PYELOLITHOTOMY	0	1
NEUROBLASTOMA/RESECTION	1	1
LOWER OESOPHAGEAL PERFORATION/DRAINAGE	0	1
PANCREATIC PSEUDOCYST/CYSTO-GASTROSTOMY	1	1
PUJ OBSTRUCTION/PYELOPLASTY	0	1
RENAL ATERY STENOSIS	1	0
RENAL CELL CARCINOMA	0	1
VESICOURETERIC REFLUX	0	1
WILMS TUMOR	2	1
TOTAL	17	18

Table 3: Indications for surgery in the laparotomy group.

6.2 PAIN SCORES AND MORPHINE REQUIREMENTS

Within the appendectomy groups (APP-SAPA & APP-CLAWI) there was a significantly lower average pain score of 2.5 in the CLAWI subgroups compared to 3.5 in the SAPA and 3.0 in the EPI subgroups. Morphine requirements were higher in the SAPA and EPI subgroups with the SAPA group requiring up to five fold the amount of morphine on average and EPI group requiring at least 50% higher the amount in the CALWI subgroup.

The pain score trends were clustered at lower levels in the CLAWI subgroups in comparison to the EPI and SAPA subgroups (*Figure 5*).

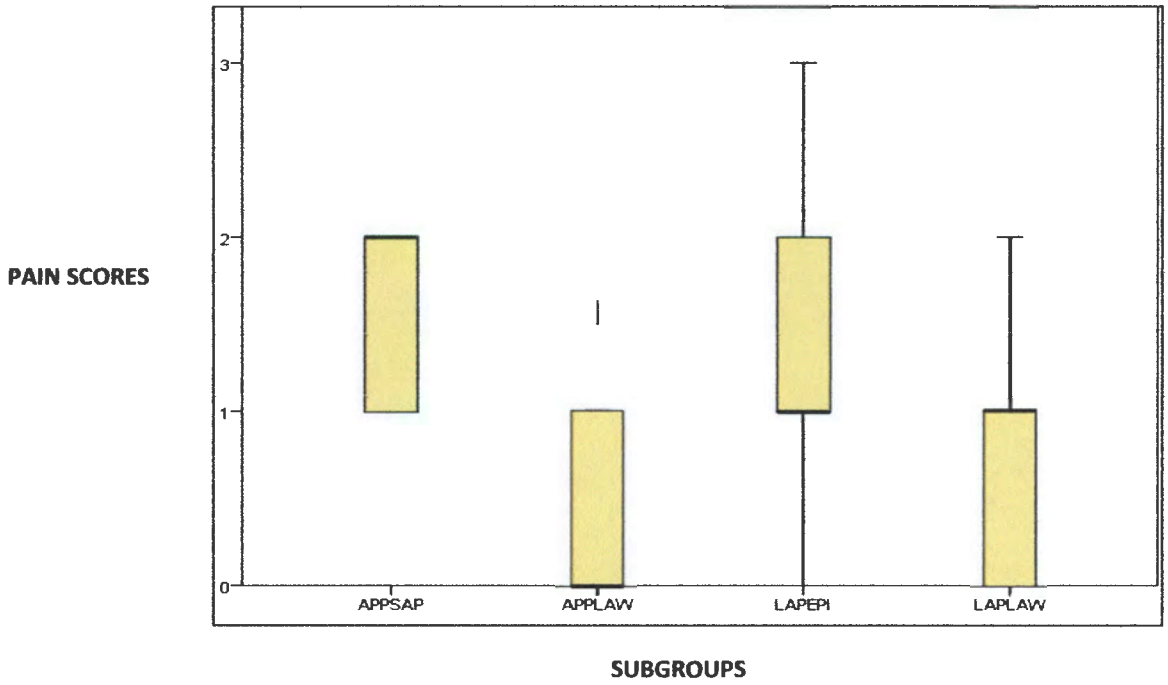

Figure 5: Pain score trends in the different study arms (APPSAP- appendectomy with standard analgesia, APPLAW-appendectomy with local anesthetic wound infusion, LAPEPI-laparotomy with epidural, LAPLAW-laparotomy with local anesthetic wound infusion).

6.3 DAYS TO MOBILISE

The days to mobilization were shorter in the CLAWI group compared to the other groups with a significant difference between the APP-SAPA and APP-CLAWI subgroups of 2 days on average. On average the LAP-CLAWI subgroup was fully mobile one day earlier than the LAP-EPI subgroup.

6.4 DAYS TO ENTERAL FEEDS AND DURATION OF HOSPITAL STAY

There was no statistical difference in length of hospital stay and time to full enteral feeds between subgroups with a tendency to shorter stay and earlier enteral feed tolerance by one day for the CLAWI subgroups.

6.5 URETHRAL CATHETERIZATION

The requirement for urethral catheterization was higher in the EPI group. On average, among the CLAWI subgroup participants who had urine catheter inserted peri-operatively, the urine catheter was removed 2 days earlier compared to the SAPA and EPI subgroups.

6.6 WOUND COMPLICATIONs

There were no surgical site infections in the EPI and CLAWI groups. 3 Surgical site infections occurred in three participants in the APP-SAPA group (two deep incisional and one organ space).

6.7 OTHER COMPLICATIONS

There were no adverse drug reactions to morphine or bupivacaine.
So far, none of the study participants has presented with incisional hernia or other delayed wound complications.

CHAPTER 7: DISCUSSION

Post-operative analgesia is critical for optimal outcomes in surgery. Historically analgesia in pediatrics was seen as unnecessary or unimportant. This has changed with recognition that children suffer pain even in the neonatal period and their physiologic response to pain is actually markedly higher. Hence the current standard of care is to provide good analgesia postoperatively.

However, there is a variation between centers on the modalities utilized for post-operative pain control. The extent of post-operative pain monitoring also varies and a dedicated pain service is not widely available especially in the resource constrained environments. Ideally, pain assessment should be one of the vital signs. The fear of adverse reactions to opiate analgesia and the lack of personnel trained in epidural analgesia for children are other important hurdles in the institution of multi-modal post-operative analgesia in pediatrics.

Continuous local anesthetic wound infusion is an attractive option since it requires little expertise for infusion catheter placement. It also has the potential to reduce the need for opiate analgesia, urethral catheterization and intensive monitoring. The use of Continuous Local Anesthetic Wound Infusion (CLAWI) has been studied in adults undergoing different operations with promising results. CLAWI use in children is limited to a few centers. Studies on its efficacy in post-operative patients in pediatric surgery are few and vary in types operations, age groups and secondary outcome measures (time to enteral feeds, mobilization and other return of function surrogate markers).

We conducted a pain assessor-blinded randomized control trial to compare continuous bupivacaine wound infusion to epidural bupivacaine analgesia and intravenous morphine in children undergoing different abdominal operations. The first part of the study included participants undergoing open appendectomy for complicated appendicitis. They were randomized to undergo either continuous local anesthetic wound infusion (APP-CLAWI) or standard post-operative analgesia (APP-SAPA). The second part of the study included participants undergoing open abdominal surgery for varied diagnoses. They were randomized to undergo either continuous local anesthetic wound infusion (LAP-CLAWI) or epidural analgesia (LAP-EPI). The two parts of the study ran concurrently between January 2013 and January 2014.

Out of 71 enrolled study participants we excluded 10. There was no significant overall variability within groups in age, gender, or type and length of incision. Pain scores were significantly in the lower trends and tended to remain low in the intervention arms (continuous local wound infusion – CLAWI) compared to the control arms. Hidas and colleagues reported lower pain ratings with continuous incisional local infusion in pediatric patients undergoing major urological procedures[31]. The appendectomy (APP-SAPA) subgroup required up to five-fold more morphine compared to APP-CLAWI subgroup. This was the total morphine requirements. Both groups received morphine infusion which was tapered off gradually. Due to ethical concerns we were not able to utilize a placebo nor could we start off without morphine infusion in both groups. This would have allowed the use of rescue morphine doses alone as an indicator of efficacy in this group.
Within the laparotomy group, the epidural arm (LAP-EPI) required up to 50% more rescue morphine compared to the wound infusion arm (LAP-CLAWI). The morphine sparing effect of continuous local infusion in pediatrics has been shown by Hermansson [47] and Wang[33]. The marked difference in the need for opioid analgesia and pain score trends which was statistically significant albeit at a lower power (80%) in this study necessitated the conclusion of the study at this point

Given the resulting smaller number of study participants in the subgroups, this study is not powered to detect a statistical difference in the other secondary outcomes. However there was a trend towards earlier resumption of full enteral feeds in the wound infusion subgroups by up to 2 days. Participants in the CLAWI subgroup also tended to mobilize earlier, few required urethral catheterization and in those whom a urine catheter was inserted, it was removed on average two days earlier. Wang et al reported earlier mobilization and reduced ileus in patients with continuous Ropivacaine wound infusion[33]. There was no difference in time to feeds and hospital stay in the study by Hermansson and colleagues[47]. It is possible that the trade-off for higher morphine doses to maintain acceptable pain control is the unwanted effect of prolonged ileus, urine retention and drowsiness.

One of the concerns regarding wound infusion is the risk of surgical site infection particularly in the setting of a contaminated surgical field with a foreign body. Although the number of participants in the APP-CLAWI group with high risk CDC wound class was 3 compared to zero in the APP-SAPA group, no wound infections occurred in the former while three infections (2 superficial and 1 deep) occurred in participants in latter. It has been shown in vitro studies that different local anesthetic agents have a bacteriostatic effect on E.coli and other organisms that commonly result in surgical site infections[48]. However this has not been replicated in human and animal studies[49, 50].

It is also possible that local anesthetic infusion alters the inflammatory response with improved tissue perfusion[51]. There are animal studies demonstrating reduced collagen production and wound strength by local anesthetics[52]. This has raised concerns regarding the risk of poor healing and resultant incisional hernias in patients undergoing continuous local anesthetic wound infusion. The 3 month, short term, follow-up of participants in this study has so far not found a case of incisional hernia. Long term follow-up is necessary to detect any cases in the future. One significant complication of continuous local anesthetic is the risk of chondrolysis which has been reported in two adult patients with intra-articular local anesthetic infusion[53].

Although CLAWI is not an indication for intensive monitoring on its own, it is crucial to ensure that the site of placement is correct, and hemostasis has been achieved. This is to avoid infusion into open vessels. Labeling of the syringes and the tubing should also be clear and all the staff taking care of the patient made aware as is the case for those on epidural analgesia.

We did not do a cost-benefit analysis comparing CLAWI to the standard post-operative analgesia. The cost of the wound infusion catheter is most likely offset by the reduced need for urinary catheterization, ease of application and reduced need for other analgesics[54]. The use of readily available and affordable material is going to reduce the cost while maintaining efficacy and safety of local anesthetic wound infusion[55].

The weak points in this study are the low numbers particularly in the different indications for surgery in the laparotomy groups. The overall low numbers make it difficult to draw robust conclusions regarding the secondary outcomes as well.

We also did not do a cost analysis for the wound infusion catheter.

CONCLUSION:

Continuous subfascial bupivacaine infusion is a reliable, safe and effective technique for post-operative pain control in children undergoing open abdominal surgery. It is comparable to current standard of care and has reduced need for intravenous analgesia with a tendency to earlier resumption of enteral feeds and mobilization.

RECOMMENDATIONS

Continuous local anesthetic wound infusion should be one of the first line options for post-operative pain control in children undergoing open abdominal surgical procedures and future studies should look into the cost-benefits of the infusion catheter as well as the secondary endpoints.

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APPENDICES

APPENDIX – I: CDC wound infection risk

Clean (class I)	Nontraumatic
	No inflammation encountered
	No break in technique
	Respiratory, alimentary, or genitourinary tract not entered
Clean-contaminated (class II)	Gastrointestinal or respiratory tract entered without significant spillage
	Appendectomy (non-ruptured)
	Oropharynx entered
	Vagina entered
	Genitourinary tract entered in absence of infected urine
	Biliary tract entered in absence of infected bile
	Minor break in technique
Contaminated (class III)	Major break in technique
	Gross spillage from gastrointestinal tract
	Traumatic wound, fresh
	Entrance of genitourinary or biliary tracts in presence of infected urine or bile
Dirty and infected (class IV)	Acute bacterial inflammation encountered, without pus
	Transection of clean tissue for the purpose of surgical access to a collection of pus
	Traumatic wound with retained devitalized tissue, foreign bodies, fecal contamination, delayed treatment, or all of these; or from dirty source

APPENDIX – II: FLACC scale

FLACC Behavioral Pain Assessment Scale

CATEGORIES	SCORING		
	0	1	2
Face	No particular expression or smile	Occasional grimace or frown; withdrawn, disinterested	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid, or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs; frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or being talked to; distractable	Difficult to console or comfort

How to Use the FLACC

In patients who are awake: observe for 1 to 5 minutes or longer. Observe legs and body uncovered. Reposition patient or observe activity. Assess body for tenseness and tone. Initiate consoling interventions if needed.

In patients who are asleep: observe for 5 minutes or longer. Observe body and legs uncovered. If possible, reposition the patient. Touch the body and assess for tenseness and tone.

Face

- Score 0 if the patient has a relaxed face, makes eye contact, shows interest in surroundings.
- Score 1 if the patient has a worried facial expression, with eyebrows lowered, eyes partially closed, cheeks raised, mouth pursed.
- Score 2 if the patient has deep furrows in the forehead, closed eyes, an open mouth, deep lines around nose and lips.

Legs

- Score 0 if the muscle tone and motion in the limbs are normal.
- Score 1 if patient has increased tone, rigidity, or tension; if there is intermittent flexion or extension of the limbs.
- Score 2 if patient has hypertonicity, the legs are pulled tight, there is exaggerated flexion or extension of the limbs, tremors.

Activity

- Score 0 if the patient moves easily and freely, normal activity or restrictions.
- Score 1 if the patient shifts positions, appears hesitant to move, demonstrates guarding, a tense torso, pressure on a body part.
- Score 2 if the patient is in a fixed position, rocking; demonstrates side-to-side head movement or rubbing of a body part.

Cry

- Score 0 if the patient has no cry or moan, awake or asleep.
- Score 1 if the patient has occasional moans, cries, whimpers, sighs.
- Score 2 if the patient has frequent or continuous moans, cries, grunts.

Consolability

- Score 0 if the patient is calm and does not require consoling.
- Score 1 if the patient responds to comfort by touching or talking in 30 seconds to 1 minute.
- Score 2 if the patient requires constant comforting or is inconsolable.

Whenever feasible, behavioral measurement of pain should be used in conjunction with self-report. When self-report is not possible, interpretation of pain behaviors and decisions regarding treatment of pain require careful consideration of the context in which the pain behaviors are observed.

Interpreting the Behavioral Score

Each category is scored on the 0–2 scale, which results in a total score of 0–10.

0 = Relaxed and comfortable
1–3 = Mild discomfort
4–6 = Moderate pain
7–10 = Severe discomfort or pain or both

From Merkel, S. I., Voepel-Lewis, T., Shayevitz, J. R., & Malviya, S. (1997). The FLACC: A behavioral scale for scoring postoperative pain in young children. Pediatric Nursing, 23(3), 293–297. The FLACC scale was developed by Sandra Merkel, MS, RN, Terri Voepel-Lewis, MS, RN, and Shabha Malviya, MD, at C. S. Mott Children's Hospital, University of Michigan Health System, Ann Arbor, MI. Used with permission.

APPENDIX – III: Human Ethics and Research Committee study approval

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences
Human Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6338 • **Facsimile** [021] 406 6411
e-mail: shuretta.thomas@uct.ac.za

10 January 2013

HREC REF: 135/2012

Dr S Machoki
Paediatric Surgery
Red Cross War Memorial Children's Hospital

Dear Dr Machoki

PROJECT TITLE: LOCAL ANAESTHETIC WOUND INFUSION VS STANDARDISED ANALGESIA IN PAEDIATRIC POST-OPERATIVE PAIN CONTROL: A DOUBLE BLIND RANDOMISED CONTROL TRIAL

Thank you for responding to the issues raised by the Faculty of Health Sciences Human Research Ethics Committee in your letter received on 8th January 2013.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year till the 15th January 2014

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/research/humanethics/forms)

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC. REF in all your correspondence.

Yours sincerely

signature removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN ETHICS
Federal Wide Assurance Number: FWA00001637.

Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

s.thomas

APPENDIX – IV: Consent & assent forms

a) ENGLISH

i) (STUDY PARTICIPANTS BELOW THE AGE OF 12 YEARS)

Patient name:
Date of birth
File no.
Study no: .....

ID STICKER

We (the RCWMCH local wound infusion investigators) are conducting a study to establish the use of continuous delivery of a local anesthetic ('pain reducer or pain medicine') to the wound by use of a sterile small tubing placed in the wound during surgery.

For study purposes, the study participant will either get the tubing plus pain medicine or not have the pain medicine delivered although he/she will have a tube. For those who will not be getting pain medicine through the tubing, a tube will be strapped on the study participant so that the one doing the study does not know who is getting extra pain medicine through the tube. The study participant and his/her parent or guardian will also not know if the pain medicine is being delivered through the tube. This is to make the results of the study more useful.

The study will not interfere in any way in the treatment of the underlying problem and the study participant will be monitored regularly for adequate pain control and for any complications resulting from the sterile tubing or pain medicine. In case of pain the study participant will have the usual pain control medicine (morphine, paracetamol, Valoron). If the study participant has any pain the doctors and nurses will give him/her additional medicine to control it. In case of complications from the tubing or pain medicine, it will be stopped and the pain medicine delivery tube removed by the doctor.

This kind of treatment has been used safely in adults without increasing complications.

The benefits of the study are to see if the medicine through the tube is better than the medicine through the veins and mouth or the back (spine). The risks of the medicine through the tube are infection, allergy or reaction to the medicine or the tube. The risks from the pain medicine through the veins and mouth include vomiting, drowsiness, allergy and other reactions. The risks from the pain medicine through to the back include low blood pressure, difficulty passing urine, allergy and other reactions. All this medicines have been used safely on the treatment of pain after surgery and you will be checked for any complications related to them.

We need consent from the parents and/or guardians in order to place a catheter into the wound of the study participant during surgery and to administer the local anesthetic continuously through the catheter for up to 72 hours after surgery.

The study participant will be monitored regularly while in the ward and will also be followed-up in the clinic after discharge.

Involvement in the study will not result in payment or promise of better care and non-involvement will not result in any bias towards treatment of the underlying condition.

I (Name & Surname).....Signature..... (Parent or legal guardian)

Do give consent for the investigators to place a wound infusion tube into the wound of the above named study participant and to administer a local anesthetic (pain medicine).

Investigator (Name & Surname):.....Signature.....
Witness (Name & Surname:.....Signature.....

Consent taken (Circle one): Personally Via Translator

In case of any complaints or comments or questions regarding the study please contact:

The Principal Investigator:

And/Or

Dr. Stanley M. Macholi
Department of Pediatric Surgery
Redcross War Memorial Childrens Hospital
P.O Box 7700 Rondebosch, Cape Town, RSA
Tel: 0216585599 or 0795911577
Email: stanmugambi@yahoo.co.ul

The Groote Schuur Human Research Ethics Committee:

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Health Sciences Faculty
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Groote Schuur Hospital
Tel: 021 406 6492
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HREC/ REF:135/2012

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ii) ENGLISH (STUDY PARTICIPANTS 7 TO 12 YEARS OF AGE)

Patient name:
Date of birth
File no. .....
Study no: .....

We are conducting a study to establish the use of continuous delivery of a local anesthetic ('pain reducer or pain medicine') to the wound by use of a sterile small tubing placed in the wound during the operation.

Should you choose to be included in the study, you will either get pain medicine through the tubing plus other pain medicine or not have the small tube in the wound but you will have pain medicine through the veins or into the back. In both cases we will watch you for any pain and increase the amount of pain medicine. The pain medicine is going to be reduced slowly as you recover and eventually changed to medicine that you can swallow orally near the time of discharge.
Even if you do not get pain medicine through the tube in the wound, you will still have a covered tube attached to the side of the operation site so that we are able to do the study effectively since you and the person checking you for pain will not know which kind of treatment you are getting. This will not mean that you will be without pain medicine.

The study will not interfere in any way in the treatment of the problem that brought you to hospital, you will be checked regularly by the doctor and the person checking for pain. In case of pain the pain medicine will be increased and we will be checking for any problems caused by the pain medicine or the tube.

This kind of treatment has been used safely in adults without increasing complications.

The benefits of the study are to see if the medicine through the tube is better than the medicine through the veins or the back (spine). The risks of the medicine through the tube are infection, allergy or reaction to the medicine or the tube. The risks from the pain medicine through the veins include vomiting, drowsiness, allergy and other reactions. The risks from the pain medicine through to the back include low blood pressure, difficulty passing urine, allergy and other reactions. All this medicines have been used safely on the treatment of pain after surgery and you will be checked for any complications related to them.
We need your permission to place the small tube into the wound during surgery and to give the local pain medicine continuously through the catheter for up to 72 hours after surgery.

Your involvement in the study will not result in payment or promise of better care and non-involvement will not result in any penalty or poor treatment of the underlying condition.

I (Name & Surname).....Signature.....
Do give consent for the investigators to place a wound infusion tube into the wound of the above named study participant and to administer a local anesthetic (pain medicine).

Investigator (Name & Surname):.....Signature.....
Witness (Name & Surname:.....Signature.....

Consent taken (Circle one): Personally Via Translator
In case of any complaints or comments or questions regarding the study please contact:

The Principal Investigator:

And/Or

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HREC/ REF:135/2012

ii) AFRIKAANS (STUDIEDEELNEMERS 7 TOT 12 JAAR OUD)

Naam van pasiënt:
Geboortedatum:
Lêernommer: .....
Studienommer: .....

ID-PLAKKER

Ons voer 'n studie uit om die gebruik van die volgehoue toediening van 'n plaaslike verdowingsmiddel ("pynverligter of pynmedisyne") aan die wond te vestig deur die gebruik van 'n steriele, klein buis wat gedurende die operasie in die wond geplaas word.

Indien u kies om aan die studie deel te neem, sal u óf pynmedisyne deur die buis plus ander pynmedisyne kry óf nie die klein buis in die wond hê nie, maar eerder pynmedisyne deur die are of in die rug kry. In albei gevalle sal ons u monitor vir enige pyn en die hoeveelheid pynmedisyne vermeerder. Die pynmedisyne sal stadig verminder word soos u herstel, en dit sal uiteindelik verander word na medisyne wat u kan mondeliks kan sluk naby die tyd dat u ontslaan word.
Selfs al ontvang u nie pynmedisyne deur die buis in die wond nie, sal u steeds 'n bedekte buis hê wat aan die kant van die operasieplek geheg is sodat ons die studie doeltreffend kan uitvoer aangesien u en die persoon wat u vir pyn monitor nie sal weet watter tipe behandeling u ontvang nie. Dit beteken egter nie dat u sonder pynmedisyne sal wees nie.

Hierdie studie sal geensins inmeng by die behandeling van die probleem wat u na die hospitaal gebring het nie; u sal gereeld ondersoek word deur die dokter en die persoon wat u monitor vir pyn. In die geval van pyn sal die pynmedisyne vermeerder word en ons sal kyk vir enige probleme wat deur die pynmedisyne of die buis veroorsaak word.

Hierdie tipe behandeling is veilig gebruik in volwassenes sonder vermeerderde komplikasies.

Die voordele van hierdie studie is om te bepaal of die medisyne deur die buis beter is as die medisyne deur die are of in die rug (ruggraat). Die risiko's van die medisyne deur die buis is infeksie, allergie of reaksie op die medisyne of die buis. Die risiko's van die pynmedisyne deur die are sluit braking, lomerigheid, allergie en ander reaksies in. Die risiko's van die pynmedisyne deur na die rug sluit lae bloeddruk, probleme om te urineer, allergie en ander reaksies in. Al hierdie medisyne is veilig gebruik om pyn na chirurgie te behandel, en u sal ondersoek word vir enige komplikasies wat hiermee verband hou.
Ons het u toestemming nodig om gedurende chirurgie die klein buis in die wond te plaas, en om die plaaslike pynmedisyne voortdurend vir tot 72 uur na chirurgie deur die kateter te voer.

U betrokkenheid by die studie sal nie lei tot betaling of die belofte van beter sorg en niedeelname sal nie in enige straf of swak behandeling van die onderliggende toestand lei nie.

Ek (Naam & Van).....Handtekening.....

Gee toestemming vir die navorsers om 'n wondinfusiebuis in die wond van bogenoemde studiedeelnemers te plaas en om 'n plaaslike verdowingsmiddel (pynmedisyne) toe te dien.

Navorser (Naam & Van):.....Handtekening.....
Getuie (Naam & Van:.....Handtekening.....

Toestemming geneem (Omkring een): Persoonlik Via Vertaler
In die geval van enige klagtes, kommentaar of vrae rakende die studie kontak gerus:

Die Hoofnavorser:

Dr. Stanley M. Macholo
Departement van Pediatriese Chirurgie
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HREC/ REF:135/2012

c) Iifomu zemvume

i) ISINGESI (ABATHABATHI NKXAXHEBA KUPHANDO BAKWIMINYAKA ENGAPHANTSI KWESHUMI ELI-7)

Igama lesigulane :
Umhla wokuzalwa
Inombolo yefayile.
Inombolo yesifundo sophando: .....

ISITIKHA SE-ID

Thina(Baphandi beRCWMCH local wound infusion) senza izifundo zophando ngokusetyenziswa kwesithomalalisi zintlungu (ilocal anesthetic) kwisilonda ngokuthi kusetyenziswe ityhubhu esuswe iintsholongwane ibekwe esilondeni ngethuba lotyando.

Ukulungiselelwa uphando, umthabathi nkxaxheba uza kufumana ityhubhu kunye nesibulala zintlungu okanye angafumani sibulali zintlungu lo gama efumene ityhubhu.Kwabo bangafumani zibulali zintlungu ngetyhubhu, ityhubhu iza kubotshelelwa kumthabathi nkxaxheba ukwenzela ukuba owenza uphando angazi ukuba ngubani oza kufumana isibulala zintlungu esongezelelweyo kusetyenziswa ityhubhu. Umthabathi nkxaxheba kunye nomzali okanye impelesi akazokuyazi ukuba isibulali zintlungu zifakiwe kwityhubhu.Le nto iza kwenza ukuba iziphumo zophando zibe luncedo.

Uphando alusayi kuphazamisana nonyango kwaye umthabathi nkxaxheba uza kusoloko ebekwe iliso ukulawula iintlungu ngendlela eyiyo nokubona naziphi na iingxaki ezinokubangelwa kukufakwa kwetyhubhu okanye isibulali zintlungu.Kumba weentlungu umthabathi nkxaxheba uya kunikwa isithomalalisi zintlungu esiqhelekileyo (imorphine,iparacetamol neValoron).Ukuba umthabathi nkxaxheba uva iintlungu oogqirha nabongikazi bakumongezelela isithomalalisi ukuzilawula.Xa kuthe kwakho ingxaki ebangelwa kukufakwa kwetyhubhu okanye isithomalalisi zintlungu, kwaku yekwa, sisuswe isithomalalisi zintlungu esifakwa ngetyhubhu ngugqirha.

Olu hlobo lonyango selukhe lwasetyenziswa ngempumelelo kubantu abadala kungabangakho kukhula kwaziingxaki..

Iinjongo zolu phando kukubona ukuba iyeza xa lifakwe kwityhubhu lingcono na kuneyeza elifakwe kwimithambo, emlonyeni okanye kumnqonqo.Iingxaki ezinokubakho ngokufakwa kweyeza ngetyhubhu, zizilo, i-aleji, ukungalungelani neyeza okanye ityhubhu.Iingxaki ezinokubangelwa kukufakwa kweyeza ngemithambo okanye emlonyeni kuquka ukugabha, ukozela, i-aleji kwanezinye iimeko zokubukula iyeza.Iingxaki ezibangelwa kukufakwa kwesibulali zintlungu kumnqonqo yilowu presha(yilow blood pressure), ukuchama nzima, i-aleji kunye nezinye iimeko zokubukula unyango.Onke amayeza asetyenziswa ngokukhuselekileyo kuthomalaliso lweentlungu emva kotyando kwaye uza kujongwa naziphi na iingxaki ezinxulumene nazo.

Sifuna imvume yabazali okanye iimpelesi khon'ukuze sibe nokufaka ikhathetha kwisilonda somthabathi nkxaxheba ngethuba loqhaqho okanye ukufakwa kwesithomalalisi zintlungu kwikhathetha kangangeeyure ezingama-72 emva kotyando.

Umthabathi nkxaxheba uya kubekwa iliso logama esewadini kwaye uyakumana ejongwa eklinikhi emva kokuba ekhululwe esibhedlele.

Ukuthabatha inkxaxheba kuphando akuzokuba nanzuzo yentlawulo okanye isithembiso sononophelo olungcono kwaye ukungathabathi nkxaxheba akuzokubangela umkhethe othile .

Mna(Igama neFani).....Umsayino..... (Umzali okanye impelesi)

Ndiyabanika imvume abaphandi ukuba bafake ityhubhu kwisilonda somthabathi nkxaxheba okhankanywe ngezantsi kwanokuba anikwe izithomalalisi zintlungu.....

Umphandi (Igama neFani):.....Umsayino.....
Ingqina (Igama neFani).....Umsayino
Imvume ndiyinikezele (Yenza isangqa kwenye): Ngokwam Ngeloliki

Ngokuphathelele kwizikhalazo okanye ukunika uluvo okanye imibuzo ngokuphathelele kuphando nceda uqhagamshelane no:

Umphandi oyiNtloko:

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HREC/ REF:135/2012

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ii) ISINGESI (ABATHABATHI NKXAXHEBA KUPHANDO BAPHAKATHI KWEMINYAKA ESI-7 neli-12)

Igama lesigulana:
Umhla wokuzalwa
Inombolo yefayile. .....
Inombolo yesifundo sophando:
.....

Senza izifundo zophando ngokusetyenziswa kwesithomalalisi zintlungu (ilocal anesthetic) kwisilonda ngokuthi kusetyenziswe ityhubhu esuswe iintsholongwane ibekwe esilondeni ngethuba lotyando.

Ukuba ukhethe ukuthabatha inkxaxheba kuphando, uya kufumana isithomalalisi zintlungu ngetyhubhu kunye nesithomalalisi zintlungu ngomlomo okanye ungafakwa ityhubhu esilondeni kodwa uyaku fumana isithomalalisi ziintlungu sifakwe emithanjeni okanye kumnqonqo.Kwezi zehlo zozibini sakujonga ukuba akukho zintlungu zikhoyo songeze isithomalalisi zintlungu.Isithomalalisi zintlungu siza kuye sicuthwa ekuye imeko ibuyela esiqhelweni ekugqibeleni utshintshelwe kwiyeza oza kuthi ulisele xa kusondele ukukhululwa esibhedlele.Nokuba akufumani sithomalalisi zintlungu esifakwe kwityhubhu esilondeni, uya kunikwa ityhubhu ethiwe nca kweli cala lenziwe utyando khon'ukuze senze uphando ngendlela eyiyo ngenxa yokuba wena nalo mntu ukujongayo ningazokuyazi ukuba loluphi uhlobo lonyango olufumanayo.Le nto ayithethi kuthi awuzokufumana izithomalalisi zintlungu.
Uphando oluzokuphazamisana nonyango lwesigulo sakho esikuzise esibhedlele, uza kujongwa rhoqo ngugqirha kwanomntu okujonga ukuba akukho zintlungwini na.Xa kukho iintlungu isithomalalisi zintlungu sakongezwakwaye kwakujongwa naziphi na iingxaki ezibangelwa sisithomalalisi zintlungu okanye ityhubhu.

Olu hlobo lonyango selukhe lwasetyenziswa ngempumelelo kubantu abadala kungabangakho kukhula kwazingxaki.

Injongo yolu phando kukubona ukuba xa iyeza lifakwa kwityhubhu kungcono na kunaxa lifakwa ngemithambo okanye kumnqonqo.. Iingxaki zokufakwa kweyeza ngetyhubhu kukubakho kwezifo, i-aleji okanye ukungalungelani neyeza okanye ityhubhu. Iingxaki ezinokubangelwa kukufakwa kweyeza ngemithambo kuquka ukugabha, ukozela, i-aleji kwanezinye iimeko zokubukula iyeza.Iingxaki ezibangelwa kukufakwa kwesibulali zintlungu kumnqonqo yilowu presha(yilow blood pressure), ukuchama nzima, i-aleji kunye nezinye iimeko zokubukula unyango. Onke amayeza asetyenziswa ngokukhuselekileyo kuthomalaliso lweentlungu emva kotyando kwaye uza kujongwa naziphi na iingxaki ezinxulumene nazo .
Sifuna imvume yabazali okanye iimpelesi khon'ukuze sibe nokufaka ikhathetha kwisilonda somthabathi nkxaxheba ngethuba lotyando okanye ukufakwa kwesithomalalisi zintlungu kwikhathetha kangangeeyure ezingama-72 emva kotyando.

Ukuthabatha kwakho inkxaxheba akuzokuba nanzuzo okanye isithembiso sononophelo olungcono kwaye ukungathabathi nkxaxheba akazokwenza kubekho isohlwayo okanye impatho mbi.

Mna(Igama neFani).....Umsayino.....
Ndiyabanika imvume abaphandi ukuba bafake ityhubhu kwisilonda somthabathi nkxaxheba okhankanywe ngezantsi kwanokuba banikwe izithomalalisi zintlungu.....

Umphandi(Igama neFani):.....Umsayino.....
Ingqina (Igama neFani:.....Umsayino.....

Imvume ndiyinikezele (Yenza isangqa kwenye): Ngokwam Ngetolika

Ngokuphathelele kwizikhalazo okanye ukunika uluvo okanye imibuzo ngokuphathelele kuphando nceda uqhagamshelane no:

Umphandi oyiNtloko:

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Inombolo yefowuni: 0216585599 or 0795911577
Ifeksi: stanmugambi@yahoo.co.ul

Ne/Okanye

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The Groote Schuur Human Research Ethics Committee
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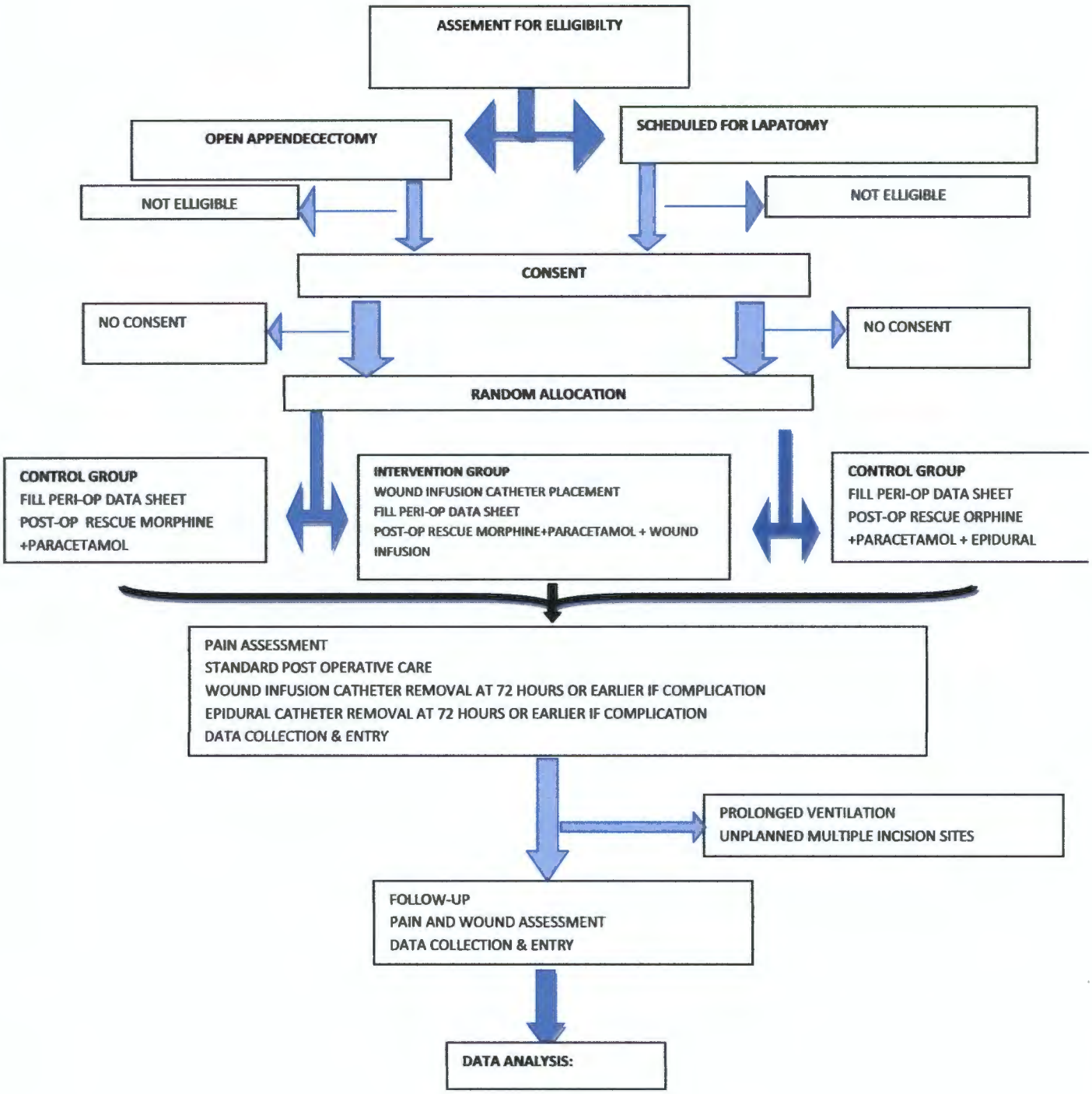
E52, Rm 24, Old Main Building
Groote Schuur Hospital
Inombolo yefowuni: 021 406 6492
Ifeksi: 021 406 6411
HREC/ REF:135/2012

APPENDIX – V: Study flow chart


ASSEMENT FOR ELLIGIBILTY
OPEN APPENDECECTOMY
SCHEDULED FOR LAPATOMY
NOT ELLIGIBLE
NOT ELLIGIBLE
CONSENT
NO CONSENT
NO CONSENT
RANDOM ALLOCATION
CONTROL GROUP
FILL PERI-OP DATA SHEET
POST-OP RESCUE MORPHINE
+PARACETAMOL
INTERVENTION GROUP
WOUND INFUSION CATHETER PLACEMENT
FILL PERI-OP DATA SHEET
POST-OP RESCUE MORPHINE+PARACETAMOL + WOUND
INFUSION
CONTROL GROUP
FILL PERI-OP DATA SHEET
POST-OP RESCUE ORPHINE
+PARACETAMOL + EPIDURAL
PAIN ASSESSMENT
STANDARD POST OPERATIVE CARE
WOUND INFUSION CATHETER REMOVAL AT 72 HOURS OR EARLIER IF COMPLICATION
EPIDURAL CATHETER REMOVAL AT 72 HOURS OR EARLIER IF COMPLICATION
DATA COLLECTION & ENTRY
PROLONGED VENTILATION
UNPLANNED MULTIPLE INCISION SITES
FOLLOW-UP
PAIN AND WOUND ASSESSMENT
DATA COLLECTION & ENTRY
DATA ANALYSIS:

Appendix - VI: Data collection sheet

INFUSION STUDY DATA COLLECTION SHEET (CASE REPORT FORM)

STICKER	
Name_Initials	
Folder_Number	
Study_Number	
Gender	M/F
Body_Weight	KG (XX.YY)
Date_of_Birth	DD-MM-YYYY
Date_of_surgery	DD-MM-YYYY
Date_of_Discharge	DD-MM-YYYY
Diagnosis	
Type_of_surgery	ELECTIVE/EMERGENCY/URGENT
Surgery_PROCEDURE	
Antibiotic1_at_induction	
Antibiotic_2_at_induction	
Antibiotic_3_at_induction	
Other Antibiotics at induction	
Incision_TIME	HH:MM
Wound_closed_TIME	HH:MM
Incision_type	
Incision_length_CMs	
Wound_infection_risk	CLEAN/CLEAN CONTAMINATED/CONTAMINATED
Preincision_analgesia	
PreIncision_analgesia_type	INTRAVENOUS/LOCAL/GAS
Infusion_catheter_IN	YES/NO
Catheter_IN_date	DD-MM-YYYY
Catheter_length_CMs	
Catheter_infusion_rate	MLS/HOUR
Catheter_infusion_boluses_totalMLs	MLS
Catheter_OUT_date	DD-MM-YYYY
Catheter_infusionMLS_total	MLS
Catheter_infusion_BLOCKED	YES/NO
Catheter_infusion_LEAK	YES/NO
Catheter_infusion_DISLODGED	YES/NO
Catheter_infusion_BLEEDING	YES/NO
Catheter_infusion_INFECTION	YES/NO
Epidural INSERTED?	YES/NO
Epidural_IN_date	DD-MM-YYYY
Epidural_rate	MLS/HOUR
Epidural_boluses_total	MLS
Epidural_OUT_date	DD-MM-YYYY
Epidural_infusionMLs_total	MLS
Epidural_BLOCKED	YES/NO
Epidural_LEAK	YES/NO

Epidural_DISLODGED	YES/NO
Epidural_BLEEDING	YES/NO
Epidural_INFECTION	YES/NO
Morphine_infusion_start_date	DD-MM-YYYY
Morphine_boluses_total	MLS
Morphine_infusion_stop_date	DD-MM-YYYY
Morphine_infusion_total	MLS
Perferalgan_total_dose	MGS
Valoron_total_dose72hrs	DROPS
Painscore0hrs	
Painscore6hrs	
Painscore12hrs	
Painscore24hrs	
Painscore36hrs	
Painscore48hrs	
Painscore60hrs	
Painscore72hrs	
Date_BOWEL_SOUNDS	DD-MM-YYYY
Date_FLATUS	DD-MM-YYYY
Date_STOOL	DD-MM-YYYY
Date_SIPS	DD-MM-YYYY
Date_ORALFLUIDS	DD-MM-YYYY
Date_FEEDS	DD-MM-YYYY
Number_VOMITS	
DATE_FULLY_MOBILE	DD-MM-YYYY
Date_Urinecatheter_IN	DD-MM-YYYY
Date_Urinecatheter_OUT	DD-MM-YYYY
Surgical_site_infection	YES/NO
Chest_infection	YES/NO
Urinary_tract_infection	YES/NO
CNS_COMPLICATION	YES/NO
CVS_COMPLICATION	YES/NO
BUPIVACAINE_ADVERSE_REACTION	YES/NO
MORPHINE_AVERSE_REACTION	YES/NO
Venous_thrombosis	YES/NO
Generalised_SEPSIS	YES/NO
MORTALITY	YES/NO
MORTALITY_DATE	YES/NO
ANY COMPLICATION AT 3MONTHS	YES/NO IF YES WRITE COMPLICATION