COLLEGE OF MEDICINE & HEALTH SCIENCES

SCHOOL OF MEDICINE & PHARMACY

DEPARTMENT OF SURGERY

# MULTIMODAL ANALGESIA WITH RESTRICTIVE USE OF OPIOID ANALGESICS: ASSESSMENT OF LEVEL OF PAIN CONTROL IN PEDIATRIC PATIENTS UNDERGOING MAJOR ABDOMINAL SURGERIES AT CHUK.

*Dissertation submitted in partial fulfilment of the requirements for the award of the Degree of Master of Medicine in General Surgery, University of Rwanda.*

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**AUGUST 30, 2021**

## DECLARATION

**The researcher:**

I hereby declare that this dissertation: **"Multimodal analgesia with restrictive use of opioid analgesics: Assessment of the level of pain control in pediatric patients undergoing major abdominal surgeries at CHUK."** and its entire content have never been submitted to any institution of higher learning for any academic award.

Signature:

Date: 30/08/2021

Dr MWISENEZA Philemon

**The supervisor:**

I hereby declare that this dissertation: **"Multimodal analgesia with restrictive use of opioid analgesics: Assessment of the level of pain control in pediatric patients undergoing major abdominal surgeries at CHUK."** was submitted by Dr MWISENEZA Philemon with my approval.

Signature:

Date: 30/08/2021

Dr NTAGANDA Edmond

**The co-supervisor:**

I hereby declare that this dissertation: **"Multimodal analgesia with restrictive use of opioid analgesics: Assessment of the level of pain control in pediatric patients undergoing major abdominal surgeries at CHUK."** was submitted by Dr MWISENEZA Philemon with my approval.

Signature:

Date: 30/08/2021

Dr URIMUBABO Jean Christian

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MWISENEZA Philemon, MD

**DEDICATION**

*To The Almighty God,*

*To my late beloved father:*

*Munyaneza James,*

*To my mother:*

*Nyamirere Alvera*

*To my sisters:*

*Violette, Beatrice and Solange.*

*To my friend:*

*Jeannine*

*I dedicate this humble work*

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**ABSTRACT**

**Background:** The management of acute postoperative pain is very important as it enhances a smooth recovery for the patient. Most of the time, pediatric patients who undergo major abdominal surgery experience severe pain which requires the use of opioid analgesics to be controlled. The use of multimodal analgesia with restrictive use of opioid analgesics is one of the ways that can be used to achieve this objective.

**Objective**: This study aimed at assessing the adequacy of pain control when the multimodal analgesia with restrictive use of opioid analgesics is used in pediatric patients undergoing major abdominal surgery at CHUK.

**Methods:** This was a prospective observational cohort study of 9 months duration from November 2020 to July 2021 assessing the level of pain control when the multimodal analgesia with restrictive use of opioid analgesics is used after major abdominal surgery in pediatric patients at CHUK. The data was collected using a pre-established questionnaire. Data analysis was done using both SPSS, version 16.0. Descriptive statistical analysis, Fisher's test, bivariate, and multivariate logistic regression analysis were used where applicable.

**Results:** Ninety patients have been enrolled in the study. 56.7% of patients recruited were males whereas 43.3% of patients recruited were females. Their mean-age was 31.98 months (SD 39.212 months). For all 90 patients who were recruited, the pain control was 100%. The multimodal analgesia was started after surgery with local anesthesia infiltration in 52.2% of the patients whereas in 47.2% of the patients, infiltration with local anesthesia was not done. Opioid analgesics were included in the postoperative multimodal analgesia in 26.6% of the patients and for the rest, that's 73.3% of patients either received paracetamol and ibuprofen or paracetamol only.

**Conclusion:** A significant proportion of patients who underwent major abdominal surgery could have their acute postoperative pain controlled with multimodal analgesia that did not include the use of opioid analgesics. Selective addition of opioid analgesics for the patients requiring it allowed to achieve pain control for all the cohort.

**Key words:**

Pediatric pain management; Pain assessment tools; Multimodal analgesia; Opioid analgesics; Non-opioid analgesics; Major abdominal surgery

## LIST OF ABREVIATIATIONS

**APS:** American Pain Society

**ASA:** American Society of Anesthesiologists

**ASAA:** American Society of Regional Anesthesia

**CHUK:** Centre Hospitalier Universitaire de Kigali

**COXIBs:** Cyclooxygenase-2 selective NSAIDs

**CRIES pain scale:** cry, requires oxygen, increased vital signs, expression, sleeplessness pain scale

**ERAS:** Enhanced Recovery after Surgery

**FLACC pain score:** Face, Legs, Activity, Cry, Consolability pain score

**FPS:** Faces Pain Scale

**NRS:** Numeric Rating Scale

**NSAIDs:** Non-steroidal anti-inflammatory drugs

**PACU:** Post-anesthesia care Unity

**PCA:** Patient-controlled analgesia

**PICU:** Pediatric Intensive Care Unity

**SPSS:** Statistical Package for Social Science

**UR-CMHS:** University of Rwanda, College of Medicine and Health Sciences

**VAS:** Visual Analogue Scale

**VDS:** Verbal Descriptor Scale

# CHAPTER I: INTRODUCTION

## 1.1 Background

Pain control is important for the patient after surgery because it improves the clinical outcome and at the same time the level of being more comfortable will increase [1]. When it is not controlled in an adequate manner, as a consequence there will be undesired events like discomfort of the patient and suffering also [2].

Proper pain management in pediatric patients undergoing major abdominal surgery is also very important as it will lead to a smooth recovery and a better postoperative evolution. Multimodal analgesia is the best option because it permits to avoid the side effects which are not good linked to the fact that opioid analgesics have been used while dealing with pain for patients who have been operated on.

The American Pain Society (APS) and the American Society of Anesthesiologists (ASA) have considered the complications which occur after opioid-based analgesia is prescribed so as to manage the postoperative pain. They came up with a guideline which would help the way pain in the postoperative period is managed. This guideline was a comprehensive one and it was also evidence-based. Among the many recommendations that were developed, four had been considered of the high-quality evidence and were recommended strongly [3].

- The use of multimodal analgesia, or using different pain medications and techniques in combination with interventions which are nonpharmacological for treating the postoperative pain in pediatric patients is requested to all clinicians.
- For patients who do not have any contraindications, paracetamol and/or NSAIDs like ibuprofen should be given as some of the components which are making the multimodal analgesia in order to treat the postoperative pain.
- The neuraxial analgesia was recommended for patients who would have major surgical procedures involving the chest and abdomen, especially for patients whose risk of having complications (like cardiac and pulmonary), or prolonged ileus is increased.
- Using regional anesthetic techniques has to be a consideration in pediatric patients where an evidence of efficacy is indicated.

Acute postoperative pain management has been always problematic in pediatric patients. For this age group, pain is still not properly treated because there are challenges related to adequate pain assessment or management [4,5]. A significant proportion of pediatric patients are non-verbal and it is not possible for them to report their pain. In the older age group, even if they can talk, their cognition is still not well developed so that they can report well their pain.

Abdominal surgery in children is among the types of surgical interventions in which children experience significant pain in the post-operative period and these interventions are more frequent in the pediatric surgery sub-speciality.

Three approaches which are used for assessing pain in pediatric patients are:

- **Self-reporting (what is reported by the child)**

The self-reporting approach most of the time is used for those children who are old enough to understand. For them, it is easier to be helped by the self-reporting methods. This implies they are not in distress and their cognition is not impaired at all.

- **Behavioural indicators (behaviours of the child visa-a-vis pain)**

Infants, toddlers and pre-verbal children will need pain assessment tools which consider behaviours. It is the same for those whose cognition is impaired or they are sedated. These kind of tools should also be used for children who are old but they are in distress.

Behaviours which indicate pain in the pediatric population are: irritability, unusual posture, reluctance to move, disturbed sleep patterns, unusual quietness, restlessness, sobbing, lethargy, screaming, increased clinging, loss of appetite, whimpering, laying scared and stiff.

- **Indicators which are physiological (child's body reactions visa-a-vis pain)**

Physiological indicators (heart rate, respiratory rate and pattern, blood pressure and oxygen saturation) should not be used alone while assessing pain in pediatric patients. In fact, other physiological changes such as fever, anxiety and exertion can influence them [6,7,8].

Another challenge is related to the appropriate analgesics which should be prescribed in order to control postoperative pain. Opioid-based analgesia is known to be the best modality which is used for managing the pain which is severe in the postoperative period. However, complications and adverse events are feared when opioid analgesics are used as postoperative pain management [9].

Some complications which are a result of using opioid analgesics are: respiratory depression, sedation, drowsiness, pruritus, skin rash, urinary retention, delayed gastrointestinal motility, and postoperative vomiting and nausea [9]. Dependency is also among the undesired side effects.

The safe use of opioid analgesics in the postoperative period requires a close monitoring. Most of our postoperative wards do not have a sufficient staff to do the close monitoring of the patients who receive opioid analgesics. It is for this reason that a permanent solution should be found in order to manage well pain in the postoperative period for patients who underwent major abdominal surgery by considering the undesired effects linked to the use of opioid analgesics.

## 1.2 Problem statement

Optimal postoperative pain control is challenged by a combined fear of opioid analgesics, associated complications, inadequate pain assessment for pediatric patients and insufficient monitoring of patients in the surgical wards [10,11,12].

In large prospective observational studies, incidences of 17% of adverse drug reactions were reported and opioid analgesics were major contributors [13]. Critical incidents while children were receiving infusions of opioid analgesics were reported at 1.7% in a large pediatric center

[14]. The respiratory depression and over-sedation caused by opioid analgesics was reported in the range of 0.11-0.41% [14]. Among patients who were at increased risk there are those whose age is under 1 year and preterm births.

Opioid-based analgesia is recommended as a modality for managing severe postoperative pain according to the existing knowledge. The limitation to this in our setting is lack of sufficient close monitoring as it was mentioned above.

Despite all these challenges, postoperative pain in pediatric patients should be well treated by basing on a properly conducted pain assessment.

It is known that acute postoperative pain which is uncontrolled will have an increase in morbidity as concequence, there will be functional impairment and the same for the quality of life will be impaired, it will take long for the patient to recover, the duration of using opioid analgesics will be prolonged, and all these will have an impact on the overall cost of care to the patient [15].

It has been demonstrated that the multimodal analgesia can be suitable for almost all cases involving controlling pain. It is possible to adapt it to different categories of cases. It will be good for the day care surgery, patients who had major surgeries will also beneft, the children who are in critical condition will also beneft from it, or the child who is very young [16].

### 1.3 Justification of the study

It is known that proper pain management should be guided by proper pain assessment using appropriate pain assessment tools.

In our setting, these pain assessment tools are not used systematically in order to guide the prescription of analgesics in pediatric patients who underwent major abdominal surgeries.

After consulting our local journals, there was no study done in Rwanda showing the level of pain control for operated patients.

Determination of the level of pain control when the multimodal analgesia with restrictive use of opioid analgesics is used in pediatric patients who undergo major abdominal surgeries would help to know the efficiency of pain management in our setting.

With the study conclusions, we hope to encourage further clinical studies evaluating the challenges related to pain management and how to overcome them in our setting.

### 1.4 Research question

Does the multimodal analgesia used at CHUK achieve a satisfactory level of pain control?

## 1.5 Objectives of the study

### 1.5.1 General objective

To assess the adequacy of pain control when the multimodal analgesia with restrictive use of opioid analgesics is used in pediatric patients undergoing major abdominal surgeries at CHUK.

### 1.5.2 Specific objectives

- To describe the demographic data of pediatric patients in this study.
- To determine the level of pain control in pediatric patients undergoing major abdominal surgeries at CHUK.
- To determine components of the multimodal analgesia used for pain control.
- To determine factors which influence the use of opioid analgesics in pediatric patients who are on the multimodal analgesia.
- To determine the rate of complications related to uncontrolled pain.

## CHAPTER II: LITERATURE REVIEW

### 2.1 WHO Analgesic Ladder

Treating pain in the post-operative period should include both pharmacological and non-pharmacological strategies. The analgesic ladder is the basis of the treatment and consists in starting with simple oral medications and if the pain is not relieved, the clinician will shift to opioid analgesics.

This approach of treating pain was developed after a group of experts at the international level have made some recommendations. This analgesic ladder underwent several modifications for many years and for this time it is used even for cancer pain management but also other painful conditions which are acute and chronic non-cancer can benefit from it.

The original analgesic ladder was made of three steps [17]:

1. For the first one, mild pain was treated by non-opioid analgesics like NSAIDs or paracetamol. Adjuvants could be added or not.
2. For the second one, moderate pain was managed by weak opioids (hydrocodone, codeine, tramadol) with or without non-opioid analgesics. Adjuvants could be added or not.
3. For the third one, the pain which is severe and also persistent was treated by opioid medications which are potent like morphine, fentanyl and many others of the same category. Non-opioid analgesics could be added or not, and it was the same for the adjuvants also.

With the updated version of this analgesic ladder from WHO, there was an addition of the fourth step. This one consisted in many procedures which are non-pharmacological and they are considered as strong recommendations for managing persistent pain. Strong opioid analgesics and other medications also can be combined with this one in order to treat pain. Procedures which require some interventions and minimal invasion are involved like epidural analgesia, administering analgesics by the intra-thecal route and anesthetic drugs administered locally with or without use of pumps are included in this group [18,19,20,21].

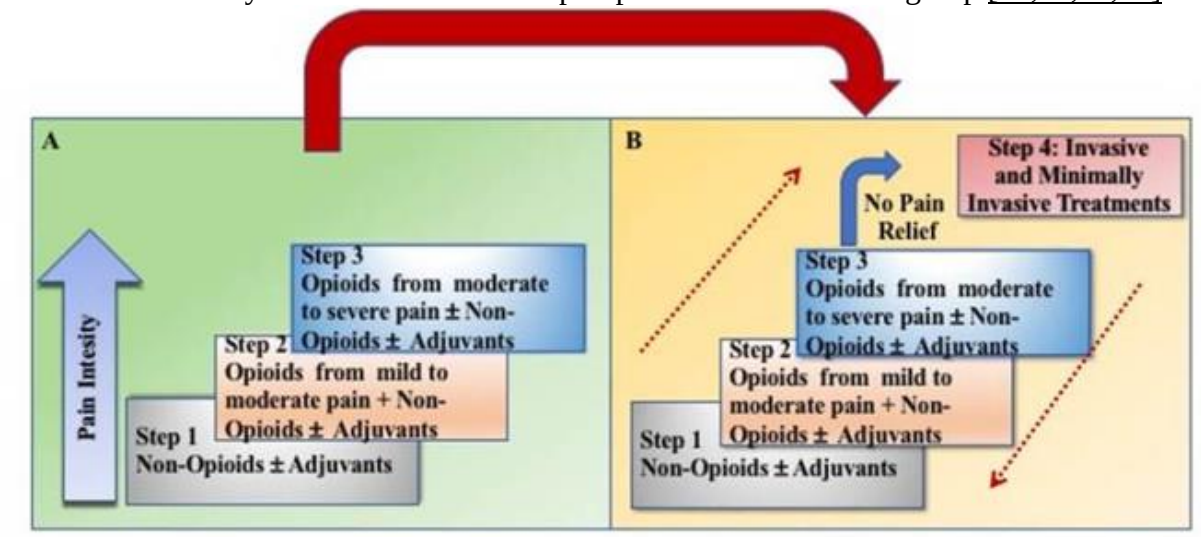


**Figure 1: WHO analgesic ladder**

The fact that there was a shift from the previous WHO analgesic ladder that was made of three steps to the one which is revised with four steps, there was an addition of the fourth step which includes techniques using some form of invasion or minimal invasion. This WHO ladder with some revisions has an approach which is bidirectional.

## 2.2 Multimodal analgesia

### 2.2.1 Introduction

Multimodal analgesia is a way of using many classes of analgesic medications with different pharmacology when receptors of different nature along the pathway of pain are targeted. The objective for it is to improve analgesia and at the same time individual class-related side effects are reduced [22].

Currently evidence is supporting the use of this approach of controlling pain routinely when the patient is admitted to the hospital especially after being operated on as it will not promote the culture of relying excessively on opioid analgesics for controlling pain and it will also help in reducing adverse events related to opioid analgesics.

Multimodal analgesia is one of the recommendations for treating pain in the postoperative period for many situations which are clinical. It is one the main focus of a joint practice which is clinical and a guideline from different societies dealing with pain worldwide.

### 2.2.2 Elements of multimodal analgesia

Multiple pain subtypes constitute the perioperative pain and for this reason, to treat it effectively will not require a single medication only. According to the surgery done, pain from it will be nociceptive, neuropathic, mixed, psychogenic, or idiopathic [23].

This protocol of multimodal analgesia can be made of opioid analgesics, non-opioid analgesics like paracetamol, NSTDs like brufen and anesthetic drug which are administered by local infiltration, regional block, or the intravenous route.

#### i. Non-opioid systemic analgesics

A successful way of prescribing pain medications is by using the multimodal analgesia where the regimen for the surgical patient in the perioperative period should be build on non-opioid analgesics. Many of these medications are very effective for treating pain in the postoperative period and at the same time they allow faster mobilisation. On top of this, there will not be side effects related to opioid analgesics.

Acetaminophen has been the first medication to be used in clinic for a long time and it was proven to be safe when used in appropriate doses. A big number of multimodal analgesia protocols used currently include acetaminophen [24,25 ,26], and the fact that side effects related to opioid analgesics are avoided and it doesn't have contraindications apart from patients for whom liver disease is severe and make it appealing.

Another class of medications with highest efficacy for managing pain for surgical patients especially in the postoperative period is NSAIDs. These medications also should be included in the multimodal analgesia protocols. Their mechanism of action is by exerting its effects through inhibition of cyclooxygenase (COX) and prostaglandin synthesis [24].

Clinicians should be careful using them for patients who have conditions of kidney injury and gastrointestinal ulcers [17]. In pediatric patients where gastrointestinal ulcers are considered as a big problem, a COX-2 selective inhibitor may be substituted for a non-selective agent in order to reduce this risk [27].

## ii. Local anesthetics

### ii.1 Regional anesthesia and analgesia techniques

Superior pain control is provided by regional anesthesia when compared to starategies of ordinary opioid-based analgesia in many different surgical interventions. It helps also for decreasing episodes nausea and at the same vomiting; it will also help to decrease the time a patient spends in the PACU (that's post-anesthesia care unit) [28].

Neuraxial anesthesia (spinal and epidural) and peripheral nerve blocks are included in the category of regional anesthesia. Nerve injury, bleeding, infection, and rebound pain are some of the complications related to the nerve block and these risks should always be weighed against their pontetial benefits.

Complications related to neuraxial blocade are: Post-dural puncture headache, backache, transient neurological symptoms, total spine anesthesia, spinal or epidural hematoma, epidural abscess, meningitis, arachnoiditis, cardiac arrest, urinary retention and drug toxicity [29].

### ii.2 Local infiltration analgesia

Local anaesthetic wound infiltration and opioid analgesia combinations in the provision of superior pain relief and reduction in opioid consumption after cardiothoracic surgery has also been demonstrated to be effective in children[30].

Various local anaesthetic regimens contribute so much to the effectiveness of the analgesia. In case of laparotomy, a long-acting agent (e.g. bupivacaine 0.5%) with a concentration of relatively high level provides superior analgesia compared to placebo while lower concentrations of bupivacaine (e.g. 0.25%) have not ensured adequate analgesia in majority of adults. In contrast, lower concentrations of ropivacaine (0.2%) achieved sufficient analgesia and lower rescue opioid requirements [30].

## iii. Opioid analgesics

Opioid analgesics have been considered as the best medications for managing pain in the perioperative period for a long time. The reason behind was that these medications were simple, predictable and familiar to those who were using them. Their mode of action consists in the fact that they interact with receptors which are found in some areas located in the central nervous system, which play a role of transmitting nociceptive afferences and they help in identifying pain [31].

Patient-controlled analgesia (PCA) is a way of self-administering predetermined doses of analgesic medications in order to treat pain [37]. This modality of controlling pain is used to manage acute and chronic postoperative pain [38]. Medications which are used for this purpose can be given through an IV line, an epidural or peripheral nerve catheter, and transdermally [40,41].

The goal for this modality is relieving pain in an efficient manner at the dosage and schedule preferred by the patient. Patients are allowed administering themselves boluses of medications which are predetermined according to their needs and they do so by pressing a button [38].

Variables which are contained in all forms of PCA modes are: initial loading dose, demand dose, lockout interval, background infusion rate and 1-hour or 4-hour limits [37]. Morphine is

the medication which is used most commonly as intravenous drug for PCA and the most studied also. Even if morphine is used as for PCA as the first choice, other opioids were also used for this option with success [37].
It has been proven that PCA is more effective for controlling pain compared with non-patient opioid injections and as a result, the satisfaction of the patient is high [39].

PCA can also be used in pediatric patients and they can benefit from it. Intramuscular injections of opioid analgesics will no longer be needed and will be eliminated [42]. The cognition and physical ability of the children should be considered when PCA is opted for managing their pain. The screening for these should be done before.

Other alternatives to patient-controlled analgesia for pediatric patients whose cognition and physical ability are impaired are family-controlled analgesia and nurse-controlled analgesia. They can be considered in some selected cases. Some of the potential adverse effects which need to be prevented and controlled are: respiratory depression, nausea, vomiting, and pruritus [42].

### 2.3 Pain assessment

Assessing pain in pediatric patients can be a big challenge. Pre-verbal children or those who are developmentally delayed may not be able to communicate the severity or even the presence of pain to those who are assessing them. In any patient and at any age, it may not be easy for distinguishing pain from agitation. Even if there are those challenges, pain in pediatric patients should be recognized, assessed, and managed immediately. The best approach for managing acute pain in the postoperative period includes an adequate tool for assessing pain. The various tools which are used to assess pain are the following:

#### 2.3.1 Neonates and infants

Tools which are used in this age group are the ones which use observation of behaviours and physiological reactions. The degree of discomfort is assessed by the combination of physiological reactions with facial expressions. The pain assessment tools used commonly for this age group are: Premature Infant Pain Profile (PIPP), CRIES postoperative pain scale, FLACC scale etc. The CRIES as a pain scale is the best tool because it encompasses both behavioural and physiologic parameters and is shown in Table 1: [32]

It was tested and validated by comparing with other pain assessment tools used in the neonatal period because it combines both behavioural and physiological scores [33].

**Table1: The CRIES pain scale**

| Indicator | Score | | |
|---|---|---|---|
| | 0 | 1 | 2 |
| Crying | No | High pitched but consolable | Inconsolable |
| Requires oxygen for<br><br>Saturation > 95% | No | FiO2 < 30% | FiO2> 30% |
| Increased Vital Signs | No | HR or BP increased < 20% | HR or BP increased > 20% |
| Expression | No | Grimace | Grimace and Grunt |
| Sleepless | No | Wakes often | Constantly awake |

*Score < 4: Initiate non-pharmacological methods*

*Score > 4: Initiate pharmacological and non-pharmacological methods*

### 2.3.2 Infants and toddlers

FLACC as a pain scale which considers behaviours when it is used for assessing pain in infants and toddlers is the best option because it has been validated by many studies. It is suitable for pediatric patients between the age of 2 months and 7 years [34]. Five behavioural descriptions are included in the scale with a score given to each such behaviour and it is depicted in Table 2. Other tools used for assessing pain which may be used in the same age group are:

- Wong-Baker Pain Rating Scale can be used for children aged 3-18 years but it is a self-reporting pain scale which means it can help only those who can communicate.
- FPS-R can also be used in the same age group between 5-12 years and it is also considered a self-reporting pain assessment tool [6,7,8].

Many children and infants found in that age group are the ones who cannot communicate properly. It is the reason why the FLACC pain assessment tool was chosen as the most used tool because it considers behaviour only.

**Table 2: FLACC behavioural Pain Score**

| Categories | Score | | |
|---|---|---|---|
| | **0** | **1** | **2** |
| Face | No particular expression<br><br>Or smile | Occasional grimace or frown,<br><br>Withdrawn, disinterested | Frequent to constant quivering chin, clenched jaw |
| Legs | Normal position or relaxed | Uneasy, restless or 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, distractible | Difficult to console or comfort |

*Total score between 0-10*

| **Pain intensity** | **FLACC score** |
|---|---|
| Relaxed and comfortable | 0 |
| Mild discomfort | 1-3 |
| Moderate pain | 4-6 |
| Severe discomfort/pain | 7-10 |

### 2.3.3 Children over the age of 8 years

This population encompasses patients who are old enough. They can understand very well the proportionality related to numbers and colours. It means that they are able to give a description of their pain easily on a Visual Analogue Scale (VAS) or Numerical Rating Scale like adults.

Children who are in this category may rate their pain which is severe as less because they had been exposed to a wide range of stimuli which are painful comparing to the younger ones who may rate the same pain as more severe [32]. It means older children may have been familiar with painful conditions and these ones will be considered as severe for those who are exposed to them for the first time.

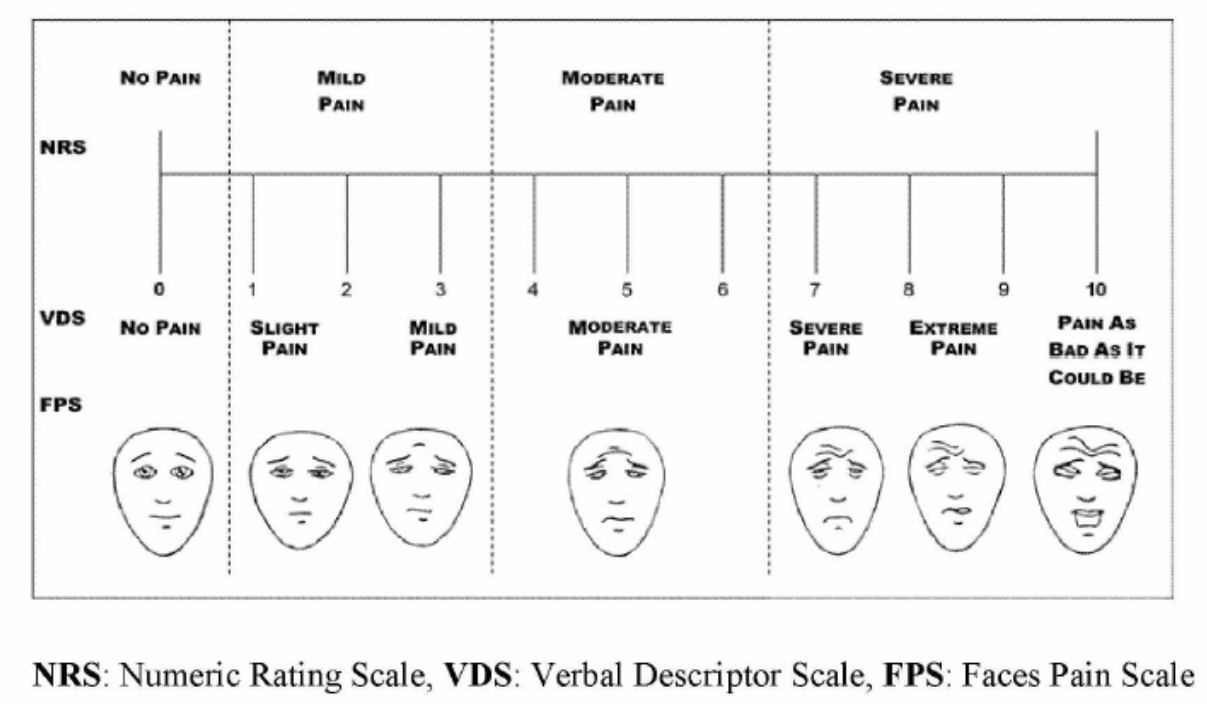


**Figure 2: NRS: Numeric Rating Scale, VDS: Verbal Descriptor, FPS: Faces Pain Scale.**

## CHAPTER III: Methodology

### 3.1 Study design:

This was a prospective observational cohort study of 9 months duration from November 2020 to July 2021 assessing the level of pain control when the multimodal analgesia with restrictive use of opioid analgesics is used after major abdominal surgeries in pediatric patients at CHUK.

### 3.2 Study setting:

The study was conducted in the department of surgery and the department of pediatrics at CHUK, a tertiary referral hospital. The hospital has a 513 beds capacity and the department of surgery counts 170 beds. Among these beds, the department of pediatric surgery counts 15 beds distributed in the 2 departments (4 beds are found in the department of surgery and the remaining are found in the department of pediatrics).

### 3.3 Study population:

All pediatric patients who underwent major abdominal surgeries in the department of surgery at CHUK during the study period were recruited.

### 3.4 Selection of the study population

**Definition of major abdominal surgery:**
Major abdominal surgery was defined as all gastrointestinal (colorectal, gastric, small bowel, hepatic) and urological (nephrectomy and other pediatric urological procedure of abdominal surgery) [20]. All surgical procedures that involved opening the abdomen (both open and laparoscopic procedures) were included in the study.

- **Inclusion criteria:** Pediatric patients who underwent major abdominal surgeries in the department of surgery at CHUK during the study period were included.
- **Exclusion criteria:** Patients who underwent major abdominal surgeries during the study period and who were admitted in the pediatric intensive care unit (PICU) on continuous sedation and mechanical ventilation were excluded.

### 3.5 Sample size calculation:
The sample size was calculated using the formula:

$$\text{Sample size} = \frac{Z_{1-\alpha/2}{}^2\, p(1-p)}{d^2}$$

Here

$Z_{1-\alpha/2}$ = Is standard normal variate (at 5% type 1 error ($P<0.05$) it is 1.96 and at 1% type 1 error ($P<0.01$) it is 2.58). As in majority of studies $P$ values are considered significant below 0.05 hence 1.96 is used in formula.

p=expected proportion of pediatric major abdominal surgeries out of other surgical interventions done at CHUK based on the registry of the operating room and is 0.05
d=absolute error or precision

The sample size was n=73 patients

### 3.6 Variables:

Clinical and demographic variables to be studied included:

- Age and sex
- Diagnosis
- Type of surgical intervention(emergency or elective)
- Type of anesthesia given
- Duration of the procedure
- Components of the multimodal analgesia used for pain control
- Prescribed post-op analgesia (non-opioids +opioids PRN)
- Pain assessment in the surgical ward over a period of 3 days.
- Complications experienced in case of uncontrolled pain.

Complications related to poorly controlled pain are many and include increased morbidity, development of chronic postoperative pain, impaired function, recovery from surgery, and quality of life, prolonged opioid use, and increased medical costs [43].

In our study, we focused in those complications which could be possible in the immediate postoperative period (that's within the first 3 days after surgery). It is for this reason we were investigating if the patient might have developed any of the following: respiratory distress, desaturation, lung atelectasis, pulmonary infection, hypertension, tachycardia and increases in urinary retention.

Other complications related to poorly controlled pain would have required much longer time to investigate them, which was not the case for our study. For this reason, they were not investigated.

### 3.7 Enrolment, data collection and management:

Patients were recruited in the study on their post-operative day one. They were evaluated for demographic data, their clinical status and diagnosis.

Some of the recorded information was: type of surgical intervention, its duration, type of anesthesia given, the components of multimodal analgesia used at the end of the operation (local infiltration, caudal block and epidural block), analgesics prescribed after surgery, then follow-up was done in the surgical ward where pain was assessed over a period of 3 days.

The end of follow-up for patients was the third day after surgery because at that time it was expected to know whether the prescribed treatment in terms of pain management was efficient or not. During the time period the study was conducted, nurses in the surgical ward and residents who were rotating in the pediatric surgery were involved in the data collection process.

**Expected outcomes are:**

- Primary outcome: The level of pain control when the multimodal analgesia with restrictive use of opioid analgesics in pediatric patients undergoing major abdominal surgery is used.
- Secondary: Complications experienced in case of uncontrolled pain.

### 3.8 Statistical analysis

A database was created using Statistical Package for Social Science (SPSS 16.0). Data entry was done using the Excel Sheet and the analysis was done using SPSS, 16.0 . The analysis of data in this study was based on frequency, distribution, charts, and figures and cross tabulation.

### 3.9 Ethical considerations & Confidentiality

Ethical approval was obtained from the Institutional Review Board of the University of Rwanda-College of Medicine and Health Sciences (UR-CMHS) prior to study enrolment. The CHUK ethics' committee approval was also obtained prior to patient's recruitment.

An informed consent was obtained from parents after clear and concise explanations of the purpose, potential risks and benefits of the study. Parents had the right to refuse the study enrolment or withdraw their consent later. Parents were informed that their decision would not have any impact on treatment decisions or medical management.

As all participants were in the pediatric age group (that's below the legal age for consent), they were requested to give an assent in addition to the consent from a parent or a legal guardian/ representative where it was applicable. A statement verifying an informed consent was visible on the first page of the questionnaire.

All data collected from participants were handled with confidentiality. The collected information was not shared or communicated to anyone.

The data was stored on a password-protected computer and patient information was de-identified prior to data analysis.

### 3.10 Limitations of the study

Some of the limitations to this study have been:
Different pain assessment tools were used for different age groups. They are not reliable at the same level even if they are all validated.

## CHAPTER IV: RESULTS

### 4.1 Description of patient demographics

Ninety patients have been enrolled in the study. 56.7% of patients were male whereas 43.3% of them were female. Their mean-age was 31.98 months (SD 39.212 months).

**Figure 3: Distribution of patients according to their age**

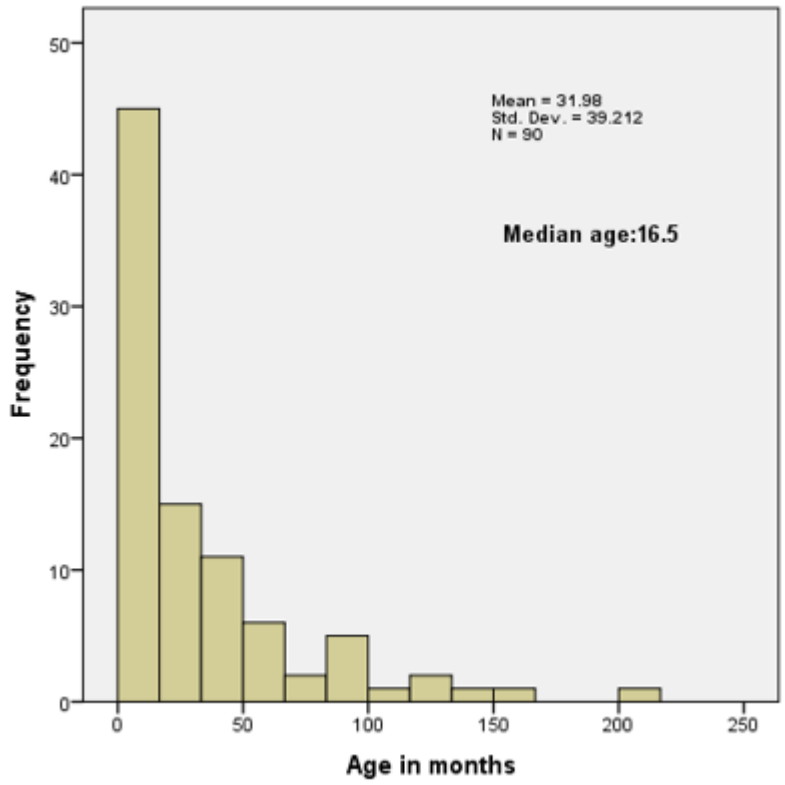


Figure 3 shows that majority of surgical pediatric patients were below 50 months old and the mean age was 32 months old while the median age was 16.5 months old.

**Figure 4: Distribution of patients according to their sex**

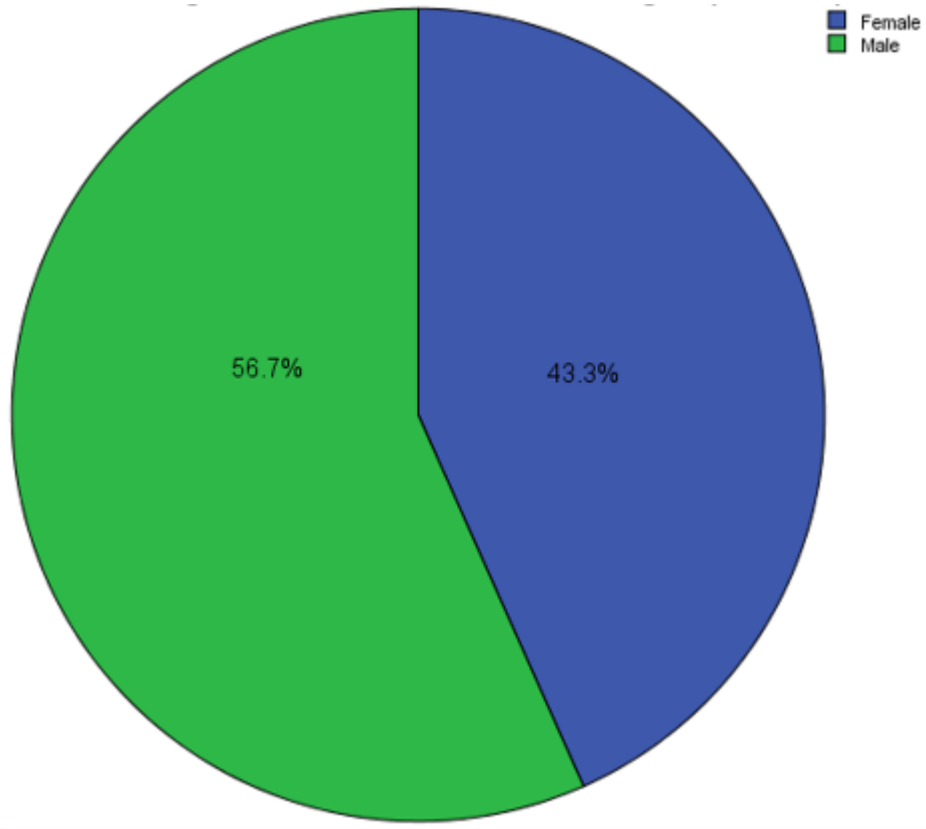


Figure 4 shows that majority of study participants were male (56.7%) while female occupy 43.3%

### 4.2 The level of pain control in pediatric patients undergoing major abdominal surgery.

For all patients who were enrolled in the study, the pain was controlled at 100%.

### 4.3 The components of multimodal analgesia used.

**Figure 5: Use of local infiltration in multimodal analgesia plans.**

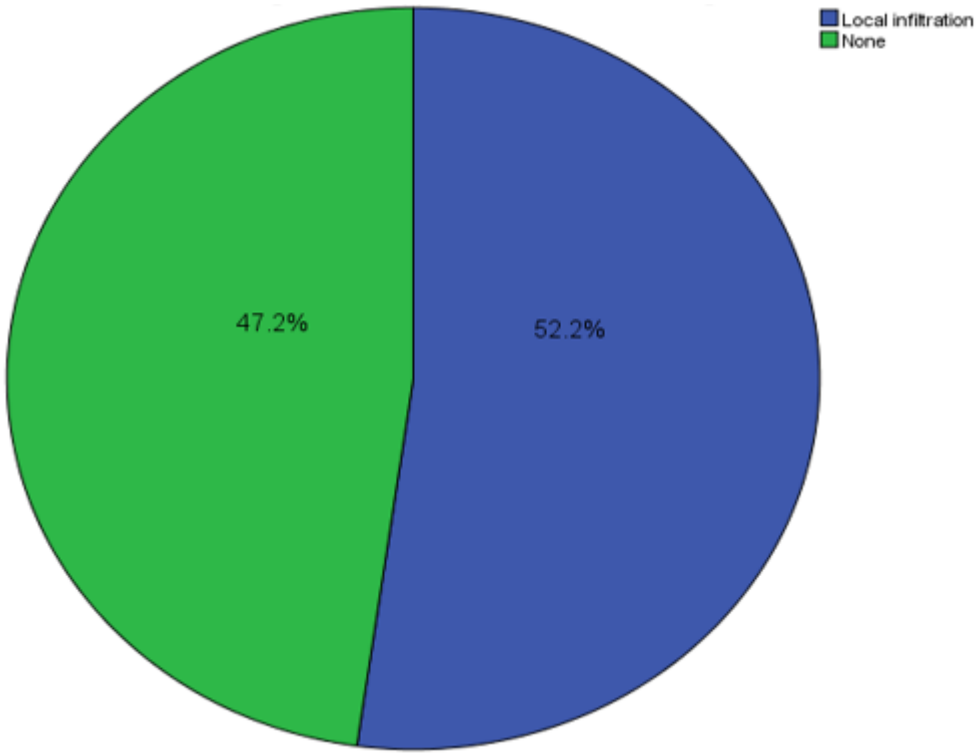


Figure 5 shows that in majority of pediatric patients who underwent major abdominal surgeries, multimodal analgesia using local infiltration was (52.2 % ) and for 47.2%, the local infiltration was not used.

**Figure 6: Other components of the multimodal analgesia in addition to local infiltration.**

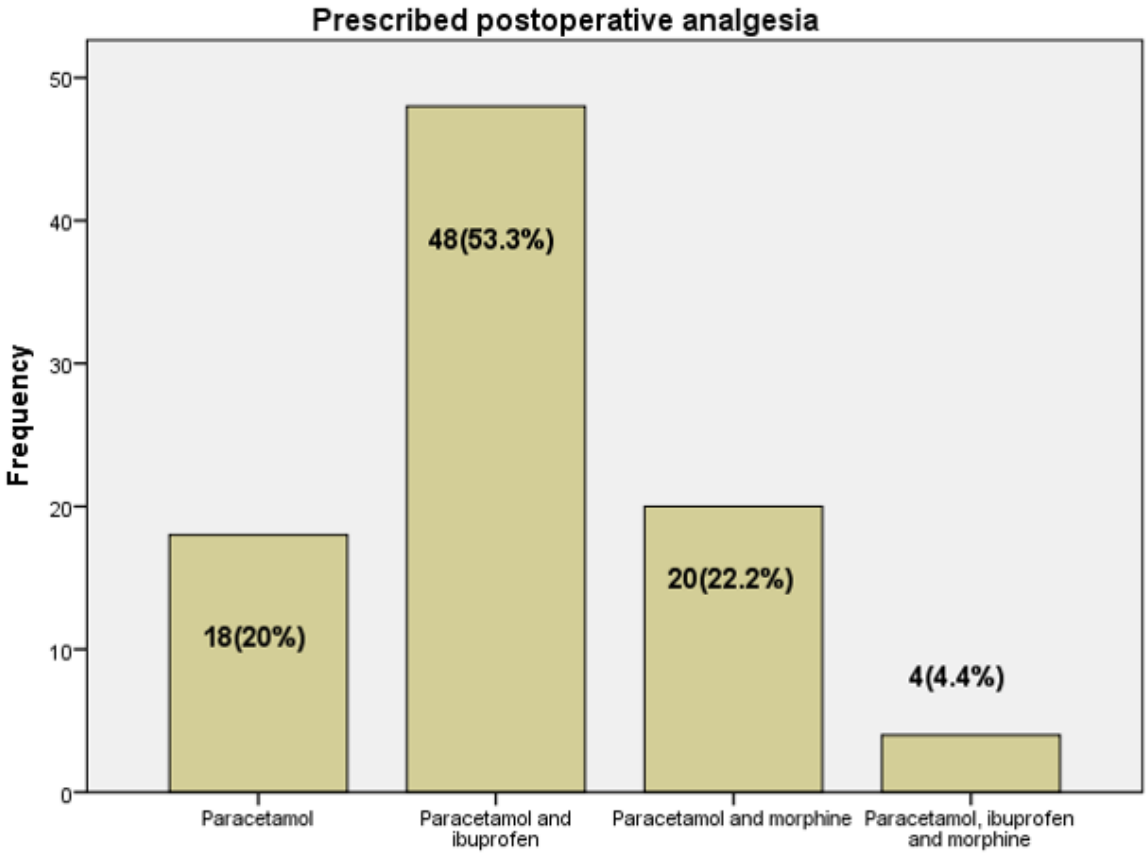


Figure 6 shows that majority of patients received only paracetamol and ibuprofen (53.3%) while opioid analgesics were only received in 26.6% of patients since 73.3% of patients received paracetamol and ibuprofen or paracetamol only

**4.4 Factors associated with the use of opioid analgesics in pediatric patients who are on the multimodal analgesia.**

| Variable | Category | Were opioids added | | | | |
|---|---|---|---|---|---|---|
| | | No | | Yes | | |
| | | Count | Percentage | Count | Percentage | p-value |
| Age group | </=24 | 40 | 59.7% | 2 | 8.7% | **<0.001** |
| | > 24 | 27 | 40.3% | 21 | 91.3% | |
| Sex | Female | 27 | 40.3% | 12 | 52.2% | 0.321 |
| | Male | 40 | 59.7% | 11 | 47.8% | |
| Pain assessment tool used | VAS | 4 | 6.0% | 5 | 21.7% | **0.007** |
| | FLACC | 47 | 70.1% | 18 | 78.3% | |
| | CRIES | 16 | 23.9% | 0 | 0.0% | |
| AVERAGE PAIN SCORE | </=2 | 64 | 95.5% | 15 | 65.2% | **<0.001** |
| | >2 | 3 | 4.5% | 8 | 34.8% | |
| Grade of severity | No pain | 21 | 31.3% | 3 | 13.0% | **0.004** |
| | Mild | 46 | 68.7% | 17 | 73.9% | |
| | Moderate | 0 | 0.0% | 3 | 13.0% | |
| Pain control level | Controlled | 67 | 100.0% | 23 | 100.0% | NA |
| Surgical intervention | Emergency | 11 | 16.4% | 4 | 17.4% | |
| | Elective | 56 | 83.6% | 19 | 82.6% | **0.012** |
| Type of anesthesia | General | 67 | 100.0% | 23 | 100.0% | NA |
| Multimodal analgesia | Local infiltration | 34 | 50.7% | 13 | 56.5% | 0.229 |
| | None | 33 | 49.3% | 10 | 43.5% | |
| Duration of intervention | </= 2h | 54 | 80.6% | 13 | 56.5% | **0.04** |
| | >2h | 13 | 19.4% | 10 | 43.5% | |

Table 3: Factors associated with the use of opioid analgesics in pediatric patients who are on the multimodal analgesia

Table 3 shows that factors associated with opioid use were age group (more than 24 months old, 91.3%, p-value <0.001), used pain assessment tool ( FLACC, 78.3%, p-value=0.007), Average pain score (</=2, 65.2%, p-value<0.001), pain severity (mild, 73.9%, p-value=0.004), type of surgery (elective, 82.6%, p-value=0.012, duration of intervention(</= 2h, 56.5%, p-value=0.04).

**4.5 The rate of complications related to uncontrolled pain**.

For all patients who were enrolled in the study, no complication related to uncontrolled pain was identified.

## CHAPTER V: DISCUSSION

Controlling pain in the postoperative period is of paramount importance as it enhances the quick recovery of patients after surgery. It is in this framework, in our setting we are trying to look for ways which can help improve the postoperative management of pediatric patients. The limited use of opioid analgesics was one of the alternative.

This study aimed at determining the level of pain control when multimodal analgesia with restrictive use of opioid analgesics was used for pediatric patients who underwent major abdominal surgeries.

In our study, it was found that the pain was controlled for all patients who were recruited. The explanation behind this is that opioid analgesics were prescribed on a case by case basis following evaluation by the treating team: where the team judged that opioid analgesics were required to achieve pain control; they were given.

The use of local anesthetics as part of a multimodal analgesia approach by infiltrating the wound with local anaesthetics was done in 52.8%. For the remaining cases, the treating team didn't opt to do infiltration of the wound with local anesthetics like in cases of peritonitis where the wound is dirty.

Among factors which influenced the use of opioid analgesics, the age was found to be one of them. We have found that prescription of opioid analgesics was much less in the younger patients. Older patients tended to have more opioids analgesics prescribed in their pain management plans. Difference in opioid analgesics prescription by age group was found to be statistically significant.

In a study done in Australia by Jane Bell, Simon P Paget, Timothy C Nielsen, Nicholas A Buckley, John Collins, Sallie-Anne Pearson and Natasha Nassar about prescription opioid dispensing in Australian children and adolescents showed that the prevalence of dispensing opioid analgesics was greater for older ages comparing with younger ages [35].

In a study done in German by R Sittl , J Tillig, H Huber, N Grießinger, G Braun, A Katalinic about PRN analgesic drug administration and PCA in children and adults following surgery for funnel chest, in their results they showed that children were receiving less opioid analgesics compared with adults. Within the same study also they showed that adults were receiving the highest total dosage of opioid analgesics compared with children [30].

With the findings of the above studies, there are similarities with the results of our study because they are showing that the rate of opioid analgesics prescription was lower for young ages. For old ages, the rate of opioid analgesics prescription was high.

It is obvious that worldwide, the fear related to the prescription of opioid analgesics to the young ages exists, which has been the same case also for our setting.

The other factor which influenced the use opioid analgesics was the duration of the procedure. It was obvious that for all procedures which took more than 2 hours, the use of opioid analgesics has increased comparing with procedures which took less than 2 hours. The duration of the intervention was also statistically significant.

Most of the procedures associated with long duration were more complexes which implies the use of opioid analgesics in the post-operative period.

The fact that the surgical intervention being either emergency or elective was also influencing the use of the opioid analgesics to the multimodal analgesia used after surgery. It was obvious

that for emergency cases, opioid analgesics were more included in the multimodal analgesia plans comparing with elective cases. This was also statistically significant.

For our study, no complication was found among those which were expected. The reason behind is that pain was controlled for all patients who were enrolled in the study. All complications were not investigated because there are some which are expected on the long term basis whereas for us we were focusing on the immediate post-operative period (that's within the first three days after surgery).

# CHAPTER VI: CONCLUSION AND RECOMMENDATIONS

## 6.1 Conclusion

Our study has shown that multimodal analgesia with restrictive use of opioid analgesics was able to control pain in patients who underwent major abdominal surgery.

The age of the patients has been identified as one of the factors that was influencing the use of opioid analgesics in the multimodal analgesia plans.

Addition of opioid analgesics in the post-operative multimodal analgesia plans was depending on the treating doctor's appreciation and there was no consensual protocol for the inclusion of this class of analgesics in the post-operative pain management plans.

Our study also revealed that infiltration of the wound with local anesthetics as a component of multimodal analgesia was the only one which was used among the loco-regional anesthesia.

## 6.2. Recommendations

We recommend that the multimodal analgesia with restrictive use of opioid analgesics should be promoted and comprehensive protocols developed to this end.

We recommend that pain assessment tools should be used for all patients in the post-operative period in order to optimize post-operative pain control.

We recommend that other methods of loco-regional analgesia like epidural analgesia, or intra-thecal injection of opioid analgesics would be included in multimodal analgesia plans for pediatric patients.

## CHAPTER VII: REFERENCES


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**APPENDIX 1: DATA COLLECTION SHEET**

Date: ……./…../……..

**Project title: MULTIMODAL ANALGESIA WITH RESTRICTIVE USE OF OPIOID ANALGESICS: ASSESSMENT OF LEVEL OF PAIN CONTROL IN PEDIATRIC PATIENTS UNDERGOING MAJOR ABDOMINAL SURGERIES AT CHUK.**

**Clinical data** Code: ……/……/…….

- Age (in years, months or days): …….
- Sex: Male ☐ Female ☐
- Pain assessement tool used: **Visual Analogue Scale (VAS)** ☐

  **FLACC behavioural Pain Score** ☐ **The CRIES pain scale** ☐

  Day 1: Pain score= Grade of severity: …….

  Pain score= Grade of severity: …….

  Pain score= Grade of severity: …….

  Day 2: Pain score= Grade of severity: …….

  Pain score= Grade of severity: …….

  Pain score= Grade of severity: …….

  Day 3: Pain score= Grade of severity: …….

  Pain score= Grade of severity: …….

  Pain score= Grade of severity: …….

  Conclusion: Pain controlled ☐ Pain not controlled ☐
- Diagnosis:……
- Intervention done:……
- Type of surgical intervention: Emergency ☐ Elective ☐
- Type of anesthesia: General anesthesia ☐ Spine anesthesia ☐
- Duration of the procedure:……..
- Type of multimodal analgesia started perioperatively:

  Local infiltration ☐ Caudal block ☐ Epidural analgesia ☐
- Prescribed post-op analgesia:……
- Were opioid analgesics added to the above multimodal analgesia?: Yes or No
- Were they received by the patient?: Yes or No
- Were opioid analgesics prescribed as PRN?: Yes or No
- Were they received by the patient?: Yes or No
- Is there any complications related to uncontrolled pain? Yes or No

- Which one of the following? (respiratory distress, desaturation, lung atelectasis, pulmonary infection, hypertension, tachycardia and increases in urinary retention)
  .....

**APPENDIX 2: ASSSENT FORM**

Project title: **MULTIMODAL ANALGESIA WITH RESTRICTIVE USE OF OPIOID ANALGESICS: ASSESSMENT OF LEVEL OF PAIN CONTROL IN PEDIATRIC PATIENTS UNDERGOING MAJOR ABDOMINAL SURGERIES AT CHUK.**

Investigators: Dr MWISENSEZA Philemon, Dr NTAGANDA Edmond,
Dr URIMUBABO Christian
Tel: +250788638790/ +250731053082
Email: pmwiseneza@gmail.com

We are doing a research on assessment of the level of pain control in pediatric patients undergoing major abdominal surgery at CHUK when multimodal analgesia with restrictive use of opioid analgesics is applied. If you decide to be part of this study, you will be asked by a clinician to answer questions related to the study.

You can ask questions any time, now or later. You can talk to the doctors, your family or someone else. If you do not want to be in this study, no one will be mad at you because it is your right. We will also ask your parents if they would like you to be in the study. Even if you say yes now, you can change your mind later.

When we finish this study, we will write a report about what was learnt. This report will not include your name or that you were in the study.

**ASSENT**

I want to take part in this study. I know I can change my mind at any time.

**Names of the child**:

……

**Verbal assent given**: Yes

**Names of the next of keen and signature:**

……

Date: …/…/……

I confirm that I have explained the study to the participant to the extent compatible with the participant understands, and that the participant has agreed to be in the study.

**Names of the person obtaining the assent and signature:**

……

Date: …/…/……

**If you have questions about the study, contact:**

Dr MWISENEZA Philemon
University of Rwanda, Postgraduate Trainee in Surgery
Telephone: +250 788638790/+250731053082
Email: pmwiseneza@gmail.com

**If you have questions about your rights in the study, contact*:***

Professor Jean Bosco GAHUTU
Chairperson, Institutional Review Board Telephone: + 250783340040
Francois Xavier Sunday
Secretary, Institutional Review Board Telephone: +250788563311
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P.O. Box 3286Kigali, Rwanda
Email: researchcenter@ur.ac.rw
Website: http://cmhs.ur/ac/rw/

**APPENDIX 3: ICYEMEZO CYUBURENGANZIRA BWO KWINJIRA MUBUSHAKASHATSI (munsi y imyaka 18)**

**UMUTWE W' IBYIGWA**: **Gusuzuma urwego rw'ububabare mu bana babazwe mu nda muri CHUK igihe haba hifashishijwe uburyo bwo kubagabanyiriza ububare hadakoreshejwe imiti ifite ubukana bukakaye(izwi nka opioid mu ndimi z'amahanga) ku gipimo cyo hejuru**.

Abashakashatsi: Dr MWISENEZA Philemon, Dr NTAGANDA Edmond,
Dr URIMUBABO Christian
Telefoni: +250788638790/+250731053082

Turakora ubushakashatsi kubijyanye no gusuzuma urwego rw'ububabare mu bana babazwe mu nda muri CHUK igihe haba hifashishijwe uburyo bwo kubagabanyiriza ububare hadakoreshejwe imiti ifite ubukana bukakaye(izwi nka opioid mu ndimi z'amahanga) ku gipimo cyo hejuru. Niwemera kwitabira ubu bushakashatsi, umuganga azagira ibibazo akubaza bijanye n' indwara ufite anagusuzume. Ushobora kubaza abaganga cyangwa umuryango wawe, cyangwa undi muntu uwo ariwe wese, igihe icyo aricyo cyose.

Ntabwo ari itegeko kwitabira ubu bushakashatsi. Ntawe uzakurakarira ntuba utabyitabiriye. Tuzabaza n'ababyeyi bawe niba bemera ko witabira ububushakashatsi. Nubwo wakwemera ubu, wemerewe kuva muri ubu bushakashatsi igihe cyose ushakiye.

Niturangiza ubu bushakashatsi, tuzandika amakuru y' ibyo twabonye ariko izina ryawe ntaho rizagaragara.

Kwemera mu magambo byabaye: Yego

Izinary'umwana……

Izina ry'uhagarariye umwana n'umukono:

……

Itariki …… / ……. /……

Ndemeza ko nsobanuriye uwitabiriye ubu bushakashatsi kurwego abisobanukirwa bituma abasha gufata icyemezo cyo kwemera cg guhakana kwitabira.

Amazina n'umukono by' uwasobanuriye umwana:

……

Itariki: ……/…..../……

**Ukeneye ibindi bisobanuro wabaza:**

Dr MWISENEZA Philemon
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Telephone: +250 788638790
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**Mu gihe uburenganzira bwawe butakubahirizwa wabaza:**

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Francois Xavier Sunday
Secretary, Institutional Review Board Telephone: +250788563311
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Website: http://cmhs.ur/ac/rw/

## APPENDIX 4: ETHICAL APPROVAL FROM UR-CMHS

UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DIRECTORATE OF RESEARCH & INNOVATION

*CMHS INSTITUTIONAL REVIEW BOARD (IRB)*

Kigali, 18th/August/2020

**Dr Mwiseneza Philemon**
**School of Medicine and Pharmacy, CMHS, UR**

**Approval Notice: No 281/CMHS IRB/2020**

Your Project Title ***"Multimodal Analgesia with Restrictive Use of Opioid Analgesics: Assessment of Level of Pain Control in Pediatric Patients Undergoing Major Abdominal Surgery at CHUK"***, has been evaluated by CMHS Institutional Review Board.

| | | Involved in the decision | | |
|---|---|---|---|---|
| | | | No ( Reason) | |
| **Name of Members** | **Institute** | Yes | **Absent** | **Withdrawn from the proceeding** |
| Prof Kato J. Njunwa | UR-CMHS | X | | |
| Prof Jean Bosco Gahutu | UR-CMHS | | X | |
| Dr Brenda Asiimwe-Kateera | UR-CMHS | X | | |
| Prof Ntaganira Joseph | UR-CMHS | X | | |
| Dr Tumusiime K. David | UR-CMHS | X | | |
| Dr Kayonga N. Egide | UR-CMHS | X | | |
| Mr Kanyoni Maurice | UR-CMHS | | X | |
| Prof Munyanshongore Cyprien | UR-CMHS | X | | |
| Mrs Ruzindana Landrine | Kicukiro district | | X | |
| Dr Gishoma Darius | UR-CMHS | X | | |
| Dr Donatilla Mukamana | UR-CMHS | X | | |
| Prof Kyamanywa Patrick | UR-CMHS | | X | |
| Prof Condo Umutesi Jeannine | UR-CMHS | | X | |
| Dr Nyirazinyoye Lactitia | UR-CMHS | X | | |
| Dr Nkeramihigo Emmanuel | UR-CMHS | | X | |
| Sr Maliboli Marie Josee | CHUK | X | | |
| Dr Mudenge Charles | Centre Psycho-Social | X | | |

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 14th August 2020, **Approval has been granted to your study.**
Please note that approval of the protocol and consent form is valid for **12 months**.

Email: researchcenter@ur.ac.rw P.O Box 3286 Kigali, Rwanda www.ur.ac.rw

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 18th August, 2020

Expiration Date: The 18th August 2021

Dr Stefan

For: Professor GAHUTU Jean Bosco
**Chairperson Institutional Review Board,**
**College of Medicine and Health Sciences, UR**

Ce:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

## APPENDIX 5: ETHICAL APPROVAL FROM CHUK

CENTRE HOSPITALIER UNIVERSITAIRE
UNIVERSITY TEACHING HOSPITAL

Quality Health Care
Training & Research

Ethics Committee / Comité d'éthique

16,Oct,2020 *Ref.:EC/CHUK/084/2020*

***Review Approval Notice***

**Dear Philemon MWISENEZA,**

*Your research project: "**Multimodal analgesia with restrictive use of opiod analgesics: Assessment of the level of pain control in pediatric patients undergoing major abdominal surgery at CHUK.** "*

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 16,Oct,2020 to evaluate your request for ethical approval of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your research project.

You are required to present the results of your study to CHUK Ethics Committee before publication by using this link:www.chuk.rw/research/fullreport/?appid=180&&chuk.

PS: Please note that the present approval is valid for 12 months.

Yours sincerely,

**Dr Emmanuel Rusingiza Kamanzi**
The Chairperson, Ethics Committee,
University Teaching Hospital of Kigali

ETHICS COMMITTEE
CHUK

*Scan code to verify.*

*" University teaching hospital of Kigali Ethics committee operates according to standard operating procedures (Sops) which are updated on an annual basis and in compliance with GCP and Ethics guidelines and regulations "*