SCHEDULED AROUND THE CLOCK VERSUS ROUTINE ANALGESIC DOSING FOR POST CAESAREAN PAIN CONTROL AT KENYATTA NATIONAL HOSPITAL,
A RANDOMISED CLINICAL TRIAL

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A research dissertation submitted in partial fulfilment of Masters of Medicine degree in Obstetrics and Gynaecology, School of Medicine, University of Nairobi.

DECLARATION AND SUPERVISORS APPROVAL

This dissertation undertaken in partial fulfilment of the Masters of Medicine in Obstetrics and Gynaecology, is my original work, and has not been undertaken or presented for a degree in any other university.

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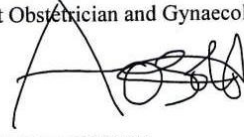
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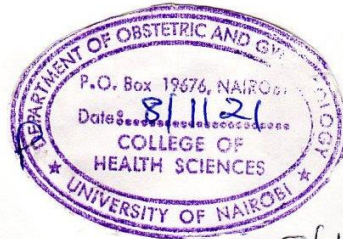Senior Lecturer-Department of Obstetrics and Gynaecology, University Of Nairobi.

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DEDICATION

To my late Dad Mulunda, my mom Nafuna, my siblings, my husband Andembe and our lovely children Jayson and Hadassah.

LIST OF ABBREVIATIONS

ACOG - The American College of Obstetricians and Gynaecologists

APS - American Pain Society

CS - Caesarean Section

IASP - International Association for the Study of Pain

KNH - Kenyatta National Hospital

NICE - The National Institute for Health and Care Excellence

NSAIDS - Non-Steroidal Anti-Inflammatory Drugs

PACU - Post Anaesthesia Care Unit

PRN - Pro Re Nata

PROSPECT - Procedure Specific Postoperative Pain Management

SATC - Scheduled Around the Clock

SPSS - Statistical package for social sciences

UoN - University of Nairobi

VAS - Visual Analogue Scale

WHO - World Health Organisation

OPERATIONAL DEFINITIONS

Around The Clock Medication: Medication given at regular schedule through the day and may include a dose at night.

Baseline Pain: The average pain intensity experienced for a duration of twelve or more hours in a day.

Breakthrough Pain: Sudden intense spikes of pain in patients on prescribed pain medication.

Caesarean Section: A procedure done to deliver a baby through surgical incisions made in the abdomen and uterus.

End of Dose Failure: The level of pain relief is not enough in the last few hours before administration of the next dose.

Labour: The process that leads to childbirth. Normal labour refers to spontaneous onset of regular uterine contractions increasing in frequency and intensity accompanied by descent of presenting part and cervical dilatation and ends with delivery of the baby and expulsion of the placenta.

Multimodal Pain Treatment: The use of two or more therapeutic interventions concurrently each with a different mechanism of action on the pain pathway within one discipline.

Scheduled Dosing of Medication: Maintenance doses administered according to a standard repeated cycle of frequency.

Unimodal Pain Treatment: Refers to a single analgesic therapeutic modality directed at a specific pain mechanism.

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ABSTRACT

Background: Post caesarean pain management is still suboptimal despite the available knowledge, research and advanced therapeutic methods. Current guidelines advocate for multimodal approach to postoperative pain treatment. At Kenyatta National Hospital, the procedure specific pain protocol for caesarean section is multimodal but not scheduled and with marked diversity in post caesarean analgesic prescription. A scheduled around the clock multimodal analgesic regimen ensures continuous pain control with optimal doses of analgesia, reduces end of dose treatment failure and opioid consumption.

Objective: To compare the differences in mean pain scores between post-caesarean patients randomized to scheduled around the clock versus routine analgesia at the Kenyatta National Hospital.

Methods: A single blind parallel, randomized controlled trial was carried out at the Kenyatta National Hospital maternity unit. Ninety-eight patients scheduled for caesarean delivery were randomised into scheduled around the clock or routine analgesia study arm. Scheduled around the clock group received six hourly subcutaneous morphine for 12 hours followed by intravenous paracetamol six hourly and rectal diclofenac 12 hourly for 24 hours. The routine arm received analgesics as prescribed by the operating surgeon and mean pain intensity scores evaluated before the first analgesic dose, at 4, 10, 24 and 48 hours using the visual analogue scale. Satisfaction with pain management was evaluated using a Likert scale at 72hrs after the surgery. Data was analysed using Statistical Package for Social Scientists software, version 25. Demographic data of patients who received scheduled around the clock analgesia and routine analgesia were compared using the Fishers test and age identified as a potential confounder. The Fishers Exact test and Cox regression were used to compare the mode of anaesthesia of patients on scheduled around the clock analgesia and routine analgesia. The independent samples T test and Analysis of Covariance were used to compare dosage of analgesia of patients on scheduled around the clock analgesia and routine analgesia, with the Fishers Exact test and Cox regression used to compare satisfaction with management of patients on scheduled around the clock and routine analgesia at 95% confidence level. All analyses were intention to treat.

Results: Between September and November 2019, 101 patients were screened and 98 randomized. The mean age was statistically significantly lower among patients who received routine analgesia, 26.7 (SD 5.5) compared to scheduled around the clock analgesia, 30.3 (SD 6.1), P<0.01. Scheduled around the clock had lower mean pain scores compared to routine analgesia at four hours, 3.6 (SD 2) vs 4.8 (SD 2.6), P<0.01). At 10 hours (4.2 vs 4.6), 24 hours (3.1 vs 3.6) and 48 hours (1.9 vs 2.4), the mean pain scores were lower for SATC than routine groups but not significant statistically. The mean (SD) dosage of prescribed morphine was significantly lower in scheduled around the clock, 2 (0) than routine group 2.9 (0.4) P<0.01. Prescribed diclofenac doses were significantly more for scheduled around the clock group mean 5 (SD 0) than routine mean 4.4 (SD 1.2) P<0.01.The dose of rescue diclofenac was higher in the routine than scheduled analgesia group mean 1 (SD 0) vs 4(SD 0) P<0.01. Side effects were similar between the two treatment regimens.

Conclusion: Scheduled around the clock analgesia significantly reduced mean pain scores at 4 hours, rescue analgesia and opioid consumption compared to routine analgesia.

Recommendation: We recommend the use of multimodal analgesia in a scheduled around the clock fashion to prevent and treat post caesarean pain.

Trial registration: PACTR202006496208237

CHAPTER ONE: INTRODUCTION

1.1 Background

Pain is an unpleasant sensation and emotional experience resulting from actual or potential tissue injury. Pain is also subjective (IASP). Post-operative pain can be categorised into acute commencing right after operation to 7 days and chronic pain that lasts more than three months after surgery.(1) The goal of post-surgical pain management is to prevent the occurrence of pain and control pain. Benefits of effective pain management include faster recovery, reduced morbidity, early discharge from hospital and decreased cost with better use of resources. Post-operative pain management is still suboptimal despite available knowledge and potent pain medication and non-pharmacological methods of managing pain.(2).

Globally more than fifty percent of patients undergoing surgery experience moderate to severe post-operative pain. Seventy-five to eighty percent of patients report acute pain after surgery. Trauma and surgery are major contributors to the global pain burden. At KNH in 2013, Mbugua conducted a cross sectional survey of 166 patients undergoing different surgeries including obstetrics and gynaecology under general anaesthesia to determine the prevalence of moderate to severe pain and adequacy of intra-operative pain management among different surgical disciplines. 10.8 % of postoperative patients reported severe, 29.9% moderate and 46.6% mild pain. The association between observed pain score and surgical speciality was not statistically significant.(3)

Multimodal or balanced analgesia, the use of at least two analgesics with different mechanisms in the pain pathway to achieve superior analgesic effect while decreasing adverse effects of individual drugs is currently the globally advocated method of postoperative pain management as opposed to unimodal treatment(4)

Pain medication should be administered on fixed regular time interval as opposed to as needed method to control baseline pain. WHO advocates for administration of analgesics around the clock. In early postsurgical period, analgesic dosing by the clock will protect from severe pain and control baseline pain.

Time scheduling of analgesics ensures steady presence of pain medication in patients system, which protects against sub optimal pain treatment and overdosing. Other benefits include reduction in severe pain, use of lower doses of medication and a decrease in side effects of drugs.

Inadequate pain treatment may result from inadequate pain assessment and inappropriate use of analgesics. Most regional studies cite discrepancies between prescription and actual analgesic administration, lack of standardised practice, absence or stock outs of pain medication and poor knowledge and attitudes among professionals as barriers to adequate pain control. (5)(6)(7)

This study proposes the of use available analgesics at the right time intervals, favourable routes of administration and regular pain assessment in a regimen to achieve adequate post-caesarean control.

2 CHAPTER TWO: LITERATURE REVIEW

2.1 Pain Pathway

Following injury, pain impulses are transmitted to the dorsal horn of spinal cord by A-delta and C fibres of primary afferent neurons.(8) . Synapse with second order neurons in the dorsal horn of the spinal cord primary afferent fibres. Second order neurons cross over to the contralateral side of the spinal cord and ascend via spinothalamic and spinoparabrachial pathways to the reticular activating system and thalamus. Processing of somatosensory information takes place in the thalamus. Perception of pain and interaction occurs in the cortex. Descending tracts are important in pain modulation and result in inhibition of pain impulse transmission in the spinal cord.

Opiate receptors are widely located in the brain, spinal cord and peripheral neurons. Opiate receptors activation at the interneuron level leads hyperpolarisation with resultant inhibition of neuronal firing and the release of substance P, culminating in blocking pain transmission. Pathophysiology of Postoperative Pain. Perioperative pain results from inflammation caused by tissue injury or nerve damage. Local tissue injury cause stimulation of pain receptors by release of chemical inflammation mediators, production of noxious stimuli and irritation of free nerve endings (8).

Inflammatory mediators can produce hyperalgesia (increased sensitivity to pain to stimulus) or allodynia (pain perception to non-painful stimuli). Postoperative pain may originate from injury to skin or deeper structures. Nociceptive somatic pain arises from skin, mucous membranes, muscles, bones and tendons. Nociceptive visceral from thoracic, abdominal and pelvic organs and neuropathic pain caused by damage or disease of nervous system. Postoperative pain is usually a combination of several types of pain. Patient education and regular staff training on pain, the use of multimodal analgesia and pain assessment at regular intervals during treatment contribute to effective post-operative pain management(1). Barriers to effective pain management include inadequate, excessive dosing interval, patient reluctance to request analgesia, attitudes and education barriers on physician and patients' and intrinsic limitation of available techniques (9)(10). Clinicians' knowledge on analgesics onset, peak and duration of action and side effects is important in effective pain management.

2.2 Consequences of Postoperative Pain

Postoperative pain treated inadequately has physiological, psychological, economic and social consequences for patients, the hospital and society (9). Suboptimal acute pain control impairs patient function and quality of life, prolongs recovery time with risk prolonged opioid use and is associated with increased morbidity (10). Changes in multiple organs systems noted with sub optimally managed acute pain including cardiovascular, pulmonary, gastrointestinal, renal, immunology and coagulation.(10). In some patients, poorly controlled acute postoperative pain has also been linked to development of chronic and or persistent pain.(11).

2.3 Multimodal Analgesics Mechanisms of Action

Pharmacologic agents used in postoperative pain management act on various points on the pain pathway to treat pain.

2.3.1 Opioid analgesics

Opioids are group of pain-relieving drugs that work by interacting with opioid receptors in the cells. They stimulate mu receptors throughout the central nervous system. Commonly used pure opioid agonists include morphine, hydromorphone, meperidine and fentanyl. Currently, opioids remain the main analgesics used for postoperative pain management. Opioids produce analgesia by mimicking the effect of endogenous opioids at specific central and peripheral opioid receptors. Sufficient doses of potent opioids will relieve most types of postoperative pain with tolerable side effects.

There are tremendous variations in dose of opioid required to control post-operative pain due to variations in pharmacokinetics and pharmacodynamics.(12). Some patients may respond certain opioids but be intolerant to others. Furthermore switching from one opioid to another may show improved symptoms and record a decrease in side effects. This calls for an individualised approach in pain treatment with opioids.

Different routes may be used administer opioids. The intramuscular route is unpredictable with wide swings in drug concentration but commonly used in clinical settings. The intravenous route gives more constant blood levels. Patient-controlled analgesia (PCA) is a method of delivering pain medication. Patients receive predetermined doses of pain medication to relieve pain by pressing a button on a computerized pump connected to a tube in the body. It is preferred due to superior analgesic effects with constant analgesic levels in patients system. IV PCA is however invasive, requires frequent monitoring and may limit patient mobility. PCA is not available universally and in the study setting.

2.3.2 Non-opioid analgesics

Paracetamol and Non-Steroidal Anti-Inflammatory Drugs (NSAIDS) are recommended for use as part of multimodal regimens. They may be used for low intensity pain, and in combination with opioid or local analgesia for high intensity pain.

NSAIDS act by blocking the action of enzyme cyclooxygenase, which converts arachidonic to prostaglandins. Prostaglandins cause pain, fever, vasodilation in response to trauma. NSAIDS may also exert central analgesic effect and provide an additional opioid sparing effect.

Ketamine is an anaesthetic agent that acts by inhibiting the N-methyl-D-aspartate (NMDA)-gated calcium channel with hypnotic, analgesic, and amnestic effects. NMDA receptors are involved in the changes in neuronal excitability and the development of allodynia and hyperalgesia.

Local anaesthetics are used in a variety of procedures, in peripheral nerve blocks and as neuraxial anaesthetics. Lidocaine acts by blocking sodium channels. IV lidocaine has analgesic, anti-hyperalgesia, and anti-inflammatory properties that make it a potential option for perioperative pain control.

Anticonvulsants (gabapentin and pregabalin) are used as adjuncts in multimodal analgesics. They bind to voltage-gated calcium channels and promote anti-nociceptive actions by inhibiting the release of excitatory neurotransmitters. When used in postoperative pain management they reduce acute pain and opioid use.

2.4   Current Recommendations on Post-operative Pain Management

Dr John Bonica, considered the father of modern pain management, cited improper or inadequate application of available information and advanced therapies as the cause of ineffective pain management.

IASP recommends multimodal, procedure-specific analgesia and acute rehabilitation after surgery. For caesarean section, Procedure Specific Postoperative Pain Management [PROSPECT initiative] recommends the use of NSAIDS and or acetaminophen, opioids as rescue and continuous infusion of wound with local anaesthetic.

American pain society [endorsed by American society for regional anaesthesia] advices the use of multimodal analgesia for postoperative pain management. Paracetamol and or NSAIDS recommended for use as part of multimodal analgesia.

Canadian pain society in a position statement support the treatment of pain as a human right with routine assessment and use of patient self-report when possible for effective pain management.

National Institute for Health and Care Excellence [NICE] has no published guidelines but advocate for, in the absence of national guidelines, development of local pain management protocols with prescribing guidance from special pain management team.

American College of Obstetricians and Gynaecologists [ACOG] recommends use of non-pharmacological and pharmacological methods in pain management with stepwise-individualised pain management using multimodal agents.

WHO analgesic ladder recommends adjustment of analgesic according to pain intensity starting from non-opioids, to weak opioids through to strong opioids. Kintu et al conducted a prospective descriptive study of 333 women delivering at Mulago National Referral Hospital in Kampala, Uganda in 2015 to assess pain management. There was diverse use of pain medication with unimodal, multimodal and some patients not receiving pain medication. Pain assessment at 0, 6 and 24 hours using VAS and satisfaction with pain control. At 0hr, pain score was lowest for pethidine only and combination group, highest for tramadol only. At 6h pain score was lowest for tramadol only and highest for intrathecal morphine while at 24h lowest score was recorded for intrathecal morphine group and highest for tramadol only group.

Yefet et al conducted randomised-controlled trial in Israel of women undergoing caesarean delivery under regional anaesthesia between February and December 2013. They compared fixed time interval [6 hourly] to as needed analgesic administration of tramadol, paracetamol and diclofenac for post caesarean pain. The fixed interval group recorded lower mean pain scores (2.8 ± 0.84 versus 4.1 ± 0.48; $P < 0.0001$) and better satisfaction with pain control (9.1 ± 1.2 versus 8.3 ± 1.5; $P < 0.0001$) despite having increased number of analgesic administration. There was no increase in adverse effects for both groups. (13).

Booth et al in 2016 conducted a randomised clinical trial of pregnant mothers delivering by elective caesarean section and predicted to have severe post-operative pain. Patients in the intervention group received a higher dose of spinal morphine [300 mcg] followed by 1-gram acetaminophen 6 hourly for 24 hours after surgery. Patients in the control group received a

lower dose of spinal morphine [150 mcg] followed by placebo tablets. Scheduled ibuprofen and IV morphine patient-controlled analgesia was given in both arms and pain assessed at 24 hours. The intervention group had lower pain record with movement at 24 hours (46 ± 25 mm in control group versus 31 ±17 mm in intervention group, P value= 0.009)(14).

Brie et al, 2016 at Trihealth Good Samaritan Hospital, Ohio, in a randomised controlled trial compared scheduled IV paracetamol to placebo [normal saline] in a multimodal protocol for post caesarean pain with Ibuprofen and oxycodone for breakthrough pain. Results showed decreased narcotic consumption in the scheduled IV paracetamol group 47mg vs 65mg (P 0.034) in the placebo. Both study arms recorded low pain scores [median 1 to 4]. (15)

Valentine et al, 2013 at Stanford University of Medicine, USA conducted a retrospective review of scheduled paracetamol with PRN oxycodone, versus combined acetaminophen-opioid PRN for post caesarean pain in a multimodal regimen. There was decreased opioid use in the scheduled acetaminophen group with more consistent acetaminophen use.(16)

Mitra et al, 2012 in India compared the analgesic efficacy of diclofenac-acetaminophen combination with diclofenac-tramadol combination in a randomized controlled trial of women undergoing caesarean section under spinal anaesthesia. In one arm, patients received rectal suppository diclofenac 100 mg (8 hourly for 24 h) combined with intravenous acetaminophen (1 g 6 hourly). The second group received diclofenac with tramadol (75 mg 6 hourly). The overall pain score was significantly lower in the diclofenac-tramadol group. Consumption of rescue analgesia for breakthrough pain was comparable between the two groups (13% vs. 12%, P value 0.872).(17)

2.5 Pain Assessment

Assessment of pain is a fundamental component of effective pain management. Pain is subjective and multidimensional and patient self-report is the most reliable indicator of pain.

The American Pain Society, American Society of Regional Anaesthesia and Pain Medicine, and the American Society of Anaesthesiologists' Committee on Regional Anaesthesia panel recommend the use of a validated pain assessment tool by clinicians. Assessment allow tracking of responses to postoperative pain treatments and adjustment accordingly.

Validated pain assessment tools include the visual analogue scale, numeric or verbal rating scales and symbols. The choice of a specific pain assessment tool depends on the patients, the setting, considering factors like age, cognitive status, level of consciousness, education level, social-cultural and language differences.

Unidimensional tools measure the intensity of pain and are ideal for acute pain of known aetiology. They include the following:

Numeric pain scale

>Numbers are used to quantify the intensity of pain – zero means no pain and 10 corresponds to the worst pain imaginable

>Six-point NRS (0-5)

>Eleven-point NRS (0-10))

>Twenty-one point NRS (0-20)
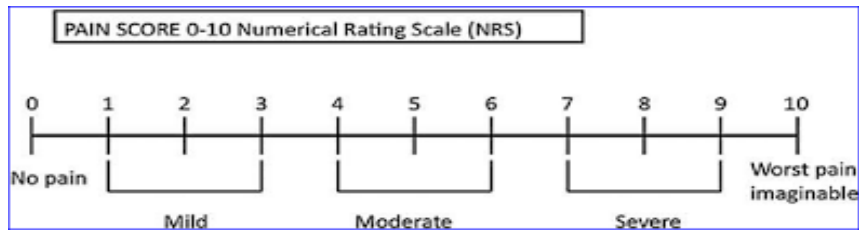
Figure 1: Eleven point Numerical Pain Scale

- Visual analogue scale

    A 10cm or 100mm continuous horizontal line used. Patients' rate pain intensity by putting a mark that best corresponds to the intensity of pain along the line at that particular time.
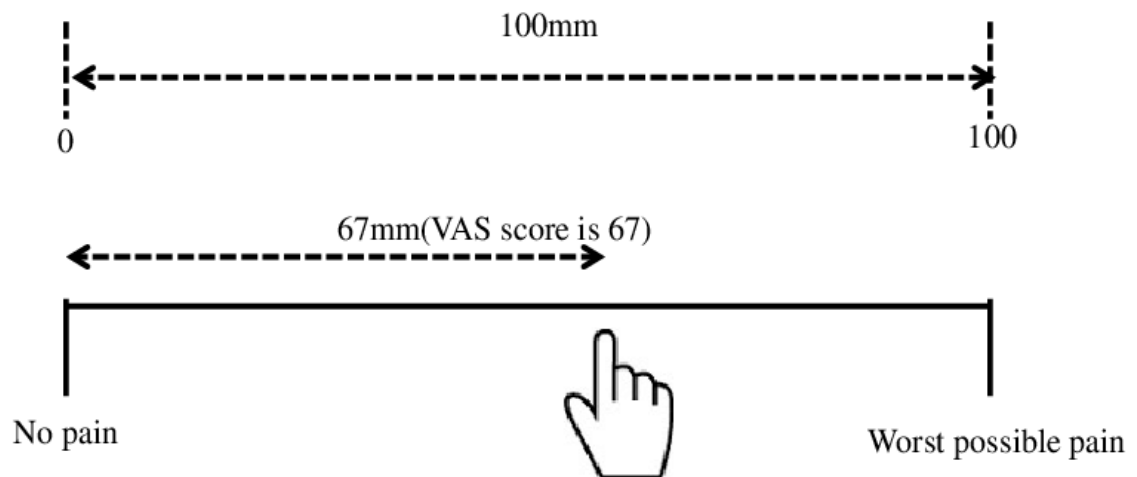
Figure 2: Visual Analogue Scale

- Verbal rating scale

    Patients use adjectives describe pain by marking the adjective that best fits the pain intensity.

    Four-point VRS

Table 1: Four Point Verbal Rating Scale

Pain intensity	Score
No pain	0
Mild pain	1
Moderate pain	2
Severe pain	3
Excruciating pain	4

Figure 3: Wong-Baker FACES Pain Rating Scale

Multidimensional tools measure pain characteristics and impact of function and or quality of life in addition to pain intensity. They encompass the moods, behaviour, thoughts and beliefs. Postoperative pain is a combination of several types of pain and multidimensional tools allow treatment of all aspects of pain.

They include pain assessment tool and flow sheet, brief pain inventory, McGill pain questionnaire, pain/comfort journal and body chart. Below is the McGill pain pain questionnaire, an example of a multidimensional tool with sensory and affective aspects of pain.

SHORT-FORM McGILL PAIN QUESTIONNAIRE
RONALD MELZACK

PATIENT'S NAME:_____   DATE:_____

	NONE	MILD	MODERATE	SEVERE
1. THROBBING	0) ____	1) ____	2) ____	3) ____
2. SHOOTING	0) ____	1) ____	2) ____	3) ____
3. STABBING	0) ____	1) ____	2) ____	3) ____
4. SHARP	0) ____	1) ____	2) ____	3) ____
5. CRAMPING	0) ____	1) ____	2) ____	3) ____
6. GNAWING	0) ____	1) ____	2) ____	3) ____
7. HOT-BURNING	0) ____	1) ____	2) ____	3) ____
8. ACHING	0) ____	1) ____	2) ____	3) ____
9. HEAVY	0) ____	1) ____	2) ____	3) ____
10. TENDER	0) ____	1) ____	2) ____	3) ____
11. SPLITTING	0) ____	1) ____	2) ____	3) ____
12. TIRING-EXHAUSTING	0) ____	1) ____	2) ____	3) ____
13. SICKENING	0) ____	1) ____	2) ____	3) ____
14. FEARFUL	0) ____	1) ____	2) ____	3) ____
15. PUNISHING-CRUEL	0) ____	1) ____	2) ____	3) ____

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|————————————————————————————————————————|
0                                        10
NO                                     WORST
PAIN                                 POSSIBLE
                                       PAIN
```

P P I

0	NO PAIN	____
1	MILD	____
2	DISCOMFORTING	____
3	DISTRESSING	____
4	HORRIBLE	____
5	EXCRUCIATING	____
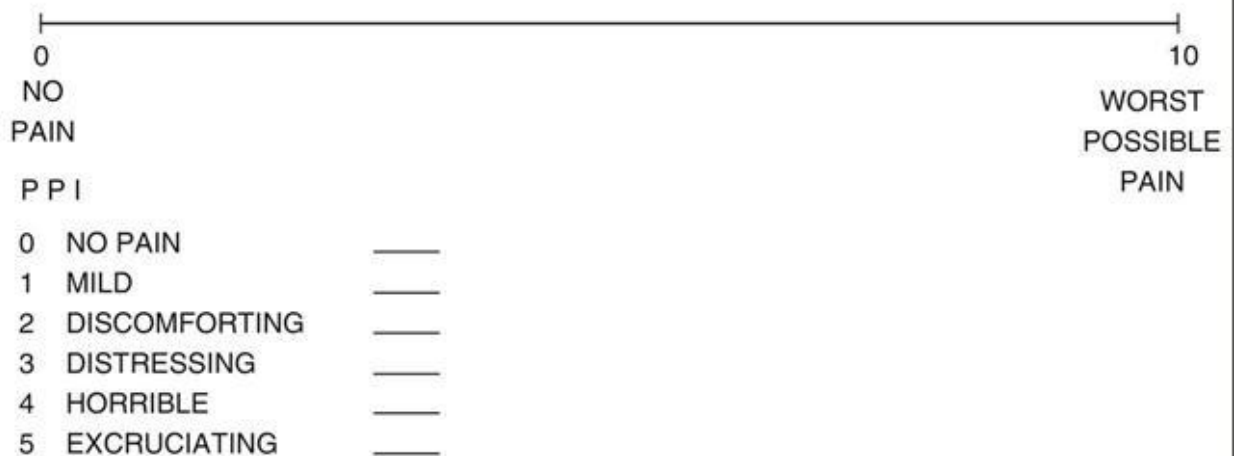
Figure 4: McGill Pain Questionnaire (short form)

2.6 Conceptual Framework

Pain is an unpleasant sensation and emotional experience and is subjective. Socio-demographic, preoperative, intraoperative and postoperative factors affect postoperative pain outcomes. Factors contributing to effective postoperative pain management include a structured pain management team, patient education, regular staff training, use of balanced analgesia and regular pain assessment. Scheduled around the clock pain protocol used shorter dosing intervals and staggering of analgesics to ensure steady analgesic levels in patients system and reduce breakthrough pain. The aim was to achieve adequate pain control, reduce opioid consumption, facilitate faster recovery and successful breastfeeding and bonding between mother and her newborn baby.

CONCEPTUAL FRAMEWORK

Factors contributing to effective pain management
- Use of balanced analgesia
- Pain management team
- Patient education
- Regular staff training
- Regular pain assessment
- Around the clock dosing analgesic administration

PATIENT OUTCOMES

Adequate pain management
- Pain control
- Improved function
- Breastfeeding and bonding with newborn
- Patient satisfaction with pain management
- Faster recovery and hospital discharge
- Reduced morbidity
- Decreased hospital costs

Inadequate pain management
- Moderate to severe pain
- Persistent or chronic pain
- Multiple organ dysfunction
- Negative quality of life

Predisposing factors to pain
- Inappropriate analgesic use
- Inadequate pain assessment
- Lack of standardized practice
- Drug stock outs
- Poor knowledge and attitude

Intra-operative factors affecting pain outcomes
- ASA status
- Length of surgery
- Intra-operative pain treatment
- Type of anaesthesia

Post-operative factors affecting pain control
- Multimodal analgesia
- Non-pharmaceutical methods of pain control
- Around the clock dosing

Figure 5: Conceptual Framework

2.7 Study Justification

Pain control at KNH [Kimani 2013] and in most countries is still inadequate despite advanced knowledge and research in mechanism of pain and its management (Kintu 2015]. This may be due to lack of standardised pain assessment, standardised practise in analgesic prescription and adherence to current analgesic protocol. Globally there is need to reduce opioid overuse and addiction. Tolerance and dependence on opioid analgesics is a growing concern and has been termed an epidemic. Strategies are needed to reduce the need and consumption of opioid analgesics without compromising post-operative pain management. Severe postoperative pain affects the quality of life of mother and new-born baby including bonding and breastfeeding initiation and maintanace.Uncontrolled acute post-operative pain has been shown to increase the risk of chronic persistent pain.

Research on specific combinations of the available analgesics suited for individual patients in our setting are lacking. There are no RCTs on scheduled dosing of analgesia previously conducted at KNH. A randomised trial will evaluate the current post caesarean pain protocol in KNH and identify optimal scheduled dosage regimens to maximise patient care. There are no local or regional RCTs on scheduled around the clock dosing of analgesia in pos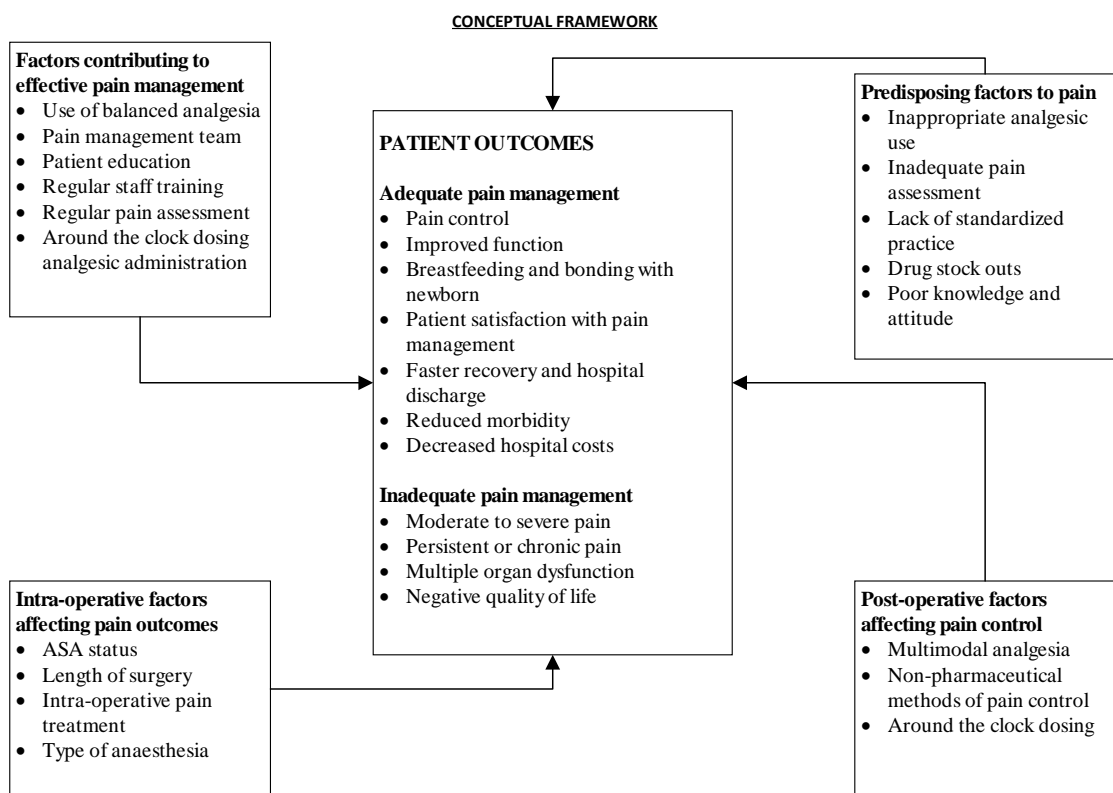t-caesarean pain treatment. In low income countries, with inadequate health care workers and inconsistent supply of pharmaceuticals and non-pharmaceuticals there is need to identify a combination of affordable and available analgesics to manage postoperative pain adequately. Globally there are few studies on scheduled around the clock dosing analgesia in post-operative pain management.

Scheduled around the clock analgesic dosing is recommended for post-caesarean section pain management to prevent and manage baseline pain, allow faster recovery, minimize maternal and neonatal side effects and improve maternal mobility. Multimodal analgesia and schedule dosing have been shown to have opioid sparing benefits. Despite the current KNH post caesarean pain management protocol being multimodal, it is not scheduled. This study evaluated the use of available analgesic agents administered at regular time intervals compared to the routine care to achieve adequate post-caesarean pain control.

2.8 Research Question

Is there difference in post caesarean pain control using scheduled around the clock analgesia compared to routine post-caesarean pain care at KNH?

2.9 Null Hypothesis

There is no difference in post caesarean pain control between patients on scheduled around the clock analgesia compared to routine post-caesarean pain care at KNH

2.10 Study Objectives
2.10.1 Broad Objective
To compare the differences in mean pain scores between post-caesarean patients randomized to scheduled-around the clock versus routine analgesia at KNH

2.10.2 Specific Objectives
2.10.2.1 Primary objectives
Among post caesarean patients receiving scheduled around the clock versus routine analgesics at KNH to compare

1. The mean pain scores at 4, 10, 24 and 48 hours
2. The need for rescue analgesia over a period of 3 days
3. The total analgesic doses used over a period of 3 days

2.10.2.2 Secondary objectives
To evaluate patient satisfaction among post-caesarean patients receiving scheduled around the clock versus routine analgesics at KNH.

3 CHAPTER THREE: METHODOLOGY

3.1 Study Design

A randomised single blind parallel clinical trial assessing the efficacy of scheduled around the clock dosing in management of post-operative pain. The study participants (patients) were blinded to the treatment regimens with an allocation ration of 1:1.

3.2 Study Setting

The study centre was Kenyatta National Hospital maternity wards and theatre. KNH is a teaching hospital for the University of Nairobi, College of Health Sciences. The Obstetrics and Gynaecology department has two operation theatres. Patients admitted from home, the antenatal clinic or referred from peripheral health facilities for caesarean section. Pre-operative preparation for caesarean operation takes place in the antenatal and labour wards for elective and emergency cases respectively. Patients transferred to operating theatre through labour ward for surgery then back to the wards. Post-caesarean patients are nursed in the maternity unit. Approximately twenty cases of caesarean sections are performed every 24 hours. The surgeons are resident doctors in obstetrics and gynaecology and routinely prescribe post-operative analgesics.
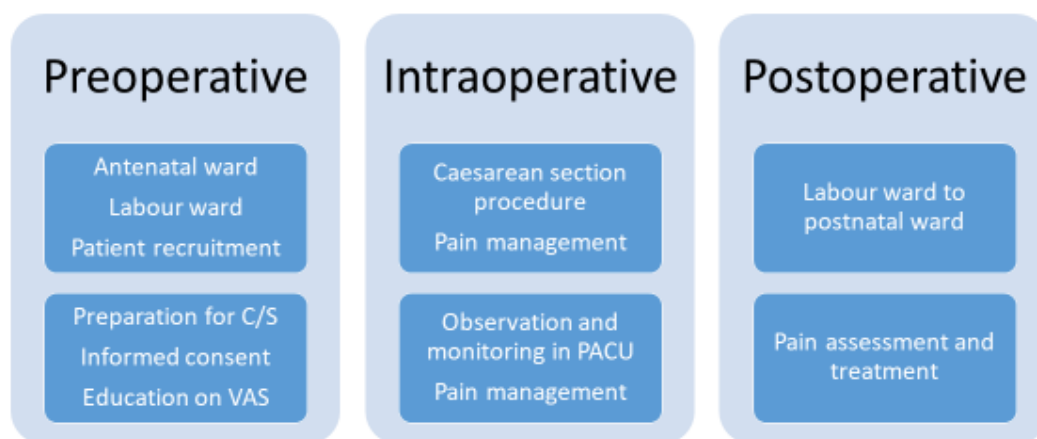
Figure 6: Patient Flow

3.3 Study Population

Patients undergoing elective and emergency caesarean section at KNH.

3.4 Population Characteristics

All expectant women age 18 to 44 years who delivered by caesarean section at Kenyatta National Hospital.

Intervention: Scheduled around the clock group
- Patients received scheduled morphine 10mg 6 hourly for 12 hours post operatively
- Paracetamol 1000mg administered intravenously every 6 hours for 24 hours starting 12 hours after the morphine dose
- Diclofenac rectally 12 hourly given 3 hours after the first paracetamol dose for 24 hours

There was no simultaneous administration of medications to allow for continuous pain control.

Control: Routine care group

Patients received routine analgesia as per the operating surgeon's preference.
- Paracetamol
- NSAIDS
- IV Opioids (Morphine/Tramadol)

Rescue analgesia; Breakthrough pain was managed with Morphine 2mg PRN for both groups.

Local wound infiltration was offered to both groups.

All analgesics administered by clinicians documented and accounted for.
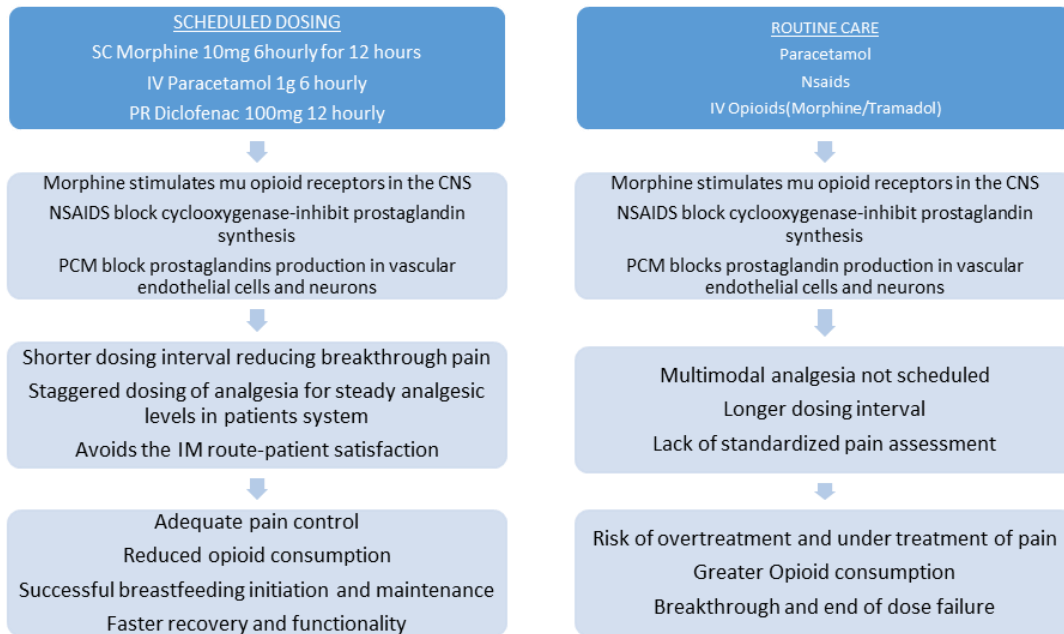
Figure 7: Intervention versus routine care regimens

Pain assessment

The primary outcome of interest was effective pain control for the two groups of patients using visual analogue scale, where score zero corresponds to no pain and 10 is worst pain. Patient education and practice in using the VAS scale took place preoperatively while pain control was assessed postoperatively. Pain intensity was assessed at 0, 4, 10, 24 and 48 hours

by the patients. Pain score above four (4) (moderate intensity) was managed with rescue analgesia if it occurred between prescribed doses.

The total doses of analgesics and doses of rescue analgesics used during the 72 hours of admission were calculated from the study questionnaire. This was collaborated with the patients' treatment charts to ensure all doses used were captured. At the point of discharge the study participants were asked to rate their satisfaction with pain control during admission using on a Likert scale.

3.5   Inclusion Criteria
- Patients undergoing elective and caesarean section
- American Society of Anaesthesiologists status (ASA) I and II
- Patients who gave written informed consent.

3.6   Exclusion Criteria
- Patients known to have adverse reactions or allergy to study medications
- Patients too sick/incapable of providing objective pain assessment e.g. mental retardation, visual and hearing impairment.
- Patients on pain treatment pre-operatively
- Patients on chronic opioid use

3.7   Sample Size Determination

The main outcome of this study was post-operative pain control among patients who had undergone Caesarean delivery at the Kenyatta National Hospital.

The sample size was calculated using the formula for comparing means as below:

$$n_1 = \frac{(r+1)}{r} \frac{\sigma^2 (Z_\beta + Z_{\alpha/2})^2}{\text{difference}^2}$$

Based on a similar study conducted by Jessica L. Booth et al 2016 (18) where there was a statistically significant difference in pain scores between the intervention 31mm and control 46mm groups,

n_1	= Size of survivors group	
r	= ratio of exposed to control group	= 1
σ	= standard deviation of the control group	= 25
Difference = clinically meaningful difference in means of the outcome: 46 – 31		= 15
Z_β	= corresponds to the power of the study	= 80%
nα/2	= corresponds to two – tailed significance level	= 1.96 for α = 0.05

Substituting the above values into the equation gives the sample size n_1

= (1+1) $\frac{25^2 (0.84 + 1.96)^2}{15^2}$

1   15^2

14

$$= 44$$

With a markup of 10% to cater for possible loss of data or crossovers in the study groups.

The recalculated n per arm= 100/90*44 = 49

3.8 Sampling Procedure

Simple random sampling was used to select the sample for the study. Patients admitted in the respective ward for caesarean section were informed about the study. The patients meeting the inclusion criteria and gave verbal consent then proceeded to give written consent.

3.9 Patient Recruitment

Research assistants were stationed at labour ward and three antenatal wards to enrol participants into the study. All patients scheduled for elective caesarean section were eligible to participate in the study if they met the eligibility criteria (inclusion and exclusion).

3.10 Consent Procedure

A pre-designed consent form outlining the study purpose, procedure, potential benefits and possible risks was used to obtain written informed consent. Patient/guardians pertinent questions or concerns regarding the study were addressed. The process was voluntary and free from coercion. Patients who opted out received routine care without discrimination. Enrolled participants were required to give written consent, counter-signed by the investigator. Records kept regarding reasons for non-participation of eligible participants.

3.11 Randomization and Blinding

Research assistants subsequently randomized consenting patients into the two treatment groups. Each patient picked an opaque sealed envelope containing computer generated random sequence codes for the different regimes. The unique codes were generated from a remote computer by the principal investigator. Only the patients were blinded and did not know the treatment regimen group allocated to them.

3.12 Data Variables

Table 2: Exposure, Outcome and Sources of Data Variables

Objective	Exposure variables	Outcome variables	Sources of data variables
Efficacy of post caesarean pain control	Prescribed scheduled analgesic Prescribed routine analgesia	Mean Pain intensity scores by VAS	Patient records Treatment sheets Patient questionnaire
Use of rescue analgesia	Schedule and supplemental doses Prescribed and	Extra doses of analgesia used for breakthrough pain	Patient records

Objective	Exposure variables	Outcome variables	Sources of data variables
	supplemental doses		
Total doses of analgesic used	Schedules ATC Routine care	Total doses of analgesic used in scheduled dosing arm Total doses of analgesic used in routine care	Patient records Pharmacy dispensed records
Patient satisfaction with pain management	Scheduled around the clock Routine care	Participant scores from excellent to poor on a scale of 1 to 5	Questionnaire

3.13 Ethical Considerations

Permission was sought from KNH-UoN ERC to carry out this study research. All information was handled with utmost confidentiality throughout the tenure of the study, held in trust by the investigator, research assistants and the study institution. A password protected computer with access by the primary investigator and research assistant was used. The participants were given study identification numbers and no information concerning the study participants will be released to an unauthorized third party without prior written approval by the study institution or the Ethics Research Committee.

All patient information and identifiers were delinked from the collected data before sending to the data analyst. The study findings have been presented to the University of Nairobi, Department of Obstetrics and Gynaecology as part of the requirement of the postgraduate course. Data and Safety Management Board [DSMB] was be constituted to review and evaluate data for study participant safety, study conduct and progress The study team consisted of members with a valid GCP certificate. Annex V

3.14 Data Collection

Collection of data commenced after obtaining formal permission from KNH administration and ethical clearance. Data was collected in the respective postnatal wards using a structured two-part questionnaire. The first part captured the sociodemographic and clinical parameters while the second consisted the VAS score and patient satisfaction components.

Training of research assistants took place before data collection; they initially observed the process of obtaining informed consent, demonstrating pain scoring to study participants and filling of the questionnaires by the principal investigator. The research assistants collected the

sociodemographic and clinical information from the study participants and patient records after obtaining informed consent.

The patients completed the pain scores, post operatively at the scheduled time intervals. Research assistants were on hand to prompt study participants timeously.

3.15 Quality Assurance

Written informed consent was obtained from each study participant during enrolment into the study ensuring confidentiality and the security of information obtained. Only the principal investigator had access to study materials. A pre-test of the study questionnaire was carried out and necessary corrections made to avoid bias, misinterpretations or ambiguity. Recruited qualified research assistants were trained on; sampling procedure, obtaining consent, data collection and entry procedures. No identifying personal information was disclosed. Verification of information from available patient records was carried out where possible. The primary data collection tool and the study questionnaire will be retained for three years after conclusion of study.

3.16 Data Management

Data were extracted from questionnaires and uploaded into the Statistical Package for Social Scientists software, version 25. Demographic data of patients who received scheduled around the clock and routine analgesia were compared using the Fishers test and age identified as a potential confounder. The Fishers Exact test and Cox regression were used to compare the mode of anesthesia of patients on scheduled around the clock and routine analgesia. The independent samples T test and Analysis of Covariance were used to compare dosage of analgesia of patients on scheduled around the clock and routine analgesia, with the Fishers Exact test and Cox regression used to compare patient satisfaction with pain management between scheduled around the clock and routine analgesia at 95% confidence level. All analysis was with intention to treat.

3.17 Study Results Dissemination Plan

Results will be published in reproductive health and anaesthesia journals. Result presentation and a written report will be submitted to the Department of Obstetrics and Gynaecology, KNH-UoN ERC, University of Nairobi and Kenyatta National Hospital and conferences.

3.18 Study Closure Plan and Procedure

Participant recruitment and intervention stopped on achievement of the desired sample size.

4   CHAPTER FOUR: RESULTS

4.1   Study Flow Chart

Between September and November 2019, 101 patients were screened and 98 randomly assigned into scheduled around the clock and routine with 49 patients in each arm. Two patients were excluded due to allergy to study medication and one declined to participate in the study. All the 49 patients per group received the respective treatment protocol and all results analysed.
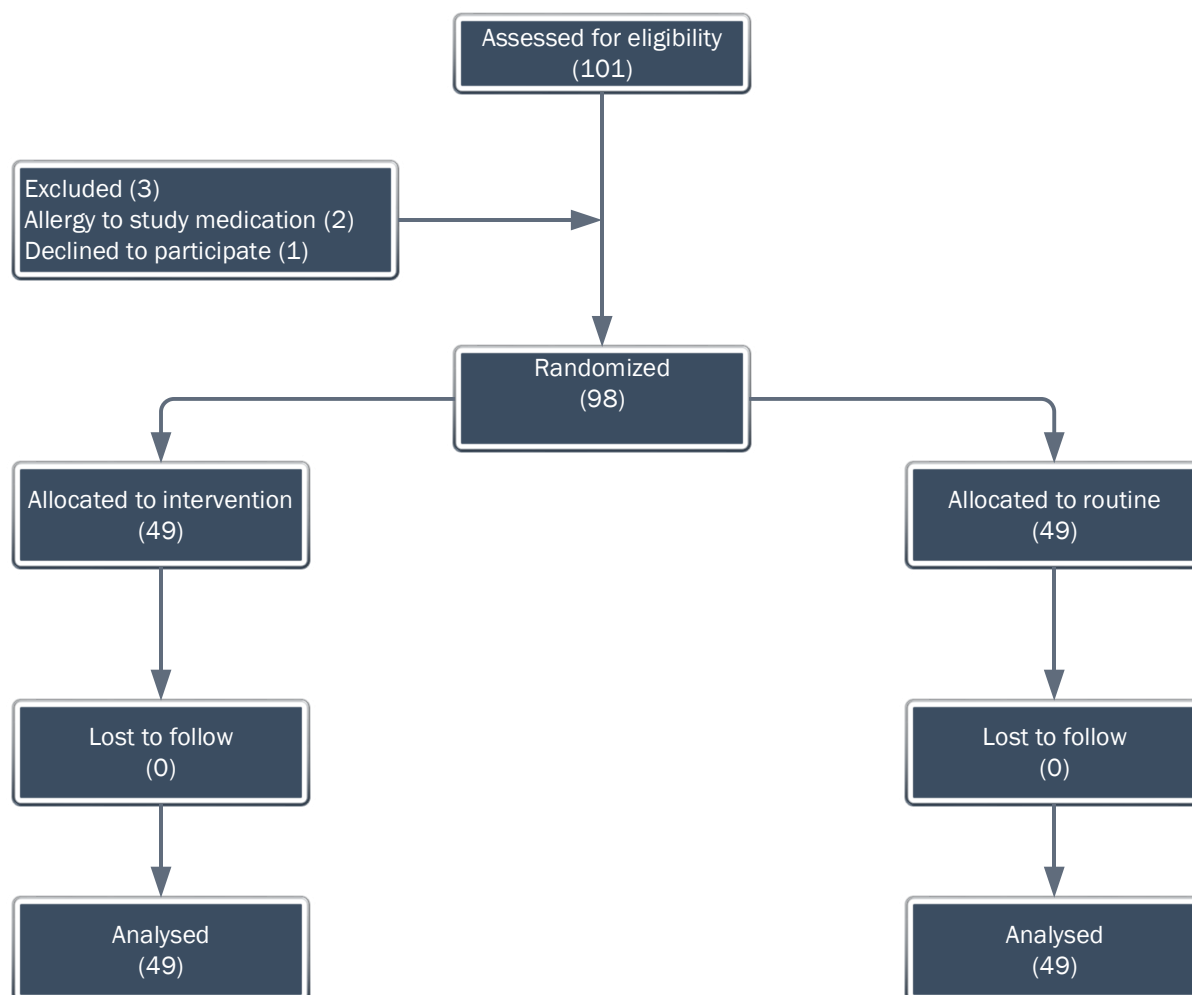
Figure 8: Study Flow Chart

4.2   Demographic and reproductive characteristics

The demographic and reproductive characteristics of participants are presented in Table 2 below. The mean age of participants on Scheduled Around the Clock (SATC) analgesia, 30.3 (SD=6.111), was significantly higher than patients on routine analgesia, 26.7 (5.5), $p<0.01$ and this is adjusted for in the main analysis. However, the marital status, education level, parity, ASA status, number of previous caesarean sections, and the duration of surgery of patients was not different between scheduled around the clock and routine analgesia groups.

Table 3: Demographic characteristics of women on around the clock versus routine analgesia for pain management after caesarean delivery

	Scheduled around the clock (n=49)	Routine (n=49)	P Value
Age, mean (SD)	30.3 (6.1)	26.7 (5.5)	<0.01
<35	38 (59.4)	26 (40.6)	0.01
35+	11 (32.4)	23 (67.6)	
Marital status			
Married	36 (48.6)	38 (51.4)	0.81
Single	13 (54.2)	11 (45.8)	
Education			
Primary	7 (43.8)	9 (56.2)	0.78
Post primary	42 (51.1)	40 (48.9)	
Parity, Mean (SD)	2.5 (1.3)	2.3 (1.3)	0.53
Primiparous	14 (46.7)	16 (53.3)	0.82
Multiparous	35 (51.5)	33 (48.5)	
No previous CS, Mean (SD)	0.9 (0.9)	0.6 (0.9)	0.26
<2	36 (46.8)	41 (53.2)	0.32
2+	13 (61.9)	8 (38.1)	
ASA status			
I	45 (50.0)	45 (50.0)	1.00
II	4 (50.0)	4 (50.0)	
Duration of surgery			
<60 minutes	43 (58.9)	30 (41.1)	0.13
60+ minutes	2 (25.0)	6 (75.0)	
Local infiltration			
Yes	48 (100)	48 (100)	1.00
No	1 (50)	1 (50)	

4.3 Mode of anaesthesia

The mode of anaesthesia was not different between patients who received scheduled around the clock compared to routine analgesia. Even though 8.2% more patients who received scheduled around the clock analgesia (100%) compared to routine analgesia (91.8%) received spinal analgesia, the difference was not statistically significant (Table 3).

Table 4: Mode of anaesthesia of women on scheduled around the clock versus routine analgesia for pain management after caesarean delivery

Anaesthesia	Scheduled Around the Clock (n=49)	Routine (n=49)	Unadjusted P value	Adjusted P value
General	0 (0.0)	2 (100)		
Spinal	49 (52.1)	45 (47.9)	0.23	0.99
Spinal plus sedation	0 (0.0)	1 (100)	-	-

| Spinal to general | 0 (0.0) | 1 (100) | - | - |

4.4 Dosage of analgesia

Number of doses of prescribed morphine was statistically significantly lower with scheduled around the clock analgesia (mean=2) compared to routine analgesia (mean=2.9), P<0.01. The number of doses of prescribed diclofenac was statistically significantly higher with the scheduled around the clock analgesia (mean=5) compared to routine analgesia (Mean=4.4), P<0.01, while the number of doses of prescribed paracetamol was lower with scheduled around the clock analgesia (Mean=7) compared to routine analgesia (Median=7.2), but not statistically significantly. The number of doses of rescue tramadol was statistically significantly lower with scheduled around the clock analgesia (Mean=1.5) than routine analgesia (Mean=2.6), P=0.01. The number of doses of rescue morphine was lower with scheduled around the clock analgesia (Mean=1) compared to routine analgesia (Mean=2), but not significantly (Table 4).

Table 5: Dosage of analgesia of women on scheduled around the clock versus routine analgesia for post caesarean pain management

Analgesia	Mean (SD)		Unadjusted P value	Adjusted P value
	Scheduled around The clock	Routine		
Prescribed				
Morphine	2.0 (0)	2.9 (0.4)	<0.01	<0.01
Paracetamol	7.0 (0)	7.2 (1.8)	0.46	0.54
Diclofenac	5 (0)	4.4 (1.2)	0.02	<0.01
Tramadol	-	3.8 (1.7)	-	-
Rescue				
Morphine	1 (0)	2 (0.8)	0.17	0.47
Paracetamol	-	2.4 (0.81)	-	-
Diclofenac	1 (0)	4 (0)	<0.01	<0.01
Tramadol	1.5 (0.5)	2.6 (1.1)	0.01	0.01
SD: Standard Deviation				

4.5 Pain scores

Pain scores of patients on scheduled around the clock analgesia (Mean=4.1) and routine analgesia (Mean=4.2) were not different at baseline statistically significantly. At 4 hours, pain scores were statistically significantly lower with scheduled around the clock analgesia (Mean=3.6) compared to routine analgesia (Mean=4.8) P<0.01. At 10 hours, 24 hours, and 48 hours, pain scores were lower with scheduled around the clock analgesia compared to routine analgesia but not statistically significantly (Table 5).

Table 6: Median pain scores of women on scheduled around the clock versus routine analgesia for pain management after caesarean delivery

	Mean Pain Score (SD)		Unadjusted P value	Adjusted P value
	Scheduled around the clock	Routine		
Before analgesic adminstration	4.1 (3.2)	4.2 (3.2)	0.85	0.92
4 hours	3.6 (2.1)	4.8 (2.6)	0.01	**<0.01**
10 hours	4.2 (3.2)	4.6 (2.8)	0.55	0.58
24 hours	3.1 (3.6)	3.6 (2.8)	0.41	0.44
48 hours	1.9 (2.3)	2.4 (2.4)	0.28	0.26

4.6 Patient satisfaction

Satisfaction with scheduled around the clock analgesia compared to routine analgesia was not different statistically significantly (Table 6).

Table 7: Patient satisfaction with SATC versus routine analgesia for pain management after caesarean delivery

	Scheduled around the clock (n=49)	Routine (n=49)	RR (95% CI)	P value	ARR (95% CI)	P value
Excellent	13 (50.0)	13 (50.0)	Reference			
Very good	20 (58.8)	14 (41.2)	1.17 (0.74-1.95)	0.60	1.40 (0.69-2.87)	0.34
Good	10 (47.6)	11 (52.4)	0.95 (0.51-1.70)	1.00	0.83 (0.34-2.06)	0.70
Fair	6 (40.0)	9 (60.0)	0.80 (0.36-1.56)	0.74	0.82 (0.28-2.39)	0.72
Poor	0 (0.0)	2 (100)	-	-	-	-
RR: Relative Risk						
ARR: Adjusted Relative Risk						
CI: Confidence Interval						

5 CHAPTER FIVE: DISCUSSION, CONCLUSIONS, AND RECOMMENDATIONS

In this study conducted among post Caesarean women at the Kenyatta National Hosptial in Kenya, we found that use of scheduled around the clock compared to routine analgesia reduced pain scores at 4 but not 10, 24 and 48 hours. The findings are similar to those of Yefet et al in 2013 in Israel, that recorded lower mean pain scores with fixed time 6 hourly paracetamol and tramadol and 12 hourly diclofenac (13). The finding of pain control at 4 and not 10, 24 and 48 hours was most likely due to the short intervention period. After 24 hours, the patients were switched to oral analgesic that were similar between the treatment groups. Similar studies used intrathecal and intravenous patient-controlled opioids (PCA) that are not available in our study setting(18). A study by Booth et al reported different findings of lower pain scores when they examined pain with movement on scheduled acetaminophen and a higher dose of morphine at 24hrs post caesarean delivery ((14)). These findings therefore support the use of scheduled around the clock analgesic dosing to reduce pain scores and optimize pain control.

The need for rescue analgesia was higher in women on routine than scheduled around the clock analgesia. This finding is similar to Valentine et al in 2013 at Stanford USA, who found that scheduled paracetamol 6 hourly used fewer IV morphine equivalents. Similarly, Brie et al in 2016 at Trihealth in Ohio, reported that using scheduled I/V paracetamol led to decreased narcotic consumption ((16)

The median dosage of prescribed morphine consumed was lower for patients on scheduled around the clock than routine analgesia. Studies by Valentine et al ((16) and Brie et al ((15) also showed decreased opioid consumption with scheduled analgesia and more consistent use of acetaminophen. However, the median prescribed dosage of paracetamol for patients on scheduled around the clock and routine analgesia was comparable between the two arms. The median dosage of diclofenac was significantly higher among women on scheduled around the clock than routine analgesics. In the study by Yefet et al (25), the number of times analgesics were administered in the fixed interval group was more compared to the as needed group due to more consistent use of medication.

Patient satisfaction with pain management was reported as adequate in both SATC and routine groups. In a study by Phillips et al which assessed the relationship between pain control and patient satisfaction, most patients were satisfied or very satisfied with overall pain management despite the pain intensity (19) concluding that pain severity scores alone may not be adequate to measure patient satisfaction with pain control. Our SATC study may not have had enough power to detect the difference in patient satisfaction with pain control.

5.1 Study Strengths
This was a single blind randomized control design. The blinding of patients, randomization and allocation concealment reduced to an extent selection bias and possible behavioural influence to the study outcomes. Several aspects (pain intensity score, patient satisfaction, adverse effects) were used to evaluate the efficacy and safety of the pain protocols.

5.2 Study Limitations
This study was limited to the analgesic modalities available to the study setting. Similar studies may have recorded lower pain scores due to availability of other pain management

modalities like intravenous patient controlled analgesia that are not available in our study setting. This study did not measure some aspects of pain including pain on movement and effect on breastfeeding. The study focussed on short-term outcomes and did not evaluate occurrence of persistent pain and long-term outcomes as possible consequences of inadequate acute pain management. We were unable to do plasma blood levels of analgesics to determine which protocol gives sustained therapeutic levels of analgesia due to financial constraints. The study instead used VAS score, a validated tool to compare effectiveness of pain control.

5.3   Conclusion

The study has shown that scheduled around the clock analgesia significantly reduced mean pain scores at 4 hours, rescue analgesia and opioid consumption compared to routine analgesia.

5.4   Recommendations

We recommend scheduling and adherence to the updated post caesarean pain management protocol at KNH in order to prevent and adequately control post caesarean pain. This may also lead to reduced opioid consumption as shown in the studies done. We also recommend larger multicentre trials to evaluate patient satisfaction with pain management.

5.5   Study Timelines

Activity	March 2019	April 2019	May 2019	June 2019	July 2019	August 2019	September to Dec 2019	Jan to Feb 2020	March to May 2020
Proposal development	■	■	■						
Ethical approval				■	■	■			
Data collection							■		
Data analysis								■	
Final result write up Result presentation and submission									■

5.6 Budget

Item	Description	Amount in Ksh
Personnel	4 research assistants allowances @Ksh. 1,000 x 30 days	120,000
	Data clerk/statistician@ 30,000Ksh	30,000
Supplies	Draft proposals printing:70pages, 3 copies @Ksh 5shs per page	1,050
	Final proposal printing: 70 pages, 3 copies @5Kshs per page	1,050
	Questionnaires printing, 4pages, @5 Ksh per page	20
	Questionnaires photocopying, 4 pages, 120copies @ 3 Ksh per page	1,440
	Airtime @ Ksh.1,000 x 4 research assistant	4,000
	2 Flash drives	1,500
Transport costs	4 research assistants x KSh. 1,000	4,000
KNH/UON ERC	Submission to ERC (twice)	2,000
Contingency	Includes analgesics stock outs	50,000
Total		Ksh. 213,060

6   REFERENCES-

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7   ANNEXES

7.1   Annex I: Consent Form

Study Title: **SCHEDULED AROUND THE CLOCK VERSUS ROUTINE ANALGESIC DOSING FOR POST CAESAREN PAIN CONTROL AT KENYATTA NATIONAL HOSPITAL**

Principal investigator: Dr. Mulunda Jackline

Introduction:

I Dr. Mulunda Jackline, a postgraduate student at the Department of Obstetrics & Gynaecology, University of Nairobi, am conducting a study on scheduled around the clock versus routine analgesic dosing for post caesarean pain at Kenyatta national hospital. You are hereby requested to participate in the study.

This information will help you make a decision on whether to participate in the study or not. You may ask any questions about the study or anything that is not clear.

Purpose of the study:

Post-operative pain remains inadequately controlled.
This study will evaluate efficacy of pain control after caesarean section.

Benefits:

Your participation in the study will help us obtain information that will assist us improve the current pain management at Kenyatta National Hospital for women undergoing caesarean section. Well managed pain after surgery aids in faster recovery, bonding between mother and baby and effective breastfeeding.

Possible risks:

The study will not have added risks compared to the current management. Possible side effects include allergy to pain medication, nausea and vomiting.

Voluntarism:

This is a voluntary exercise and you can withdraw at any point during the study with no repercussions. The management you receive at the hospital will be routine and not influenced by your decision.

Compensation:

No compensation will be offered for participation in the study.

Procedure:

As a study participant, the researcher and research assistants will obtain some information from your medical records and conduct a short interview with you and your responses filled in a questionnaire. You will be randomly assigned into one of two groups. Randomization means you will be allocated to one of the groups by chance and both you and the researcher will not choose the treatment group.

The scheduled around the clock will receive morphine every six hours for the first twelve hours. This will be followed by paracetamol injection every six hours and rectal diclofenac every twelve hours. Subsequently painkillers will be taken by mouth

The routine group will receive pain medication currently in use at Kenyatta National Hospital. Morphine, paracetamol and diclofenac injections every eight hours for one day. Subsequently painkillers will be taken by mouth from the second day

You will be required to report the intensity of pain truthfully on the questionnaire at 0, 4, 10, 24 and 48 hours after surgery.

Before discharge from the hospital you will be requested to rate your satisfaction with pain control after surgery to the time of discharge.

Confidentiality:

The information from you and from the medical records will be confidential. No names or any information identifying you will be included in the questionnaires and the fin al report.

Contact information:

If you have any questions regarding the study, you can contact Dr. Mulunda Jackline through telephone number 0721 497 284. You may also contact the KNH/UoN/ERC Commitee-0735-274 288/0721-665 077.

Or

The chairperson,

KNH/UON Ethics and Research Committee

P.O. Box 20723-00202, Nairobi.

Telephone number: (254-020) 2726300-9 Ext 44355

Email: uonknh_erc@uonbi.ac.ke

Your participation in the study will be highly appreciated.

Consent:

I_____ hereby voluntarily consent to participate in the study. I acknowledge that a thorough explanation of the nature of the study has been given to me by Dr./Mr./Mrs._____. I clearly understand that my participation is voluntary.

Signature of Participant _____ Date _____

Signature of Researcher/ Assistant _____ Date _____

7.2 Annex II: Consent Form (Swahili)

FOMU YA ITHINI:

Kichwa Cha Utafiti:

Dawa za kupunguza uchungu yaliyopangwa kwa muda wote dhidi ya dawa za kupunguza uchungu yanayotumiwa kufuata taratibu za kawaida baada ya kujifungua kwa njia ya upasuaji katika hospitali kuu ya Kenyatta
Mtafiti Mkuu: Dkt. Mulunda Jackline

Utangulizi:

Mimi Dkt. Jackline Mulunda, mwanafunzi wa shahada katika Idara ya Uja uzito na Magonjwa ya wanawake, Chuo kikuu cha Nairobi, ninafanya utafiti juu ya dawa za kupunguza uchungu zilizopangwa kwa muda wote dhidi ya dawa zinazotumiwa kufuata taratibu za kawaida baada ya kujifungua kwa njia ya upasuaji katika hospitali kuu ya Kenyatta.
Unaombwa kushiriki katika utafiti huu.
Maelezo haya yatakusaidia kufanya uamuzi juu ya kushiriki katika utafiti huu. Unaweza kuuliza swali lolote kuhusu utafiti au chochote katika fomu hii kukuwezesha kuelewa zaidi.

Kusudi la utafiti:

Maumivu/uchungu baada ya upasuaji hayajathibitiwa vikamilifu.
Utafiti huu utachunguza ufanisi wa dawa za kupunguza uchungu yaliyopangwa kwa muda didhi ya dawa zinazofuata taratibu za hospitali kuu ya Kenyatta.

Faida:

Kushiriki kwako katika utafiti huu kutatusaidia kupata habari ambazo zitatumika kuunda hatua na sera za kuwatayarisha wagonjwa hawa kwa maisha baada ya matibabu. Utafiti huu unatarajiwa kufaidi familia yako, jamii yako, nchi na wanawake duniani.

Hatari zinazowezekana:

Utafiti huu hautakuwa na athari zozote kwako na utahitajika kujibu maswali machache. Hakutakuwa na hatari zaidi ya huduma ya kawaida kama ile iliyopewa wagonjwa wengine.

Hiari:

Hili ni zoezi la hiari na unaweza kujiondoa wakati wowote wakati wa utafiti bila lawama. Usimamizi unaopokea kwenye hospitali utakuwa wa kawaida na hautaathiriwa kwa ajili ya uamuzi wako.

Fidia:

Hakuna fidia itatolewa kwa kushiriki katika utafiti huu.

Utaratibu:

Kama mshiriki wa utafiti, mtafiti na msaidizi wa utafiti watapata maelezo kutoka kwenye kumbukumbu zako za matibabu na kufanya mahojiano mafupi nawe. Washiriki watagawanywa kwa vikundi viwili kwa njia ya nasibu. Kama mshiriki hauna fursa ya kuchagua kikundi cha dawa za kupunguza uchungu. Kikundi cha dawa zilizopangwa kwa muda wote kimoja kitapokea dawa ya morphine kila masaa sita kwa muda wa mass kumi na mbili kisha kufuatwa na dawa za paracetamol na diclofenac kwa muda wa siku moja. Baada ya hapo, dawa za kupunguza uchungu zitamezwa.

Washiriki wa kikundi cha kufuata utaratibu wa hospitali kuu ya Kenyatta kitapokea dawa ya morphine, paracetamol na diclofenac kwa kila masaa nane kwa siku moja na kufuatwa na dawa za kumeza kuanzia siku ya pili.

Utahitajika kujaza kiwango cha uchungu kwa uwazi ukitumia uzani baada ya upasuaji

Utakapopata ruhusa ya kutoka hospitalini utaulizwa kujaza jinsi ulivyoridhishwa na udhibiti wa dawa za kupunguza uchungu.

Usiri:

Taarifa kutoka kwako na kutoka kwa kumbukumbu za matibabu itakuwa siri. Hakuna majina wala maelezo yoyote ya kukutambulisha yatakayonukuliwa kwenye ripoti ya utafiti huu.

Maelezo ya mawasiliano:

Ukiwa na swali lolote kuhusu utafiti huu, unaweza kuwasiliana na Dkt. Mulunda Jackline kupitia namba ya rununu 0721 497 284. Unaweza pia kuwasiliana na KNH / UoN / ERC Committee kupitia nambari 0735-274 288 / 0721-665 077.

Ama:

Mwenyekiti,

KNH / UON Kamati ya Maadili na Utafiti

S. L. P. 20723-00202, Nairobi.

Nambari ya simu: (254-020) 2726300-9 : 44355

Barua pepe: uonknh_erc@uonbi.ac.ke

Tunakushukuru sana kwa ushiriki wako katika utafiti huu.

Idhini:

Mimi_____ nimeamua kwa hiari yangu mwenyewe kushiriki katika utafiti huu baada ya maelezo ya kina kutoka kwa Dkt. / Bwana / Bi._____. Ninaelewa wazi kwamba ushiriki wangu ni kwa hiari.

Sahihi ya Mshiriki _____   Tarehe _____

Saini ya Mtafiti / Msaidizi _____   Tarehe _____

7.3 Annex III: Study Questionnaires

SCHEDULED AROUND THE CLOCK VERSUS ROUTINE ANALGESIC DOSING FOR POSTCAESAREAN PAIN CONTROL AT KENYATTA NATIONAL HOSPITAL

Patient Code:_____

Phone (Mobile)_____Phone (Alternative)_____

1. Age:_____Parity:_____Number of previous caesarean deliveries:

2. Marital Status:

Married: ☐   Separated: ☐   Widowed: ☐ Single: ☐Living together: ☐

3. Gestational age: …………….weeks…………..days

4. Highest level of education achieved

None ☐   Primary☐   Secondary☐   College ☐   University ☐

5. ANC profile:
HB………. g/dL Blood Group ………
VDRL………….HIV…………Urinalysis………….

6. ASA status: ASA 1 ☐   ASA II ☐

7. Mode of anesthesia:
Spinal ☐   Spinal with sedation ☐   Spinal to general ☐   GA ☐

8. Duration of surgery:
Time of incision…………….Skin closure time…………………Time taken…………………

9. Intraoperative analgesia used

…………………………………………

   Dosage: ……………..

   Dosage: ……………

   Dosage: …………….

10. Local anesthesia wound infiltration: Yes ☐   No ☐
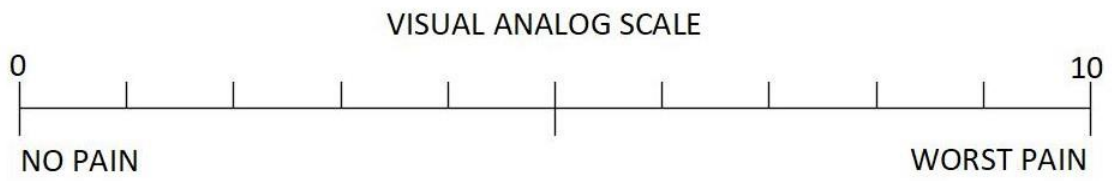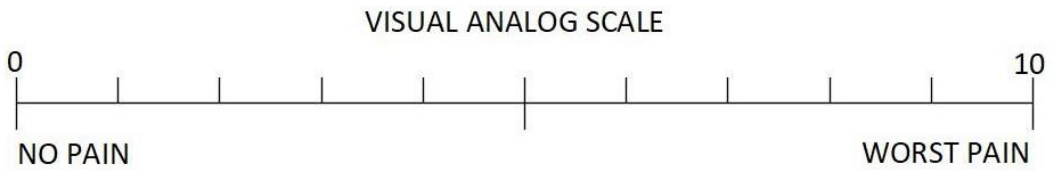   Type
11. Pain Score
Please put a mark that best describes the level of pain on the scale below
(Tafadhali weka alama kwenye mizani stahiki inayoashiria kiwango cha maumivu)
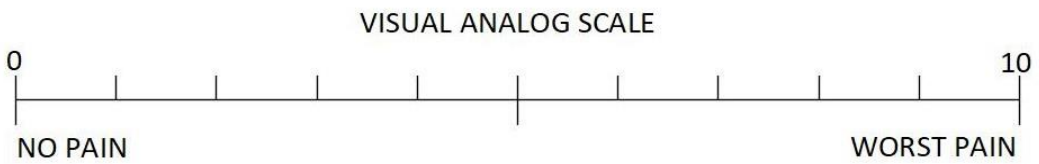**Before analgesia administration**

VISUAL ANALOG SCALE

0   10

NO PAIN   WORST PAIN

At 4 hours

VISUAL ANALOG SCALE

0   10

NO PAIN   WORST PAIN

At 10 hours

VISUAL ANALOG SCALE

0   10

NO PAIN   WORST PAIN

At 24 hours

VISUAL ANALOG SCALE

0   10

NO PAIN   WORST PAIN

At 48 hours

VISUAL ANALOG SCALE

0   10

NO PAIN   WORST PAIN
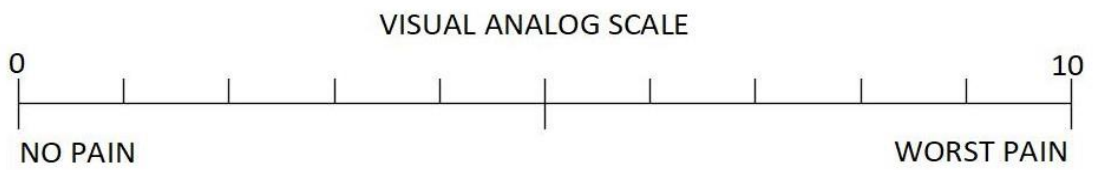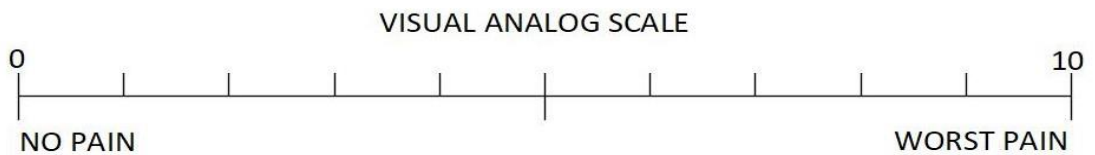
12. Postoperative analgesics used

	Drugs	Dosage	Frequency	Time given
Day 1				
Day 2				
Day 3				

13. Rescue analgesics given

	Drugs	Dosage	Frequency	Time given
Day 1				
Day 2				
Day 3				

14. Other multimodal pain management techniques used
Please check the appropriate box and give comments.

YES	NO	Treatment type	Improved	No change	Worsened
		Physical therapy			
		Occupational therapy			
		Mobilizations			

Allergies – Have you had an allergic reaction to any medication?
(An allergy means a rash, swelling, difficulty in breathing.) **YES** ☐   **NO** ☐
If you have please list them**:**

15. Overall satisfaction with pain control during admission
Excellent☐   2. Very Good ☐   3. Good ☐   4. Fair ☐   5. Poor ☐

Completed by: …………………………

Relationship to Patient: …………………………

Date: …………………………

7.4 Annex IV. Postoperative care

	Scheduled around the clock	**Routine Care**	**P Value**
Mean pain score at time Before analgesia admistration, 4 , 10 ,24 and 48 hours			
Proportion of breakthrough analgesics used			
Analgesic doses used 1. Opioids 2. Paracetamol 3. Diclofenac 4. Other analgesics used			
Patient satisfaction with pain management on scale 1 to 5 1-Excellent 2-Very good 3-Good 4-Fair 5-Poor			

7.5 Annex V. Data And Safety Monitoring Board

Study Title: **SCHEDULED AROUND THE CLOCK VERSUS ROUTINE ANALGESIC DOSING FOR POST CAESAREAN PAIN CONTROL AT KENYATTA NATIONAL HOSPITAL.**
PI Dr. Mulunda Jackline
Members Dr. Ng'anga Kuria W MBChB Moi, M.Med (ANAESTHESIA) UoN,

Consultant Anaestheologist, Kenyatta National Hospital

Dr. Enock Ondari MBChB, M.Med (OBS/GYN)

Consultant Obstetrician and Gynaecologist, Kisii Teaching and Referral Hospital

Mr. Andrew Aballa, Statistician

Objective: To compare the differences in mean pain scores between post-caesarean patients randomized to scheduled-around the clock versus routine analgesia at the Kenyatta National Hospital.
Methodology: A single blind parallel, randomized controlled trial carried out at the Kenyatta National Hospital maternity unit.
DSMB Responsibilities
Oversight of the study trial and constituting meetings to monitor safety of patients and occurrence of adverse events.

7.6 Annex VI. ERC Approval

UNIVERSITY OF NAIROBI
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P O BOX 19676 Code 00202
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KENYATTA NATIONAL HOSPITAL
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Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/329

3rd September, 2019

Dr. Jackline Mulunda
Reg. No.H58/89066/2016
Dept.of Obstetrics and Gynaecology
School of Medicine
College of Health Sciences
University of Nairobi

APPROVED
0 3 SEP 2019
KNH/UoN-ERC

Dear Dr. Mulunda

RESEARCH PROPOSAL: SCHEDULED AROUND THE CLOCK VERSUS ROUTINE ANALGESIC DOSING FOR POST CAESAREAN PAIN CONTROL AT KENYATTA NATIONAL HOSPITAL: A RANDOMIZED CLINICAL TRIAL (P466/06/2019)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 3rd September 2019 – 2nd September 2020.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study.
This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Protect to discover

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For more details consult the KNH- UoN ERC website http://www.erc.uonbi.ac.ke

Yours sincerely,

PROF.M.L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c.   The Principal, College of Health Sciences, UoN
        The Director, CS, KNH
        The Chairperson, KNH- UoN ERC
        The Assistant Director, Health Information, KNH
        The Dean, School of Medicine, UoN
        The Chair, Dept.of Obstetrics and Gynaecology, UoN
        Supervisors: Dr.Alfred Osoti, Dept.of Obs/Gynae,UoN
                      Dr. Rosa Chemwey, Dept.of Obs/Gynae,UoN
                      Dr.Rose Jepchumba Kosgei, Dept.of Obs/Gynae,UoN

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