THE EFFICACY OF PECTORAL NERVE BLOCKS FOR ACUTE PAIN MANAGEMENT FOLLOWING MODIFIED RADICAL MASTECTOMY FOR BREAST CANCER AT THE KENYATTA NATIONAL HOSPITAL

A RANDOMISED CONTROL TRIAL

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H58/79141/2012

A RESEARCH DISSERTATION SUBMITTED AS PART FULFILMENT FOR THE AWARD OF MASTER OF MEDICINE IN GENERAL SURGERY, UNIVERSITY OF NAIROBI

DECLARATION

I declare that this dissertation is my original work and has not been presented for the award of any degree at any other institution or university.

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To my mother, whose love, support, endurance and mentorship guides me, through my journey in life and to my sons, who are a blessing to me and the constant support from my life partner, my husband.

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LIST OF ABBREVIATIONS

ALND –	Axillary lymph node dissection
KNH –	Kenyatta National Hospital
MRM –	Modified Radical Mastectomy
PAR –	Pain at rest
POM –	Pain on movement
PECS –	Pectoralis
PEC I –	Pectoralis I nerve block
PEC II –	Pectoralis II nerve block/ 'modified Pecs' block
PMm –	Pectoralis major muscle
Pmm –	Pectoralis minor muscle
VAS –	Visual Analogue Scale
NRS –	Numerical Rating Scale
PMPS –	Post mastectomy pain syndrome
UoN –	University of Nairobi
KNH –	Kenyatta National Hospital
SPSS –	Statistical Package for Social Sciences
IV/iv –	Intravenously
IM -	Intramuscular

ABSTRACT

Background: Management of acute pain following breast surgery remains a challenge to both the surgeon and the anesthesiologist. There are various recommendations from anesthesia and surgical groups on multimodal anesthesia regimens; however there remains no consensus specific for patients who have undergone modified radical mastectomy for breast cancer. Some studies have indicated modified pectoral nerve block can provide good analgesia for surgery as well as post operatively.

Objective: This study aimed to compare the efficacy of the modified pecs block for acute pain management following modified radical mastectomy for breast cancer.

Methodology: This was single blinded randomized clinical trial of patients scheduled to undergo modified radical mastectomy for breast cancer in Kenyatta National Hospital. They were randomized into two groups using random generated numbers, sealed in envelopes. The control group received standard analgesia while the intervention group received the Pecs II block. Post operatively they were followed up at 4, 12, 18 and 24 post-operative hours. Pain intensity was scored using the visual analogue scale, carried out by a blinded research assistant. Patients need for rescue analgesia, time to rescue analgesia, post-operative complications and patient pain satisfaction scores were also collected. Morphine injection was used for rescue analgesia. Data was entered into SPSS and analyzed for mean, median and proportion. Comparisons were done using Man Whitney U-test, Chi square and Fischer's exact test as appropriate. Logistic regression was done for multivariate analysis. Statistically significant was taken at p-value <0.05.

Results: We recruited 40 patients that randomized into intervention group $^{(18)}$ and into control group $^{(22)}$. There was no significant difference in all baseline characteristic s except for weight that was found in logistic regression to be independently associated with higher risk for poor pain control post operatively. There were significantly lower visual analogue scale scores in the Pecs II group, at the 4^{th} post-operative hour as compared to those who received standard analgesia, with median scores of 0 (0-1) versus 4 (2-5) $p<0.001$.We also found a longer time to rescue analgesia in the block group, with a median of 13 hours, as compared to 7.5 hours in the control group. The incidence of side effects in the block group was 27.8% and 68.2% in the control group. The most common side effect was nausea, with 5.6 % and 36.4 % in the block and standard analgesia groups, respectively.

Conclusion: The Pecs block provides for a safe mode of post-operative analgesia that provides excellent acute post-operative pain, within the first 24 hours, and is associated with few administrations associated complications. Its efficacy is also comparable to standard analgesia, with fewer side effects.

CHAPTER ONE: INTRODUCTION

Modified radical mastectomy (MRM) with axillary node dissection (ALND), is the most commonly performed surgery for breast cancer, with or without neo-adjuvant or adjuvant chemo-radiotherapy. Patients in our setting are usually diagnosed with locally advanced or metastatic breast disease due to delays in presentation and diagnosis. [1] In Kenyatta National Hospital (KNH), over the course of last year an estimated one hundred patients underwent MRM and ALND.

A modified radical mastectomy, is a complete mastectomy with axillary node dissection. A complete mastectomy, involves the complete removal of the entire breast tissue from its extents, medially the sternum, laterally the anterior axillary line the inframammary crease inferiorly, and the clavicle superiorly, as well as complete resection of the pectoralis major fascia.

Following surgery, acute post - operative pain, remains a concern to manage for both the surgeon and the anesthesiologist. Acute post-surgical pain has been found to affect up to 60 percent of patients who have had surgery for breast cancer [2]

Inadequate pain management, is associated with prolonged length of admission, poor post – operative mobilization and negatively impacts the life quality of the patient [3]. Acute post-surgical pain is also a recognized risk factor for development of chronic post mastectomy pain which affects up to 50 percent of women who undergo a mastectomy. [4]

Regional analgesia, opioids, and several other oral and parenteral analgesics are used for treatment of acute pain following breast surgery, each of which has a varied effect on post-surgical comorbidity. Current studies have shown that regional techniques have better outcomes, with better post-operative pain control and patient's satisfaction in terms of quality of recovery [5, 6]. Of the regional techniques, paravertebral blocks are the most studied, and have shown efficacy for anesthesia as single anesthetic agents as well as acute pain management therapies [7, 8, 9, 10] A new regional technique known as the pectoral nerve block is emerging, as a safer option for regional anesthesia, and studies are ongoing on its efficacy in postoperative pain control. The pectoral nerve block provides, a safe, easy to administer, regional block for intra and post-operative pain control [10, 11, 1 2]

This study assessed the efficacy of pectoral nerve blocks in management of acute post-surgical pain following modified radical mastectomy for breast cancer.

CHAPTER TWO: LITERATURE REVIEW

Breast cancer remains the most common cancer in women, throughout the world, and the second most common cause of malignancy related deaths according to the American cancer society. It makes up 25% of all new cases of cancer in women globally, with the Global Cancer Incidence, Mortality and Prevalence database (GLOBOCAN) estimating an incidence of more than 2 million new cases annually and a mortality of 11.6%,of all cancer related mortality[13]. In Africa patients typically present at an earlier age as compared to high income countries [14], and in Kenya the median age of presentation at 44 years. [15]

Reviews done of surgery in breast cancer patients in Africa, has shown that modified radical mastectomy is the most common surgery performed, [14] and with the increasing screening programs, more and more women are diagnosed at earlier stages, undergo surgery as the primary modality of treatment and currently live longer following treatment for breast cancer.

An inherent complication following surgery, secondary to tissue and nerve trauma is pain, which can range from a severity of mild to very severe. Historically, post-operative pain has been managed principally y use of opioids, and effective pain control, as an outcome of surgery had not been established. Moreover, patients have generally anticipated and accepted that acute pain will be present after their surgical procedures, resulting in widespread under treatment of acute post-surgical pain. [14]

In has been found that more than 80% of patients who undergo surgery will have poorly controlled postoperative pain, of whom 75% will report it as being either extreme, moderate or severe[16,17] In addition, despite advances in medical research and changes in available treatment options available, there has been little change in post-surgical pain management over two decades. [14, 17, 18]

Studies done have also shown that less than half of patients undergoing surgery will experience adequate postoperative pain control.[17]This in turn is associated with poor quality of recovery, increased post-operative complications and increases the risk of developing chronic post-surgical pain.[3, 19]

Poor control of acute severe pain may result in stimulation of the pituitary-adrenal axis, causing a decrease in immunity. Sympathetic activation secondary to pain, has been shown to cause systemic changes like renal, cardiac and gastrointestinal system changes. Acute post-operative

pain also leads to a reluctance to move and ambulate in patients, both of which are principal factors in early post-operative recovery. Poor ambulation in turn contributes to post-surgical complications like deep venous thrombosis, myocardial infarct, and poor wound healing and chronic pain syndromes. Unrelieved acute pain also has psychological sequelae like anxiety, poor moral and depression.

The recent understanding on the magnitude of untreated post-surgical pain, has led several accredited professional bodies to develop guidelines on management of perioperative pain, however these are not specific surgery guided and uptake and use remains low. [14, 16, 17, 18]

Specific to surgery for breast cancer, 40-60 percent of patients experience clinically significant pain, indicating that post-operative pain treatment is not sufficient. [3, 18], and of these, severe pain persists for 6 – 12 months in 10 percent of the patients.

Various risk factors for acute post-surgical pain have been identified, and include, young patients, the more invasive the surgery, and those with a high level of preoperative anxiety. [2]

Consequences of unmanaged severe acute post-operative pain include, increased postoperative morbidity, longer hospital stays and immobility, severe post-operative nausea and vomiting. [3]

It is also an identified risk factor for the occurrence of chronic post mastectomy, a recognized clinical entity that is associated with poor postoperative quality of life for breast cancer patients and survivors. [19, 20] Chronic post mastectomy pain has been shown to occur in up to 50% of patients who have had breast cancer surgery. In view of the known high association of this syndrome with acute postoperative pain, it is important to effectively manage acute postoperative pain following breast cancer surgery. [22]

Chronic pain is a known, frequently occurring complication after breast cancer surgery, and risk factors for its development include; the intensity of acute postoperative pain, the presence of pain prior to surgery especially moderate to severe pain, and the type of surgery performed, inter-coastobrachialis nerve injury, adjuvant radiotherapy, and possibly psychological factors like preoperative anxiety or depression [22, 23]

Chronic post mastectomy pain as defined by the International Association for the Study of Pain, as pain attributable to a particular type of surgery and persisting beyond the anticipated normal healing time of three months. It was first described by Wood et al in 1970s, following mastectomies, who characterized it as a dull, burning and aching sensation in the anterior chest, arm and axilla, exacerbated by movement of the shoulder girdle. Further studies identified the

syndrome in patients who underwent other breast surgeries like breast reconstruction, augmentation and lumpectomies, with or without prosthetic reconstruction. It has been shown to occur more frequently following reconstruction especially with prosthetic devices and after lumpectomies versus mastectomies. [24] While the cause remains unclear, it is thought to have an association with nerve damage during surgery, either the inter-coastobrachialis, neuroma formation or axillary dissection. [24, 25]

CPMS remains a difficult condition to manage, despite multiple prospective studies undertaken, to identify optimal treatments for it.

Multiple therapeutic interventions have been proposed and studied, with the aim of preventing or reducing the intensity of acute post-operative pain following surgery for breast cancer. [26, 27, 28, 29] and assessing their efficacy in reducing the incidence of chronic post mastectomy pain denoting the challenge in the treatment of acute and chronic pain following mastectomies. Multimodal analgesia, described as the use of a combination of analgesic medications and techniques that have different mechanisms of action in the peripheral and/or central nervous system and have additive effects to each other, leading to more effective pain relief compared with single-modality interventions, has been recommended by the American Pain Society. [30, 31] However, no recommendations are available for specific surgeries e.g. MRM and despite the various modes of analgesia available for use, acute pain management remains under treated.

Of the various analgesics available, local and regional techniques have been widely studied. Paravertebral blocks (PVB) have been widely studied for use in multimodal anesthesia, single use as anesthetic and with general anesthesia for acute pain control. [8, 21, 32] PVB has been shown to be effective for pain management as well reducing post-surgical morbidity. PVB were compared to the gold standard that is thoracic epidural blocks, but are associated with less complications. Neural blockade is the most effective way of providing post-operative pain relief, while also reducing the metabolic response to trauma. [33]

A newer regional nerve block, described as the pectoralis nerve block, has emerged for use in breast cancer. It was initially described by Blanco et al, as an interfascial block targeting the pectoral nerves, for use in breast surgeries, done as day cases. [11] 50 patients, over a two year period had the block administered prior to breast surgery, and post operatively achieved good pain control, with added paracetamol and dexketoprofen, and he described it as the ‘Pecs’ block.

A modification of the block , termed 'Pecs II' block, by Blanco et al, is also described, aimed at targeting the pectoral nerves, inter-coastobrachial, long thoracic and inter-coastal nerves 3- 6 nerves. [34] Use of both the Pecs I and II blocks, in modified radical mastectomy, has been assessed, against use of general anesthesia alone, and has been found to provide acceptable postoperative pain control, with minimal opioid use and reduced surgical morbidity. [11]

The Pecs block, provides a new loco regional analgesia for breast cancer surgery, with fewer complications and better outcomes, compared to PVB. [10, 11, 32,]

2.1 Technique

The Pecs block, is a loco regional analgesic technique that targets the pectoral nerves as they run in the interfascial space between pectoralis major and minor muscles. The technique as originally described by Blanco, involves administration of 0.4mls/kg of levobupivacaine into the interfascial plane, which involve identification of the pectoral branch of the thoraco-acromial artery, adjacent to which runs lateral pectoral nerve.

The Pecs block principally targets the medial and lateral pectoral nerves. A modified block of the same described as the Pecs II block or 'modified Pecs block', targets the same nerves as well as the inter-coastal nerves 3, 4, 5 and 6, inter-costobrachial nerve, and the long thoracic nerve.

The Pecs II block is performed as follows: a linear probe is placed along the outer third of the clavicle, identifying the pectoral artery and infiltrating local anesthetic at this site. Subsequently, above the 3rd rib, targeting the serratus anterior muscle, local anesthetic is administered.

The patient will be placed in the supine position and the arm is positioned perpendicular to the trunk. Thereafter the ultrasound probe is placed, inferior to the clavicle, at the mid-clavicular level and the axillary artery and vein located. Moving the probe laterally, the pectoralis muscles are identified, and the pectoral artery running between them. The skin is then infiltrated with lidocaine 2%, and the needle is pushed in the plane of the probe from medial to lateral until the tip enters the potential space between pectoralis muscles and levobupivacaine, 10 mls is injected. Thereafter, the needle is advanced further until it lies in the potential space between pectoralis minor and serratus anterior muscles, and levobupivacaine 15 mls is deposited in this space.

Observation of the patients is done for thirty minutes following block administration. Successful take of the block is then assessed by examining the dermatomal sensation levels of T1 – T8, and this will be done by a blinded observer. The total number of dermatomes that have less pain to pin prick compared to the opposite side will be noted. If the pin-prick sensation is not decreased

in any segment for up to 30 min, it is considered as a block failure. The patient's electrocardiogram and oxygen saturation (SpO2) will be monitored continuously, and their heart rate (HR) and non-invasive blood pressure are recorded at baseline, after performing the block, and every 5 min for 30 min. Anticipated complications following block administration include injection to the thoraco-acromial artery and pneumothorax, however so far no complications have been reported in studies done to assess the pectoralis nerve block.

2.2 Post Mastectomy Pain Syndrome

Chronic pain following breast surgery was initially described by in 1978 by Wood, who described pain following mastectomy, attributed to inter-coastobrachial nerve entrapment. He described it as a dull, burning, aching pain on the anterior chest wall, axilla and arm, exacerbated by movement of the shoulder girdle. [25]

However, no standard definition of PMPS has been agreed on since. The International Association for the Study of Pain, has defined it as pain following surgery, which persists beyond the expected normal healing time, which is postulated to be three months, however for research purposes, they extended the time to six months. [35]

A review by Rockwell and Waltho has attempted to redefine the syndrome by reviewing previous trials and has described it as; pain that occurs following any breast surgery; and is of at least moderate severity; has neuropathic qualities; is located in the ipsilateral breast/chest wall, axilla, and/or arm; lasts at least 6 months; occurs at least 50% of the time; and may be worsened by movements of the shoulder girdle. This includes all chronic pain following breast surgery and gives a more concise definition and time period. [36]

However, despite a lack of consensus on its definition, PMPS has been a subject of many studies. Several studies have assessed the incidence following breast surgery. A retrospective analysis of pain following mastectomies with or without reconstruction, found that 60% of the patients experienced clinically significant acute pain, with pain persisting in 10% of them at 6-12 months. [37] On the other hand a prospective study of PMPS following surgery for breast cancer found and incidence of 52.9% of the population studied. In relation to sensitive alteration, 52.6% patients had shown inter-coastobrachialis pain, 1.3% neuroma and 3.2% have related phantom breast pain. Pain on the shoulder and/or thoracic-scapular area as a consequence of breast cancer surgical treatment was observed in 27.2% patients [22]

Risk factors associated with development of PMPS include: younger age < 40 years of age, axillary lymphadenectomy, radiation therapy after surgery, severe acute post-operative pain, and presence of pain at other sites other than the surgical site. [4, 22, 38,] Of these, the modifiable risk factor is acute postoperative pain, whose effective management, would help decrease the incidence of chronic post mastectomy pain.

2.3 Pain Scales

Assessment of the intensity of pain in patients, has historically been dine using scales, which aim to objectively quantify a patient's subjective feeling. Multiple pain scales have been developed, either specific for certain medical conditions or for general use. The most commonly used scales are: the visual analogue scale, numerical rating scale and the verbal rating scale. Of these, the VAS is the most studied, has been validated, and has been found to be reliable in acute pain measurement.

2.4 Statement of the Problem

Multiple studies have led to development of clinical guidelines on acute postoperative pain treatment, however management remains ineffective. There is no local data on the same.

2.5 Research Question

Can the 'modified Pecs block' be used as for efficient management of acute post-operative pain, following MRM with ALND?

2.6 Study Justification

Management of acute post-operative pain remains dismal, despite decades of studies on prevalence of post-surgical pain, its etiology and pathogenesis and recognized consequences. While few studies have been done in Africa, studies done in Western countries have led to development of perioperative management guidelines by multiple health professional bodies like anesthesiologists, pain specialists and surgical societies. They have provided general guidelines to postoperative pain management, that give recommendations that are not surgery specific, and uptake to implementation has been low, however key to these recommendations is use of multimodal analgesia, with an aim of reducing opioid induced side effects, by use of local and regional techniques.

No studies have been done on post-operative pain at the Kenyatta National Hospital, and so the prevalence remains unknown, however known consequence of poor pain management remain universal, driving the need for adequate post-operative pain treatment. This study aims to assess the efficacy of post-operative pain management using pectoral nerve blocks in MRM with ALND.

2.7 Objectives

2.7.1 Broad Objective

The aim of the study was to assess the effectiveness of the 'modified Pecs' block, in pain management in patients undergoing modified radical mastectomy, for breast cancer, at the Kenyatta National Hospital.

2.7.2 Specific Objectives

a) Determine the post-operative pain intensity within the first 24 hours in both groups.

b) Compare the time to first rescue opioid analgesia between the study and control groups.

c) Determine the effectiveness in pain control of the modified Pecs block as compared to standard analgesia.

CHAPTER THREE: MATERIALS AND METHODOLOGY

3.1 Study Design

This was a double blinded randomized control study.

3.2 Study Site

Kenyatta National Hospital surgical wards. KNH is the largest public hospital in Nairobi, the only teaching and referral hospital, with specialist surgical and oncology services, serving a population of more than 3 million citizens. It was suited for this study, because of the volume of patients presenting to breast and oncology clinics, also, where multidisciplinary approaches to management of breast cancer patients is advocated, and knowledge from this study will further help to improve the care provided to breast cancer patients. The knowledge gained may also trigger the establishment of a pain specialized unit, available to patients for their pain management.

3.3 Study Population

Patients with breast cancer, admitted to undergo modified radical mastectomy.
Eligibility

3.5 Inclusion Criteria

- Patients with stage 1 – 3 breast cancer, admitted to undergo MRM.
- Age: 18 years and above
- Patients who had given informed consent as study participants.

3.6 Exclusion Criteria

- Patients with breast cancer admitted for surgeries other than MRM.
- Patients who have undergone prior surgery e.g. BCS and now come for completion mastectomy.
- Patients with a contraindication to bupivacaine use
- Patients with contraindications to NSAID use and paracetamol
- Patients with coagulopathies

3.7 Methods

Patients with breast cancer, who presented to breast clinic and underwent staging, were admitted for MRM, following their case discussion at the breast multidisciplinary meeting. Admissions for MRM were done into the general surgery wards.

Following admission, the principal investigator informed all the potential participants about the study, its purpose, what it entails and likely complications that may occur secondary to receiving the modified Pecs block. Thereafter, all willing participants gave written informed consent, for enrolment into the study. The patient consented to entry into both arms of the study.

They were then randomized into either arms of the study. The randomization was done through simple randomization at 1:1 ratios, using random numbers generated from random number tables. The random number generation was by the principal investigator. The numbers corresponded to either arms of the study, and patients picked a sealed envelope containing a number. The principal investigator then opened it and attached them to an arm, either for regional block or for standard analgesia. The procedure of block infiltration was done under general anaesthesia, therefore blinding the patients as to which arm they are in .A copy of the visual analogue scale had been presented to them, and a full description on how to score the various pain levels had been done. The research assistant who was also blinded was the one to assess the pain intensities post operatively. The research assistant was a surgical resident who was trained on pain assessment and scoring. The anesthesiologist giving the nerve block was informed thereafter, and availed themselves for the surgery. Consecutive sampling was done, however the desired sample size was not achieved.

Following this, routine preoperative care was done, involving, history taking and clinical examination, laboratory investigations and anesthesiologist assessment. Patients bio data i.e. name, age, sex, weight, clinical history regarding stage of breast cancer, and any history of exposure to preoperative chemo/radiotherapy was taken.

The two arms of the study were group 1 who received standard analgesia and group 2 who received the modified Pecs block as well as dexketoprofen 50mg intravenously (IV) given 12 hourly and paracetamol 1 gram given 6 hourly IV for the first 24 hours. Standard analgesia described for this study was as follows: Paracetamol 1 gram iv given 6 hourly, tramadol given at 1 –mg/kg 6 hourly iv and dexketoprofen 50mg/iv 12 hourly. Group 2 received the modified Pecs block, given as a single shot of 0.25% bupivacaine at 0.2mg/kg i.e. 10mls for pec I and 0.4mg/kg

i.e. 20mls pec II administered, under ultrasound guidance, in theater, after administration of general anaesthesia. The ultrasound machine used was the GE Healthcare venue 50 anaesthetic ultrasound machine, which was always available in the main theater.

The nerve block was administered by anesthesiologists who have specialized in regional anaesthesia, and who agreed to participate in this study, in both a supervisory role and anesthesia provider role. The bupivacaine was drawn from the same batch of medication, for all the patients on the nerve block arm. It was released from the main pharmacy to main theater, where it was stored in the head of department's office and availed to the anesthesiologists for use on patients involved in the study only.

Reconstitution of the medication was done in a standard way by anaesthesiologists. The bupivacaine was provided as a formulation of 0.5% buvipacaine in 10mls per vial. Reconstitution was as follows: dilution into equal volumes was done using distilled water for injection to make a volume of 30 mls, with addition of dexamethasone 2mg. Post operatively, pain assessment was done at 4, 12, 18 and, 24hours. Pain scores were determined using the visual analogue scale for both groups.

For patients in both arms, whom despite use of the prescribed medications were still in pain, were given morphine at a dose of 0.01mg/kg given intravenously and reassessed after 10 minutes. If pain persisted the dose was to be repeated until patient comfort was achieved. However, no patient who required rescue analgesia was given more than a single shot of morphine. The primary outcome measure was pain scores, while secondary measures were post-operative complications like nausea and vomiting, and patient satisfaction scores. Time to initial request for recue analgesia was also evaluated for both groups. Interpretation of the visual analogue scores, in millimeters, was to be as follows: 0 -4 – no pain, 5 – 44 mild pain, and 45 – 74 as moderate pain and 75 – 100 as severe pain. Patients with VAS of >3 will have additional analgesia given. Where the numbers were small. All statistical tests were interpreted at 5% level of significance (p value less or equal to 0.05).

3.8 Sample Size Calculation

According to KNH data, retrieved from the hospital records, approximately100 modified radical mastectomies were carried out in the year 2018. Out of this population, a sample will be drawn and the sample size for a clinical superiority design will be as follows:

3.8.1 Hypothesis:

- Null Hypothesis: with respect to post-operative pain control, pectoral nerve blocks is not superior to conventional analgesia for pain control
- Alternative hypothesis: the pectoral nerve block is superior to conventional analgesia for post-operative pain control
- Effect size: The smallest effect size that is of scientific interest would be:
- From the literature review, 40 – 60% of patients who have had surgery for breast cancer will experience acute postoperative pain. For a two tailed unpaired t-test at 95% confidence interval and assuming that the two groups Q1 and Q2 are equal, and that the standard deviations are the same, $(\sigma_1 = \sigma_2 = \sigma)$:
- For 90% power, π_1 = 60 %and π_2 = 40% are the proportion estimates.
- Thus from the above, and using the **Wilcoxon-Mann-Whitney** test which is based on the nonparametric relative treatment effect formula adjusted for the minimization of the N for the optimality of the balanced design, we use the following formula:
- $$N = \left(\frac{Z_{\alpha/2} \sqrt{\pi_c(1-\pi_c)(Q_1^{-1}+Q_2^{-1})} + Z_\beta \sqrt{\pi_1(1-\pi_1)/Q_1 + \pi_2(1-\pi_2)/Q_2}}{\pi_1 - \pi_2} \right)^2$$
- Alpha, α=0.05 is the level of significance
- According to statistical tables $Z_{\alpha/2}$ =1.96 and $Z_\beta = Z_{0.10}$=1.282
- π_c=0.6*0.5+0.40*0.5=0.5
- Q_1=0.5
- Q_2=0.5
- π_1=0.6
- π_2=0.4
- $$N = \left(\frac{1.96 \sqrt{0.5(1-0.5)(0.5^{-1}+0.5^{-1})} + 1.282 \sqrt{\frac{0.25(1-0.25)}{0.60} + 0.77(1-0.77)/0.40}}{0.25-0.77} \right)^2$$
- N = 81
-
- N1= 0.5*81= 40
- N2 = 0.5*81= 40
- Hence, 81 Participants will be needed for the study. Sample size **81** in the ratio 1:1 each group Q_1 and Q_2

3.9 Data Management

3.9.1 Data Collection

The data collected included the following:

a) Patient's bio data i.e. name, age , inpatient number, sex

b) Clinical stage of diagnosis

c) History of exposure to neo-adjuvant chemo/radio therapy

d) Pain scores following surgery at the assigned time intervals

e) Any post-operative complications

The filled questionnaires were stored by the principle investigator, at all times in a locked drawer, while soft data was stored under password encryption, in a laptop only accessible by the principle investigator.

3.10 Data analysis and presentation

Data was collected using approved prepared data collecting questionnaires. It was then entered into Microsoft Excel data entry sheet, cleaned and exported into SPSS version 23.0 for statistical analysis. Categorical data was presented as frequencies and proportions. These were then presented as bar charts and tables. Continuous data was presented as means and standard deviation. Multivariate analysis was done to assess relationship of acute pain levels to the different patient characteristics.

3.11 Data Dissemination

The results will be made available to the University of Nairobi research library, KNH/UON Ethics and research committee and will be available for review by participants. The findings will also be presented for publication, with the department of surgery UON and KNH affiliated with the publication.

3.12 Quality Assurances

Data collection was subjected to strict quality control:

- A study protocol was developed and adhered to by all persons involved in the study.
- The study only commenced once approval was been given by the ethics and research committee.
- All participants voluntarily agreed to participate in the study, by giving informed consent, and were allowed to withdraw at any point without this interfering with their access to health care
- On admission, after giving written consent, pre-operative preparation was done.
- Patients were randomized to either arm of the study
- The nerve block was performed after administration of general anaesthesia. The nerve block was given by anesthesiologists who have specialized in regional anesthesia.
- The nerve block was given in the standard method and reconstitution was done be in a standard fashion by all the anesthesiologists.
- Postoperatively, pain intensity was scored using the visual analogue scale, and assessed at 4, 12, 18 and 24 hours after surgery.
- If the patient's pain control is poor despite all measures outlined in the study, the patient will be reviewed by both anesthesiologists for further management.

3.13 Ethical Considerations

The study was started in February 2020 following approval from the Department of Surgery and Ethics and Research Committee (Ref: KNH-ERC/A/26).Patients admitted for surgery, were counseled on the surgery and post-operative care, thereafter informed consent was taken for participation in the study. Those who decline participation were excluded. Refusal to participate in the study bore no repercussions and quality of care was to be up held for non-participants. Data collected was stored by the principal investigator under lock and key and those entered into the computer were under password protection. No access was given to anyone except the statistician for analysis. Data will be stored for up to 3 years after publication, thereafter it will be destroyed.

3.14 Study Limitations

Pain is a subjective emotion, with subjects pain threshold varying, therefore there may be patients at higher pain levels that what they would record on the pain scale. Patients may need more analgesia that what is offered in the study and this will have to be given, as they cannot be left in pain.

CHAPTER FOUR: RESULTS

We recruited a total of 40 patients, 18 were randomized to receive the Pecs II block intra operatively while 22 patients were randomized to receive standard post-operative pain management after undergoing a modified radical mastectomy.

The mean age of the intervention group was 50.6 years and 48.7 years for those who received standard treatment (Table 1). There was no statistical significant difference between the two groups except mean weight (p<0.001) (Table1).

Table 1: Patients' characteristics at baseline

Variable	**Block (n=18)**	**Standard drug (n=22)**	**P value**
Mean age in years (SD)	50.6 (16.8)	48.7 (15.3)	0.706
Mean weight in Kgs (SD)	63.0 (8.5)	74.9 (10.2)	<0.001
Education			
Primary	10 (55.6)	14 (63.6)	0.604
Secondary	8 (44.4)	8 (36.4)	
Stage of disease			
I	0	1 (4.8)	0.446
II	2 (11.1)	2 (9.5)	
III	9 (50.0)	15 (71.4)	
III A	1 (5.6)	1 (4.8)	
III B	5 (27.8)	2 (9.5)	
III C	1 (5.6)	0	
NACT			
Yes	8 (44.4)	4 (18.2)	0.071
No	10 (55.6)	18 (81.8)	

Comparison of pain intensity at 4, 12, 18 and 24 hours was done and adjusted for age, weight, stage of disease, use of NACT and use of morphine. Patients on block intervention showed significantly lower pain scores while at rest compared to those on standard treatment, aOR 0.49 (95% CI 0.25-0.93), p=0.030 (Table 2).

Table 2:Multivariate analysis of patient factors to pain intensity

Variable	At rest		On movement	
	OR (95% CI)	P value	OR (95% CI)	P value
At 4 hours	0.49 (0.25-0.93)	0.030	0.65 (0.38-1.11)	0.112
At 12 hours	0.73 (0.11-4.71)	0.741	0.68 (0.28-1.68)	0.405
At 18 hours	0.75 (0.31-1.82)	0.520	1.02 (0.58-1.80)	0.946
At 24 hours	0.02 (0.00-12.63)	0.241	0.45 (0.12-1.67)	0.230

4.1 Pain Intensity within 24 Hours

The median pain score measured at 4 hours after mastectomy was 0 at rest (Figure 1) and 1 on movement (Figure 2), compared to 4 at rest and 4 on movement in the control group.

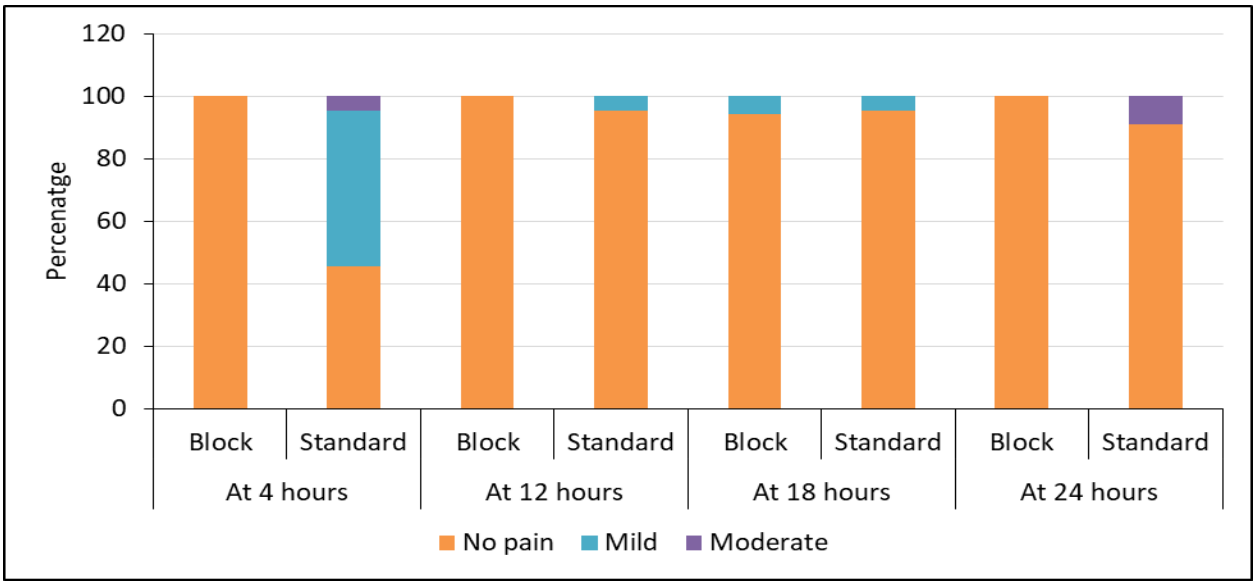


Figure 1:Pain intensity at different time points for patient at rest

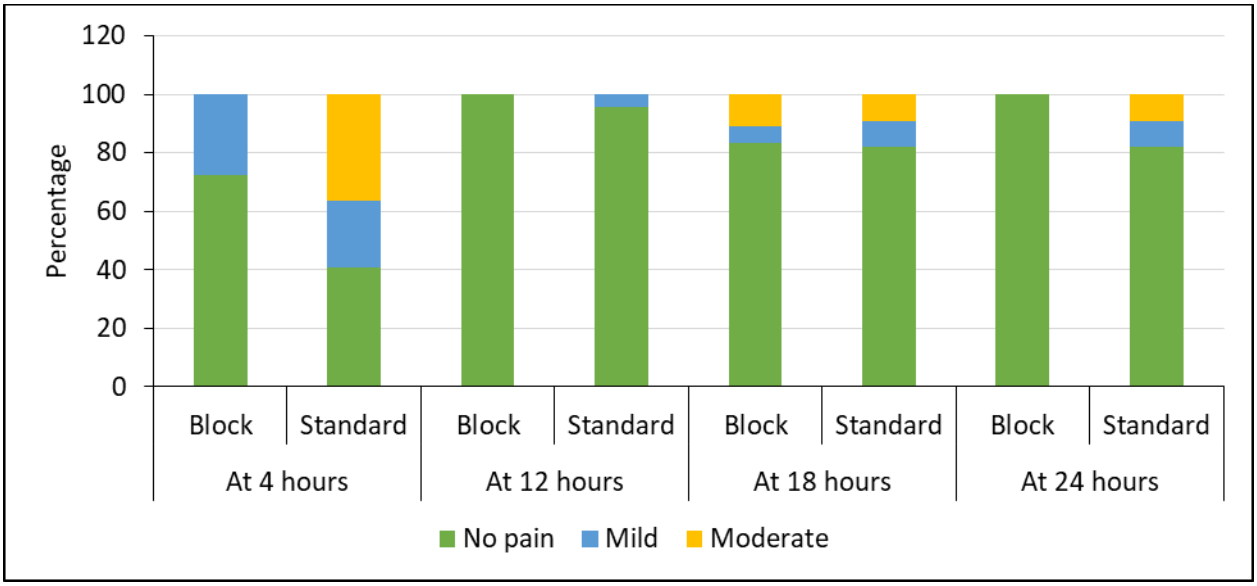


Figure 2: Pain intensity at different time points for patient on movement

This was statistically significant lower with a p value <0.001 on Mann Whitney U (Table 3).

Table 3: Pain scores within 24 hours

Variable	At rest			On movement		
	Block (n=18)	**Standard drug (n=22)**	**P value**	**Block (n=18)**	**Standard drug (n=22)**	**P value**
At 4 hours						
Median (IQR)	0 (0-1)	4 (2-5)	<0.001	1 (0-5)	4 (3-6)	0.001
Category, n (%)						
No pain	18 (100.0)	10 (45.5)	<0.001	13 (72.2)	9 (40.9)	0.009
Mild	0	11 (50.0)		5 (27.8)	5 (22.7)	
Moderate	0	1 (4.5)		0	8 (36.4)	
At 12 hours						
Median (IQR)	0 (0-0)	0 (0-0)	0.925	0 (0-1)	0 (0-2)	0.697
Category, n (%)						
No pain	18 (100.0)	21 (95.5)	1.000	18 (100.0)	21 (95.5)	1.000
Mild	0	1 (4.5)		0	1 (4.5)	
At 18 hours						
Median (IQR)	0 (0-0)	0 (0-2)	0.229	0.5 (0-2.0)	2 (0-3)	0.125
Category, n (%)						
No pain	17 (94.4)	21 (95.5)	1.000	15 (83.3)	18 (81.8)	1.000
Mild	1 (5.6)	1 (4.5)		1 (5.6)	2 (9.1)	
Moderate	0	0		2 (11.1)	2 (9.1)	
At 24 hours						
Median (IQR)	0 (0-0)	0 (0-2)	0.084	1 (0-1)	1.5 (1-2)	0.017
Category, n (%)						
No pain	18 (100.0)	20 (90.9)	0.492	18 (100.0)	18 (81.8)	0.242
Mild	0	0		0	2 (9.1)	
Moderate	0	2 (9.1)		0	2 (9.1)	

4.2 Rescue

The time to rescue analgesia was a median of 13hours and 7.5 hours for the block and control groups, respectively. (Table 4)

Table 4:Time to rescue

Variable	**Block (n=18)**	**Standard drug (n=22)**	**P value**
Rescue given			
Morphine	2 (11.1)	8 (36.4)	0.082
None	16 (88.9)	14 (63.6)	
Time to rescue(hours)	13 (8-18)	7.5 (5-13.5)	0.400

4.3 Side Effects

The patients in the block group experienced fewer side effects as compared to the control group.

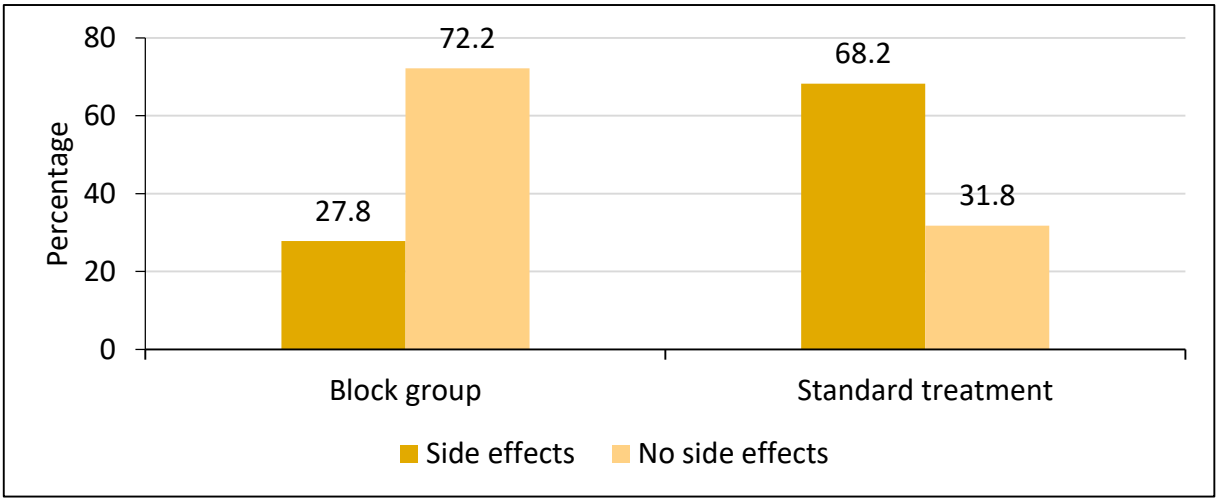


Figure 3:Incidence of side effects

The most common side effect was nausea, and this had a markedly lower occurrence as compared to the control group (Table 4).

Table 4: Post op complications

Variable	Block (n=18)	Standard drug (n=22)	P value
Nausea			
Yes	1 (5.6)	8 (36.4)	0.027
No	17 (94.4)	14 (63.6)	
Vomiting			
Yes	0	3 (13.6)	0.238
No	18 (100.0)	19 (86.4)	
Sedation			
Yes	1 (5.6)	6 (27.3)	0.105
No	17 (94.4)	16 (72.7)	
Blurry vision			
Yes	0	1 (4.5)	1.000
No	18 (100.0)	21 (95.5)	
Dizziness			
Yes	4 (22.2)	10 (45.5)	0.125
No	14 (77.8)	12 (54.5)	
Weakness			
Yes	0	2 (9.1)	0.492
No	18 (100.0)	20 (90.9)	
Any side effects			
Yes	5 (27.8)	15 (68.2)	0.011
No	13 (72.2)	7 (31.8)	

4.4 Satisfaction Levels

There was no significant difference between patients in the block group and those in the standard intervention in relation to satisfaction (Table 5).

Table 5:Satisfaction levels

Variable	**Block (n=18)**	**Standard drug (n=22)**	**P value**
Satisfaction	5 (4-5)	4.5 (4-5)	0.878
Satisfaction 4 5	 8 (47.1) 9 (52.9)	 11 (50.0) 11 (50.0)	 0.855

CHAPTER FIVE: DISCUSSION

Acute post-operative pain following modified radical mastectomy is still a management challenge, despite the large body of evidence showing the negative outcomes associated with poor pain control, [3] and in spite of the numerous studies [7,8,9,10] done experimenting with different agents both singly and in combination, in an attempt to find the optimal pain regimen, that is safe to use while minimizing side effects. The Pecs II nerve blocks provide a safe regional approach to blocking the nerves supplying the breast and are implicated in pain following mastectomies. These are the pectoral, inter-coastobrachial, and inter-coastal nerves III-VI and long thoracic nerve, therefore providing adequate analgesia postoperatively.

Whereas the age, stage of breast cancer, socio-economic status , and administration of neoadjuvant chemotherapy were not found to be significantly different between the two groups, weight was statistically significantly different. A multivariate analysis carried out against different patient characteristics, found that weight was an independent predictor of post-operative pain. Fecho et al, on retrospective analysis of women who had undergone mastectomies for breast cancer, found that obesity, Non-white race, high PACU scores were factors that increased the likelihood of patients experiencing pain at one month post operatively [44]. Poleshuck et al found that a younger age, greater preoperative pain and anxiety, single women, and more invasive surgeries were risk factors for sever acute pain at two days postoperatively [2]. These studies however had a different methodology to ours, hence the different results.

In this study we found that, the Pecs II block provided adequate acute post-operative analgesia that was optimal at the fourth postoperative hour at rest and at the twenty fourth post-operative hour on movement as compared to those who received standard analgesia. This is comparable to Blanco et al, who found adequate pain control, for up to 8 hours postoperatively, for patients who underwent mastectomies as day surgeries, and had received the Pecs II block [12].

Time to rescue analgesia was a median of 13 hours in the intervention group versus 7.5 hours in the control group. The proportion of patients, who required rescue within 24 hours in Pecs II group versus the control group, was 11.1% versus 36.4% respectively. While not statistically significant, due to the small sample size in the study, the clinical significance of this is means less opioid consumption with Pecs II use. Bashandy et al noted a similar outcome in patients who underwent radical mastectomies, with Pecs II block use [11]. They found a reduced total morphine

consumption post operatively and reduced fentanyl use intraoperatively. The analysis also shows a longer time to need for the rescue analgesia, with a clinical significance of this is that the block provided a longer duration of initial analgesia as compared to control group. These results are also comparable to Bashandy et al, who found that post-operative morphine consumption in patients who received the Pecs block, was lower in the first 12 hours after surgery [(11)].

The need for rescue analgesia, goes hand in hand with the frequency of occurrence of side effects. In this regard, the results we found show a higher frequency of opioid side effect in the control group, in whom 68.2% experienced side effects, while 27.8 % in the block group. The most common side effect was nausea, which 5.6% of patients in the block group experienced, versus 36.4% in the control group. Bashandy et al, also found a lower occurrence of nausea, vomiting and sedation in the post anaesthesia care unit, in patients who received the Pecs block for breast surgery [(11)]. The implication of this means a better recovery experience for the patients, and reduced length of hospital stay.

The overall patient satisfaction with their pain control was comparable in both groups, with patients in either group happy with the pain control. One patient developed a subcutaneous hematoma following block infiltration. The other patients who received the block had no complications from it. In conclusion, we had found that the Pecs II block, is a safe and easy to administer under ultrasound guidance, with a short learning curve. It has few complications, and provides adequate analgesia for the first 24 post-operative hours.

REFERENCES

1. V. Vanderpuye, S. Grover, N. Hammad et al. An update on the management of breast cancer in Africa. Infectious Agents and Cancer volume 12, Article number: 13 (2017)
2. J.Ellen, L.Poleshuck, H.Andruse, Laura A.HoganbBeth F.JungfDale I.KulickgRobert H.Dworkin. Risk factors for acute pain and its persistence following breast cancer surgery. Pain. Volume 119, Issues 1–3, 15 December 2005, Pages 16-25
3. Wu, Christopher L., Naqibuddin, Mohammad, Rowlingson, Andrew J., Lietman et al, The Effect of Pain on Health-Related Quality of Life in the Immediates Postoperative Period . Anesthesia & Analgesia: October 2003 - Volume 97 - Issue 4 - p 1078-1085
   Doi: 10.1213/01.ANE.0000081722.09164.D5
4. E.L.Poleshuck, J.Katz, C.H.Andrus, et al, Risk factors for chronic pain following breast cancer surgery: A prospective surgery. The Journal of Pain, Volume 7, Issue 9, September 2006, Pages 626-634
5. S.H.Chang, V.Richard M.Langford Acute and chronic pain following breast surgery, Acute Pain, Volume 11, Issue 1, March 2009, Pages 1-14, doi.org/10.1016/j.acpain.2009.01.001
6. F. Amaya, T. Hosokawa, A. Okamoto, et al. Can Acute Pain Treatment Reduce Postsurgical Comorbidity after Breast Cancer Surgery? A Literature Review. BioMed Research International. Volume 2015, Article ID 641508 .doi.org/10.1155/2015/641508
7. A. Schnabel, S. U. Reichl, P. Kranke, E. M. Pogatzki-Zahn, P. K. Zahn. Efficacy and safety of paravertebral blocks in breast surgery: a meta-analysis of randomized controlled trials. British Journal of Anaesthesia, Volume 105, Issue 6, December 2010, Pages 842–852, doi.org/10.1093/bja/aeq265
8. Klein, Stephen M., Bergh, Arthur, Steele, Susan M., Georgiade, Gregory S., Greengrass, Roy A. Thoracic Paravertebral Block for Breast Surgery. Anesthesia & Analgesia: June 2000 - Volume 90 - Issue 6 - p 1402–1405 doi: 10.1097/00000539-200006000-00026
9. Sherif Samir Wahba, Sahar Mohammed Kamal, Thoracic paravertebral block versus pectoral nerve block for analgesia after breast surgery Pages 129-135 | Received 23 Aug 2013, Accepted 31 Oct 2013, Published online: 17 May 2019doi https://doi.org/10.1016/j.egja.2013.10.006

10. S. Kulhari, N. Bharti, I. Bala, S. Arora, G. Singh. Efficacy of pectoral nerve block versus thoracic paravertebral block for postoperative analgesia after radical mastectomy: a randomized controlled trial. British Journal of Anaesthesia, Volume 117, Issue 3, September 2016, Pages 382–386, https://doi.org/10.1093/bja/aew223
11. GMN Bashandy, DN Abbas. Pectoral nerves I and II blocks in multimodal analgesia for breast cancer surgery. Regional anesthesia and pain 2015
12. . R. Blanco. The 'pecs block': a novel technique for providing analgesia after breast surgery. The Association of Anaesthetists of Great Britain and Ireland: 11 August 2011 doi.org/10.1111/j.1365-2044.2011.06838.x
13. Carol Warfield, MD; Cynthia Kahn, MD. Acute Pain Management: Programs in U.S. Hospitals and Experiences and Attitudes among U.S. Adults. Anesthesiology 11 1995, Vol.83, 1090-1094.
14. N.A. Othieno-Abinya, L.O. Nyabola, H.O. Abwao, P. Ndege. Post – surgical management of patients with breast cancer at Kenyatta National Hospital, East African Medical Journal 2002, pp 156 – 162
15. Tong J Gan, Ashraf S. Habib, Timothy E Miller, William White, Jeffrey L. Afelbaum. Incidence, patient satisfaction, and perceptions of post-surgical pain: results from a US national survey. Current Medical Research and Opinion. Volume 30, 2014 - Issue 1. doi.org/10.1185/03007995.2013.860019
16. Deloatch, Lauren J., Higgins, Michael S. Caplan, Amy B. Stiff, Judith L. The Visual Analog Scale in the Immediate Postoperative Period: Intrasubject Variability and Correlation with a Numeric Scale. Anesthesia & Analgesia: January 1998 - Volume 86 - Issue 1 - p 102-106 doi: 10.1213/00000539-199801000-00020
17. Apfelbaum, Jeffrey L., Chen, and Connie, et al. Postoperative Pain Experience: Results from a National Survey Suggest Postoperative Pain Continues to Be Undermanaged. Anesthesia & Analgesia: August 2003 - Volume 97 - Issue 2 - p 534-540 doi: 10.1213/01.ANE.0000068822.10113.9E
18. R.SeanMorrisonaJayMagazinerbMaryAnnMcLaughlincGretchenOroszaStacey BSilberzweigaKenneth JKovaldAlbert LSiuc. The impact of post-operative pain on outcomes following hip fracture. Pain. Volume 103, Issue 3, June 2003, Pages 303-311

19. Raymond Sinatra, MD, PhD. Causes and Consequences of Inadequate Management of Acute Pain. *Pain Medicine*, Volume 11, Issue 12, December 2010, Pages 1859–1871 doi.org/10.1111/j.1526-4637.2010.00983.x
20. Rob W. Hutchison. Challenges in acute post-operative pain management. American Journal of Health-System Pharmacy, Volume 64, Issue 6_Supplement_4, 15 March 2007, Pages S2–S5, doi.org/10.2146/ajhp060679
21. EricaAlves Nogueira FabroaAnkeBergmannbBlendado Amaral e SilvabAna CarolinaPadula RibeirocKarende Souza Abrahão et al. Post-mastectomy pain syndrome: Incidence and risks. The Breast. Volume 21, Issue 3, June 2012, Pages 321-325
22. Frederick M. Perkins, M.D.; Henrik Kehlet, M.D., Ph.D. Chronic Pain as an Outcome of Surgery: A Review of Predictive Factors. Anesthesiology 10 2000, Vol.93, 1123-1133.
23. R.C.Tait, K.Zoberi, M.Ferguson, K.LevenhagenPT, et al. Persistent Post-Mastectomy Pain: Risk Factors and Current Approaches to Treatment. The Journal of Pain, Volume 19, Issue 12, December 2018, Pages 1367-1383
24. Wood K.M. Intercostobrachial nerve entrapment syndrome. Southern Medical Journal [01 Jun 1978, 71(6):662-663]
25. Fassoulaki, Argyro, Patris, Konstantinos, Sarantopoulos, Costantine, Hogan, Quinn. The Analgesic Effect of Gabapentin and Mexiletine After Breast Surgery for Cancer. Anesthesia & Analgesia: October 2002 - Volume 95 - Issue 4 - p 985-991
doi: 10.1213/00000539-200210000-00036
26. A.Fassoulaki, C. Sarantopoulos, A.Melemeni, Q.Hogan. EMLA reduces acute and chronic pain after breast surgery for cancer. Regional Anesthesia and Pain Medicine. Volume 25, Issue 4, July 2000, Pages 350-355
27. S. Y. KIM, J. W. SONG, B. PARK, S. PARK, Y. J. AN, Y. H. SHIM. Pregabalin reduces post-operative pain after mastectomy: a double-blind, randomized, placebo-controlled study. 02 February 2011 doi.org/10.1111/j.1399-6576.2010.02374.x

28. A.O. Cortés-Flores, J.J.Tornero, G. Morgan-Villela, M. Delgado-Gómez, C. J. Zuloaga-Fernández del Valle et al. Effects of preoperative dexamethasone on postoperative pain, nausea, vomiting and respiratory function in women undergoing conservative breast surgery for cancer: Results of a controlled clinical trial. European Journal of Cancer Care. 04 May 2017, https://doi.org/10.1111/ecc.12686
29. RogerChou∗Debra B.Gordon†Oscar A.de Leon-Casasola‡Jack Rosenberg§StephenBickler et al. Management of Postoperative Pain: A Clinical Practice Guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council The Journal of Pain. Volume 17, Issue 2, February 2016, Pages 131-157
30. W.Cairns SSmithaDiBourneaJanetSquairaDeanO. PhillipsaWAlastair Chambers, A retrospective cohort study of post mastectomy pain syndrome. PAIN, Volume 83, Issue 1, 1 October 1999, Pages 91-95. doi.org/10.1016/S0304-3959 (99)00076-7
31. F. W. Abdallah, P.J. Morgan, M Tulin Cil,et al. Ultrasound-guided Multilevel Paravertebral Blocks and Total Intravenous Anesthesia Improve the Quality of Recovery after Ambulatory Breast Tumor Resection.. Anesthesiology 03 2014, Vol.120, 703-713. doi:10.1097/ALN.0000436117.52143.bc
32. P. A. LönnqvistJ. MacKenzieA. K. SoniI. D. Conacher. Paravertebral blockade: Failure rate and complications. Journal of the Association of Anaesthetists. Volume50, Issue9, September 1995, Pages 813-815. doi.org/10.1111/j.1365-2044.1995.tb06148.x
33. M.Pérez; O.s Duany; Patrcia de la Torre; Redefining PECS Blocks for Post mastectomy Analgesia. Regional Anesthesia and Pain Medicine. 40(6):729–730, NOV 2015 DOI:10.1097/AAP.0000000000000243
34. International Association for the Study of Pain (IASP) Classification of chronic pain. Descriptions of chronic pain syndromes and definitions of pain terms. The International Association for the Study of Pain, Subcommittee on Taxonomy. Pain. 1986; 3:S1–226.
35 D.Waltho, and G. Rockwell, Post–breast surgery pain syndrome: establishing a consensus for the definition of post-mastectomy pain syndrome to provide a standardized clinical and research approach — a review of the literature and discussion. Canadian Journal of Surgery. 2016 Oct; 59(5): 342–350

36. K. Fecho, N. Miller, S. Merritt, N. Klauber-DeMore et al MD, PhD, Acute and persistent postoperative pain after breast surgery, Pain Medicine, Volume 10, Issue 4, May 2009, Pages 708–715, doi.org/10.1111/j.1526-4637.2009.00611.x
37. R. Gärtner, M. Jensen, J. Nielsen, et al. Prevalence of and Factors Associated With Persistent Pain Following Breast Cancer Surgery. JAMA. 2009; 302(18):1985-1992. doi:10.1001/jama.2009.1568
38. Bray F1, Ferlay J2, Soerjomataram I3, Siegel RL4, Torre LA5, Jemal A6. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018 Nov; 68(6):394-424. doi: 10.3322/caac.21492. Epub 2018 Sep 12.
39. Kehlet, Henrik, Wilmore, Douglas W. Evidence-Based Surgical Care and the Evolution of Fast-Track Surgery. Annals of Surgery: August 2008 - Volume 248 - Issue 2 - p 189-198 doi: 10.1097/SLA.0b013e31817f2c1a
40. H.Kehlet, T. S.Jensen, C. J. Woolf. Persistent postsurgical pain: risk factors and prevention. The Lancet. Volume 367, Issue 9522, 13–19 May 2006, Pages 1618-1625
41. Scott SReubenMDGraceMakari-JudsonMDShari DLurieMD. Evaluation of efficacy of the perioperative administration of venlafaxine X R in the prevention of post mastectomy pain syndrome. Journal of Pain and Symptom Management. Volume 27, Issue 2, February 2004, Pages 133-139
42. BarbaraVersyckMDaGeert-Janvan GeffenMD, PhDbPatrickVan HouweMDa. Prospective double blind randomized placebo-controlled clinical trial of the pectoral nerves (Pecs) block type II . Journal of Clinical Anesthesia. Volume 40, August 2017, Pages 46-50
43. Sidiropoulou, Tatiana, Buonomo, Oreste, Fabbi, Eleonora, Silvi, Maria Beatrice, et al, A Prospective Comparison of Continuous Wound Infiltration with Ropivacaine Versus Single-Injection Paravertebral Block After Modified Radical Mastectomy. Anesthesia & Analgesia: March 2008 - Volume 106 - Issue 3 - p 997-1001, doi: 10.1213/ane.0b013e31816152da

APPENDICES

Appendix I: Study Questionnaire

Patient Data

Name initials:……

Age: …….

Weight:…….

Level of education:……..

Ward:……..

Inpatient Number:……

Date of admission:……

Gender:……

Clinical stage:……

Pre-op chemo/radiotherapy:……

Randomization identifying number:…….

Intra operative analgesia used:

MEDICATION	GIVEN
PARACETAMOL	
MORPHINE	
TRAMADOL	
FENTANYL	
OTHERS	

Pain Score Table

PAIN SCORE	AT REST	ON MOVEMENT
4 HOURS		
12 HOURS		
18 HOURS		
24 HOURS		

Time to rescue analgesia and analgesic used

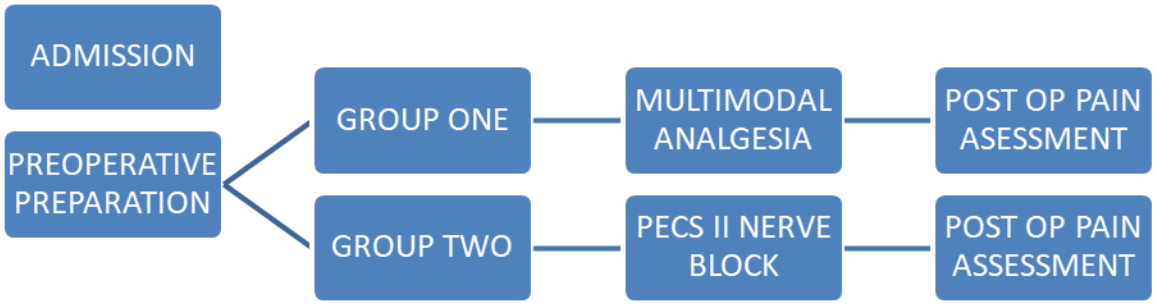
POST-OP HOUR	ANALGESIC USED

Post-op complications experienced:

POST-OP COMPLICATIONS	
NAUSEA	
VOMITING	
SEDATION	
OTHERS	

Patients satisfaction score: ……

Duration of hospital stay: ……



Adverse Event/Reaction Form

Study Title:

Protocol No: **Site ID:**

Project Code:

S.No.	Subject ID	Adverse Event	Serious[1]	Severity[2]	Relationship to Inv. Agent	Start Date/Time (dd/mm/yy) (24Hrs)	End Date/Time (dd/mm/yy) (24Hrs)	Investigator Initial and Date	Comments[3]
			☐ Yes ☐ No	☐Mild ☐ Moderate ☐ Severe ☐Life-threatening	☐Unrelated ☐Possible ☐Probably ☐Definitely	Date: Time:	Date: Time:		
			☐ Yes ☐ No	☐Mild ☐ Moderate ☐ Severe ☐ Life-threatening	☐Unrelated ☐Possible ☐Probably ☐Definitely	Date: Time:	Date: Time:		
			☐ Yes ☐ No	☐Mild ☐ Moderate ☐ Severe ☐ Life-threatening	☐Unrelated ☐Possible ☐Probably ☐Definitely	Date: Time:	Date: Time:		

NOTE:

1. The definitions of severity are the following:

Mild – Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required.

Moderate – Mild to moderate limitation in activity, some assistance may be needed; no or minimal medical intervention/therapy required.

Severe – Marked limitation in activity, some assistance usually required; medical intervention/therapy required hospitalizations possible.

Life threatening – Extreme limitation in activity, significant assistance required; significant medical intervention/therapy required hospitalization or hospice care probable.

2. Treatment or Procedure or Study Discontinuation (Please Specify)

Signature of the Principal Investigator:

Date:

STUDY SCREENING TOOL

Study Title:

Complete this log for every subject screened for inclusion in the study.

S.No	**Subject ID**	**Gender**	**Date of birth** (dd/mm/yyyy)	**Date screened for eligibility** (dd/mm/yyyy)	**Eligibility criteria fulfilled**	**Subject Eligible?**	**If ineligible, specify reason for ineligibility**	**Investigator Initials and Date**
		M ☐ F ☐				Y ☐ N ☐		
		M ☐ F ☐				Y ☐ N ☐		
		M ☐ F ☐				Y ☐ N ☐		
		M ☐ F ☐				Y ☐ N ☐		
		M ☐ F ☐				Y ☐ N ☐		
		M ☐ F ☐				Y ☐ N ☐		

Signature of the Principal Investigator:

Date:

Appendix II: Informed Consent (English Version)

This informed consent is for patients, presenting to Kenyatta National Hospital to undergo modified radical mastectomy, for breast cancer. We are requesting these patients to participate in this research project whose title is "efficacy of pectoral nerve blocks in acute pain management following modified radical mastectomy: a randomized controlled trial"

The informed consent has three parts

1. Information Sheet - to share the information about the research with the participants
2. Certificate of consent- signed sheet upon agreement to participate in the study
3. Statement by the researcher/ person taking the consent

Part 1:

Information Sheet

My name is Dr. Beryl Achieng', a postgraduate student at the department of Surgery University of Nairobi.

Purpose of the Research

The University Of Nairobi in partnership with Kenyatta National Hospital regularly carries our research in different areas in order to improve the quality of care offered to patients and to better understand illnesses. One of the illnesses that is currently under study is breast cancer and in this study we want to know how well we can control pain after surgery, by using a specific medicine called bupivacaine. Bupivacaine has already been studied and found to be effective in pain control after surgeries. We would like to confirm this in our Kenyan population, to better help patients' comfort and recovery after surgery for breast cancer. Following admission for surgery to the ward, you will be prepared for surgery by taking blood samples for tests and thereafter you will give written informed consent for the operation, as well as written consent to participate in this study.

The procedure involves injecting the medicine on the side of the surgery, by a specialist doctor and after theater checking whether you are in pain. There will be a special table for you to use, to describe how much pain there is.

This table will be provided for you to keep at all times. My assistant will explain to you how to use this table. Should there be pain, medication is available to you at all times to ensure that you are comfortable. In theater, after you are given general anaesthesia, the medicine will be injected and surgery performed. After your surgery, my assistant will come regularly, to check on how well the pain is controlled by using the pain score table.

Participation

You are hereby invited to participate in the study. Your participation is voluntary and there is no penalty for refusal to participate in the study. You are also free to withdraw from the study at any point that you may wish to, and this will not interfere with your healthcare. You are entitled to ask any questions and seek clarifications before you decide to participate in the study, I and my co-investigators will be glad to respond to your questions comprehensively.

Quality care will be given to you despite refusal to participate in this study and you will receive no repercussions.

The Process

In order to conduct the study, the participants, assist us with some information, which is treated with confidentiality, and we assign to you a unique number to hide your identity, and it is only the researchers who have access to the information you give. Results arrived at following this research will be used by doctors, policy makers and health planners to improve care of patients with breast cancer.

Risks and Benefits

This is not a new procedure, and has been in use for breast surgeries for years. Though complications are rare, the following may occur: bleeding, failure of medication to work, infection and lung collapse. Should any of these complications occur, and interventions are taken, this cost will not be passed on to you. Results from this study will help in improving the health care given to breast cancer patients at Kenyatta National Hospital. If you are satisfied with the explanation and agree to participate in the study, kindly sign the section below.

Who to Contact

This proposal has been reviewed and approved by the KNH/UoN – ERC, for a duration of one year following its presentation to the Department of Surgery

Should you have any questions, you may contact the following for further information and clarifications;

Principal Investigator:

Dr. Beryl Achieng

Department of Surgery, School of Medicine, University of Nairobi

P.O. BOX 19676 KNG, Nairobi 00202

Tel :0720 99 22 67

Supervisors:

Dr. Daniel Ojuka

Consultant General Surgeon MBChB, M.MED (Gen. Surg), FCS (ECSA)/

Senior Lecturer

P.O. BOX 00202 – 19676, KNH, Nairobi

Dr. Marilynn Omondi

Tutorial Fellow and Consultant General Surgeon

MBChb, M.MED (Gen Surg),

P.O. BOX 00202 – 19676, KNH, Nairobi

Tel: 020-2726300

KNH/ UoN – ERC

Secretary

Tel: 020 – 2726300-9, EXT 44355

Email: KNHplan@Ken.Healthnet.org

Tel: 020- 2726300

PART II

Certificate of consent

I have read the given information, or it has been read to me and have had the chance to ask questions and seek clarification, and these have been answered to my satisfaction. Anticipated complications following involvement in the study have been explained to me and I consent voluntarily to participate in this study.

Name:……..

Signature:……. Date:……..

Witness:…….

If illiterate:

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the chance to ask questions, which have been answered to their satisfaction. I confirm that the individual has given consent freely.

Name of participant:

Signature/ thumb print of participant:

Date:

Statement by the Researcher

I have accurately read out the information sheet to the participant, and in detail explained its contents and intent, and they in turn have understood the information given. Thereafter, the following options are available to them:

- Voluntary acceptance to participate in the study.
- Refusal to participate in the study, which does not compromise the care of treatment to follow.

I confirm that the participant was given ample opportunity to learn about the study, understand its intention, ask questions and detailed answers were given. Therefore no coercion has been done to enter into the study and acceptance was freely given.

A copy of this consent has been provided to the participant.

Name of researcher taking consent:…….

Signature of researcher taking consent:…… Date: …….

Appendix III: Informed Consent (Kiswahili Version)

Utangulizi

Jina langu ni daktari Beryl Achieng, na mimi ni mwanafunzi wa kuhitimu masomo ya juu, katika chuo kikuu cha Nairobi, idara ya masomo ya upasuaji.

Umuhimu wa Utafiti

Chuo kikuu cha Nairobi, pamoja na hospitali ya Kenyatta, wako na ushirikiano ya kufanya uchunguzi ya magonjwa tofauti tofauti kila mwaka, ili kuboresha uhuduma na matibabu wagonjwa wanapata na kuzidisha kuelewa vizuri hayo magonjwa.

Kati ya magonjwa ambazo tunachunguza ni saratani ya matiti, na katika uchunguzi huu ambayo nataka kufanya, nikuangalia jinsi dawa ya bupivacaine inaweza kutumika baada ya upasuaji wa titi kuboresha matibabu ya uchungu. Dawa hii tayari imedhibitishwa kusaidia sana kupunguza uchungu baada ya upasuaji ya kutoa titi kwasababu ya ugonjwa wa saratani ya titi. Ningependa kufanya utafiti hii katika idadi ya wanawake hapa Kenya kuona kama matokeo ni kama yale ya tafiti zingine kama hii. Matokeo itawezesha kuboresha matibabu ambayo tunawapa wagonjwa wetu.

Kwa kukubali kujiunga na utafiti huu matibabu yako yataendelea hivi. Baada ya kulazwa kwa ward, utafanyiwa mtihani wa maabara kukutayarisha kupelekwa ukumbi wa upasuaji. Tutahitaji pia idhini ya kuandikwa, kukubali kuwa ungependa kujihusisha na utafiti huu na idhini nyingine ya kukubali kufanyiwa upasuaji. Katika ukumbi wa upasuaji, dakitari wa kupatiana madawa ya kulala, atatumia mashini ya picha, kuangalia upande wa kufanya upasuaji, na kudunga sindano mbili za dawa ya bupivacaine.Baada ya hayo utafanyiwa upasuaji, na utakapo aamka kwa chumba cha wagonjwa kuangaliwa baada ya upasuaji, nitakuja kukuona na kudhihirisha kiwango cha uchungu ambayo unasikia kama utakuwa na uchungu. Hata kama hii ni utafiti ya uchungu baada ya upasuaji, haimanishi kuwa utakuwa unahisi uchungu ya zaidi baada ya upasuaji.

Hatungependa uwe na usumbufu wa uchungu baada ya upasuaji, kwa hivyo madawa yako ya kupunguza uchungu, na utapewa kila wakati utakapoitisha kama unahisi uchungu. Dawa hii imetumika kwa njia hii kwa miaka na zipo utafiti zingine zimefanywa nchi za ulaya kudhibitsha utumishi wake katika upasuaji wa matiti juu kwasababu ya saratani ya titi. Licha ya hii, kumepatikana adhara wakati unapodungwa dawa hii. Dawa inweza kukosa kufanya, au kuvuja damu kidogo, ama kudunga sehemu ya mapafu. Ingawa adhara na utaratibu wa kupewa dawa hii

ni nadra sana, ni jukumu letu kuwaelezea juu zao. Ikiwa adhara yeyote itafanyika, tutaitatua bila wewe kulipishwa pesa zaidi ya ile ungelipia mwanzoni.

Ushirika wa Hiari

Kujiunga na utafiti huu ni kwa hiari yako baada ya kusoma na kuelewa maelezo haya. Wale amabao hawataki kujihusisha na utafiti huu, bado watapata matibabu sawa na wale ambao wamejiunga, bila maangamizo yoyote. Ukiwa na maswali yoyote, mimi na wapelelezi wenzangu tuko tayari kuyajibu na kuondoa mkanganyiko yoyote.

Madhara

Kuhusika na utafiti huu hautakuwa na madhara makubwa dhidi ya afya yako. Ile dawa ambayo tunatumia kukinga uchungu, haitakuwa na madhara kwako, ni dawa ambayo hivi tayari intatumiwa kwa njia zingine tofauti, kukinga uchungu, na kabla ya kuruhusiwa nyumbani, itakua imeondoka kwenye mwili wako.

Adhara ya njia ya kudunga dawa hii zipo, lakini ni nadra sana, na katika utafiti zingine, hakuna adhara yeyote amabayo ilitokea.

Siri Na Faida

Kwa kuhusika katika utafiti huu, hatutatumia jina lako, na taarifa yoyote amabayo untatupa ita wekwa kwa siri na baada ya kumalizika kwa utafiti huu, matokeo yatakayopatikana, utaruhusiwa kuyajua.

Utafiti huu, utasaidia sana kujua jinsi ambavyo tunaweza kusaidia wagonjwa amabao wanfanyiwa upasuaji, kwa sababu ya ugonjwa wa saratani ya titi.

Unaweza kuuliza maswali yeyote kuhusu utafiti huu na ukiridhika tafadhali ijaze fomu ya idhini iliyopo hapa chini. Unaweza pia kuuliza swali lolote baadaye kwa kupiga simu ya mtafiti mkuu ama mkuu wa idara ya upasuaji katika chuo kikuu cha Nairobi ama walimu wasimamizi wa utafiti ukitumia nambari za simu zifuatazo;

Katibu wa utafiti, hospitali kuu ya Kenyatta na chuo kikuu cha Nairobi, sanduku la posta 20723 KNH, Nairobi 00202. Nambari ya simu: 2726300-9

Kwa mawasiliano zaidi:

Mtafiti Mkuu

Daktari Beryl Achieng

Idara ya upasuaji

Nambari: 0720992267

Wasaidizi Wakuu:

Daktari Marilynn Omondi

Idara ya upasuaji

Chuo kikuu cha Nairobi

Sanduku la posta 19676 KNH Nairobi 00202

Tel: 0202726300

Daktari Daniel Ojuka

Idara ya upasuaji

Chuo kikuu cha Nairobi

Sanduku la posta 19676 KNH Nairobi 00202

Tel: 0202726300

Formu Ya Kudhibitish Uingiaji Kwa Utafiti Kwa Hiari Idhini Ya Mgonjwa

Mimi (jina)……. kwa hiari yangu nimekubali kushiriki katika utafiti huu unaofanywa na Daktari Beryl Achieng kutokana na hali ambazo nimeelezwa na sio kwa malipo ama shurutisho lolote.

Nimeelewa kwamba nina weza kujiondoa wakati wowote nitakapo na hatua hii haita hatirisha matibabu ninayoyapata. Matokeo ya utafiti yaweza kuwa na manufaa kwangu ama kwa wagonjwa wengine kwa jumla na hata madaktari wenyewe, kwa kuendeleza elimu. Matokeo nitaelezwa siku nyengine nitakapokuja kliniki.

Sahihi/alama ya kidole cha gumba……

Tarehe…….

Siku/Mwezi/Mwaka

Jina la shahidi…….

Sahihi……Tarehe…….

Siku/ Mwezi/Mwaka

Dhibitisho la Mtafiti Mkuu

Hii nikuidhinisha ya kwamba nimemueleza mgonjwa kuhusu utafiti huu na pia nimempa nafasi ya kuuliza maswali. Nimemueleza yafuatayo;

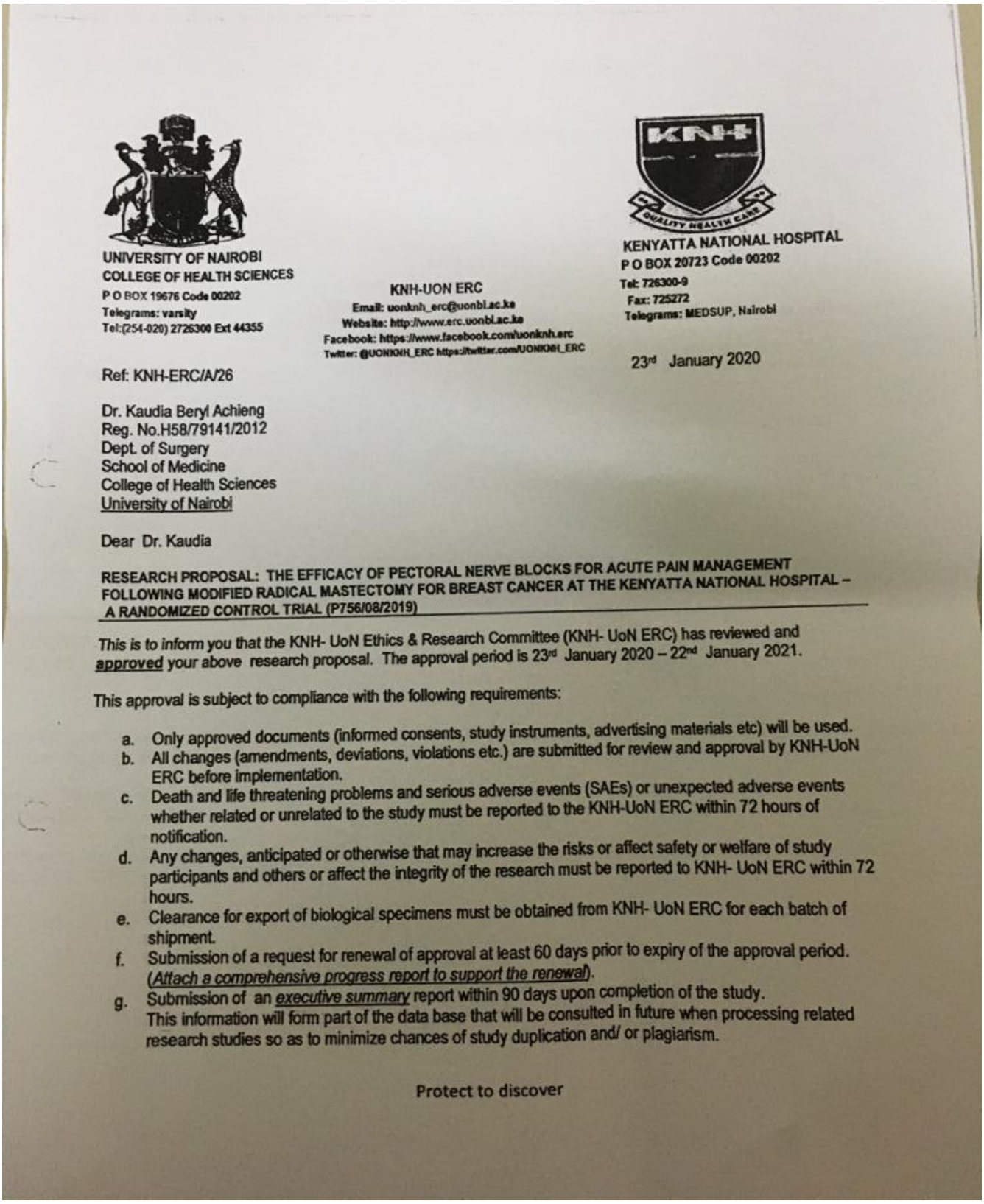
- Kwamba kushiriki ni kwa hiari yake mwenyewe bila malipo.
- Kushiriki hakutasababisha madhara ama kuhatarisha maisha kamwe.
- Anaweza kujiondowa kutoka kwa utafiti huu wakati wowote bila kuhatirisha matibabu anayoyapata katika hospitali kuu ya Kenyatta
- Habari ambazo atapeana hazita tangazwa hadharani bila ruhusa kutoka wake na pia kutoka kwa mdhamini mkuu wa utafiti wa hospitali kuu ya Kenyatta na chuo kikuu cha Nairobi.

Jina la mtafiti……

Sahihi……Tarehe……

Siku/Mwezi/ Mwaka

Appendix IV: KNH/UON-ERC Letter of Approval



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KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

23rd January 2020

Ref: KNH-ERC/A/26

Dr. Kaudia Beryl Achieng
Reg. No.H58/79141/2012
Dept. of Surgery
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Kaudia

RESEARCH PROPOSAL: THE EFFICACY OF PECTORAL NERVE BLOCKS FOR ACUTE PAIN MANAGEMENT FOLLOWING MODIFIED RADICAL MASTECTOMY FOR BREAST CANCER AT THE KENYATTA NATIONAL HOSPITAL – A RANDOMIZED CONTROL TRIAL (P756/08/2019)

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 23rd January 2020 – 22nd January 2021.*

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

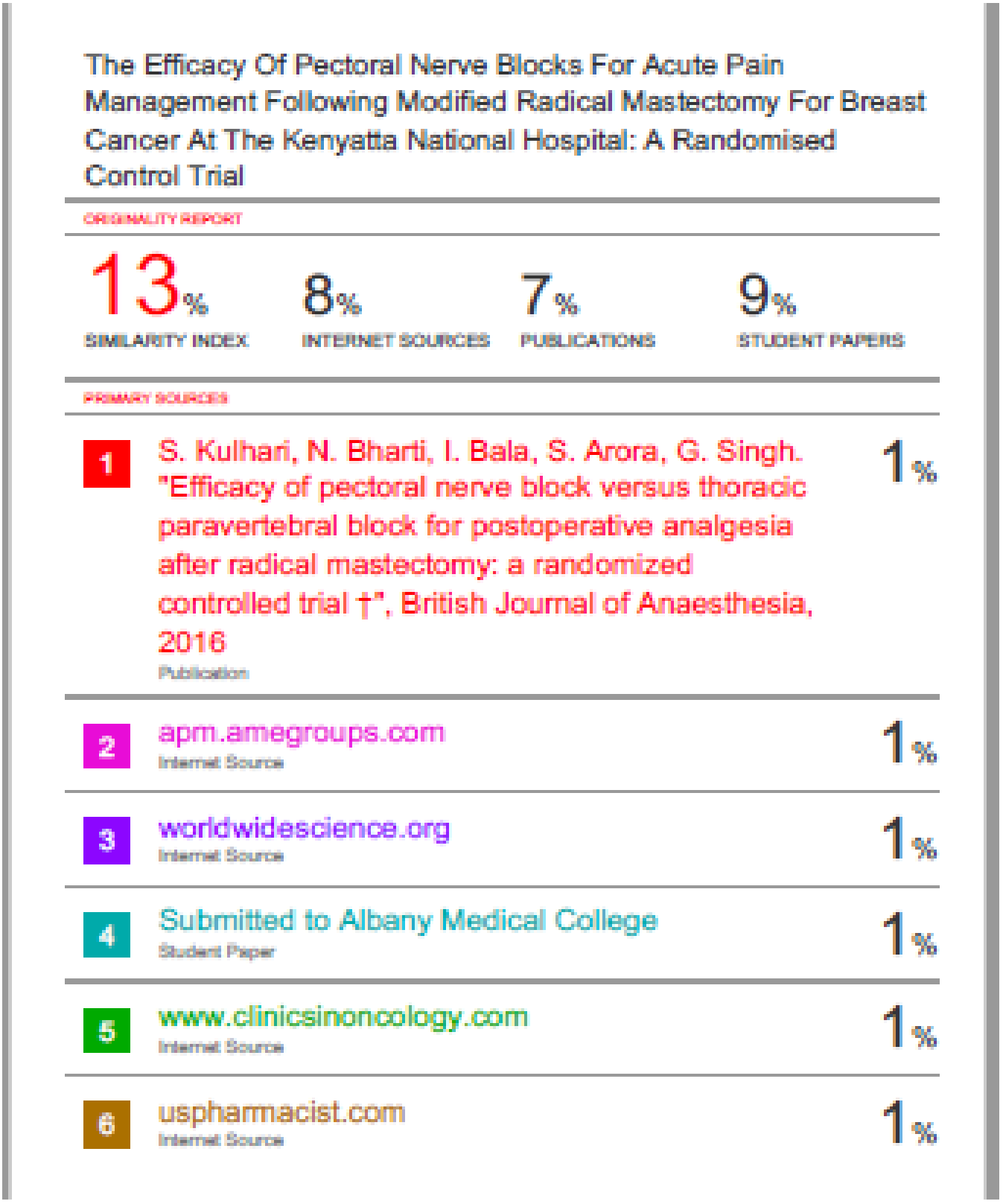
For more details consult the KNH- UoN ERC website http://www.erc.uonbi.ac.ke

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 Surgery, UoN
Supervisors: Dr. Daniel Ojuka, Dept. of Surgery, UoN
Dr. Marilynn Omondi, Dept. of Surgery, UoN
Dr. Timothy Mwiti, Dept. of Anaesthesia, UoN
Dr. Kevin Arunga, Dept. of Anaesthesia, KNH

Appendix V: Plagiarism Certificate



The Efficacy Of Pectoral Nerve Blocks For Acute Pain Management Following Modified Radical Mastectomy For Breast Cancer At The Kenyatta National Hospital: A Randomised Control Trial

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