The efficacy of a simple standard multimodal analgesic protocol on acute post-operative pain after major abdominal surgery at Kenyatta National Hospital.

A dissertation submitted in part fulfillment of the requirements for the Master of Medicine in General Surgery degree of the University of Nairobi.

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April, 2013

Declaration

Candidate

I hereby declare that this study is my original work and has not been presented at any other institution or university.

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Dedication

To Kamene for your patience and support

Nyaboke, Kemunto and Kerubo my source of inspiration when things were hard

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Abstract

Background: Management of post-operative pain is regarded as routine in surgical practice. Many studies have however shown that its management is often poor. Opioid analgesics are most commonly used in treatment of moderate to severe pain after major abdominal surgery. Intramuscular pethidine given in varying dosages has been shown to be the most common analgesic used in Kenyatta National Hospital (KNH). This method has received numerous criticisms from various authors. Multimodal analgesia is a strategy of combining different classes of analgesics by various routes of administration to reduce side effects of opioids and increase analgesic effect.

Objectives: To assess the effect of a standardized multimodal analgesic post-operative pain management protocol in patients recovering from major abdominal surgery at KNH

Methodology: This was an age matched case control study of patients undergoing major abdominal surgery in the General Surgical Wards at KNH. The cases were patients who post-operatively received the study analgesic protocol of pethidine combined with diclofenac. The control group consisted of patients whose post-operative treatment was a single analgesic agent either an opioid or Non-Steroidal Anti-Inflammatory Drug (NSAID). The study period was 3 months during which convenient (non-random) sampling was utilized to enrol study participants meeting the enrolment criteria until the desired sample size of 50 in each arm was attained. The main Outcome variables were pain scores measured at rest in the first 72 hours using the Visual Analogue Scale and the incidence of common opioid side effects i.e. nausea; vomiting and sedation. These were compared in the two study arms. Data collected was entered and verified in Microsoft Excel and data analysis performed using SPSS version 17.

Results: patients who received the study's multimodal analgesic protocol had significantly lower pain scores. Mean VAS score at 12 hours was 5.125 and 1.062 at 72 hours compared with 6.175 at 12 hours and 1.66 at 72 hours. P value was <0.05. There was no significant difference in the occurrence of sedation, nausea or vomiting between the two groups.

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List of Abbreviations

APS -	Acute Pain Service
ASA -	American Society of Anesthesiologists
KNH -	Kenyatta National Hospital
IASP-	International Association for the Study of Pain
IM -	Intra-Muscular Injection
MEAC-	Minimum Effective Analgesic Concentration
MPQ -	McGill Pain Questionnaire
NRS -	Numerical Rating Scale
NSAIDs-	Non-steroidal Anti-Inflammatory Drugs
PCA -	Patient Controlled Analgesia
PRN -	Pro-Re-Nata (as required)
VAS -	Visual Analogue Scale
WHO -	World Health Organization

Definition of operational terms

Multimodal Analgesia:

The use of several analgesics or modalities that act by different mechanisms in combination to maximize analgesic efficacy and minimize side effects (International Association for the Study of Pain)

Major Abdominal Surgery:

Abdominal surgery requiring laparotomy

Early post-operative period:

The first 72 hours after surgery

1. Introduction

1.1 Background

Post-operative pain is a frequent occurrence in the surgical setting. Kehlet describes it as "a constellation of unpleasant sensory, mental and emotional experiences precipitated by surgical trauma"[1]. Autonomic, emotional and behavioral reactions are usually elicited and these may adversely affect the individual. Despite the numerous medical advances in recent times, the ability to provide total pain relief has not been achieved[1].

The treatment of pain is a routine feature of everyday practice and is often considered straight forward. Its management is however commonly reported to be poor [2]. A study by Ocitti showed that 60% of patients had inadequate pain relief in the first 72 hours after major abdominal surgery. Intermittent intramuscular opioid analgesia was the most commonly used analgesic regime with little attention to the patients' response and exaggerated concern about the adverse effects of opioid analgesics [3]. Many health workers routinely dismiss pain resulting from surgical or diagnostic procedures as inevitable, yet to patients it is perceived to be one of the major negative consequences of the procedures carried out on them [4]. Surveys done have shown that inadequacies in pain evaluation and treatment are frequently reported among health care workers. These inadequacies result from insufficient knowledge of pharmacology of the most commonly used analgesics, the existence of poor prescription practices, a lack of concern for adequate relief of procedural pain, failure to follow prescribed analgesic regimens, and the fear of known or perceived side effects of the drugs used [1, 3 & 5].

Effective pain management is considered a mark of a civilised society by some authors, and they have argued that it should be considered a basic human right [6]. In addition to humanitarian reasons, effective post-operative pain relief has been shown to have physiologic benefits. These include reduction in occurrences of pulmonary and vascular complications including atelectasis, hypostatic pneumonia, deep venous thrombosis, post-surgical hypertension and tachycardia. Post-operative ileus, emesis and acute urinary retention rates have also been shown to reduce with better post-operative pain management[7, 8 & 9]. Improved post-operative pain management also decreases hospital stay and allows patients to resume their usual lifestyles earlier. The incidence of chronic post-operative syndromes has also been shown to reduce with adequate post-operative pain management [10].

As pain is a subjective experience, researchers have shown consistently that patient self reports provide the most valid measure of this experience. The Visual Analogue Scale (VAS), Numeric Rating Scale (NRS) and the McGill Pain Questionnaire (MPQ) are some of the frequently used self-rating instruments both in research and routine care of patients [11]. The MPQ is designed to assess the multidimensional nature of pain and has been shown to be reliable, valid and consistent. It is however a cumbersome questionnaire to use and requires the users to be fluent in the language used [12]. Myles et al. showed that the VAS is an accurate linear scale for the measurement of post-surgical pain intensity and changes in the score consistently reflected change in the intensity of pain experienced[13]. Bodian et al. demonstrated that changes in VAS scores in post laparotomy patients of 10 points using a 100 point VAS was associated with a significant clinical presentation demonstrated by either an increase or decrease in analgesic requirement[14].

As a result of understanding the frequency and burden of post-operative pain many health bodies globally have adopted policy statements that advocate for the systematic and institutional approaches to its management. These include policy statements from the World Health Organisation (WHO), The Royal College of Surgeons, The American Pain Society and The Joint Commission on Accreditation of Healthcare Organizations[15, 16]. These recommendations emphasize on routine assessment of pain as the fifth vital sign, standard multimodal pain treatment and continuous quality evaluation. They also include setting up of formal teams of surgeons, anesthesiologists and nurses in formation of an acute pain service [17].

1.2 Study question

What is the efficacy of a simple standardized multimodal analgesic protocol on acute post-operative pain after major abdominal surgery?

2. Literature review

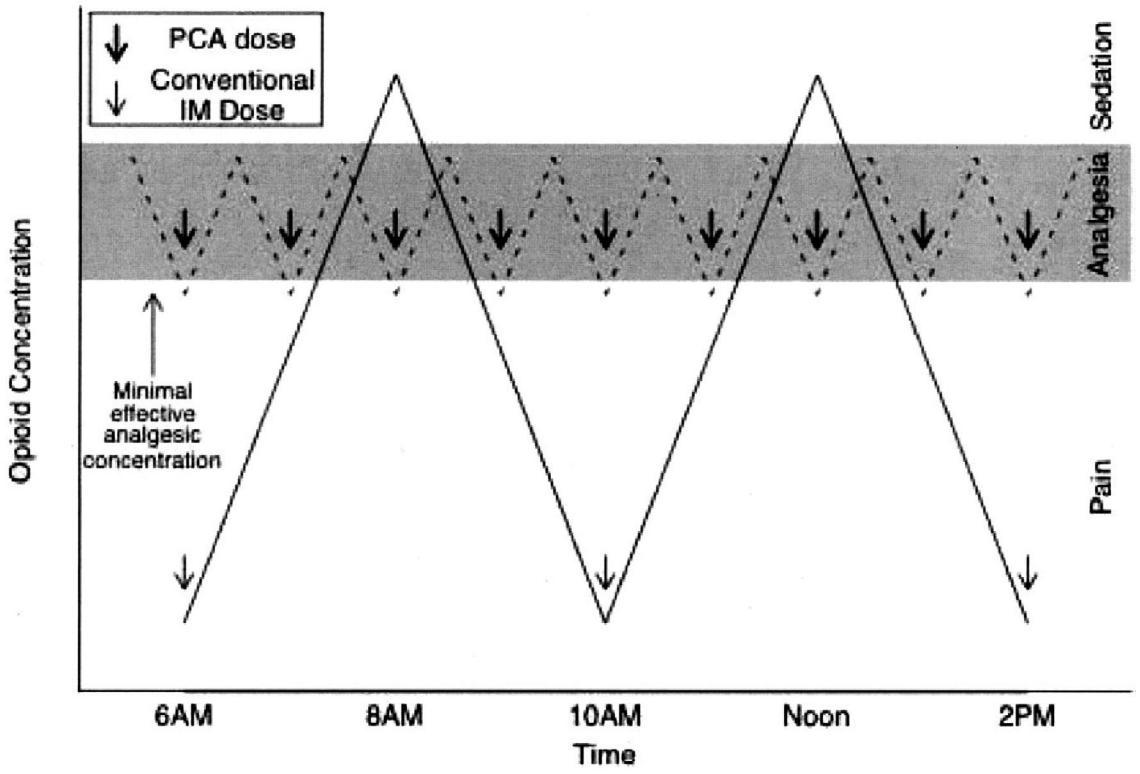
The International Association for the Study of Pain defines pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"[18]. Pain receptors are the free nerve endings that are found in virtually all tissues. Nociceptive impulses are transmitted through A-delta and C fibers for somatic pain and afferent sympathetic fibres for visceral pain to the central nervous system. In the dorsal horn of the spinal cord modulation of these impulses occurs before ascent to the hypothalamus, reticular formation and brainstem through spinothalamic and spinoreticular tracts. Eventually these impulses reach the cerebral cortex. Inhibitory descending pathways mediated by serotonin, norepinephrine and encephalins play an important role in pain modulation. Segmental reflexes in the spinal cord can trigger peripheral responses that may affect the individual further. These include increased muscle tone, decreased chest compliance, and decreased gastric motility leading to ileus, nausea and vomiting [1, 19].

Acute pain following major surgery is frequent. Warfield and Kahn reported that 70% of adult patients reported incidences of pain after surgery with 80% of the respondents describing their pain as moderate to severe in intensity [20]. To this effect studies have been under taken to determine predictors of severe post-operative pain. Caumo et al. identified American Society of Anaesthesiologist (ASA) status, age, acute preoperative or chronic pain, high trait anxiety levels and depressive mood states as predictors of developing moderate to severe pain after surgery [21].

Opioid analgesics have been the main stay of postoperative analgesia in patients with moderate to severe pain. Ocitti demonstrated that intermittent intramuscular pethidine was the most common opioid used after major abdominal surgery in Kenyatta National Hospital (KNH) [3]. Intramuscular opioid has received widespread criticism as it produces variability in pain control [22]. This is because intramuscular route produces periods of low plasma concentration (troughs) of opioid when little analgesic effect is achieved and peaks or overshoots when adverse effects such as sedation and respiratory depression are common with little added value in overall pain control (see figure 1)[23]. Intramuscular Pro-Re-Nata

(PRN) method is however low cost and less demanding on the nursing staff hence its continued usage especially in resource poor settings [3].

Figure 1: Graphic comparison of analgesia achieved by intermittent intramuscular route and patient-controlled analgesia [23]



Sechzer demonstrated that small intravenous doses of opioid given on demand by either nurse or machine produced better analgesic effect than the intramuscular route [24]. Further work by various authors on the pharmacokinetics and pharmacodynamics of opioids resulted in the acceptance of two fundamental prerequisites for effective analgesia in opioid use. The first is the concept of individualized dosage titrated to achieve the Minimum Effective Analgesic Concentration (MEAC) and establish analgesia. The second prerequisite is the ability to maintain constant plasma concentration and avoid the peaks and troughs. These are not achievable by PRN or round the clock intramuscular injections. This herald the paradigm of Patient Controlled Analgesia (PCA), the use of on-demand, intermittent analgesia under patient control. [25]

The route of administration of PCA can be oral, subcutaneous, epidural, peripheral nerve catheter, transdermal or intravenous if the analgesic is delivered on immediate patient demand in sufficient quantities [2]. However the 'traditional' PCA commonly refers to intravenous administration of opioid analgesia using sophisticated microprocessor-controlled infusion pumps that deliver programmed dosage when patients press a demand button [25]. Morphine, hydromorphone and fentanyl are the most commonly used opioids in the United States of America for PCA. Pethidine (meperidine) though commonly used is discouraged by some authorities for use in PCA [26]. This is due to the side effects of its active metabolite normeperidine which causes sedation, respiratory depression with no analgesic benefit.

Walder et al published a systematic review that concluded that Intravenous PCA with opioids compared with conventional intermittent intramuscular opioid use improved analgesia and was preferred by patients in the post-operative pain setting [27] .This method however is more costly than conventional intramuscular route when given in frequent dosage to achieve similar analgesic effect. Though reduction in nursing time favoured PCA, this gain was offset by the significantly higher cost of materials. In addition PCA still has frequent opioid related adverse effects with post-operative nausea and vomiting being the most common [23].

The concept of multimodal analgesia was introduced to improve pain control and reduce the opioid related side effects. The rationale of this strategy is the use various combinations of different classes of analgesics that have different mechanisms of action. The aim of these combinations is to reduce the dosage and thus limit the occurrence of adverse effects due to any one particular analgesic whilst providing adequate analgesia to the patient. This method is advocated by various bodies with interest in post-operative pain management including the American Society of Anesthesiologists, the Royal College of Surgeons and the Royal College of Anaesthesiologists [15, 28].

A met-analysis of double and single blind studies investigating the use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) with opioids by Jin et al showed that majority of patients experience lower pain scores, require fewer analgesics and have prolonged time to analgesic requirement after surgery [29]. Other agents that have been used as adjuncts to

opioids include cyclooxygenase-2-selective inhibitors, N-Methyl-D-aspartate (NMDA) receptor antagonists e.g. low dose ketamine and magnesium sulfate. Alpha-2 adrenergic agonist e.g. clonidine and dexmedetomidine have also been used in combination with opioids. Other drugs that have demonstrated opioid sparing effects include gabapentin, pregabalin and glucocorticoids [30]. Local anaethesia used properly has been shown to be opioid sparing and can give good analgesic effect. Carney et al. demonstrated this using a transversus abdominis plane block in patient undergoing abdominal hysterectomy [31].

Gould et al described improvement in post-operative pain scores by introducing changes in post-operative pain management in seven sequential steps. These began with an audit of current hospital practice, followed by sequential introduction of pain assessment charts, an algorithm to allow for more frequent intramuscular (IM) analgesia, increased use of local anaesthesia and regional techniques, introduction of a pain information sheet for patients and finally PCA[17]. Harmer et al showed the effect of introduction of formal pain assessment and use of a simple algorithm that allows for more flexible IM opioid use improved pain control both at rest and during movement after surgery [32].

3. Study justification and Hypothesis

3.1. Study Justification

There is paucity of literature concerning post-operative pain management in the low resource setting. Kituyi et al showed that clinicians had many knowledge gaps in the assessment and management of post-operative pain [5]. Ocitti demonstrated that at KNH post-operative pain management was inadequate, with 60% of patients reporting inadequate analgesia in the immediate post-operative period. He recommended further studies and improved techniques in pain management [3].

Most studies done on multimodal analgesia for major surgery have included Patient Controlled Analgesia (PCA) methods as one of their modalities in their protocols. This method is both expensive, time consuming and is not readily available in public hospitals in developing countries.

Few studies have been done on the more readily available analgesia in a resource poor situation as is commonly encountered in a public hospital in a developing country like Kenya. This study looked at the effect of locally and readily available analgesia used in a multimodal manner coupled with frequent and routine pain assessment.

It is hoped that the results of this study may be a step in formation of a formal acute pain service at Kenyatta National Hospital.

3.2. Hypothesis

- There is no difference in the efficacy of a simple standardized multimodal analgesic protocol and single analgesic use.

4. Study objectives

4.1 Main Objectives

- To assess the efficacy of a standardized post-operative pain management protocol in patients undergoing major abdominal surgery in KNH

4.2 Specific objectives

- To compare pain severity scores of patients treated under the protocol and the current practice in the early post-operative period. (First 72 hours)
- To compare analgesic induced post-operative complications in patients under protocol and current practices in the early post-operative period. (First 72 hours)

5. Methodology

5.1 Study setting

The study was conducted in the general surgical wards of Kenyatta National Hospital in Nairobi Kenya after approval from the department of surgery, University of Nairobi (UON) and The KNH/UON Ethics and Research Committee.

5.2 Study population

Patients undergoing major abdominal surgery at the Kenyatta National Hospital General Surgery wards were the study population.

5.3 Study design

The study was an age matched case control study. The cases consisted of patients who were managed using the study's multimodal analgesic protocol. The controls were patients matched for age (using a ten year age bracket) and gender. The ratio of cases to controls was 1:1.

The patients were recruited from all the three general surgical wards of KNH.

Taking cognizance of the fact that there are no standardized analgesic practices in the general surgical wards [7], patients recruited into the control arm of the study were those whose analgesic regimen consisted of a single opioid analgesic agent or multiple agents including opioids and NSAIDs administered sequentially after a minimum period of 24 hours. Patients on multiple analgesic regimens concurrently were not recruited.

5.4 Sampling

5.4.1. Sample size determination

Sample size was calculated using the formula below. This formula was chosen because the study involved comparison of two arms of equal proportion and the main outcome measure (VAS) is a continuous variable [33].

$$\underline{n=2[(a+b)^2\sigma^2]}$$

$$(\mu_1 - \mu_2)^2$$

Where:

n = the sample size in each of the arms of the study

μ_1= population mean in the protocol group

μ_2 = population mean in the control group

$\mu_1 - \mu_2$ = clinically significant difference to be detected equal to 10%. Represents a change in the VAS score of 10 points [14]

σ^2 = population variance = Standard deviation= 25

a= conventional multiplier for alpha (probability for type I error) = 1.96

b= conventional multiplier for beta (probability for type II error) = 0.842

$n=2[(1.196+.842)^2(25)^2/ (10)^2=49.070025$

Therefore the minimum sample size in each arm was 50 patients.

5.4.2. Sampling Method

Sampling was non-random (purposive) with all eligible patients being recruited sequentially until the above sample size was met.

5.5 Inclusion criteria

- Patients who were 18 years and older

- Patients scheduled for major abdominal surgery either electively or as emergency
- Patients who gave written consent
- Patients with ASA status of I and II

5.6 Exclusion criteria

- Patients with known psychiatric disorders
- Patients with known addictions or substance abuse
- Patients with pre-existing medical condition that was a contraindication for NSAID use e.g. renal insufficiency
- Polytrauma patients
- Patients who had preoperative chronic pain syndromes and had been on long term analgesia.
- Patients who required admission to the Intensive Care Unit (ICU) in the peri-operative period
- Patients who received regional analgesia

5.7 Implementation of the protocol

- Patients in the interventional arm of the study were started on a multimodal analgesia protocol using opioid analgesics and NSAIDS. Post-operative analgesia was administered on arrival to the general ward after discharge from the Post Anaesthesia Care Unit (PACU). A rescue analgesic algorithm was included in the protocol and was also available for those in the control group. The postoperative treatment sheets were written by the operating surgeon and counter checked in the

ward by the principle investigator for conformity to the study protocol. (Appendix 5)

- Preemptive anaesthesia was not used in the protocol.
- Patients were recruited in the pre-operative period.
- The prescribed analgesia was administered by the nursing staff on duty and treatment sheets inspected daily by the investigator and assistants to ensure adherence.
- Intramuscular route of administration was used in the protocol because of the ease of use and less demand on the nursing staff.
- Intra-operative analgesia used was recorded.

5.8 Pain assessment

- Pain scores were measured at 12 hour intervals for the first 72 hours after surgery using a Visual Analogue Scale (VAS) by the principle investigator and research assistant.
- All patients recruited into the study were taught how to score their pain using the Visual Analogue Scale prior to surgery.

6. Data management

Data for the study was collected through a structured data sheet. (Appendix 2)

6.1 Data variables collected included:

- Age and Gender.
- Indication for the surgery and procedure performed
- Intra-operative analgesia used.
- Pain scores using the VAS at 12, 24, 36, 48, 60 and 72 hours after surgery.
- Vital signs (pulse, blood pressure, respiratory rate) taken at the same time as the pain scores.
- Occurrences of sedation, nausea and vomiting were recorded as these are the most common side effect of opioid analgesia in the post-operative setting.
- Type of analgesia used post operatively in both study arms was recorded.

6.2 Data Analysis

- Collected data was entered into a Microsoft Excel spread sheet for verification and cleaning. The data was then coded and analyzed using Statistical Package for Social Sciences version 17.0(SPSS 17.0).

- Descriptive statistics derived from demographic data were used to describe the study population using means, ranges and medians for continuous variables of age. Ordinal variables e.g. gender, had their frequencies and subsequent proportions calculated. These were in turn compared between the two groups.

- Pain scores obtained from the VAS at 6 intervals were analyzed for the mean and trend. These were then plotted in a graph. Analysis of Variance (ANOVA) was used to check for statistical significance.

- Frequency of sedation, nausea and vomiting in each group was obtained and compared for statistical significance using Pearson's Chi square test.

- Statistical significance was set at 0.05

- After analysis the results were presented in form of tables, charts, scatter plots and graphs

7. Ethical considerations

- The study was presented to the KNH/UON Ethics and Research committee through the department of surgery, University of Nairobi. Approval to conduct the study was given on 6th December 2012.

- Written informed consent was obtained from all patients recruited into the study and there was no adverse consequence of any sort to those who declined to enroll.

- The right to withdraw from the study at any time was guaranteed to all patients.

- Patients' information was treated with confidentiality.

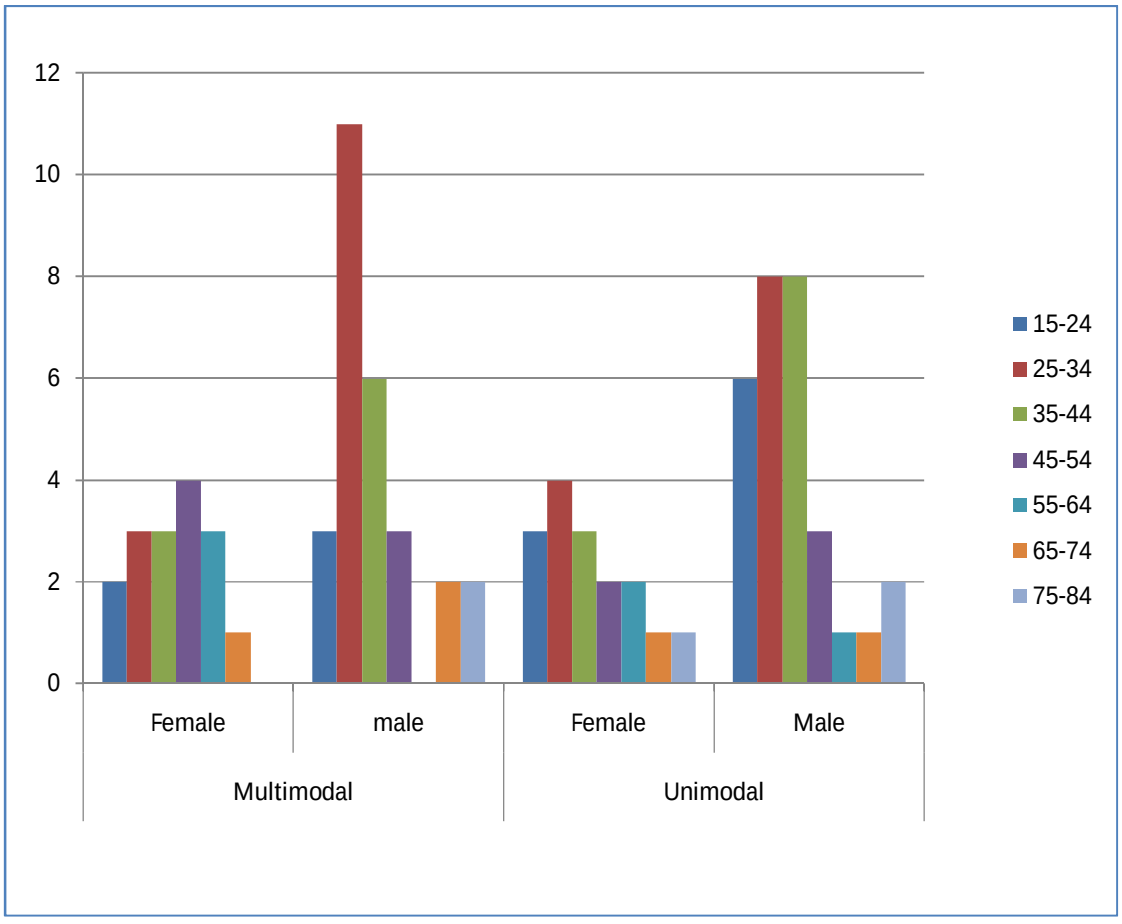
- No harm was intended in this study

- Provision of rescue analgesia for both arms of the study was provided (Appendix 5).

8. Results

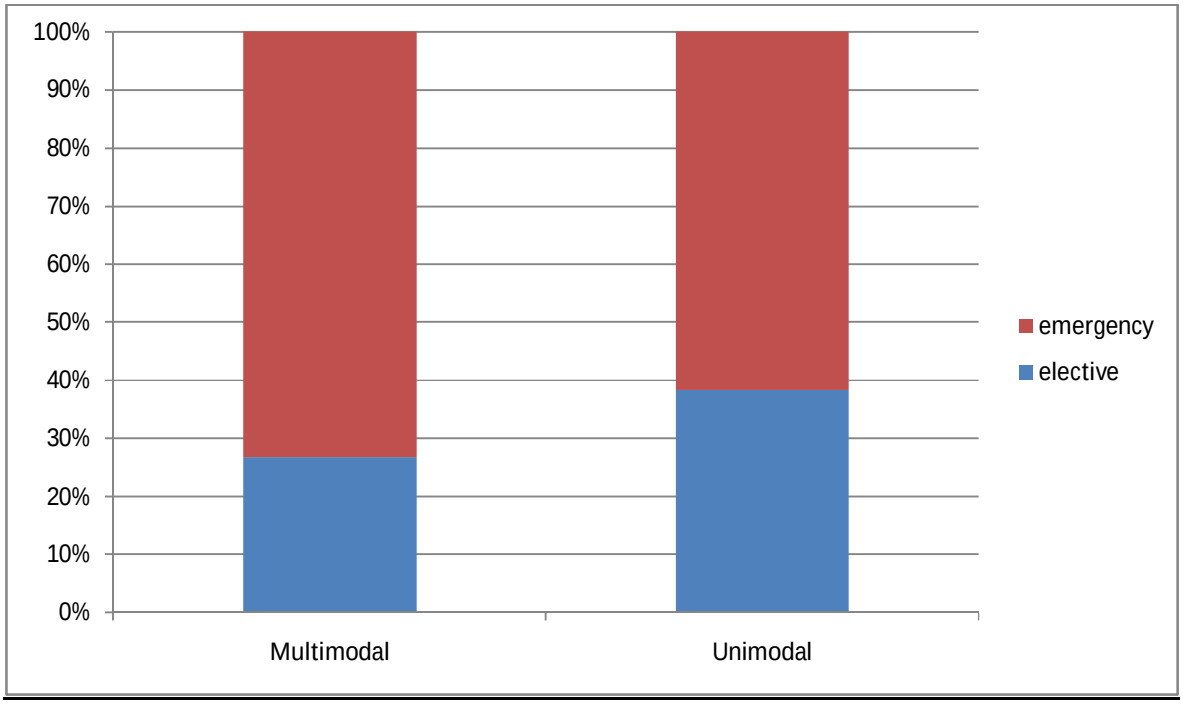
Over a twelve week period from December 2012 to April 2013, one hundred patients undergoing laparotomy were approached and recruited into the study. Patients were assigned into one arm of the study to match for age frequency and type of surgery (elective vs. Emergency). Seven of the patients recruited were discharged before 72 hours elapsed, 4 patients' treatment sheets were inconsistent and one withdrew from the study. The results of the remaining eighty eight patients were analyzed and are subsequently presented below.

Figure 2: Bar graph showing age distribution of study subjects



The patients' ages were grouped in ten year age brackets. In the multimodal group the ages ranged from 19 to 72 years with a mean of 40.45 years. The median age was 37 years. In the unimodal group the ages of subjects ranged from 18 to 82 years with a mean age of 40.9 years. The median age in this group was 36 years. Female to male ratio was 1:1.5 in the multimodal group and 1:1.8 in the unimodal group.

Figure 3: Bar chart showing proportions of the emergency vs. elective surgery in both groups



Elective surgeries were 11 (26.8%) in the multimodal group and 18 (38.3%) in the unimodal group. In the multimodal group 30 (73.2%) patients had emergency surgery performed while it was 29 (61.7%) patients in the unimodal group. (Figure 3) Four patients in the multimodal group had bupivacaine or lidocaine injected into the wound at the end of surgery.

Table 1: Summary of the pathologies encountered

Type of Surgery	Pathology Identified	Unimodal group	Multi-modal Group
Elective	Biliary	5	3
	Spleen	1	1
	Gastric Pathology	2	3
	Large bowel disease	3	2
	small bowel disease	5	1
	Urinary system	2	1
	Miscellaneous masses	4	1
		22	**12**
Emergency	Intestinal Obstruction	5	11
	Penetrating Abdominal Trauma	8	4
	Blunt Trauma	2	1
	Peritonitis	3	13
	Appendicular mass/abscess	5	2
		23	31

Biliary tract pathology accounted for the most frequent elective pathology (8 cases) encountered with most of these patients having bypass surgery performed on them. Intestinal obstruction and peritonitis were the most common reasons for emergency laparotomy (16 cases each) Penetrating abdominal injury was common in the males of 15-15 years (12 cases).

Figure 4: Comparison of Trend of Mean VAS scores

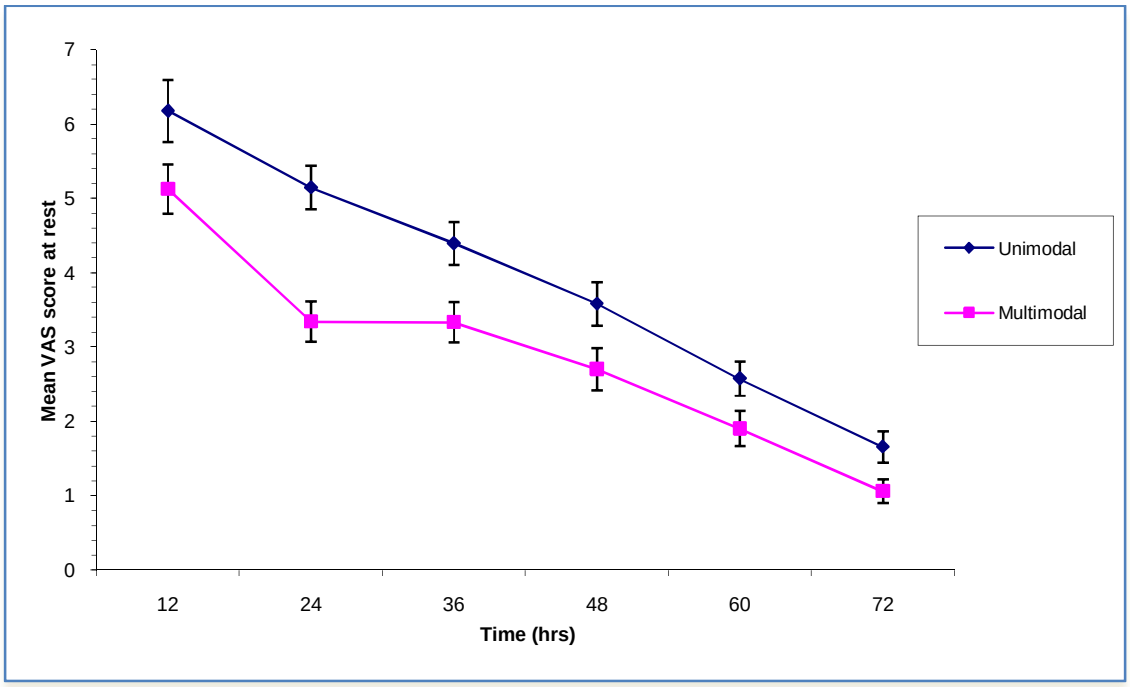


Table 2: Mean VAS scores over time

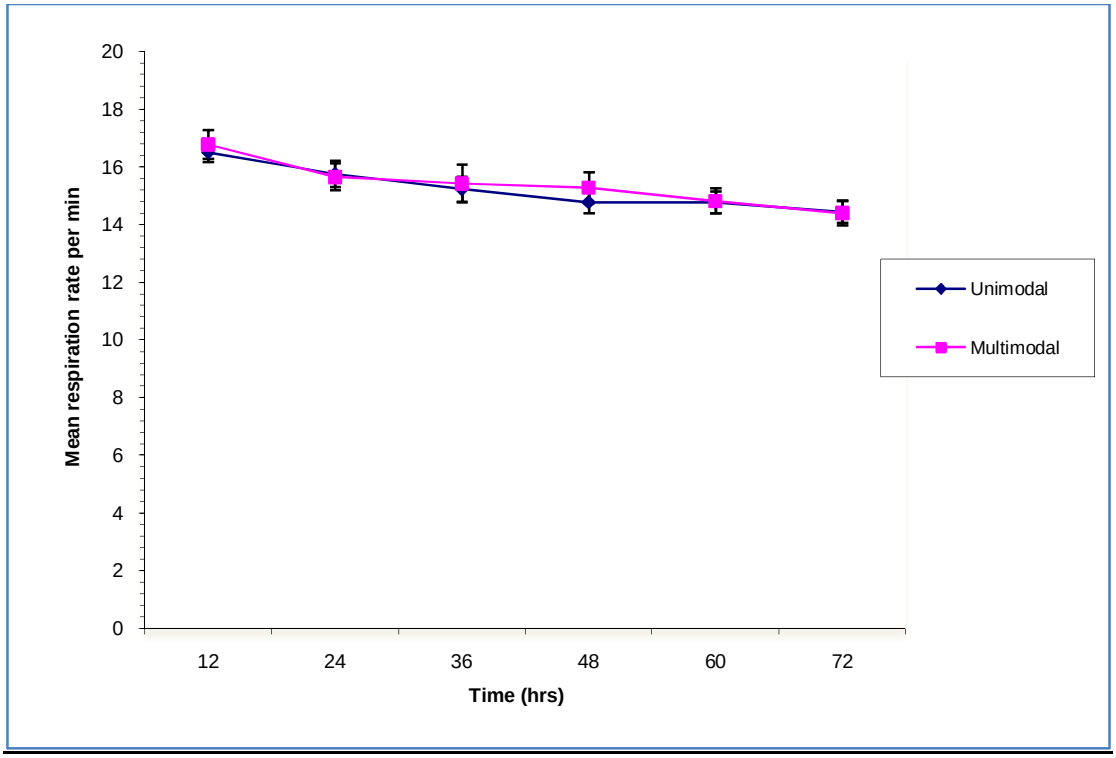
Group	Time in hours					
	12	24	36	48	60	72
Unimodal Group	6.175	5.145	4.395	3.58	2.575	1.66
Multimodal group	5.125	3.343	3.335	2.705	1.905	1.062

Table 3: ANOVA for VAS

Variate: VAS						
Source of variation	**d.f.**	**s.s.**	**m.s.**	**F**	**P**	
Group	1	122.21	122.21	39	<.001	Significant
Time	5	924.584	184.917	59.01	<.001	Significant
Group.Time	5	18.723	3.745	1.19	0.311	Not significant
Residual	468	1466.583	3.134			
Total	479	2532.1				

The mean VAS scores were lower in the multimodal group as compared to the unimodal group during all the intervals measured. This difference was statistically significant ($p<0.001$). The mean VAS scores in both groups reduced at every interval. The highest scores were obtained at 12 hours and the lowest scores at 72 hours. There was however no statistical significance in the rate of change between the two groups ($p=0.311$). (Table 2 and Figure 4)

Figure 5: Comparison of Respiratory rate



There mean respiratory rates were computed and presented in the graph above. There was no statistically significant difference between the groups at any time ($p=0.57$). The overall trend showed a reduction in the mean respiratory rates in both groups over time. The difference in the rates at the various time intervals was statistically significant ($p=<0.001$). (Figure 5 & Table 4)

Table 4: ANOVA for Respiratory rate

Respiration rate/min					
Source of variation	**d.f.**	**s.s.**	**m.s.**	**F**	**P**
Group	1	2.7	2.7	0.32	0.57
Time	5	244.892	48.978	5.88	<.001
Group.Time	5	4.875	0.975	0.12	0.989
Residual	468	3901.4	8.336		
Total	479	4153.867			

There was no significant difference between the groups ($F_{[1,468]}$=0.320, p=0.570) in Respiration rate per minute for patients.
There was a significant difference between the various times ($F_{[1,468]}$=5.88, p<0.001).in Respiration rate per minute for patients.
However, the interaction between group and time is not significant ($F_{[5,468]}$=0.12, p=0.989) in Respiration rate per minute for patients.

Figure 6: Comparison of Mean Arterial Pressure (MAP)

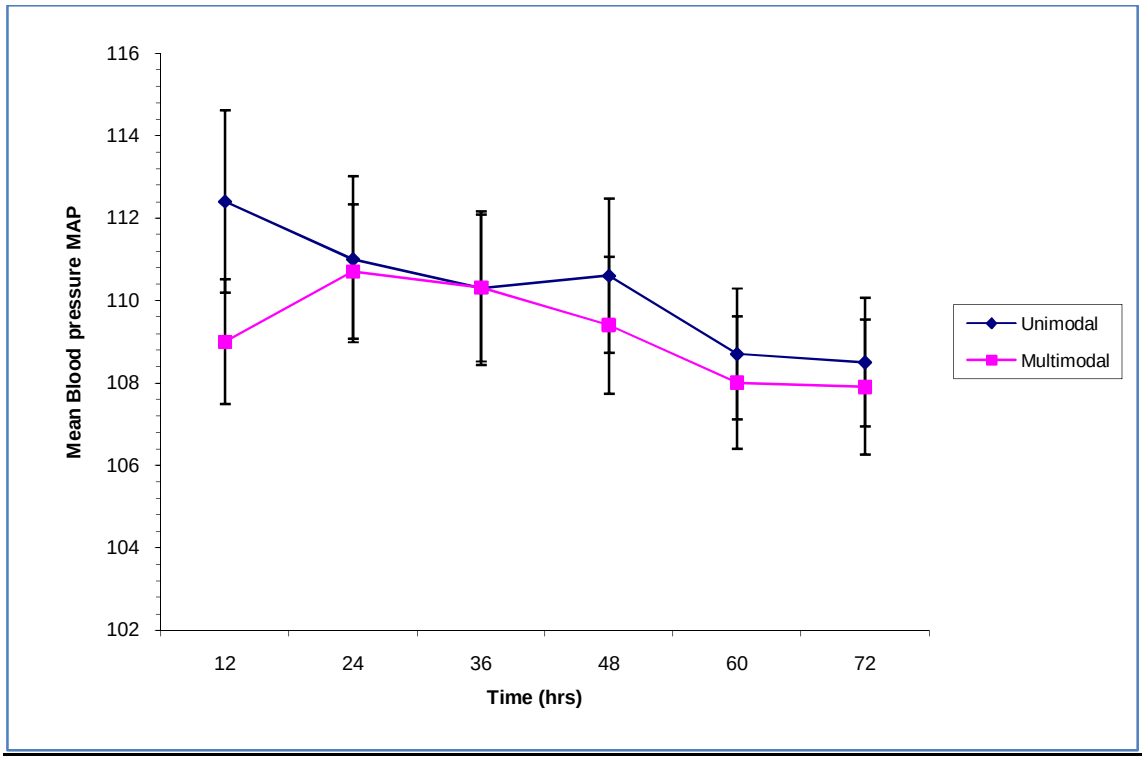


Table 5: ANOVA for Mean Arterial Pressure (MAP)

Variate: Blood pressure (MAP)					
Source of variation	**d.f.**	**s.s.**	**m.s.**	**F**	**P**
Group	1	131.6	131.6	1.06	0.303
Time	5	543.8	108.8	0.88	0.494
Group.Time	5	156.6	31.3	0.25	0.938
Residual	468	57843	123.6		
Total	479	58675			

There was no significant difference between the groups ($F_{[1,468]}$=1.06, p=0.303) in Blood pressure (MAP) for patients after operation.
There was no significant difference among the various times ($F_{[5,468]}$=0.88, p=0.494).
There was also no significant difference between group and time ($F_{[5,468]}$=0.25, p=0.938).

The Mean Arterial Pressure for every subject was calculated by taking a third of systolic pressure and added to diastolic pressure. Means for every time interval were calculated for each group and plotted in a graph. (Figure 6) There was no statistically significant difference between the two groups at any single time interval (p=0.303) or over the entire period of the 72 hours (p=0.494). (Table 5)

Figure 7: Comparison of Pulse rate

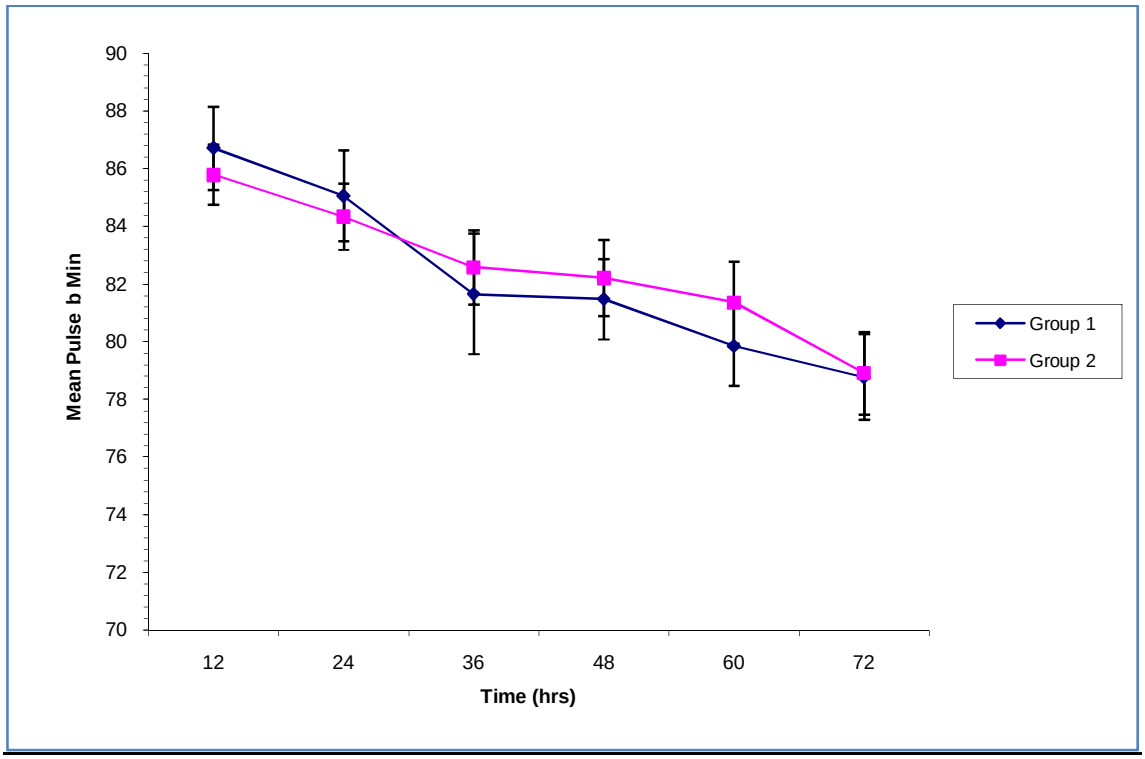


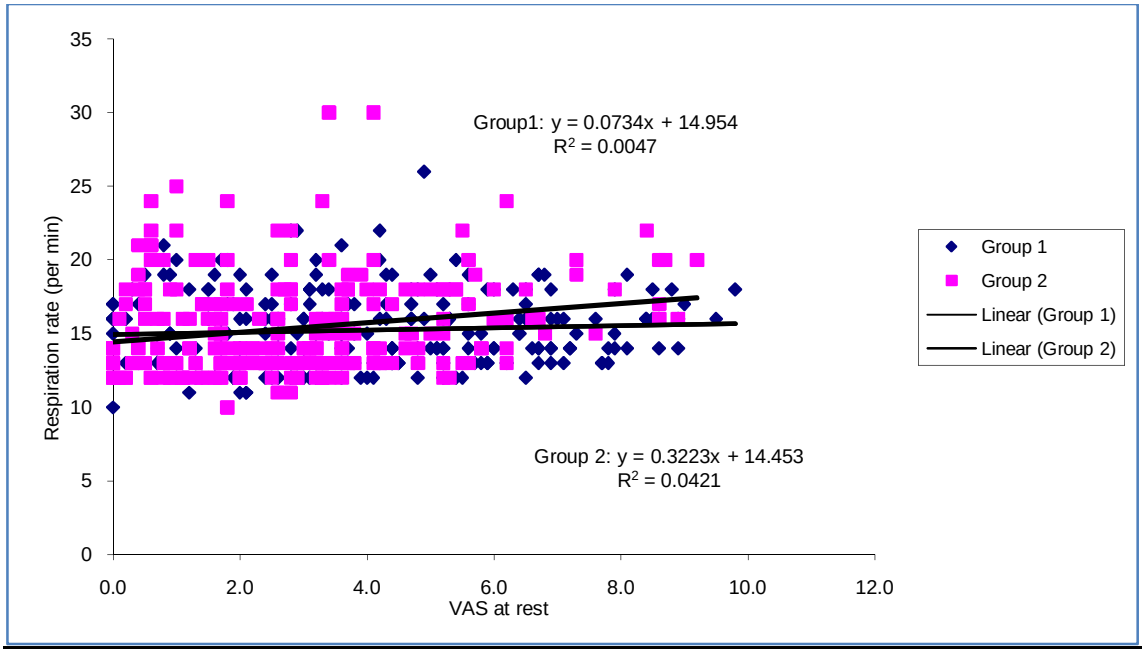
Table 6: ANOVA for pulse rate

Variate: Pulse/Min					
Source of variation	**d.f.**	**s.s.**	**m.s.**	**F**	**P**
Group	1	8.8	8.8	0.11	0.745
Time	5	2903.06	580.61	7	<.001
Group.Time	5	91.76	18.35	0.22	0.953
Residual	468	38806.08	82.92		
Total	479	41809.7			

There was no significant difference between group 1(unimodal) and group 2(Multimodal) ($F_{[1,468]}$=0.11, p=0.745) in Pulse rate for patients after operation.
There was a significant difference among the various times ($F_{[5,468]}$=7.0, p<0.001).
There was no significant difference between group and time ($F_{[5,468]}$=0.22, p=0.953).

The mean pulse rate for each group was calculated for every time interval and plotted on the above graph. (Figure 7) The mean pulse rate reduced at every interval in both groups. There was no statistically significant difference between the two groups overall (p=0.745) nor was the interaction between group and time significant (p=0.953). There was a significant difference noted in the change of mean pulse rate at the various times in both groups (p<0.001). (Table 6)

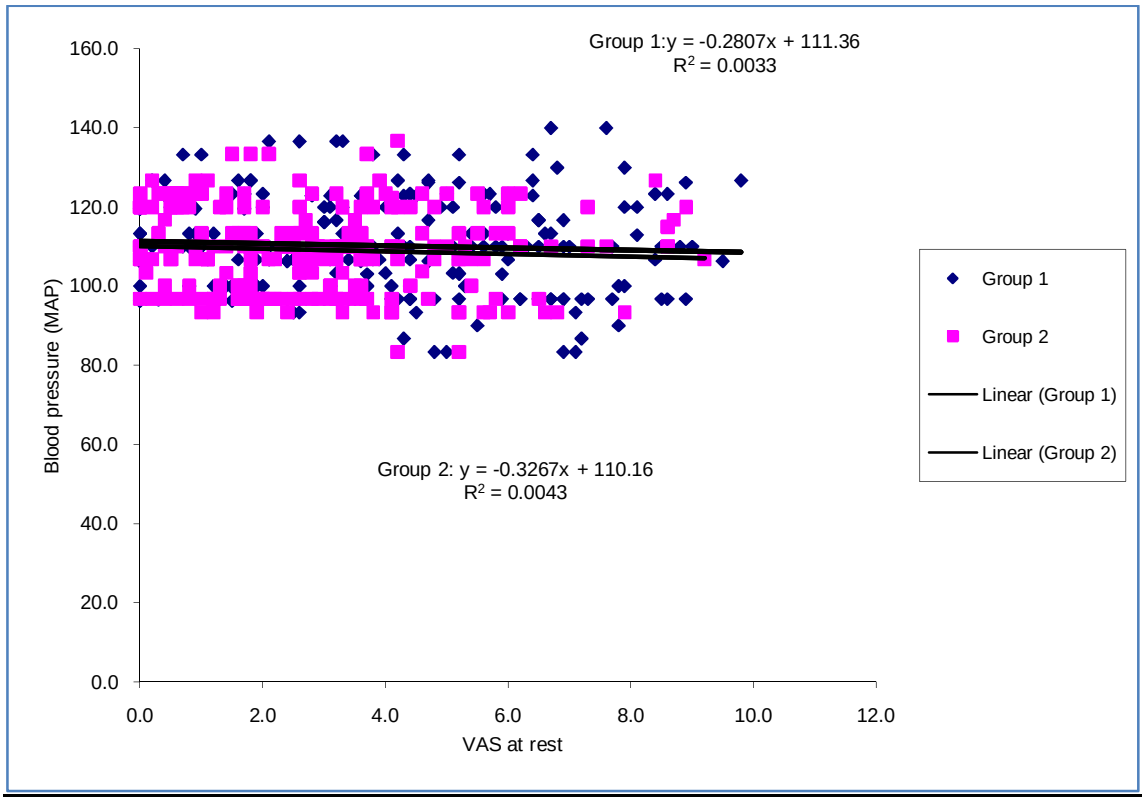
Figure 8: Correlation between VAS and Respiratory rate



NB. Group 1 is Unimodal Group, Group 2 is Multimodal group.

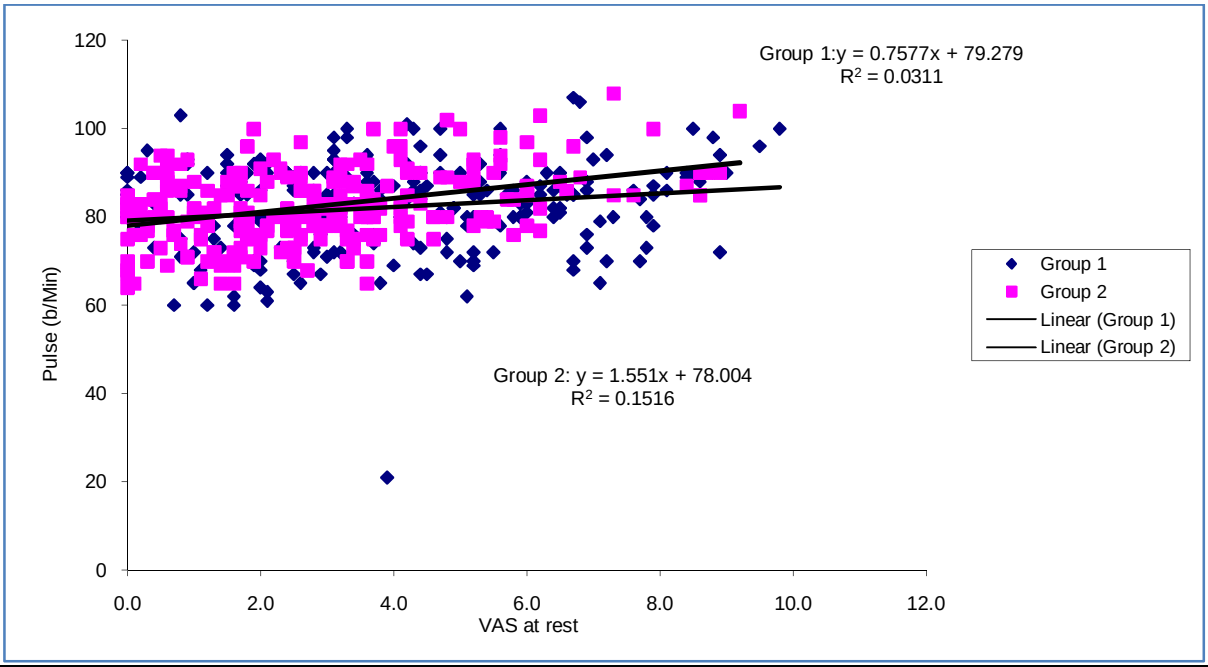
Pearson's correlations were obtained for VAS-respiratory rate, VAS-Pulse rate and VAS-Mean Arterial Pressure. There were positive linear correlations between the VAS score – respiratory rate (r=0.129, p=0.005) and VAS score – pulse rate (r=0.255, p<0.001). (Figures 8, 10 & Table 7) The correlation between VAS and Mean Arterial Pressure was linear but did not show any significance.

Figure 9: Correlation between VAS and Mean Arterial Pressure



NB. Group 1 is Unimodal Group, Group 2 is Multimodal group.

Figure 10: Correlation between VAS and Pulse rate



NB. Group 1 is Unimodal Group, Group 2 is Multimodal group.

Table 7: Correlation cross-tabulation for VAS and Vital signs (Resp. rate, MAP and Pulse)

		VAS	Respiration.rate (per min)	Blood.pressure (MAP)	Pulse (b/Min)
VAS	Pearson Correlation	1	.129**	-.049	.255**
	Sig. (2-tailed)		.005	.284	<0.001
	N		480	480	480
Respiration.rate (per min)	Pearson Correlation		1	.265**	.462**
	Sig. (2-tailed)			<0.001	<0.001
	N			480	480
Blood.pressure (MAP)	Pearson Correlation			1	.214**
	Sig. (2-tailed)				<0.001
	N				480
Pulse (b/Min)	Pearson Correlation				1
	Sig. (2-tailed)				
	N				

**. Correlation is significant

The results indicate that there is significant (r=0.129, p=0.005) positive correlation between VAS and Respiration rate among patients.

The results indicate that there is no significant (r=-0.049, p=0.284) correlation between VAS and Blood pressure among patients.

The results indicate that there is significant (r=0.255, p<0.001) positive correlation between VAS and Pulse among patients.

Figure 11: Incidence of sedation in Unimodal group by percentage over time

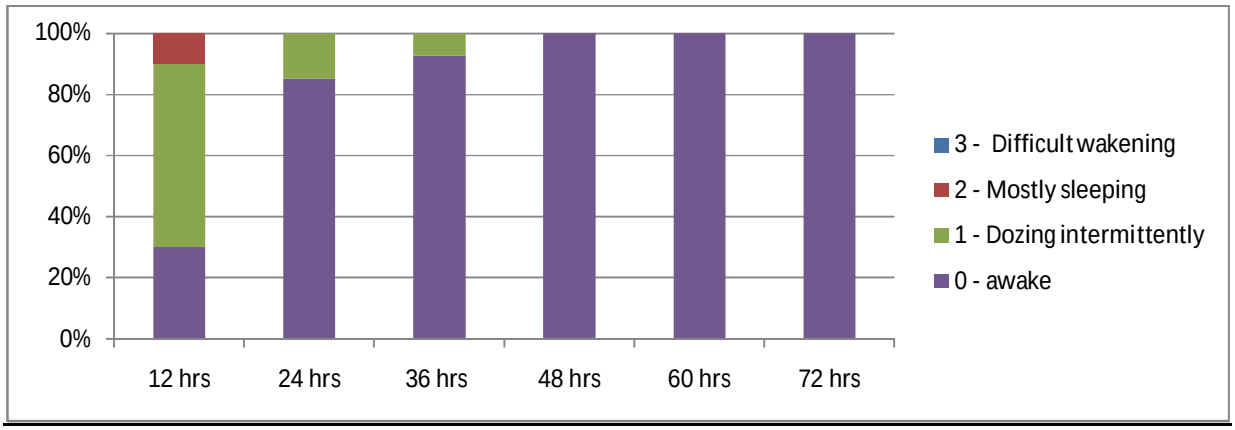
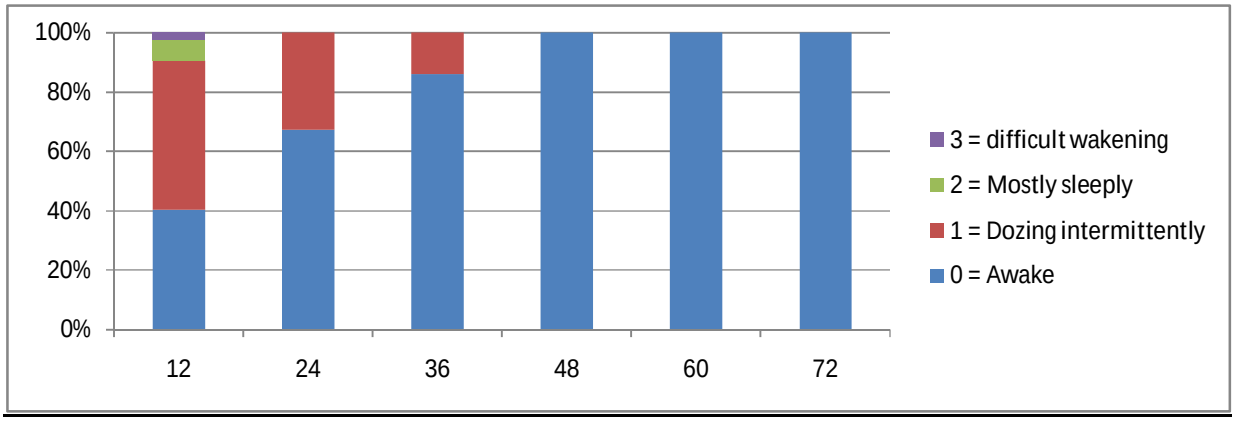


Figure 12: Incidence of sedation in Multi-modal group by percentage over time



At every 12 hour interval for the first 72 hours, each patient was scored for sedation. (Appendix 2) The frequency of each score was obtained for every time interval and represented as on the above bar graphs. (Figure 11 & 12) By 48 hours 100% of the patients had sedation scores of zero in both groups. Only 2% of the patients in the multimodal group had sedation scores of 3 in the first 12 hours. No patients in the unimodal group had s sedation score of 3 at any time.

There was no statistically significant difference between the two groups when compared using a Pearson Chi Square (p=0.519).

Table 8: Cross tabulation for sedation between the Groups

			Group		Total
			Unimodal	**Multimodal**	
Sedation Score	0	Count	196	204	400
		% within Sedation Score	49.0%	51.0%	100.0%
	1	Count	40	34	74
		% within Sedation Score	54.1%	45.9%	100.0%
	2	Count	4	2	6
		% within Sedation Score	66.7%	33.3%	100.0%
Total		Count	240	240	480
		% within Sedation Score	50.0%	50.0%	100.0%

Chi-Square Tests					
	Value	df	p-value		**Conclusion**
Pearson Chi-Square	1.313	2	0.519		There is no significant difference between the groups

Figure 13: Incidence of Nausea in Unimodal group by percentage over time

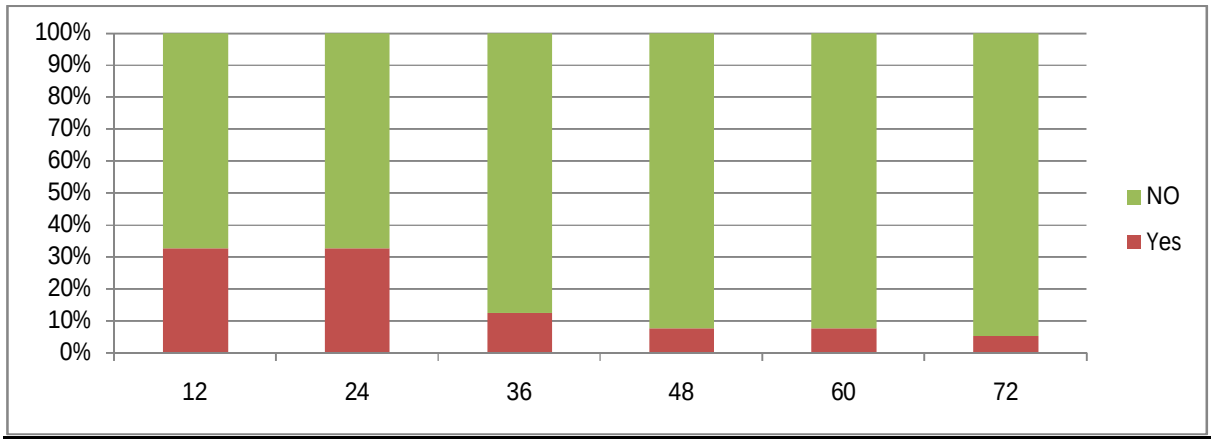


Figure 14: Incidence of Nausea in Multi-modal group by percentage over time

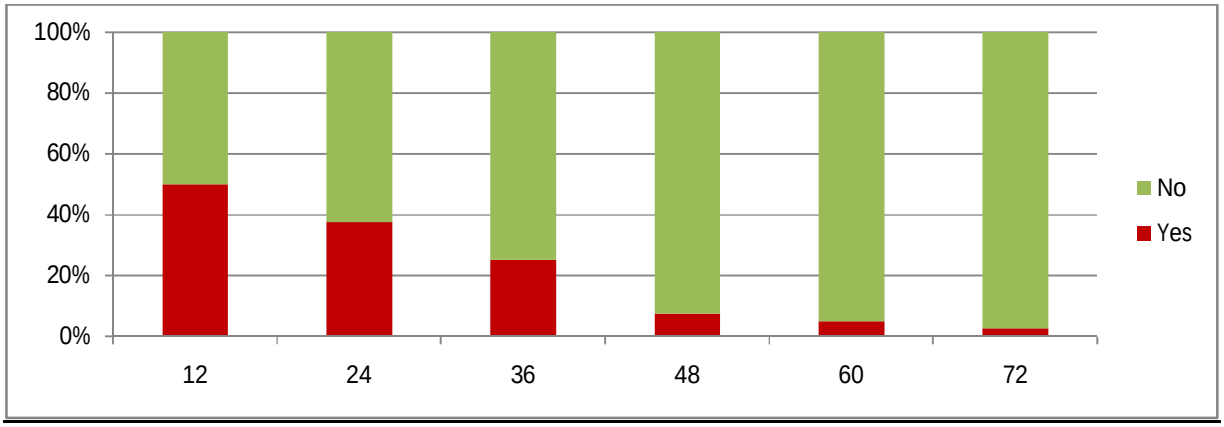


Table 9: Cross tabulation for Nausea between the Groups

			Group		Total
			Unimodal	Multimodal	
Nausea	**no**	Count	194	199	393
		% within Nausea	49.4%	50.6%	100.0%
	yes	Count	46	41	87
		% within Nausea	52.9%	47.1%	100.0%
Total		Count	240	240	480
		% within Nausea	50.0%	50.0%	100.0%

Chi-Square Tests					
	Value	df	p-value		**Conclusion**:
Pearson Chi-Square	0.351	1	0.554		There is no significant difference between the groups

Figure 15: Incidence of Vomiting in Unimodal group by percentage over time

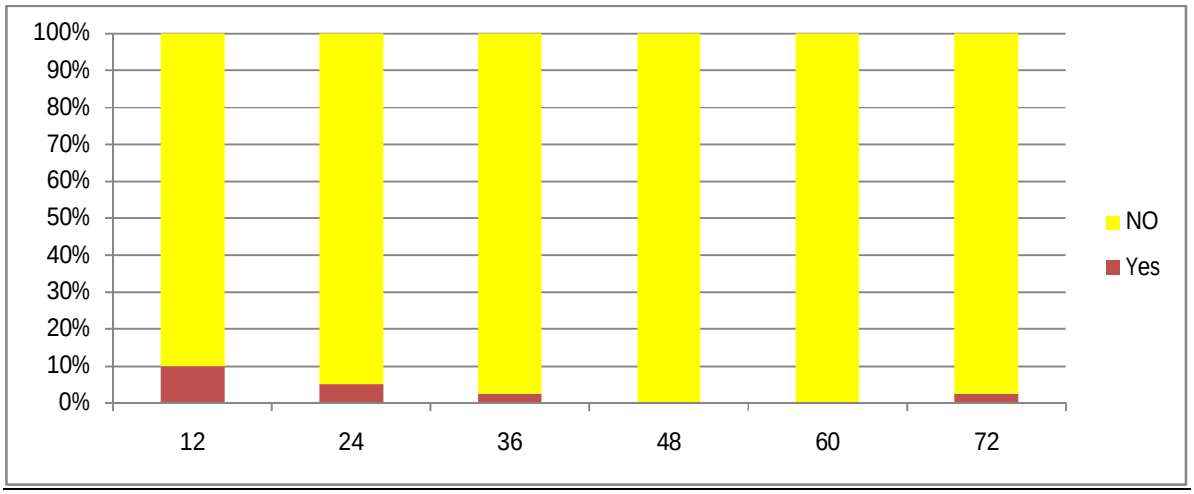


Figure 16: Incidence of Vomiting in Multi-modal group by percentage over time

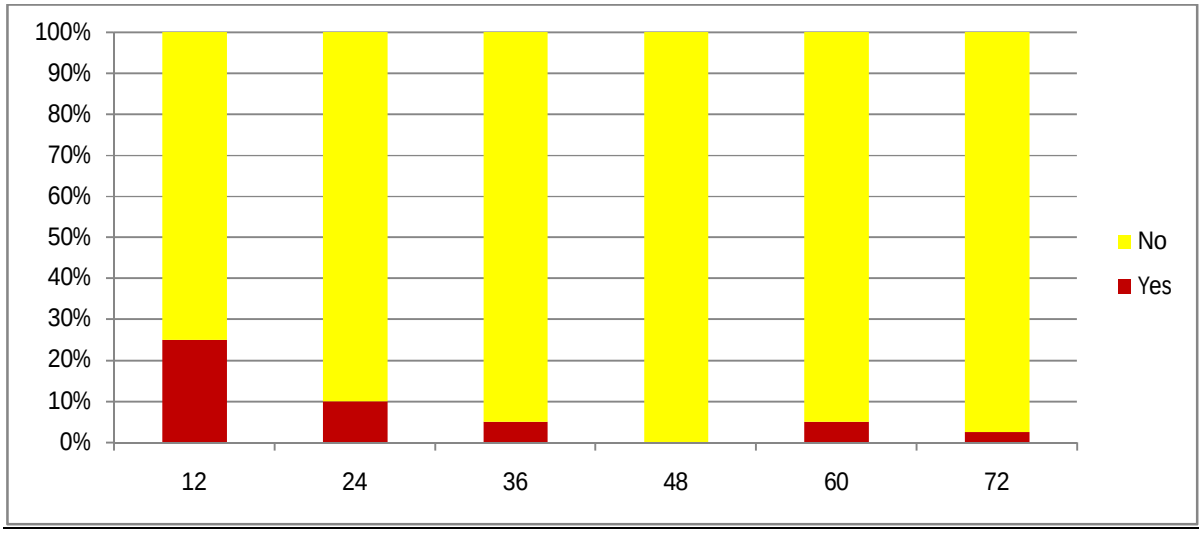


Table 10: Cross tabulation for Vomiting between the Groups

			Group		Total
			Unimodal	Multimodal	
Vomiting	no	Count	223	230	453
		% within Vomiting	49.2%	50.8%	100.0%
	yes	Count	17	10	27
		% within Vomiting	63.0%	37.0%	100.0%
Total		Count	240	240	480
		% within Vomiting	50.0%	50.0%	100.0%

Chi-Square Tests					
	Value	df	p-value		**Conclusion**:
Pearson Chi-Square	1.923	1	0.166		There is no significant difference between the groups

The incidence of nausea and vomiting were obtained as frequencies at every 12 hour interval. These frequencies are presented as percentages in the above bar graphs. (Figures 13, 14, 15 & 16)

There were more incidences of both nausea and vomiting in the unimodal group than the multimodal group. These differences were however not statistically significant when Pearson Chi square cross-tabulations were performed with p value of 0.554 for Nausea and 0.166 for Vomiting. (See table 9 and 10)

8. Discussion

Post-operative pain still remains a challenge despite advances in medicine[1]. In East Africa, the most common analgesia used in the immediate post-operative period after laparotomy was single opioid either pethidine or morphine with the intramuscular route of administration being the most preferred [3]. This study set out to evaluate the efficacy of a standardized multimodal analgesic protocol of pethidine and diclofenac when compared to the aforementioned analgesic practice.

The multimodal group had an age range of 19 to 72 years with a mean of 40.45 years while the unimodal group ranged from 18 to 82 years with a mean age of 40.9 years. The median ages were 37 years in the multimodal group as compared to 36 years in the unimodal group. These age ranges were comparable to Ocitti's study of 106 laparotomy patients where he found the median age was 39 years with ages ranging from 15 to 82 years [3]. The pain scores of the Ocitti study can therefore be compared with those found in this study which showed unsatisfactory pain control when opioids were used in a unimodal manner administered by intermittent intramuscular route.

Elective surgery accounted for 38.6% of the procedures performed in this study. Of these surgeries, biliary pathology was the most common with 23.5% of the cases followed by small bowel pathology 17.6%. This differed from Basweti's study in which he found that stoma closure was the most common indication for elective laparotomy at KNH [35.] Kheri showed that penetrating abdominal trauma was the leading cause of emergency laparotomy accounting for 50.7% of his study subjects [36]. In this study the intestinal obstruction and peritonitis were the most common indications for laparotomy with 29.6% of the cases. Penetrating abdominal trauma made up 22.2% of the cases that underwent laparotomy. Although the most frequent indications for abdominal surgery may have differed slightly from the aforementioned two recent studies at KNH, most of the surgeries performed were for commonly encountered pathologies in the general surgery for which this multimodal regimen used in the study could be applied.

The study compared the pain scores, vital signs and occurrence of nausea and vomiting between two groups. The mean pain scores were significantly lower in the protocol group than in the unimodal group over a 72 hour period. This concurs with observations from a study by Kiswezi on post-operative pain management after laparotomy at Mulago Hospital

Uganda which showed better pain scores when diclofenac and pethidine were used in combination [37]. Different combinations of NSAIDs with opioids have been shown to provide better pain relief, fewer analgesic requirements and a prolonged time to analgesia requirement as shown by Jin ET al [29].

The mean pain scores in the first 24 hours were found to be higher in both the unimodal group and the multimodal group as compared to studies undertaken using Patient Controlled Analgesia [38]. Unlugenc et al showed that mean pain scores at 12 hours were 1.2, 1.3 in their study population while using IV morphine via PCA as compared to 6.175 and 5.125 in this study. At 24 hours they had reduced pain scores of 1.2 and 1.0 while this study had mean scores of 5.145 and 3.345 at 24 hours [38]. This difference in pain scores may be attributed to the poorer pain control achieved by multiple intermittent intramuscular injections and was demonstrated by Austin in his study on morphine [22]. Ferrante et al also described the peaks and troughs that resulted in poor analgesic effect of intermittent intramuscular injections [23]. (Figure 1) There is therefore need to consider introduction of modalities of patient controlled analgesia to this setting that will be cost effective and provide better control of pain in the immediate post-operative setting.

Four patients in this multimodal group had local analgesia infiltrated into the surgical incision at the end of surgery. The use of local analgesia has been shown to be effective on minor abdominal surgeries like herniotomy. After major abdominal surgery infiltration of local anaesthesia into the wound does not have a significant effect on the overall pain scores [39]. Continuous wound irrigation with local anaesthetic has however been shown to improve pain scores, reduce post-operative opioid consumption in a PCA setup and results in earlier return to function [40]. Local anaesthetics have been shown to be efficacious in pain control when used as regional analgesia e.g. as transversus abdominis plane blocks [31].

The Visual Analogue Scale was used in the assessment of pain. This scale is preferred because of its ease and brevity of administration. It is also minimally intrusive, has good sensitivity to detect intervention-based changes in pain and is simple to understand [41]. Ocitti had done his study using a 10 point numerical rating scale while Kiswezi used a 10cm Visual Analogue scale [3, 37]. These two methods of measuring pain have been shown to have similar sensitivity for acute post-operative pain intensity both experimentally and in clinical practice. [42]. The numerical scale is however preferred by patients as it is easier to understand and administer in a routine clinical setup [43]. Pain assessment as part of the routine observations

done by health care workers managing post-operative patients as been shown be beneficial even in resource poor settings. The tools of assessment are both cheap and easy to use and can be adopted for the local variations [44].

A met-analysis of 165 studies on effect of postoperative management strategies on respiratory depression and hypotension by Cashman et al showed that I.M analgesia had incidence of respiratory depression of 0.1% to 1.7 % using respiratory rate as an indicator [45]. In this study no patient was observed to have any respiratory depression in either group. No hypotension was reported in this study as the lowest mean arterial pressure was 83.3 mmHg. The presence of hypotension affects the delivery of analgesia to the tissues and has been associated with worsening pain scores [46].

Acute pain may be associated with physiological changes that arise from sympathetic stimulation. Increase in heart rate, blood pressure and respiratory rate often accompany a painful event [47, 48]. In this study there was a weak correlation between the respiratory rate and VAS scores ($r=0.129$, $p=0.005$), heart rate and the VAS scores ($r=0.255$, $p<0.001$). There was no correlation with the mean arterial blood pressure ($r=-0.049$, $p=0.284$). Such correlations have not been consistently shown in other studies.

Lord et al. showed that pre-hospital VAS scores in adult patients did not correlate with the heart rate and blood pressure. However there was a mildly statistically significant correlation between respiratory rate and pain score [49]. Etri and Adib-Hajbaghery in their study on effects of acupressure on pain and vital signs of patients after small abdominal surgeries also did not show a correlation[50]. Bendall et al however showed that the respiratory rate had a weak but significant correlation with pain scores in adults presenting with acute pain [51] .The same study showed that pulse rates above 100/min had increased odds of associated severe pain. This weak correlation found in this study between respiratory rate, heart rate and pain scores may however not be of clinical significance. This is because the changes in the heart rate and respiratory rate occur also due to sympathetic nervous system activation as part of the stress response to trauma of surgery [52].

The incidence of post-operative nausea and vomiting has a strong relationship with use of opioid [53]. This is most often seen when intravenous opioids are used in a patient controlled setting (IV PCA). This study did not demonstrate any significant difference in the incidence of nausea and vomiting in the two groups. The overall incidence of nausea was 19.2% and

17.1% in the unimodal and multimodal groups respectively. The overall incidence of vomiting was 7.1% and 4.2% respectively. This was comparable to a meta-analysis by Dolin of 181 studies on post-operative management where the overall incidence for nausea was 17% for intramuscular analgesia and 25% for IV patient controlled analgesia [9]. This study had a lower incidence of vomiting than Dolin's study which showed an overall incidence of 20.9% for intramuscular analgesia and 20.7 for IV PCA. It is thus safe to combine NSAIDs and opioid analgesics to reduce the incidence of opioid related side effects and achieve good analgesic control.

Sedative effect of opioids especially morphine is a major concern to clinicians and contributes to the apprehension in their use for post-operative pain management [5]. This study did not demonstrate a statistically significant difference between the two groups. Most of the sedation occurred between the first 24 hours after general anaesthesia. There were no sedative effects noted after 36 hours. Mild sedation is a known effect of opioid use. However excessive sedation is more common when intravenous opioid is given in a PCA setting. Intramuscular opioid use still has significantly higher sedative side effects than epidural route of administration [9]. The effect of general anaesthesia on post-operative sedation may have contributed to the higher occurrence of sedation in the first twenty four hours after surgery although this was beyond the scope of this study.

Use of NSAIDs in combination with opioid analgesics has been shown to reduce the total opioid requirement and there is resultant reduction in the incidence of opioid side effects [54]. This effect may be inferred in this study as the overall nausea, vomiting and sedation scores were low in the multimodal group. Other agents such as paracetamol have also been shown to produce comparable opioid sparing effects and may be considered for use especially when NSAIDs are contradicted [55].

Blinding was not used in this study due to the technicalities involved. Blinding would have improved the validity of the results obtained in this study by reducing the Hawthorne effect seen when either trial subjects or assessors are not blinded and therefore modify their responses or have bias in their observations [56]. In order to blind the subjects, the nursing staff and observers the drug packaging, syringe doses and frequency of administration in both groups would have had to be identical. This was not possible with the available resources and timeframe.

9. Conclusion

This study demonstrates that a simple multimodal protocol of pethidine as an opioid and diclofenac as an NSAID produce better pain scores than the more commonly practiced unimodal approach to post-operative analgesia at KNH. This is seen from the improved pain scores using a Visual analogue scale.

It should be noted that although there was improvement in the pain scores, these pain scores were still higher than those reported in studies were better analgesic methods were used i.e. Patient Controlled Analgesia.

This multimodal approach is without any significant side effects to the patients. There were no significant deleterious side effects from this protocol.

10. Recommendations

- Use of a multimodal approach in management of post-operative pain should be the standard of practice at KNH.

- Routine monitoring of pain in the immediate post-operative period should be considered for all patients who undergo major surgery.

- An acute pain service should be instituted at KNH to constantly evaluate pain management and look for ways of improving the same.

- Patient controlled analgesia should be explored as a way of reducing post-operative pain after major surgery.

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12. Appendices

12.1 Appendix 1. Informed consent forms (Adopted from WHO) [57]

12.1.1 English version

This Informed Consent form is for patients of hospitalized at the Kenyatta National Hospital general surgical wards who are to have major abdominal surgery during the study period. We are requesting these patients to participate in this research project whose title is **"The efficacy of a simple standard multimodal analgesic protocol on acute post-operative pain after major abdominal surgery in KNH".**

Principal investigator: Dr. Janai A. Mariita Ondieki

Institution: School of Medicine, Department of surgery- University of Nairobi

Supervisors: Dr Joseph Kimani Wanjeri & Dr Timothy M. Mwiti

This informed consent has three parts:

1. Information sheet (to share information about the research with you)
2. Certificate of Consent (for signatures if you agree to take part)
3. Statement by the researcher

You will be given a copy of the full Informed Consent Form.

Part I: Information sheet

My name is Dr. Janai A. Mariita Ondieki, a Post-Graduate student at the University of Nairobi's School of Medicine. I am carrying out a study on the efficacy of a simple multimodal analgesic protocol on post-operative pain management after major abdominal surgery. Multi modal analgesia refers to the use of two or more analgesic drugs that have different mechanisms of action. This is aimed at improving the pain control and minimizing side effects of either drug.

This study aims to check the efficacy of a simple multimodal analgesic regimen.

I am inviting you to participate in my study and you are free to either agree immediately after receiving this information or later after thinking about it. You will be given the opportunity to ask questions before you decide and you may talk to anyone you are comfortable with about the research before making a decision. After receiving this information concerning the study, please seek for clarification from either myself or my assistant if there are words or details which you do not understand.

If you agree to participate, you will be asked to provide personal information and other details related to the condition you are suffering from including the amount of pain experienced. All the information which you provide will be kept confidential and no one but the researchers will see it. The information about you will be identified by a number and only the researchers can relate the number to you as a person. Your information will not be shared with anyone else unless authorized by the Kenyatta National Hospital/University of Nairobi – Ethics and Research Committee (KNH/UoN-ERC).

Your involvement in this research will be through an interview and clinical evaluation and you will not expose yourself to any risks if you consent to participate. Your participation is voluntary and refusal to participate in the research or withdrawal from it will not affect the treatment which you receive at this hospital. All the information that you give us will be used for this research only.

All patients undergoing major abdominal surgery during the study period are being invited to participate. Recruitment of patients into the study will take three months from the date approval to conduct the study is given.

This research has been reviewed and approved by the KNH/UoN-ERC which is a committee whose work is to make sure research participants like your self are protected from harm. It was submitted to them through the Chairman of the Department of Surgery at School of Medicine of the University of Nairobi with the approval of the two university supervisors. The contact information of these people is given below if you wish to contact any of them for whatever reason;

- Secretary, KNH/UoN-ERC

  P.O. Box 20723 KNH, Nairobi 00202

  Tel 726300-9

Email: KNHplan@Ken.Healthnet.org

- Chairman,
  Department of Surgery, School of Medicine– University of Nairobi

  P.O. Box 19676 KNH, Nairobi 00202

  Tel # 0202726300

- University of Nairobi research supervisors

  Dr Joseph Kimani Wanjeri,
  Department of Surgery, School of Medicine, University of Nairobi

  P.O. Box 19676 KNH, Nairobi 00202

  Tel # 0202726300

  Dr. Timothy M. Mwiti,

  Department of Anaesthesia, School of Medicine, University of Nairobi

  P.O. Box 19676 KNH, Nairobi 00202

  Tel # 0202726300

- Principle researcher:

  Dr. Janai A. Mariita Ondieki

  Department of Surgery, School of Medicine, University of Nairobi

  P.O. Box 19676 KNH, Nairobi 00202

  Mobile phone # 0724925705

Part ii: Consent certificate

I……..freely give consent of myself or for my proxy (Name…….) to take part in the study conducted by Dr. Janai A. Mariita Ondieki, the nature of which has been explained to me by him/his research assistant. I have been informed and have understood that my participation is entirely voluntary and I understand that I am free to withdraw my consent at any time if I so wish and this will not in any way alter the care being given to me or my proxy. The results of the study may directly be of benefit to me or my proxy and may improving postoperative pain management after abdominal surgery.

……
…

Signature/left thumb print (Participant/Next of kin)

Date……
…

Day/Month/Year

Thumb print of participant if illiterate (a witness must sign below)

Statement by the witness if participant is illiterate

I have witnessed the accurate reading of the consent form to the participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of witness……

Signature of witness……..

Date……

Day/Month/Year

Part iii: Statement by the researcher

I have accurately read out the information sheet to the participant, and to the best of my ability made sure that the participant understands that the following will be done:

- Refusal to participate or withdrawal from the study will not in any way compromise the care of treatment.
- All information given will be treated with confidentiality.
- The results of this study might be published in a scientific journal.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Informed Consent Form has been provided to the participant.

Name of researcher taking consent……

Signature of researcher taking the consent……

Date……
……

Day/Month/Year

12.1.2 Kiswahili version

Fomu ya idhini

(i) Sehemu ya kwanza – Maelezo:

Mimi ni Dkt Janai A. Mariita Ondieki, kutoka shule ya Afya ya upasuaji ya Chuo Kikuu cha Nairobi (University of Nairobi). Ninafanya utafiti kuhusu upunguzaji wa maumivu baada ya upasuaji wa tumbo kwa kutumia utaratibu maalum ya madawa hapa hospitali kuu ya Kenyatta.. Ningependa kukuchagua wewe ama mgonjwa wako katika utafiti huu wangu. Lengo ni kutambua jinsi utumizi ya madawa aina bili zina weza kupunguza maumivu mgonjwa anayohisi baada ya upasuaji wa tumbo. Katika utafiti huu utatakiwa kutoa taarifa yako binafsi, taarifa kuhusu ugonjwa yako na pia maumivu unayo hisi.. Habari zote zitakazo kusanywa zitashughulikiwa kwa siri na hazitatambazwa ila tu kwa ruhusa kutoka kwa jopo maalum ya utafiti ya chuo kikuu cha Nairobi na hospitali kuu ya Kenyatta(KNH/UoN-ERC).

Kuhusika kwako kwenye utafiti huu hauna malipo yeyote ila ni kwa hiari yako mwenyewe na pia unaweza kujiondoa kwa utafiti wakati wowote bila kuhatarisha matibabu yako katika Hospitali Kuu ya Kenyatta. Naomba mimi ama wasaidizi wangu wakuulize maswali ambayo yatajibiwa kwa fomu maalum. Habari yote ambaye utatuarifu ni ya siri kati yako nasi watafiti na haitaenezwa kwa watu wengine.

Utafiti huu unatarajia kuchukuwa jumla ya miezi tatu kuaanzia siku idhini ya kufana utafiti takapopewa na jopo maalum yaa utafiti ya chuo kikuu cha Nairobi na hospitali kuu ya Kenyatta(KNH/UoN-ERC).

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 wasimamiza 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 726300-9.
- Mwenye kiti, Idara ya upasuaji katika chuo kikuuu cha Nairobi. Sanduku la Posta 19676 KNH Nairobi 00202. Nambari ya simu: 0202726300
- Walimu wasimamizi wa Chuo kikuu cha Nairobi:
    1. Dkaktari Joseph Kimani Wanjeri, Sanduku la Posta 19676 KNH, Nairobi 00202. Nambari ya simu: 0202726300
    2. Daktari Timothy M. Mwiti, Sanduku la Posta 19676 KNH, Nairobi 00202. Nambari ya simu:0202726300
- Mtafiti: Daktari Janai A. Mariita Ondieki, Idara ya Upasuaji ya Shule ya Utabibu – Chuo kikuu cha Nairobi, Sanduku la Posta 2678 KNH Nairobi 00202. Nambari ya simu ya rununu 0724925705

(ii) Sehemu ya pili - Idhini:

Mimi (Jina)……..kwa hiari yangu ama kwa hiari ya mgonjwa wangu (Jina la Mgonjwa).....

……. nimekubali kushiriki katika utafiti huu unaofanywa na Daktari Janai A. Mariita Ondieki kutokana na hali ambazo nimeelezwa na sio kwa malipo ama shurutisho lolote.

Nimeelewa kwamba nina weza kujiondoa wakati wowote nitakapo na hatua hii haita hatarisha matibabu ninayopata ama anayoipata mgonjwa wangu. Matokeo ya utafiti yaweza kuwa ya manufaa kwangu ama kwa wagonjwa wengine kwa jumla na yaweza kusaidia kupunguza maumivu baada ya upasuaji..

Kidole cha gumba kwa wale wasiojua kuwandika (Shahidi atie sahihi hapa chini)

…….

Sahihi/ama alama ya kidole cha gumba katika sanduku →

Tarehe…….....

Siku/Mwezi/Mwaka

Jina la shahidi……

Sahihi…….
Tarehe…….

(Siku/Mwezi/Mwaka)

(iii) Sehemu ya tatu – Dhibitisho la mtafiti

Hii nikuidhinisha ya kwamba nimemueleza mshiriki ama msimamizi wake kuhusu utafiti huu na pi nimempa nafasi yakuuliza maswali. Nimemueleza yafuatayo;

- Kwamba kushuriki ni kwa hiari yake mwenyewe bila malipo.
- Kushuriki hakutasababisha madhara ama kuhatarisha maisha kamwe.
- Anaweza kujiondoa kutoka kwa utafiti huu wakati wowote bila kuhatarisha matibabu anayo ipata katika hospital kuu ya Kenyatta.
- Habari ambazo atapeana hazita tambazwa hadharani bila ruhusa kutoka kwake (mshiriki) na pia kutoka kwa mdhamini mkuu wa utafiti wa hospital kuu ya Kenyatta na chuo kikuu cha matibabu.

Jina la mtafiti ama msimamizi wake……

Sahihi……..

Tarehe…….

(Siku/Mwezi/Mwaka)

12.2 Appendix 2. Patient Assessment Chart

Patient Chart Study ID _____

Name_____ Age _____

IPNO._____ Sex _____

Ward _____

Diagnosis_____

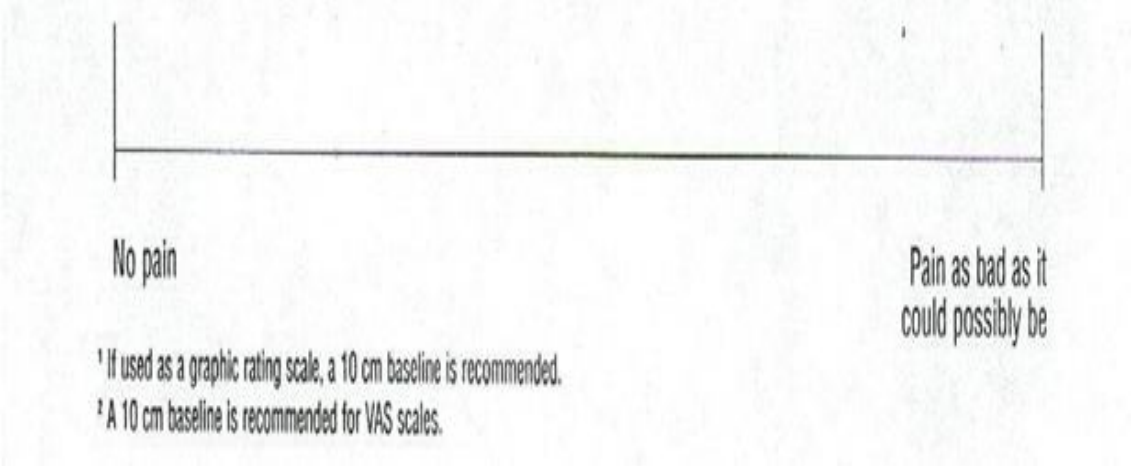
Intra Operative Details	
Intra-operative analgesia used	
Intra-operative local anaesthesia given	

Post-operative analgesia given			
	Drugs	Dosage	Frequency
Day 1			
Day 2			
Day 3			

VAS Scores						
	Day 1		**Day 2**		**Day 3**	
	12 hrs	**24 hrs**	**36 hrs**	**48 hrs**	**60 hrs**	**72 hrs**
At rest						

	1st Post-operative day								2nd Post-operative day								3rdPost-operative day								
Date																									
Time																									
BP (mmhg)																									Pulse
250																									250
240																									240
230																									230
220																									220
210																									210
200																									200
190																									190
180																									180
170																									170
160																									160
150																									150
140																									140
130																									130
120																									120
110																									110
100																									100
90																									90
80																									80
70																									70
60																									60
50																									50
40																									40
30																									30
RESP																									
Sedation																									
Pain Score																									
Nausea																									
Vomiting																									

12.3 Appendix 3. Visual Analogue Scale [58]



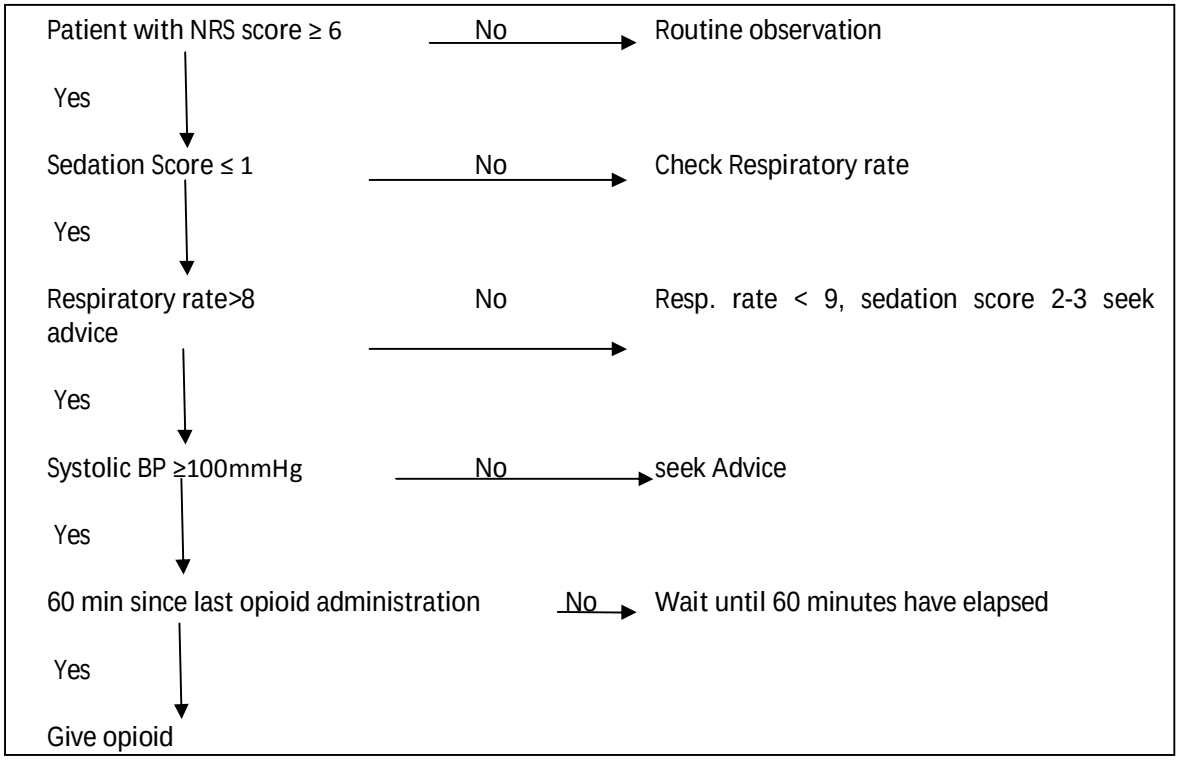
12.4 Appendix 4. Sedation Score [32]

0	Awake
1	Dozing intermittently
2	Mostly sleeping
3	Difficult wakening

12.5 Appendix 5. Pain Management Protocol [32]

Drug		Pt weight (kg)	Dosage	Route of administration
Strong opioid	Pethidine	40-65	75 mg 4 hourly	Intramuscular
		65-100	100mg 4 hourly	Intramuscular
NSAID	Diclofenac	40-100	50mg 8 hourly or 75mg 12 hourly	Intramuscular

Rescue Analgesia algorithm [32]



12.6 Appendix 6. Copy of Ethical Approval

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
(254-020) 2726300 Ext 44355
Ref: KNH-ERC/A/330

KNH/UON-ERC
Email: uonknh_erc@uonbi.ac.ke
Website: www.uonbi.ac.ke
Link:www.uonbi.ac.ke/activities/KNHUoN

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi
6th December 2012

KENYATTA NATIONAL HOSPITAL
APPROVED
06 DEC 2012
ETHICS & RESEARCH COMMITTEE

Dr. Janai A. Mariita Ondieki
Dept.of Surgery
School of Medicine
University of Nairobi

Dear Dr. Ondieki

RESEARCH PROPOSAL: EFFICACY OF A SIMPLE STANDARD MULTIMODAL ANALGESIC PROTOCOL ON ACUTE POST-OPERATIVE PAIN AFTER MAJOR ABDOMINAL SURGERY IN KENYATTA N.HOSPITAL (P312/06/2012)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above revised proposal. The approval periods are 6th December 2012 to 5th December 2013.

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 severe 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) 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*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
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.

For more details consult the KNH/UoN ERC website **www.uonbi.ac.ke/activities/KNHUoN**

Yours sincerely

PROF. A.N. GUANTAI
SECRETARY, KNH/UON-ERC

c.c. The Deputy Director CS, KNH
The Principal, College of Health Sciences, UoN
The Dean, School of Medicine, UoN
The Chairman, Dept.of Surgery, UoN
The HOD, Records, KNH
Supervisors: Dr. Joseph Kimani Wanjeri, Dept. of Surgery, UoN
Dr. Timothy M. Mwiti. Dept.of Surgery, UoN

12.7 Appendix 7. Declaration of Originality Form for Students

UNIVERSITY OF NAIROBI

Declaration of Originality Form

This form must be completed and signed for all works submitted to the University for Examination

Name of Student: ____**Dr Janai Abaya Mariita Ondieki**_____
Registration Number: _**H58/70986/09**_____
College Of_____ **Health Sciences**_____
Faculty/School/Institute **of Medicine**_____
Department _____**of Surgery**_____
Course Name: **Master of Medicine in General Surgery**_____
Title of the work: **"The efficacy of a simple standard multimodal analgesic protocol on acute post-operative pain after major abdominal surgery at Kenyatta National Hospital".**

DECLARATION

1. I understand what Plagiarism is and I am aware of the University's policy in this regard
2. I declare that this _**Dissertation**_____ (Thesis, project, essay, assignment, paper, report, etc) is my original work and has not been submitted elsewhere for examination, award of a degree or publication. Where other people's work or my own work has been used, this has properly been acknowledged and referenced in accordance with the University of Nairobi's requirements.
3. I have not sought or used the services of any professional agencies to produce this work
4. I have not allowed, and shall not allow anyone to copy my work with the intention of passing it off as his/her own work
5. I understand that any false claim in respect of this work shall result in disciplinary action, in accordance with University Plagiarism Policy.

Signature _____

Date _____

Declaration Form for Staff

UNIVERSITY OF NAIROBI

Declaration of Originality Form

This form must be completed and signed for all scholarly works produced.

Name of Staff _____**Dr Joseph K. Wanjeri**_____

Payroll Number _____

College _____**Health Sciences**_____

Faculty/School/Institute_**of Medicine**_____

Department _____**of Surgery**_____

Title and bibliographic details of the work: **"The efficacy of a simple standard multimodal analgesic protocol on acute post-operative pain after major abdominal surgery at Kenyatta National Hospital".**

DECLARATION

1. I understand what plagiarism is and I am aware of the University's policy in this regard.
2. I declare that this _____**Dissertation**_____ scholarly work (Paper, book chapter, monograph, review, etc) is my original work. Where other people's work, or my own work has been used, this has properly been acknowledged and referenced in accordance with the University of Nairobi's requirements.
3. I have not allowed, and shall not allow anyone to copy my work with the intention of passing it off as his/her own work.
4. I understand that any false claim in respect of this work shall result in disciplinary action, in accordance with University Plagiarism Policy.

Signature _____

Date _____

Declaration Form for Staff

UNIVERSITY OF NAIROBI

Declaration of Originality Form

This form must be completed and signed for all scholarly works produced.

Name of Staff _____**Dr Timothy M. Mwiti**_____

Payroll Number _____

College _____**Health Sciences**_____

Faculty/School/Institute_**of Medicine**_____

Department _____**of Anaesthesia**_____

Title and bibliographic details of the work: **"The efficacy of a simple standard multimodal analgesic protocol on acute post-operative pain after major abdominal surgery at Kenyatta National Hospital".**

DECLARATION

1. I understand what plagiarism is and I am aware of the University's policy in this regard.
2. I declare that this __**Dissertation**_____ scholarly work (Paper, book chapter, monograph, review, etc) is my original work. Where other people's work, or my own work has been used, this has properly been acknowledged and referenced in accordance with the University of Nairobi's requirements.
3. I have not allowed, and shall not allow anyone to copy my work with the intention of passing it off as his/her own work.
4. I understand that any false claim in respect of this work shall result in disciplinary action, in accordance with University Plagiarism Policy.

Signature _____

Date _____