A randomised controlled trial comparing the effect of adjuvant intrathecal 2MG midazolam to 20-micrograms fentanyl on post-operative pain for patients undergoing lower limb orthopaedic surgery under spinal anaesthesia

Francis Otieno Codero
Aga Khan University

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A RANDOMISED CONTROLLED TRIAL COMPARING THE EFFECT OF ADJUVANT INTRATHECAL 2MG MIDAZOLAM TO 20-MICROGRAMS FENTANYL ON POST OPERATIVE PAIN FOR PATIENTS UNDERGOING LOWER LIMB ORTHOPAEDIC SURGERY UNDER SPINAL ANAESTHESIA

By

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A dissertation submitted in part fulfilment of the requirements for the degree of

Master of Medicine in Anaesthesiology

NAIROBI, KENYA

2nd July, 2013
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DEDICATION

This dissertation is dedicated to my wife Maryline Achieng Mireku whose presence in my life has brought inspiration and fulfilment.
ABSTRACT

Background

Intrathecal adjuvants are added to local anaesthetics to improve the quality of neuraxial blockade and prolong the duration of analgesia during spinal anaesthesia. As an intrathecal adjuvant, fentanyl improves the onset and quality of spinal blockade as compared to plain bupivacaine and confers a short duration of postoperative analgesia. However, its use is associated with several adverse effects that range from pruritus to life threatening respiratory depression. Intrathecal midazolam as an adjuvant has been used and shown to improve the quality of spinal anaesthesia and prolong the duration of postoperative analgesia. No studies have been done comparing intrathecal fentanyl with bupivacaine and intrathecal 2mg midazolam with bupivacaine.

Objective

To compare the effect of intrathecal 2mg midazolam to intrathecal 20 micrograms fentanyl when added to 2.6 ml of 0.5% hyperbaric bupivacaine, on post-operative pain, in patients undergoing lower limb orthopaedic surgery under spinal anaesthesia.

Study design

Single blinded Randomized Controlled Trial

Methods

A total of 40 patients undergoing lower limb orthopaedic surgery under spinal anaesthesia were randomized to two groups

Group 1; 2.6mls 0.5% hyperbaric bupivacaine with 0.4mls (20micrograms) fentanyl

Group 2; 2.6mls of 0.5% hyperbaric bupivacaine with 0.4mls (2mg) midazolam
Results

The duration of effective analgesia was longer in the midazolam group 384.05min as compared to the fentanyl group 342.6min. There was no significant difference (‘P’ 0.4047). The time to onset was significantly longer in midazolam group 17.1min as compared to the fentanyl group 13.2min (‘P 0.023’). The visual analogue score at rescue was significantly lower in the midazolam group 5.55 as compared to the fentanyl group 6.35 (‘P - 0.043’).

Conclusion

On the basis of the results of this study, there was no significant difference in the duration of effective analgesia between adjuvant intrathecal 2mg midazolam as compared to intrathecal 20micrograms fentanyl for patients undergoing lower limb orthopaedic surgery.
# LIST OF ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>ASA</td>
<td>American Society of Anaesthesiologists</td>
</tr>
<tr>
<td>BP</td>
<td>Blood pressure</td>
</tr>
<tr>
<td>B/min</td>
<td>Beats per minute</td>
</tr>
<tr>
<td>CSF</td>
<td>Cerebrospinal Fluid</td>
</tr>
<tr>
<td>GA</td>
<td>General Anaesthesia</td>
</tr>
<tr>
<td>HR</td>
<td>Heart rate</td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
</tr>
<tr>
<td>IM</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>IT</td>
<td>Intrathecal</td>
</tr>
<tr>
<td>mg</td>
<td>Milligrams</td>
</tr>
<tr>
<td>mls</td>
<td>Millilitres</td>
</tr>
<tr>
<td>mmHg</td>
<td>Millimetres of mercury</td>
</tr>
<tr>
<td>N₂O</td>
<td>Nitrous oxide</td>
</tr>
<tr>
<td>NSAID</td>
<td>Non-steroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>RA</td>
<td>Regional Anaesthesia</td>
</tr>
<tr>
<td>RR</td>
<td>Respiratory rate</td>
</tr>
<tr>
<td>SA</td>
<td>Spinal anaesthesia</td>
</tr>
<tr>
<td>SPSS</td>
<td>Statistical package for the social sciences</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual Analogue Scale</td>
</tr>
</tbody>
</table>
ACKNOWLEDGEMENT

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I am appreciative of the services of Dr. Thikra Sharif who assisted in the proofreading and editing of my paper, to Dr. Lucy Mwaura who assisted with other technical aspects and to Ms. Kamanda Ciru of the Research Support Unit at AKUH who organized the research seminars.

My gratitude goes to the library staff as well for their support.

Thank you all.
DECLARATION

I declare that this dissertation does not incorporate without acknowledgement any material previously submitted for a degree or diploma in any university, and that to the best of my knowledge it does not contain any material previously published or written by another person except where due reference have been made in the text.

The editorial assistance provided to me has in no way added to the substance of my dissertation, which is the product of my own research endeavors.

(Signature of candidate)

2nd July, 2013
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INTRODUCTION

Acute postoperative pain is one of the most common postoperative problems, with an incidence up to 70% in certain categories of surgical patients (1). Apfelbaum et al (2) conducted a national survey in the United States and concluded that, acute postoperative pain continues to be undermanaged with up to 60% of patients experiencing moderate to severe pain at hospital discharge. A recent unpublished study carried out at the Aga Khan University Hospital investigated the incidence of postoperative pain after day care surgery and concluded, that 56% of patients suffer from moderate to severe pain after day care surgery (3).

Acute postoperative pain is a complex physiological reaction to tissue injury which may result in unpleasant, unwanted sensory and emotional experiences (4). It can result in delayed healing, delayed mobilization and increased risk of myocardial infarction or ischemia, risk of tachycardia and dysrhythmia. Other published reports indicate that postoperative pain can lead to thromboembolic events, peripheral vasoconstriction, and metabolic acidosis (5,6). Controlling post-operative pain has the potential to allow for earlier hospital discharge and may improve the patient's ability to tolerate physical therapy.

In the past few years various pharmacological and non-pharmacological methods have been introduced to provide post-operative pain-relief. Systemic analgesics and conventional pain treatment modalities are effective in controlling postoperative pain for majority of patients. However, many other patients such as those with complex trauma, and extensive injuries, require more aggressive therapy to directly modulate pain transmission in the central nervous system; and a high dose of systemic analgesics may cause significant side effects such as alteration in mental processes, respiratory depression, and other cardiovascular instability. The use of intrathecal opioids in controlling post-operative pain has developed from an understanding for the role of the spinal cord for modulating and processing nociceptive stimuli, and the discovery of opioid receptors in the spinal cord (7). Several agents have
been administered epidurally and intrathecally with and without local anaesthetic; such as opioids, benzodiazepines, neostigmine, clonidine, non-steroidal anti-inflammatory agents, vasoconstrictors. The objective of adding such agents is to provide more adequate analgesia, reduce the use of oral analgesics with unwanted side effects, and to prolong the duration of analgesia.

A vast number of research have demonstrated the efficacy of intrathecal administration of opioids such as fentanyl and other agents such as midazolam in controlling postoperative pain (8–11). Most of those studies have demonstrated benefits and side effects using different doses of fentanyl and midazolam in controlling postoperative pain (8,10–12). Only one recent study by Talwar et al in 2008 has been done to compare fentanyl 20 micrograms with 1mg midazolam in which they investigated the net effect on postoperative pain and side effects. The purpose of this study is to compare the effect of intrathecal bupivacaine with 2mg midazolam to intrathecal bupivacaine with 20 micrograms fentanyl on postoperative pain for patients undergoing lower limb orthopaedic surgery under spinal anaesthesia.
2.0 LITERATURE REVIEW

2.1 General versus spinal anaesthesia

Spinal anaesthesia has several advantages over general anaesthesia especially for lower limb surgery such as better pain relief after surgery, selective analgesia, reduction of systemic analgesic consumption and elimination of opioid related side effects (13–16). Several studies have been undertaken to compare the perioperative and postoperative outcomes including postoperative pain of patients undergoing surgery under general and spinal anaesthesia. Urwin et al in their meta-analysis of 15 randomized controlled trials compared general and spinal anaesthesia, concluded that there was, a reduced 1-month mortality and incidence of deep vein thrombosis in the regional anaesthesia group; they also noted that there was a tendency towards a lower incidence of myocardial infarction, confusion and postoperative hypoxia in the regional anaesthetic group (13).

William and colleagues conducted a meta-analysis of ten independent trials involving 330 patients under general anaesthesia and 348 patients under neuraxial block. They reported that neuraxial block significantly decreased the incidence of radiographically diagnosed deep venous thrombosis and pulmonary embolism; they noted that neuraxial block is associated with a decrease in intraoperative blood loss and the number of patients requiring blood transfusions (14).

A systematic review done to estimate the effect of neuraxial blockade compared to general anaesthesia on post-operative morbidity and mortality their results showed further benefits of neuraxial anaesthesia. There was reduced mortality by one third, reduced risk of deep venous thrombosis, pulmonary embolism, transfusion requirements, pneumonia, respiratory depression, myocardial infarction and renal failure(15).

A meta-analysis on the comparison of regional versus general anaesthesia for ambulatory anaesthesia indicated potential advantages for regional anaesthesia, such as decreased post anaesthesia care unit use, nausea, and postoperative pain (16).
Based on the above evidence, there seems to be a general consensus that for orthopaedic, vascular and other surgeries in the lower limbs, central neuraxial blocks confer several advantages over general anaesthesia with less morbidity and mortality. These advantages include less postoperative pain and early mobilization, less respiratory complications, less blood loss and transfusion requirements, with fewer events of deep venous thrombosis and pulmonary embolism.

2.2 Clinical implications of post-operative pain

Millions of patients worldwide undergo surgery each year. They do benefit from knowledge, skills, and sophisticated technology that characterize most aspects of modern surgical treatment, including pain management.

Effective pain control is essential for optimal care of surgical patients. However, many patients continue to experience considerable discomfort despite advances in knowledge of neurobiology, pharmacology of analgesics, and the development of more effective techniques for postoperative pain control. There appears to have been little improvement in this aspect of care of surgical patients over the past several decades (17,18).

Postoperative pain is one of the most common forms of acute pain (5,19). Its suboptimal management has been recognized as a problem by clinicians for the past 50 years, and has been formally identified as a public health concern by various societies and government institutions in the USA, Australia and Europe (5,17–19).

Moderate to severe pain can affect nearly every organ system. Cardiovascular effects include hypertension, increased heart rate, arrhythmias, increased systemic vascular resistance, increased cardiac output, or decreased cardiac output with compromised left ventricular function- all of which can aggravate ischemia. Respiratory effects include increased carbon dioxide production, increased minute ventilation, and increased work of breathing. Gastrointestinal (GI) effects include decreased GI motility; increased acid
production, possibly leading to ulcers; nausea and vomiting; and constipation. Endocrine responses include increased catecholamine’s, cortisol, and glucagon; decreased insulin and testosterone; and sodium retention. Hematologic effects include hypercoagulation and decrease in immune function. Pain also causes sleep and affective disturbances (19).

Pain causes stimulation of sympathetic neurons and subsequent tachycardia, increased stroke, cardiac work, and myocardial oxygen consumption. The risk of myocardial ischemia or infarction may be increased when fear of aggravating pain results in reduced physical activity, venous stasis, and platelet aggregation.

Following surgery, ileus, nausea, and vomiting can occur for a number of reasons that include nociceptive impulses from viscera and somatic structures. Pain can also cause hypomotility of the urethra and bladder and consequent difficulty with urination. These effects can be very unpleasant for patients, and, especially in the case of ileus, may prolong hospital stay (20). Suprasegmental reflex responses to pain result in increased sympathetic tone, hypothalamic stimulation, increased catecholamine and catabolic hormone secretion (cortisol, ACTH, ADH, GH, cAMP, glucagon, aldosterone, renin, angiotensin II), and decreased secretion of anabolic hormones (insulin, testosterone).

### 2.3 Intrathecal adjuvants for spinal anaesthesia

A single intrathecal injection of bupivacaine alone provides anaesthesia and analgesia for approximately 2–3 hours (21). However, most patients require adequate pain control for a longer duration of time, during the surgical intervention and during the immediate post-operative period.

Several adjuvants have been added to local anaesthetics to increase the density of the neuraxial blockade and to prolong the duration of analgesia. The drugs that have been administered for this purpose include benzodiazepines, opioids, neostigmine, clonidine,
non-steroidal anti-inflammatory agents, vasoconstrictors etc. each with its advantages and disadvantages

2.4 Intrathecal opioids

To prolong the duration of post-operative analgesia and to improve the density of the neuraxial block, several opioids have been administered including fentanyl, morphine, hydromorphone, sufentanyll each with its advantages and disadvantages

Of the opioids, fentanyl and sufentanyl are the best studied and most commonly used lipophilic drugs for intrathecal delivery. In a systematic review investigating the use of intrathecal lipophilic opioids as adjuncts to spinal anaesthesia, Hamber and Viscomi 1999 (8) recommended using 20-30 micrograms fentanyl to supplement bupivacaine for spinal anaesthesia. The addition of this dose led to faster onset of block, improved intraoperative and postoperative analgesia that lasted 2-5 hours.

2.5 Complications of intrathecal opioids

Intrathecal opioids are associated with numerous complications including respiratory depression, urinary retention, pruritus, nausea and vomiting. The most feared complication is respiratory depression. The mechanism is through the rostral spread immediately after injection and with fentanyl and sufentanyll occurs within 20-30min after injection. Evidence from small controlled studies and large observational studies (22) show an incidence of 0.07%-0.49% clinically significant, dose dependent, and non-drug specific respiratory depression. Pruritus is the most common complication with incidence of 30-100% (23,24) and the management requires the administration of opioid antagonists naloxone and naltrexone (25,26) which in larger doses may reverse the analgesic effect (26).
2.6 Intrathecal fentanyl

The use of intrathecal fentanyl in controlling postoperative pain has developed from an understanding for the role of the spinal cord for modulating and processing nociceptive information, and the discovery of opioid receptors in the spinal cord (7). Fentanyl is a highly lipophilic compound with a high affinity for mu opioid receptors with a rapid onset of action following intrathecal injection. It mediates its analgesic effect through activation of the spinal opioid mu and kappa receptor and thereby modulating activity in the nociceptive pathway (27). Its administration into the intrathecal space increases the duration and spread of sensory block but does not prolong the motor block (28).

2.7 Intrathecal midazolam

There has been much recent attention towards the use of benzodiazepine midazolam as an intrathecal drug in treatment of acute and chronic pain (29).

Intrathecal midazolam exerts a spinally mediated antinociceptive action by binding with GABA\(_\alpha\) receptors leading to activation of a spinal cord delta opioid pathway (30) for spinal anaesthesia its administration to the intrathecal space improves the quality of spinal anaesthesia and prolongs the duration of post-operative analgesia.

A meta-analysis by K.M Ho et al on the use of intrathecal midazolam to improve perioperative analgesia conclude that intrathecal midazolam appears to improve analgesia and reduce nausea and vomiting during caesarean section (31).

Several other clinical studies showed that the systemic side effects of intrathecal midazolam are uncommon compared to plain bupivacaine and other adjuvants (31–34)
and adding intrathecal midazolam to other spinal medications may reduce the risk of perioperative nausea and vomiting (10,31).

In most of those above mentioned studies, midazolam has been administered in the dose of 1mg and 2mg intrathecally and up to 6mg per day of midazolam has been used safely as an intrathecal infusion for relief of chronic refractory pain (35).

Several studies have been done to compare plain bupivacaine and bupivacaine with midazolam at various dosages. Bharti et al (33) et al used 1mg of intrathecal midazolam for patients undergoing lower abdominal surgery and found that intrathecal midazolam significantly improves the duration and quality of spinal anaesthesia and provides prolonged perioperative analgesia without significant side effects. Yegin et al (36) used 2mg intrathecal midazolam for patients undergoing perianal surgery and found that it produces a more effective and longer analgesia as compared to bupivacaine alone.

Nanjegowda N et al (32) conducted a study comparing the effects of intrathecal 2mg midazolam on the duration of analgesia in patients undergoing knee arthroscopy and found that the addition of preservative free midazolam 2mg to intrathecal 0.5% hyperbaric bupivacaine prolongs the duration of analgesia without any observed side effects.

Only one study however conducted by Talwar et al (37) compared intrathecal 1mg midazolam and 20 micrograms fentanyl for lower limb surgery. This study was conducted on 58 patients and the dose for hyperbaric bupivacaine was 13mg. The variables observed in this study were the duration of sensory blockade and motor blockade and duration of effective analgesia. The authors concluded that intrathecal fentanyl combined with bupivacaine provided a longer duration of sensory and motor
blockade as compared to midazolam but in addition a greater possibility of a mild sedative effect.

A study conducted by Kim et al (33) however compared various doses of intrathecal midazolam 1mg and 2mg plain 0.5% hyperbaric bupivacaine, and found that time to first analgesia was significantly greater in the IT group compared to plain bupivacaine and even more so for the 2mg group.

Based on the above stated author’s reviews it seems that 2mg intrathecal midazolam has an obvious advantage over 1mg intrathecal midazolam as far as the density of the neural blockade and duration of postoperative analgesia

Therefore, this study is proposed to compare the effect of intrathecal midazolam with fentanyl on post-operative pain for patients undergoing lower limb orthopaedic surgery.
3.0 JUSTIFICATION

According to the previous conducted randomized controlled trials, the authors concluded that the use of intrathecal 2mg midazolam is superior to 1mg midazolam. However, all the published studies, up-to-date, have compared intrathecal fentanyl to midazolam at 1mg intrathecally. None of the published studies have compared fentanyl with intrathecal 2mg midazolam, in spite of the fact that 2mg midazolam has advantages over 1mg midazolam such as improved density blockade, longer duration of effective analgesia.

This study was designed to compare the effect of intrathecal bupivacaine with 2mg midazolam to intrathecal bupivacaine with 20 micrograms fentanyl on postoperative pain for patients undergoing orthopaedic surgery under spinal anaesthesia.

3.1 Aim of study

This study was designed to compare the duration of postoperative pain relief between intrathecal 2mg midazolam with fentanyl 20 micrograms for patients undergoing lower limb orthopaedic surgery.
4.0 RESEARCH QUESTION

Is the duration of postoperative pain relief following intrathecal 2mg midazolam combined with bupivacaine as long as that of intrathecal 20 micrograms fentanyl combined with bupivacaine in lower limb orthopaedic surgery?

4.1 Null hypothesis

There is no difference in duration of postoperative pain relief between intrathecal 2mg midazolam and intrathecal 20 micrograms fentanyl for patients undergoing lower orthopaedic surgery
5.0 OBJECTIVES

5.1 Primary objective
To compare the effect of intrathecal 2mg midazolam to intrathecal 20 micrograms fentanyl when added to 2.6 ml of 0.5% hyperbaric bupivacaine, on post-operative pain, in patients undergoing lower limb orthopaedic surgery under spinal anaesthesia.

5.2 Secondary objective
To evaluate and explore the intraoperative and postoperative side-effects following intrathecal 20micrograms fentanyl compared to intrathecal 2mg midazolam
6.0 METHODOLOGY

6.1 Study design
Prospective single blinded randomized controlled trial; the patients were blinded on the nature of the intervention made.

6.2 Study site
The study was conducted at Aga Khan University Hospital, Nairobi; this tertiary not for profit hospital with a bed capacity of 240 beds and postgraduate medical education programs in various disciplines. Since Nairobi is a cosmopolitan city, the patients served by this hospital cut across most racial groups present within the country. Patients were recruited from the outpatient pre-anaesthesia clinics and as well inpatients from the wards.

6.3 Reference population
The target population included all patients admitted for lower limb orthopaedic surgery at the Aga Khan University Hospital, Nairobi.

6.4 Sample population
The sample population included all ASA I, II and III patients scheduled for theatre for lower limb orthopaedic surgery between October 2012 and January 2013.

6.5 Feasibility of recruitment
Regarding feasibility, theatre records for the first quarter of 2012 indicated that 141 procedures were undertaken for patients who would have met the inclusion criteria for the present study.
6.6 Study population
It comprised all eligible patients scheduled for lower limb orthopaedic surgery who had given consent for the study.

6.7 Eligibility criteria

6.7.1 Inclusion criteria

All ASA I-III patients scheduled for lower limb orthopaedic surgery

6.7.2 Exclusion criteria

1. Patient refusal
2. Patients <18 years and >76 years
3. Failure to reach the sub arachnoid space and converted to GA
4. Patients with contraindications to neuraxial anaesthesia
   a. Puncture site infection
   b. Hypovolemic shock
   c. Coagulopathy
   d. Sepsis
5. Patients with psychological / mental instability
6. Patients with known psychiatric condition
7. Patient involved in any other clinical studies
6.8 SAMPLE SIZE DETERMINATION

Sample size calculation was based on the expected difference in mean duration of analgesia between intrathecal midazolam and fentanyl effect. Sample size formula for comparing two means given below is used to determine the required sample size.

\[ n = \frac{2(z_{1-a/2} + z_{1-\beta})^2 \times (\sigma_1 + \sigma_2)^2}{(\mu_1 - \mu_2)^2} \]

- \( n \) is required minimum sample size per comparison group
- \( \mu_1 \) is the expected mean duration for analgesia for the first comparison group
- \( \mu_2 \) is the expected mean duration for analgesia for the second comparison group
- such that the quantity \((\mu_2 - \mu_1)\) is the size of the magnitude of group difference it is desired to be able to detect
- \( \sigma_1 \) and \( \sigma_2 \) are expected standard deviations for the mean for the respective comparison groups being compared
- \( z_{1-a/2} \) is the z-score corresponding to the degree of confidence with which it is desired to be able to conclude that an observed difference of size \((\mu_2 - \mu_1)\) would not have occurred by chance (statistical significance), and
- \( z_{1-\beta} \) is the z-score corresponding to the degree of confidence with which it is desired to be certain of detecting a change of size \((\mu_2 - \mu_1)\) if one actually occurred (statistical power).

The reported mean duration of block for fentanyl is 296 (sd=73.64) (37) and for midazolam 2mg is 399 (sd=60) (38). Using this information in the formula above
assuming 5% significance level and power of 90%, the required sample size was 20 patients in each group (total of 40 patients).

A sample size of 40 patients was determined as sufficient to demonstrate a 103 minute mean difference in the duration of effective analgesia between patients undergoing spinal anaesthesia with adjuvant 2mg midazolam and those with adjuvant fentanyl at the Aga Khan University Hospital. The study was powered at 90%. Type 1 error was set at 0.05. The above formula was used since the aim of the study was to determine the mean difference in the duration of effective analgesia between the two intrathecal adjuvant medications.
6.9 SAMPLING PROCEDURES

6.9.1 Recruitment

The study participants were recruited from the preoperative anaesthesia clinic (during the pre-anaesthetic review) and the inpatient surgical wards. All potential participants received oral and written explanation (appendix 1) on the purpose and procedure of the study from the principal investigator; and written signed informed consent sought (appendix 2). The patients who gave written informed consent were then be enrolled into the study and randomized. Their files were tagged with a special colour sticker for ease of identification on admission and in theatres.

6.9.2 Randomization

Simple randomization was done using a computer program; the principal investigator generated a random sequence of numbers. Each of the random numbers was sequentially assigned to either;

Group 1; 2.6mls 0.5% hyperbaric bupivacaine with 0.4mls (20micrograms) fentanyl

Group 2; 2.6mls of 0.5% hyperbaric bupivacaine with 0.4mls (2mg) midazolam

6.9.3 Informed consent

Informed consent was obtained by the Primary investigator after a detailed explanation of the nature of the study and any queries shall be addressed with the patient. In case an enrolled and consented patient withdrew consent, the next consecutively randomized patient was selected as a replacement.
6.9.4 Pre-operative education

At the pre-operative visit, an anaesthesiologist and/or trained research nurse familiarized the patients with the procedure of recording the postoperative pain scores using a Visual analogue scale (VAS) - chart, which consists of a 10cm line with 0 equalling “no pain” and 10 equalling “worst pain possible”.
Flow diagram of patient distribution

64 - Assessed for Eligibility

22 excluded
- 16 - Patient refusal
- 5 - Outside age bracket
- 1 - Hypovolemic shock

42 Randomized

21 - Intrathecal midazolam group

21 - Intrathecal fentanyl group

1 - Lost to follow up

40 Analysed
6.10 Anaesthetic procedure

This study was undertaken at the Aga Khan University Hospital, Nairobi operating theatres, ASA physical status I-III patients scheduled for lower limb orthopaedic surgery and were randomized to either receive 2.6mls of 0.5% hyperbaric bupivacaine with 0.4mls (20mcg) fentanyl or 2.6mls of 0.5% hyperbaric bupivacaine with 0.4mls (2mg) midazolam intrathecally at L3-S1 interspace. The anaesthesiologist conducting the procedure (principal investigator or research assistant) received together with the data entry form the randomization group and administered the study drugs as per randomization group.

On arrival to the operating theatres, standard monitoring was applied with automated non-invasive blood pressure measurement, electrocardiography and pulse oximetry, with the objective of obtaining the baseline cardiovascular parameters. Prior to performing the spinal anaesthesia the patient would receive 500mls of Ringers lactate solution intravenously.

After a local infiltration of 2ml 2% lidocaine solution, a midline puncture with a 25 French gauge pencil point needle was performed at L3L4, L4L5 interspace, with the patient in the sitting or lateral decubitus position. After obtaining free flow of CSF, the study drugs previously prepared by anaesthesiologist as per randomization group were administered. Patients were then be turned supine and the sensory block level to both light touch and temperature were checked at 2.5min intervals until there was no change in 3 consecutive readings, the time of maximal block were documented as the time of onset of the block. After this, the anaesthesiologist assessed the modified Bromage motor score (1 - able to move hip, knee and ankle; 2 - unable to move hip, able to move knee and ankle; 3 - unable to move hip and knee, able to move ankle; 4 - unable to move hip, knee and ankle). Surgery was allowed to commence as soon as the sensory block height to light had been tested pre-incision and reached the desired level. Subsequently the sensory block height, the Bromage score, the vital signs (NIBP, heart rate and oxygen saturation) and VAS were determined and recorded every hour.
If pain or discomfort was felt, analgesia options of either GA or supplementary analgesia with IV adjuncts such as fentanyl 1-2mcg/Kg and IV paracetamol 1g was given.

Hypotension (defined as a reduction in MAP of more than 20% from baseline determined just before the administration of regional anaesthesia) was treated with ephedrine boluses of 6 mg. Bradycardia (defined as heart rate less than 60bpm) was treated with atropine. The presence of intraoperative nausea, vomiting, pruritus, and shivering was also noted and treated appropriately; rescue antiemetic drugs using a combination of IV ondansetron 4mg or granisetron 1mg were administered at the discretion of the anaesthesiologist. Other complications that patients developed were noted (inadequate blocks, conversion to general anaesthesia, bradycardia, pruritus, hypotension, respiratory discomfort, ephedrine use, colloids use, and crystalloid use). All the complications that occurred were noted by the anaesthesiologist. At the end of surgery, the patient received IV paracetamol 1g and IM diclofenac 75mg.

The principal investigator together with the research assistants followed up the patients in the wards with hourly monitoring of the VAS, Bromage score, sensory block height and vital signs (NIBP, HR and arterial oxygen saturation). The time to request first analgesia was taken as the first time the patient requests for analgesia or the VAS \( \geq 4 \).

Intraoperative data were collected by PI or trained RA using the data collection form (appendix 3).
6.12 DATA MANAGEMENT

Upon collection data were entered into the statistical software (SPSS version 15) on the same day in a coded form and saved, awaiting analysis. All data entered was verified by the principal investigator. In case of missing data the principal investigator conducted a follow up and collected the missing data from the patient or from the patient medical records. Every precaution was taken to respect the privacy of the patients whose data were collected and analysed in this study. Patient data were identified by a unique identifier number. However, in the course of monitoring data quality and adherence to the study protocol only the study supervisors referred to the recruited patient’s medical records; after analysis the data were stored in soft copy with the research support unit. The hard copies will also be stored by the anaesthesiology department for a period of 5 years from the completion of the study. A notice for destruction of the data will be given to the research committee and once approval is granted the data will be destroyed upon expiry of the 5 years.

6.12.1 DATA ANALYSIS

Data analysis was undertaken using the SPSS version 15 with the input of a statistician who has been involved since the beginning of the study.
Descriptive statistics were used to compare patients’ characteristics in terms of age, sex, height, weight. Student’s T test was used to compare if the 2 sample sizes were statistically different. The unpaired student’s t test was used to compare the differences between duration of effective analgesia and VAS at administration of rescue analgesia. The Chi test was used to compare the proportions of various complications between the two groups. Survival time analysis (Kaplan Meir) was used to analyze the duration of effective analgesia. Log rank test was used to compare duration of effective analgesia.
6.13 ETHICAL CONSIDERATIONS

The study was performed following approval from the Department of Anaesthesia and the Research and Research Ethical Committees of the Aga Khan University.

Patients were recruited after having signed an informed consent, which clearly stated that it is a research study being conducted and that their information kept confidential and may be published. The patients were made to understand that they would receive health care as all other patients who came to theatre, and that they would not be denied care if they declined to participate in the study. For those who do not understand English the above information, the pain scale and instructions were explained in Swahili by the principal investigator and further data collection by the research assistants were done in Swahili.

An explanation on the study procedure was given to the patient both verbally and using a written form. It was also made clear there shall be no direct benefit to the patient arising from participation in the study, but that the results could be used to change local practice in the future. There were no added expenses to the patient.

The patients voluntarily signed the consent form and were recruited in the pre-anaesthesia review before coming to the operating theatres.

The operation did not start until testing pre-incision was done that the anaesthesia was adequate.

In case of discomfort or pain, I.V paracetamol and fentanyl 1-2mcg/Kg was administered and the patient offered the option for conversion to general anaesthesia. At the end of surgery, the patient received IV paracetamol 1g and IM diclofenac 75mg.

In case of a serious adverse event occurring to the patient in the course of the study including prolonged lower limb weakness and loss of sensation for greater than 24hours, severe allergic reaction, severe refractory hemodynamic or respiratory collapse a written report was to be written and forwarded to the REC. In the study period there were no
serious adverse events noted. During the procedure adverse events like hypotension, nausea and vomiting were managed with vasoactive agents, ephedrine and phenylephrine and for nausea or vomiting with ondansetron or granisetron.

The patient was free to withdraw from the study at any stage and still be accorded standard care.
7.0 RESULTS

7.1 Recruitment
Data collection was carried out over four months, October 2012 to January 2013. A total of 40 participants were recruited from the outpatient clinic and surgical wards and randomised for the study. All the participants recruited were followed up and included in the data analysis, twenty in each arm.

7.2 Demographics
Age, weight, height, ASA status were similar in both groups. There was a significant difference in the number of males and females in either group (Table 1). There was no significant difference in age, weight, height and ASA status of the patients.
### Table 1: Patient’s baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Midazolam</th>
<th>Fentanyl</th>
<th>‘P’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>44.6 (18.1)</td>
<td>52.6(17.6)</td>
<td>0.164</td>
</tr>
<tr>
<td>Height</td>
<td>163.9(15.9)</td>
<td>158.3(19.6)</td>
<td>0.324</td>
</tr>
<tr>
<td>Weight</td>
<td>75.8(11)</td>
<td>76.1(12.7)</td>
<td>0.947</td>
</tr>
<tr>
<td>ASA status</td>
<td>2.1(0.9)</td>
<td>2(0.9)</td>
<td>0.713</td>
</tr>
<tr>
<td>Sex (Male)</td>
<td>7</td>
<td>15</td>
<td>0.002</td>
</tr>
<tr>
<td>Sex (Female)</td>
<td>13</td>
<td>5</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Note: Mean age, height, weight and ASA are presented as Mean +/-SD; t-test used for analysis

#### 7.3 Types of surgical procedures done

The majority of the procedures conducted were knee arthroscopy contributing to 32.5% of procedures conducted and the least was above knee amputation that contributed 2.5% of the total surgical procedures done. Table 2 shows the distribution of the procedures in each group.
Table 2: Types of surgical procedures

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Midazolam group</th>
<th>Fentanyl group</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee arthroscopy</td>
<td>8(40%)</td>
<td>5(25%)</td>
<td>13(32.5%)</td>
</tr>
<tr>
<td>Knee replacement</td>
<td>4(20%)</td>
<td>3(15%)</td>
<td>7(17.5%)</td>
</tr>
<tr>
<td>Hip replacement</td>
<td>0</td>
<td>3(15%)</td>
<td>3(7.5%)</td>
</tr>
<tr>
<td>ORIF femur</td>
<td>3(15%)</td>
<td>3(15%)</td>
<td>6(15%)</td>
</tr>
<tr>
<td>ORIF Tibia</td>
<td>1(5%)</td>
<td>1(5%)</td>
<td>2(5%)</td>
</tr>
<tr>
<td>ORIF ankle</td>
<td>3(15%)</td>
<td>5(25%)</td>
<td>8(20%)</td>
</tr>
<tr>
<td>Above knee amputation</td>
<td>1(5%)</td>
<td>0</td>
<td>5(2.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>20</td>
<td>40(100%)</td>
</tr>
</tbody>
</table>
7.4 Outcomes

The duration of effective analgesia in the midazolam group 384.05min as compared to the fentanyl group 342.6min; this was not significant (‘P’ 0.4047). The time to onset was significantly longer in midazolam group 17.1min as compared to the fentanyl group 13.2min (‘P 0.023’). The visual analogue score at rescue was significantly lower in the midazolam group 5.55 as compared to the fentanyl group 6.35 (‘P - 0.043’) (table 3).

Table 3: Primary outcome

<table>
<thead>
<tr>
<th>Variable</th>
<th>Midazolam Mean (sd) (CI)</th>
<th>Fentanyl Mean (sd) (CI)</th>
<th>Mean difference (CI)</th>
<th>‘P’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to maximum block (minutes)</td>
<td>17.1(6.5) (14.08-20.12)</td>
<td>13.2(3.8) (13.8-14.9)</td>
<td>3.95(0.6-7.3)</td>
<td>0.023</td>
</tr>
<tr>
<td>VAS at rescue</td>
<td>5.55(1.099) (5.04-6.06)</td>
<td>6.35(1.31) (5.74-6.96)</td>
<td>0.8(0.02-1.57)</td>
<td>0.043</td>
</tr>
<tr>
<td>Duration of effective analgesia</td>
<td>384.05(158.99) (309-458)</td>
<td>342.6(152.04) (271-413)</td>
<td>41.45(0-141)</td>
<td>0.4047</td>
</tr>
</tbody>
</table>

Time to maximum block, VAS at rescue and duration of effective analgesia are presented as Mean +/- SD and confidence intervals; t - test used for analysis
Table 4: incidence of intraoperative complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>Midazolam</th>
<th>Fentanyl</th>
<th>‘P’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea / Vomiting</td>
<td>2 (10%)</td>
<td>4 (20%)</td>
<td>0.661</td>
</tr>
<tr>
<td>Hypotension</td>
<td>2 (10%)</td>
<td>2 (10%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Pruritus</td>
<td>0</td>
<td>11 (57.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sedation</td>
<td>4 (20%)</td>
<td>1 (5%)</td>
<td>0.342</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Intraoperative there was a higher incidence of pruritus in the fentanyl group 57.9% as compared to none in the midazolam group (‘p <0.001’). There was no significant difference in the intraoperative incidences of nausea/vomiting and sedation in the midazolam group as compared to fentanyl group (table 4). Post operatively there was also no significant difference in the incidence of side effects (table 5).
### Table 5: Incidence of post-operative complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>Midazolam</th>
<th>Fentanyl</th>
<th>‘P’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary retention</td>
<td>1(5%)</td>
<td>3(15%)</td>
<td>0.605</td>
</tr>
<tr>
<td>Headache</td>
<td>5(25%)</td>
<td>5(25%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Dizziness</td>
<td>4(20%)</td>
<td>4(20%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Nausea / Vomiting</td>
<td>1(5%)</td>
<td>4(20%)</td>
<td>0.106</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>0</td>
<td>1(5%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3(15%)</td>
<td>2(10%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Hypotension</td>
<td>3(15%)</td>
<td>4(20%)</td>
<td>1.0</td>
</tr>
</tbody>
</table>
8.0 DISCUSSION

In this single blind randomized control study of 40 patients undergoing lower limb orthopaedic surgery under spinal anaesthesia, there was no statistically significant difference between the duration of effective analgesia of adjuvant 2mg intrathecal midazolam as compared to 20mcg intrathecal fentanyl.

The rationale for the use of intrathecal midazolam focuses on the awareness that it is an agonist at the benzodiazepine binding site, a subunit of the pentameric gamma-aminobutyric acid (GABA A) receptor. Agonist occupancy of the benzodiazepine binding site enhances the activity of GABA at the GABA A receptor. This receptor is a chloride ionophore that, when activated, typically stabilises the transmembrane potential at, or near, the resting potential. In neurons, this typically serves to decrease excitability. Intrathecal benzodiazepine-induced analgesia is spinally mediated. Binding sites are GABA receptors, abundantly present in the dorsal root nerve cells, with the maximum concentration found within lamina II of the dorsal nerve cells, a region that plays a prominent role in processing nociceptive and thermoceptive stimulation(38). The present cumulative experience with intrathecal midazolam across species broadly confirms the safety thereof, the analgesic activity of the molecule and its benzodiazepine pharmacology, and the lack of irreversible effects(39).

In the present study it was observed, that there is no statistically significant difference in the duration of effective analgesia, this finding is different from that of a previous study comparing the two drugs (37). This relationship may be explained by another study comparing (33) different doses of intrathecal midazolam that found that 2mg dose of adjuvant midazolam had a longer duration of effective analgesia as compared to the 1mg dose. The confidence intervals obtained for the primary outcome were very wide, since the study was powered for this outcome, the reason could have been due to equivalence but the study was not powered to determine this.
The ‘P’ obtained for the time to maximum block and VAS score showed there may be a difference but this was not statistically significant since there was an overlap of the confidence intervals in duration and pain score obtained between the two groups. In addition, the study was not powered to measure this difference and assess its significance.

The incidence of nausea and vomiting noted in this study was determined to be 5% both intraoperatively and post-operatively and this was lower than that of intrathecal fentanyl; these findings are similar to one done (40) to compare fentanyl, midazolam and placebo and found the highest reduction in incidence of nausea was in the midazolam group.

The incidence of respiratory depression in the present study was 5% of patients in the fentanyl group as compared to that of previous studies that found an incidence of up to 3.4% (22). This may be explained by the fewer number of patients who were recruited in our study and the 5% incidence is attributable to one patient who developed respiratory depression both intraoperatively and postoperatively. The mechanism of intrathecal opioid induced respiratory depression is due to the rostral spread.

Various studies have found different incidences of sedation following intrathecal midazolam. In the study conducted by Talwar and colleagues (37), the incidence of sedation was higher in the intrathecal fentanyl group than in the intrathecal midazolam group. In the present study the incidence of sedation was higher in the midazolam group than in the fentanyl group. This difference may have occurred due the higher intrathecal dose of midazolam (2mg) that was used in the present study.

Erdine and colleagues conducted neurotoxicologic studies in animals by studying histologic and vascular lesions in animal spinal cord samples, indicating the neurotoxic effects of intrathecal midazolam (41). Therefore, they advised against the use of intrathecal midazolam in humans. Subsequent studies in humans (9,42), found no adverse neurological symptoms in those who had received intrathecal midazolam. In agreement with these studies, the present study observed no significant adverse neurological effects in any patient during the study period. Further current reports
suggest that midazolam in a dose of 1-2mg at a concentration not exceeding 1mg/ml is not accompanied by an increase in adverse events (39).
8.1 Limitations of the study

One of the limitations of this study is that despite randomization there was heterogeneity as concerns the nature of the procedures, these procedures varied from arthroscopy to total hip replacement. This therefore meant the difference in the extent of tissue damage and thereby the nociceptive input was large and may have had an effect on the duration of effective analgesia.

Another limitation is the lack of standardization as concerns the use of local anaesthetic infiltration at the surgical site. This may have resulted in the longer duration of effective analgesia for certain procedures due to the routine use of local anaesthetic infiltration at the end of surgery by some surgeons.
9.0 CONCLUSION

On the basis of the results of this study, there was no difference in the duration of effective analgesia between adjuvant intrathecal 2mg midazolam as compared to intrathecal 20micrograms fentanyl for patients undergoing lower limb orthopaedic surgery.
10.0 RECOMMENDATIONS

A large, controlled multicentre study involving one type of procedure to investigate the side effects since the present study was not adequately powered to investigate the side effects of intrathecal midazolam. Further, larger studies need to be done to determine equivalence.

11.0 DISSEMINATION OF FINDINGS

The findings of this study can potentially change practice in the use of intrathecal adjuvants for spinal anaesthesia. This is through the more widespread use of intrathecal midazolam as an adjuvant to prolong the duration of effective analgesia. Therefore, the results will be shared with all clinicians (anaesthesiologists) at the Aga Khan University, Nairobi. In addition, the findings will be submitted to a peer reviewed medical journal for possible publication.
12.0 REFERENCES


13.0 APPENDICES

13.1 APPENDIX I:

EXPLANATION FORM

A RANDOMISED CONTROLLED TRIAL COMPARING THE EFFECT OF ADJUVANT INTRATHECAL 2MG MIDAZOLAM WITH 20 MICROGRAMS FENTANYL ON POST OPERATIVE ANALGESIA FOR PATIENTS UNDERGOING LOWER LIMB ORTHOPAEDIC SURGERY UNDER SPINAL ANAESTHESIA

Name of principal investigator: Dr. Francis Codero

Name of the institution: Aga Khan University Hospital, Nairobi

Introduction

I am a medical doctor training for a postgraduate degree in Anaesthesiology at the Aga Khan University, Nairobi.

I am conducting a study to compare the duration of adequate pain relief of two different medications administered in the spinal space to improve the quality of spinal anaesthesia during surgery. As you read this form, there may be some words that you do not understand. Please do not hesitate to ask me to clarify or ask me to stop as we go through the information and I will take time to explain.

Purpose of the research

Acute pain after surgery affects up to 70% of patients. The reason we are undertaking this study is to determine the drug that gives a longer duration of adequate pain relief after surgery. Your care during this study will not be affected in any negative way if you agree to participate.
Type of research intervention

For this research you will receive standard treatment at AKUH, N. For your surgical procedure, we will use the standard medication and either of the study medication as part of the spinal anaesthesia. Before being recruited in this research you will be asked a series of questions to ensure that you will not suffer any adverse effects from having the spinal anaesthetic.

Participant selection

You are being asked to participate as part of a group of patients who will need spinal anaesthetic for lower limb orthopaedic surgery.

Procedures

If you agree to participate, we shall be performing a spinal anaesthetic in the routine standard procedure and using the standard equipment. The only difference will be the addition of either of the study medications to the standard drug for spinal anaesthesia.

Risks and discomforts

You are not expected to have additional risks by participating in this study. Should you develop any pain or discomfort during the operative we will use what is called a “rescue medicine” that has been proven to control pain. If you are still uncomfortable, you shall be offered general anaesthesia (GA).

Benefits

The knowledge obtained by this project will improve our understanding of the duration of pain relief after a spinal anaesthetic. This may result in better ways of pain control in the future.
Study outcome

If you are interested we could communicate the results of this study to you through electronic mail or post office mail.

Compensation

You will receive no compensation for participating in this study.

Confidentiality

Any information you provide during the study will be kept strictly confidential. You full name will not appear on any study document and only staff participating in this study will have access to the information you provide.

Right to refuse or withdraw

Your participation in this research is entirely voluntary. You are free to choose whether or not you wish to participate. Your decision whether or not to participate will not affect you current or future relations with Aga Khan University Hospital, Nairobi. You will suffer neither penalties or loss of any benefit should you decided not to participate. If for any reason, you are not eligible for the study, or decide not to participate, you will receive normal care and standard treatment and medications. You are also free to withdraw from the study at any time should you wish to do so, for any reason.

Your co-operation is appreciated

Should you have any questions feel free to communicate with me concerning the study on the following address,
Dr. Francis O. Codero

Tel number 0722449575

P.O Box 30270-00100

Aga Khan University Hospital, Nairobi, Kenya
13.2 APPENDIX II

13.2.1 CONSENT FORM

I, Dr. Codero confirm that I have fully explained to my patient what this research involves and hereby undersign.

Date........................................ Signature.........................................................

I hereby consent to participate in this study, having been fully informed of the nature of the study by Dr. Codero

Date........................................ Signature.........................................................
**13.3 APPENDIX III:**

**EXPLANATION FORM TRANSLATED TO SWAHILI**

**A RANDOMISED CONTROLLED TRIAL COMPARING THE EFFECT OF ADJUVANT INTRATHECAL 2MG MIDAZOLAM WITH 20 MICROGRAMMES FENTANYL ON POST OPERATIVE PAIN FOR PATIENTS UNDERGOING LOWER LIMB ORTHOPAEDIC SURGERY UNDER SPINAL ANAESTHESIA**

**Jina la Mtafiti Mkuu:** Dkt. Francis Codero

**Jina la chuo:** Hospitali ya Chuo Kikuu cha Aga Khan kilichoko Nairobi

**Kitangulizi**

Mimi ni daktari wa matibabu kwenye mafunzo ya uzamili idara ya nusu kaputi (Anaesthesiology), chuo kikuu cha Aga Khan kilichoko Nairobi.

Ninafanya utafiti unaolinganisha muda wa kupunguza maumivu hadi kwenye kiwango kinachoridhisha kati ya dawa mbili tofauti zinazowekwa kwenye nafasiiliyo nje ya uti wa mgongo ili kuboresha upunguzaji wa maumivu kupitia mishipa ya uti wa mgongo wakati wa upasuaji. Unaposoma fomu hii, utakabiliana na maneno mengine yatakayokushinda kuelewa. Tafadhali usisite kuniomba nifanue au kuniomba nitamatishe tunapopitia habari na nitachukua muda kukelewa.

**Dhamira ya utafiti**

Maumivu makali yanaoonezekwa kwa haraka baada ya upasuaji hukabili wagonjwa wanaotimia hadi 70%. Dhamira yetu ya kutekeleza utafiti huu ni ili tupate kujuia dawa inayopunguza maumivu hadi kwenye kiwango kinachoridhisha kwa muda mrefu baada
ya upasuaji. Huduma yako haita athirishwa wakati wa utafiti huu iwapo utakubali kushiriki.

**Aina ya mradi wa utafati**

Kwa utafiti huu, utapokea matibabu ya kawaida katika hosiptali ya chuo kikuu cha Aga Khan kilichoko Nairobi. Kwa taratibu zako za upasuaji, tutatumia dawa za kawaida na mojawapo ya dawa zinazochunguzwa kama sehemu ya taratibu ya kupunguza maumivu kupitia nafasi iliyo nje ya uti wa mgongo. Kabla ya kusajiliwa kwenye utafiti huu utaulizwa maswali kadhaa ili kuhakikisha ya kwamba hautakumbwa na athari yoyote kutokana na kutumia dawa ya kupunguza maumivu kupitia nafasi iliyo nje ya uti wa mgongo.

**Uchaguzi wa washiriki**

Unaombwa kushiriki kama mmoja katika kundi la wagonjwa watakaohitaji kupunguzwa maumivu kupitia nafasi iliyo nje ya uti wa mgongo kwa minajili ya upasuaji wa miguu.

**Taratibu**

Iwapo utakubali kushiriki, tutapunguza maumivu kupitia nafasi iliyo nje ya uti wa mgongo wakati wa taratibu ya kawaida tukitumia pia vyombo vya kawaida. Tofauti itakuwa tu kwa kuongeza mojawapo ya dawa zinazochunguzwa kwenye dawa inayotumika kwa kawaida kupunguza maumivu kupitia nafasi iliyo nje ya uti wa mgongo.

**Athari na kero**

Hautarajiwi kukabiliwa na athari za ziada kwa kushiriki katika utafiti huu. Iwapo utahisi maumivu au kero wakati wa taratibu tutaumia kile kinachojulikana kama “dawa ya kuokoa” iliyothibitishwa kuweza kudhibiti maumivu. Iwapo bado unahisi kero, utapewa
dawa ya kuzuia maumivu kwa kufanya mwili wako wote ukufe ganzi (general anaesthesia GA).

**Faida**

Elimu itakayopatikana kupitia utafiti huu itaboresha ufahamu wetu wa muda wa kudhibiti maumivu baada ya kutumia dawa ya kupunguza maumivu kupitia nafasi ilio nje ya uti wa mgongo. Hii inaweza kusababisha uwepo wa njia bora zaidi za kudhibiti maumivu katika siku za usoni.

**Fidia**

Hautapata fidia yoyote kwa ajili ya kushiriki katika utafiti huu.

**Siri**

Habari yoyote utakayopeana wakati wa utafiti itawekwa kama siri. Majina yako kamili hayatatokezea kwenye hati zozote za utafiti na ni wafanyakazi wanaoshiriki katika utafiti huu pekee watakaoweza kufikia habari utakayopeana.

**Haki ya kukataa au kujiondoa**

Ushirikiano wako unathiminiwa

Iwapo una maswali yoyote jisikiye huru kuwasiliana nami kuhusu utafiti katika anwani ifuatayo,

Dkt. Francis O. Codero

Nambari ya simu 0722449575

S.L.P 30270-00100

Hospitali ya Chuo Kikuu cha Aga Khan University, Nairobi, Kenya

FOMU YA IDHINI

Mimi nakubali kushiriki katika utafiti huu, baada ya kuelezewa kamili madhumuni ya utafiti huu na Dkt. Codero

Tarehe.............................. Sahihi...........................................

Mimi, Dr. Codero nadhibitisha ya kwamba nimemueleza mgonjwa huyu kamili madhumuni ya utafiti huu

Tarehe.............................. Sahihi...........................................

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13.4 APPENDIX IV

Data collection tool

IP no. ........................................

Elective. ........ Emergency. ............

Age .................

Height .................

Weight ...............

Baseline vital signs

HR (b/min) ......................

NIBP (mmHg) systolic ..............

Diastolic ..............

MAP ..................

Time completed SA .............

Time to maximum block ..........

Duration of surgery ............
Need to convert to GA

Yes

No

Reason for conversion to GA

Reason for conversion to GA

Complications

Nausea /Vomiting Yes___ No___

Hypotension Yes___ No___

Pruritus Yes___ No___

Sedation Yes___ No___

Respiratory depression Yes___ No___
Time | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 24
--- | --- | --- | --- | --- | --- | --- | --- | --- | ---

**VAS**

**NIBP (systolic)**

**NIBP** (Diastolic)

**MAP**

**HR**

**Bromage score**

**Sensory level**

-Time of administration of rescue analgesia are:

-VAS score at administration of rescue analgesia are:

**Vitals signs**

-Systolic BP are:

-Diastolic BP are:

-MAP are:

-HR are:

-Spo2 are:

**Complications observed in the ward**
<table>
<thead>
<tr>
<th>Condition</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine retention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory depression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Highest sensory level
### Bromage score

<table>
<thead>
<tr>
<th>Grade</th>
<th>Criteria</th>
<th>Degree of block</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Free movement of legs and feet</td>
<td>Nil (0%)</td>
</tr>
<tr>
<td>II</td>
<td>Just able to flex knees with free movement of feet</td>
<td>Partial (33%)</td>
</tr>
<tr>
<td>III</td>
<td>Unable to flex knees, but with free movement of feet</td>
<td>Almost complete (66%)</td>
</tr>
<tr>
<td>IV</td>
<td>Unable to move legs or feet</td>
<td>Complete (100%)</td>
</tr>
</tbody>
</table>
Patient is to be taught on how to score pain using the VAS

**Visual Analogue Scale (VAS)**

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Worst</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Possible</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pain</td>
</tr>
</tbody>
</table>