COLLEGE OF MEDICINE AND HEALTH SCIENCE

DEPARTMENT OF ANESTHESIOLOGY

Comparison of Spinal Morphine and Transversus Abdominis Plane Block for Postoperative Pain Management in Patients Undergone Cesarean Section Under Spinal Anesthesia at Hawassa University Comphrensive and Specialized Hospital Ethiopia 2019: Randomized control trial

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DILLA, ETHIOPIA

AUGUST 2020

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Thesis Submitted In Partial Fulfillment The Requirements For Master of Science In Advanced Clinical Anesthesia of Dilla University School Of Medicine Department Of Anesthesiology.

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Abstract

Background: Pain after cesarean section is common and associated with long hospital stay, infections, less infant care and it may leads to chronic pain. Caesarean Section (CS) has been one of the most frequently performed major surgical interventions, and causes severe postoperative pain and subsequent manipulation performed through Pfannenstiel incision is associated commonly with significant degree of pain in the postoperative period, up to 79% of women experience pain at the incision site that can last for up to 2 months. Spinal opioid & abdominal field block has been investigated as effective analgesia for postoperative pain and reduce the need of systemic medications and their associated side effect. The aim of this study is to compare spinal morphine and transversus abdominis plane block for postoperative pain management.

Method: In this prospective, randomized controlled trial 108 pregnant mothers scheduled for Cesarean section under spinal anesthesia was allocated randomly to receive either spinal morphine 0.1mg (group SM; *n* 56) or transversus abdominis plane block 20ml of 0.25% (group TAP;*n* 52). Patients were followed postoperatively to assess time to first analgesic request, analgesic consumption and pain intensity through numerical rating scale for the first 24 hours, at 2, 4, 6, 12, and 24 hours. Comparison of numerical variables between study groups was done using unpaired student t- test and Manny Whitney U test for symmetric and asymmetric data respectively. Time to event variable was analyzed by using Kaplan Meir survival function. P-value less than 0.05 were considered as statistically significant.

Result: One hundred twenty patients were screened for this prospective, randomized, doubled-blind, controlled study. Of these, One hundred and fourteen patients were recruited and randomly assigned and received interventions. Among them, One hundred and eight patients completed this study. Time to first analgesic request was significantly shorter in TAP with a median (IQR) of 240 (180-390) minute vs 360 (270-480) minute in SM. Twenty four hour median morphine consumption was reduced in spinal morphine group 0 (0-4) mg compared to TAP block group 4 (0-6) mg ($p<0.001$). Median postoperative NRS score during movement and rest at 2nd hour, 6th hour, 12th hour and 24th hour were statistically significant different between groups ($p <0.001$).

Conclusion: In conclusion preservative free 100µg spinal morphine for cesarean section provides prolonged postoperative analgesia time, better postoperative analgesia, and less postoperative analgesic consumption than TAP block.

Keywords: Spinal morphine; TAP; analgesia; cesarean section

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Acknowledgement

I would like to forward my deepest gratitude to my advisors Mr. Bedru Jemal and Mr. Engida Eyob for their meticulous advice and valuable comments starting from the selection of the research topic to preparation of this proposal.

I would like to thank Dilla University for giving me chance to carry out this thesis and granting financial support. Finally my deepest gratitude goes to Hawassa university referral hospital academic and administrative staffs for their support in giving me their offer to collect my data from their work area.

Acronyms and Abbreviation

CD	Caesarean delivery
CS	Cesarean section
DBP	Diastolic Blood pressure
DURH	Dilla University referral Hospital
HR	Heart Rate
HUCSH	Hawassa university comphrensive and specialized hospital
ITM	Intrathecal morphine
IQR	Inter Quartile Range
L3	Lumbar Vertebrae 3
L4	Lumbar Vertebrae 4
NRS	Numerical Rating Scale
NIBP	None Invasive Blood Pressure
OR	Operating Room
RR	Respiratory rate
SBP	Systolic Blood Pressure
SOP	Standard Operative Procedure
SPSS	Statistical Package for Social Sciences
TAP	Transversus Abdominis Plane Block
VAS	Visual Analogue Scale
VRS	Verbal Rating Scale

1: Introduction

1.1 Background

The international figure of surgical delivery approximate here as 15%.the numbers are larger in advanced countries and in Latin America and the Caribbean, however lower in underdeveloped nations. The mean of CS deliveries is 3.5%in Africa, from this south Africa have taken (15.4%),

Egypt is the second on rank (11.4%) and the third is Tunisia (8%)and in Ethiopia the percentage reached 0,6% compare with other world it shows lowest rate.(1)

In 1985, the World Health Organization stated that 'There is no justification for any region to have caesarean section (CS) rates higher than 10–15 %.(2)

According to the 2011 Ethiopian demographic and health survey DHS the rate of CS (22%) in Addis Ababa was far more than 10-15% rate recommended by WHO. Amongst the 835 women delivered at health facilities ,19% through cesarean section and the prevalence based on medical indication was 91.3%, however 6.9%of cesarean section performed had no medical indication .(3, 4)

The technique of anesthesia for CS delivery is made by balancing women preference with the risk and benefit of the technique to mother and baby. In both developed and developing country Spinal anesthesia is gaining popularity and its use is increasing gradually in both elective and emergency CD.(5)

Cesarean section is the most frequently performed major surgical procedure and it cause severe postoperative pain, so the provision of effective post-operative analgesia is important to facilitate early mobilization of mother, infant care, prevention of post-operative morbidity, increase patient satisfaction and decrease duration of hospital stay.(6-8)

Post cesarean section pain is the result of incisional pain as well as pain from uterus. Incisional pain is experienced following CS due to tissue trauma from surgical incision, dissection, and direct nerve damage from nerve transection and compression. Tissue trauma causes release of local inflammatory mediators that can produce increased sensitivity to stimuli in the areas surrounding to injury.(9)

Cesarean section is associated with more postpartum pain than vaginal birth and leads to acute and chronic postpartum pain. Postpartum pain has various negative consequence which can lead to difficulty in mobility, increased risk of venous thrombosis , interfere optimal interaction with the new born and predispose to splinting and chest infection .(10, 11)

An ideal method of postoperative analgesia for cesarean section is controversial however, different interventions have been proposed for post cesarean section pain management like systemic opioids, Intrathecal opioids, Epidural analgesia, Transverse abdominus plane block (TAP), illioinguinal, and illiohypogastric nerve block, wound infiltration and combination of the above mentioned interventions .(12, 13)

Small dose of spinal morphine is an effective option for long-lasting postoperative pain relief following spinal anesthesia for cesarean section. This technique has been used without serious problems to date and it has been well practiced in this patient group. It is associated produces less adverse effect than systemic administration of morphine. However with low dose there are no reports about undesirable effect.(14-20)

Respiratory depression is also recognized adverse effect, but has not been noted at this small dose used for Intrathecal in normal parturient. Earlier researches show that the decrease in dose of spinal morphine might preserve quality and prolong the analgesic potency as long as decreasing the occurrence of adverse effects. Thus alternative approach to Intrathecal morphine are needed especially in presence of contraindication that limiting the use of Intrathecal morphine.(21, 22)

The transversus abdominis plane (TAP) block is a regional analgesic technique, which blocks T6–L1.This neural afferents course through the neurofascial plane between the internal oblique and transverse abdominius. On the basis of some anatomic studies, lumbar triangle of petit is a potential access point to this neurofascial plane. This space is surrounded by posteriorly by latissimus dorsi muscle and anteriorly by oblique, with iliac crest forming the base of the triangle external oblique, with iliac crest forming the base of the triangle. By introducing local anesthetics in to transverse abdominius plane via triangle of petit, it is possible to block the sensory innervation of the lower anterior abdominal wall to provide postoperative analgesia for lower abdominal surgeries including cesarean section.(23-26)

1.2 Statement of the problem

Postoperative pain is mainly nociceptive, but central sensitization also occurs. At the periphery, inflammatory mediators (prostaglandins, histamine, serotonin, bradykinin, and substance P) increase the sensitivity of nociceptors. (27)

The skin, abdominal wall, and uterine incision for cesarean delivery generate postoperative pain. The skin and visceral (uterine) nociception are transmitted by different nerve fibers, primarily C-fibers with some A delta fibers in uterine by contrast the majority of afferent fibers that rely nociceptive stimuli from the skin are A delta fibers. This component may cause different sensation of pain that might benefit from different types of pain management protocol.(28) The involvement of this two nerve fibers in post cesarean section pain cause difficulty and unsatisfactory in managing after cesarean delivery.(27)

Post cesarean pain has both somatic and visceral components. Somatic pain emerge from nociceptors within the abdominal injury and has the two skin and skin elements. Visceral pain presents unique challenge because the pain is diffuse in character often poorly localized and associated with strong autonomic reactions and changing visceral function. Effective pain management needs to be based on understanding of the autonomic and physiologic basis of visceral function and pain.(14)

The cesarean section rates in developing country continue to rise as result of changing pattern in obstetrics practice and maternal request for this mode of delivery. Postoperative pain after cesarean section can be severe and is reported that equivalent to abdominal hysterectomy. Management of postoperative pain frequently substandard, with30%-80% of patients experiencing moderate to severe postoperative pain.(29)

Caesarean delivery has been the most commonly carryout surgical procedure, and it results extreme post-operative pain. Caesarean Section (CS) and subsequent manipulation performed through Pfannenstiel incision is associated commonly with significant degree of pain in the postoperative period, up to 79% of women experience pain at the incision site that can last for up to 2 months.(30)

The potential complication of pain after cesarean section are pulmonary infection (28%), post-operative deep vein thrombosis ,pulmonary embolism, prolonged return of GI function ,cardiovascular complications; such as tachycardia, hypertension, increased cardiac work and myocardial oxygen consumption leads myocardial infarction. Inadequate postoperative pain relief after Caesarean delivery (CD) also affect ambulation, breastfeeding, early maternal infant bonding and poor pain control in the post-operative period can lead to chronic pain syndromes (34.5%) and poor quality of life.(18, 31, 32)

Adequate pain management after-caesarean section will benefit not only the mother and her baby, but also a healthcare system. Optimal pain control may shorten the time spent in hospital after caesarean section and, therefore, reduce healthcare costs.(33)

Although different options for pain management had exist, ideal form of postoperative analgesia is unknown, conventional & routine methods of pain relief had never been satisfactory and without side effects in these population.(6, 8)

Systemic opioids have previously been a routine way to relieve pain postoperatively. They are simple, inexpensive and have a long tradition in health care. The drawback are that it frequently need repeated inoculation for an ideal pain relief any problem in injection of the drug can result irritation as the pain increases.(16, 34) It is not adequately practice usually a congested workload in the wards which can result in a delay for medical help. Another option is patient controlled analgesia may not be the optimal method for administration of analgesics in all postoperative settings, because it requires education of staff and patients.(13)

NSAIDs are effective in the treatment of visceral pain, reduce the inflammatory process associated with surgery and affect the nociceptive responses associated with acute pain. Secondly, NSAIDs improve the effect of systematically or neuraxially given opioids and decrease opioid related adverse effects due to their opioid sparing effect. There have been concerns against NSAID because of potential gastrointestinal side effects and dysfunction of platelets.(27)

Surgical site local anesthetics infiltration is one of the techniques for additional analgesia for abdominal surgery but in women who receive spinal morphine under spinal anesthesia, the merit of single shoot local anesthetic incision site infiltration is minimal. Single shoot local anesthetic

surgical site infiltration at the time of procedure in doesn't probably last further than duration of spinal anesthesia impact only somatic, and has variable efficacy.(15)

Morphine has been approved by Food and Drug Administration (FDA) for neuraxial administration since 1984 .spinal administration of morphine provides superior post cesarean analgesia than that of provided by systemic opioids. Morphine produce postoperative pain control for up to 24hr and a minimal dose which is100mcg is safe in women underwent CS.(14)

The transversus abdominis plane (TAP) block, abdominal wall block its effect on pain control in many abdominal procedures has been approved, has also been suggested for post-operative pain control in mother underwent elective CS under spinal anesthesia. However the analgesic usage of TAP block is still controversial, many trials were comparing it placebo described marked advantages, while others found no analgesic importance.(34-40)

The aim of this study was to compare analgesic efficacy of Intrathecal morphine and TAP in patient undergoing cesarean section under spinal anesthesia.

1.3 Significance of the study

Managing post-operative pain with administration of systemic opioids and non-opioid analgesics is not adequate and has exaggerated side effects. Detecting and managing this side effect postoperatively can be problem in resource limited and understaffed countries.

Currently most of the post-operative pain in western nations is managed by epidural analgesia. However, the supply of epidural kit is limited, costly, and technically invasive and needs experts to perform the procedure.

Spinal morphine is one of widely used technique that might have greater post-operative analgesic efficacy after CD. It is technically easy, not time consuming and no additional equipment's are needed for administration. Spinal morphine has minimal side effects but no significant side effects when using dose of 100mcg.

TAP are well known, easy to perform and currently these blocks are done in the study area for post CD pain management and there is no enough data concerning the efficacy of TAP versus spinal morphine in the management of post-operative pain in parturient undergoing a caesarean section.

Despite this, most of the studies related with these techniques were conducted in developed countries. There are also controversies regarding analgesic efficacy between spinal morphine and TAP block for postoperative pain management.

Therefore, the choice between spinal morphine and TAP for post-cesarean section pain control with regard to pain severity, duration of analgesia & analgesia consumption needs investigation for better practice of perioperative pain control and patient care. In addition, in a resource-limited area like our set up investigating the best choice between the two techniques for pain relief has a paramount importance.

2: Literature review

A study conducted by H. Loane and colleagues (2012) investigated RCT comparing Intrathecal morphine and TAP block for post cesarean delivery analgesia. They found that between 10 and 24 hr. Mean 24 hr. morphine consumption in TAP group (7.5mg) was greater than that of Intrathecal morphine group (2.7mg) which were statistically significant. Pain intensity measured by VRNS was not different at 2hr, 4hr, and 6hr between groups. However, there was statistically significant difference at 10hr.VRNS pain score in-patient receiving TAP and ITM group. Regarding the side effect, the TAP group experienced less nausea vomiting and pruritus than ITM.(41)

A. Kwikiriza et al (2018) conducted study on the analgesic efficacy between ITM and TAP. They found that mean postoperative pain score by NRS at rest, coughing, and movement were significantly lower in ITM group compared with TAP group at 24 hr. postoperative pain score were similar at the remaining time interval. The need for rescue medication was similar in both groups. None of the patients in the study had respiratory depression. The incidence nausea vomiting, pruritus and sedation were similar in both groups.(42)

Another RCT study that compare analgesic efficacy of subarachnoid morphine(SAM) with TAP block after CS shows that patient receiving subarachnoid morphine had longer time to first analgesic request 8hr(2-36hrs) compared to TAP group 4hr (0.5-29hrs) at p-value=0.005. The median tramadol consumption was lower in SAM compared to TAP group between 0 - 12hr. However, tramadol consumption was same between 13hr to 24 hrs. Postoperative VAS visceral pain score at rest at 0hr, 2hr, and 4hr and on movement at 2hr and 4hr were significantly lower in SAM group compared to TAP group. However, no difference was noted in somatic pain score between both groups. Nausea vomiting and pruritus were higher in SAM group compared to TAP but sedation score were comparable in two groups.(43)

A prospective, randomized double-blinded controlled study done by McMorrow et al which were compared the analgesic efficacy spinal morphine versus TAP block for postoperative pain relief after cesarean section. They found that median pain scores on movement at 6hr were lower in spinal morphine group compared to TAP block and no statistically significant difference pain score at other time point. The median morphine consumption were lowest in groups receiving

spinal morphine compared to TAP block at 6hr (4.0 mg), 12hr (2.0 mg), 24hr ((5.0 mg). Sedation scores and patient satisfaction did not differ between groups. Pruritus was most common in the Spinal morphine than TAP group.(39)

Systematic review and meta-analysis of TAP block for postoperative analgesia after CD reveals that TAP block reduce the mean 24Hr morphine consumption by 24mg when Intrathecal morphine not as part of postoperative analgesia. TAP block also significantly reduce 24hr VAS score by 0.8 cm compared to placebo, the difference was not significant in the presence of Intrathecal morphine group.(44)

Randomized double blind placebo-controlled study by Allison J. Lee et al To determine analgesic efficacy of transversus abdominis plane (TAP) blocks administered in conjunction with Intrathecal morphine and Intrathecal morphine alone found that at the two-hour evaluation, the TAP group reported less pain at rest and with movement. At rest all patients in TAP group reported pain score =<4 compared to 67% in morphine only group (P = 0.002). With movement 76% of patients in the TAP group had pain score=<4 as compared to 29% in the morphine only group. Analgesic request significantly differed between groups two hours after the block. No patient in TAP plus morphine group request analgesia in the PACU whereas 25% of patient in the morphine only group (p=0.06).(45)

Another review of randomized control trial conducted by F. W. Abdullah et al on the analgesic effects of TAP block compared with control shown TAP block group has reduced pain score by VAS 17mm at 12 h (P, 0.00001), by 13 mm at 24 h. TAP block also significantly reduced morphine consumption which is 23.2 mg.(46)

RCT conducted by John G. et al to determine the analgesic efficacy of TAP for postoperative analgesia after abdominal surgery. They found that VAS score were significantly reduced by TAP block compared with control group at all-time point (TAP versus control, mean (1+1.4 vs 6.6 +2.8, P = 0.05)). TAP block had a longer time to first request for morphine and reduced cumulative postoperative morphine consumption. Sedation, nausea, and vomiting were reduced in TAP group.(47)

Anna Kupiec et al conducted a trial on the analgesic efficacy of TAP block after cesarean delivery. They found that TAP block were significantly less consumption of tramadol than

control group (p = 0.005). There were also significantly lower VAS values in all time point. Regarding side effect there were no complications related to the TAP block.(48)

Another randomized control trial done by Mankikar et al to assess efficacy of TAP block for post CD pain under spinal anesthesia conclude that TAP block compared with control group have reduced post-operative VAS score. Time to rescue analgesia in the study group was prolonged from 4.1 to 9.53 hr. Mean requirement of tramadol in the first 24 h was reduced in the study group.(49)

A Randomized Controlled Trial conducted by Ayedi et al to compare analgesic efficacy of TAP block by using 0.5% or 0.25% bupivacaine reveled TAP block confers additional analgesia for Cesarean section patients compared to placebo. There were also statistically significant difference in the mean pain Scores between the TAP and control group and statistically difference in the number of PCA boluses between the TAP groups and control group at 3 h, 6 h, 24 h .(50)

Randomized, double blinded control trial done by D. Belavy et al evaluated the analgesic efficacy of the ultrasound (US)-guided TAP block in patients undergoing Caesarean delivery. They found that Cumulative morphine use at 24 h was significantly lower in the TAP group and time to first morphine demand was longer in the TAP group compared to control group. There were no serious local complications in the US guided TAP block.(34)

In meta-analysis done by Popping *et al*. (2012) on opioids added to LA for single-shot Intrathecal anesthesia in patients undergoing minor surgery, morphine (0.05–2 mg), and fentanyl (10–50 µg) added to bupivacaine were tested. Duration of postoperative analgesia was prolonged with morphine. Morphine consumption and VAS score were lower in morphine than fentanyl group. There were no significant differences among the groups in the incidences of postoperative nausea, vomiting, cardiorespiratory and pruritus.(51)

A study done by A. R. Milner et al (1996) compared quality of analgesia and incidence of adverse effects with two doses of Intrathecal morphine (0.1mg versus 0.2mg) in patients undergoing elective cesarean section. In both groups, good quality analgesia was obtained and there was no statistically significant difference in VAS scores. Not statistically significant difference in morphine consumption in both groups. There was a significant reduction in the

incidence of nausea and vomiting in-group 0. 1 mg ITM compared with group 0.2 mg ITM (7 versus 14, p = 0.044) and Respiratory depression was not observed in any of the patients of either group.(52)

A Qualitative and Quantitative Systematic Review of Randomized Controlled study by *Jørgen B.* et al to investigate the effect of Intrathecal opioids added to spinal anesthesia during intraoperative and postoperative pain management and adverse effects after cesarean section. In these reports, 535 patients were given four different opioids (morphine, fentanyl, sufentanil, buprenorphine) in 32 treatment arms and 23 different doses and 281 patients served as controls. prolonged postoperative pain relief of .>50% as measured with VAS score with morphine 0.1 mg and 0.25 mg compared with control. Median time to first analgesic with the various effective doses of morphine was 27 h (range, 11–29h). Supplemental Analgesics Consumption at Morphine doses of 0.05 mg, 0.1 mg, and 0.2 mg were decreased postoperatively in all comparisons. The incidence of pruritus was less with fentanyl group compared with morphine.(53)

A randomized control trial done by Wojciech et al investigated Perioperative analgesic efficacy of Intrathecal fentanyl and morphine or morphine alone for cesarean section. They found that time to first postoperative analgesic request was significantly longer in the morphine group when compared with fentanyl group and fentanyl and morphine group ($p<0.05$). Patients in fentanyl and fentanyl and morphine groups made significantly more request for supplementary analgesia ($p<0.01$). There were no significant differences among groups intraoperative and postoperative nausea, vomiting and pruritus incidences.(54)

Regarding safety concern, Pruritus, nausea vomiting and respiratory depression during Intrathecal usage of morphine but there had been not observed after Intrathecal administration of morphine at doses of 0.1to 0.2mg for CS. Reviews and other studies on this topic report that respiratory depression after Intrathecal opioids is rare and mild in the obstetric population, and that the risk is no higher than after parenteral opioid administration. There was no reported relationship between Intrathecal opioid administration and neonatal Apgar scores in previous studies.(55-59)

3: Objective

General Objective

To compare analgesic efficacy of spinal morphine versus transverses abdominius plane block (TAP) for management of post cesarean section pain as part of multimodal analgesia in Hawassa university comprehensive and specialized hospital, July 2019 to July 2020.

Specific objective:

1. To compare time to first analgesic request between spinal morphine and transverse abdominius plane block.
2. To compare total analgesic consumption between spinal morphine and transverse abdominius plane block over 24 hours.
3. To compare the severity of post-operative pain using NRS between spinal morphine and transverse abdominius plane block at rest/movement.
4. To compare side effect between spinal morphine and transverse abdominius plane block

4: Methodology

4.1 Study area

Hawassa comprehensive specialized teaching hospital is one of the biggest government hospitals in Ethiopia serving as teaching and regional referral hospital since 2005E.C. It is located in Hawassa, which is the capital of SNNPR to provide health care service to the patient referred by other health centers, clinics, hospitals in the region. The hospital had been progressively increasing its capacity of beds and health care services to ever-increasing number of patients. In the year 2018, the surgery department has about 9 surgical tables and 2 obstetrics operation bed and about 100 surgical beds (gynecologic and general surgery) with a perceived 100% occupancy rate.

4.2 Study design and period

Study design was institutional based prospective parallel randomized controlled trial. The study was conducted from July 2019 to July 2020.

4.3 Population

4.3.1 Source population: All mothers admitted to obstetric ward to undergo cesarean section under spinal anesthesia in Hawassa university comprehensive and specialized hospital.

4.3.2Study population: Pregnant mother scheduled for elective cesarean section under spinal anesthesia during study period and who fulfill inclusion criteria.

4.4 Inclusion and exclusion criteria

4.4.1Inclusion criteria

All parturient who were undergo elective caesarean delivery via Pfannenstiel incision under spinal anaesthesia.

4.4.2 Exclusion Criteria

- Patient refusal
- ASA 3 and 4 patients
- Caesarean delivery requiring epidural analgesia or combined with spinal
- Preeclampsia
- Mothers with chronic pain disorder

- History of benzodiazepines taking
- Allergy to local anaesthetics and morphine
- Cognitive impairment (Dementia, Alzheimer)

4.5 Study variables:

4.5.1 Dependent variable:

- Analgesic efficacy (measured by time to first analgesic request, pain intensity and analgesic consumption)

4.5.2 Independent variables:

- Intervention groups (TAP and SM)
- Socio demographic characteristics: age, weight ,height and BMI ,experience of surgeon ,residency of patient ,ethnicity)
- Duration of surgery and duration of anesthesia
- Level of motor block
- Level of sensory block
- Postoperative hemodynamic status

4.6 Operational Definition

Time to first analgesic request: The time between the end of operation and the first time analgesics was given.

Numerical Rating Scale: A valid pain assessment tool in which patients is asked to rate his/her pain by using the number assigned from 0-10 to represent severity of pain 0= no pain 1-3= mild pain 4-6= moderate pain 7-10= severe pain(48, 60)

Total opioid consumption: The amount of opioids given in the first 24 hour.

Total tramadol consumption: The amount of tramadol given for the patient in the first 24hrs.

Analgesic adequacy: Patients who achieve NRS score <3cm at rest and movement

Pruritus-is a subjective, unpleasant, and irritating sensation that provokes an urge to scratch any body part. (0)-none, (1)-mild, (sometimes, slight itching), (2)-moderate, (persistent or intermittent itching not disturbing sleep) and (3)-severe (irritative itching disturbing sleep)

Respiratory depression: when respiratory rate less than10 breath/minute and oxygen saturation less than 90 % after Intrathecal administration of morphine with in 24hrs postoperatively.

Nausea: is an unpleasant sensation and discomfort perceived as an urge to vomit. 0 = no 1=mild 2=moderate 3=severe

Vomiting: is the involuntary, forceful expulsion of the contents of one's stomach through the mouth,

Sedation: is the depression of a patient's awareness to the environment and reduction of his or her responsiveness to external stimulation was assess by using RAMESSY score 0 paralayed 1 awake 2 lightly sedated 3 follows simple commands 4 responds to non-painful stimuli 5 responds only to painful stimuli 6 unresponsive to painful stimuli

4.7 Sample size and sampling procedure

4.7.1 Sample Size Determination

The study was designed to detect 50% increment in tome to first analgesic request for a patient receiving spinal morphine with 80% statistical power and 5% significance level. Based on this assumption we estimated that sample size of 57 participants per group was needed.

$$n = 2[\frac{(Z\alpha\backslash 2+Z\beta)^2}{(\mu 1-\mu 2)^2}(s^2)]$$

Where n=the sample size in each of the groups

µ1=population mean in spinal morphine group

µ2=population mean in TAP group

µ1-µ2=the difference the investigator wishes to detect

s^2=pooled variance

$Z_{\alpha\backslash 2}$=conventional multiplier for alpha =0.05, which is 1.96

Z_{β}=conventional multiplier for beta =0.80 which is 0.842

From the literature(43) the mean time to first analgesic request for Intrathecal morphine were µITM=8hrs, and for TAP group µTAP =4hrs and pooled standard deviation Sp =7.6 by substituting the numbers on the above formula the sample size calculated was 57 and adding 5% for dropout it was 60 per group. Finally we enrolled 114 patients and 108 patients were complete the study.

4.7.2 Sampling procedure

Preoperatively selections of parturient scheduled for cesarean section under spinal anesthesia at Hawassa university comprehensive specialized teaching hospital were assessed for eligibility. Those who fulfill eligibility were randomized in allocation ration of 1:1 to participate in this randomized control trial.

Randomization and Blinding

Patients were allocated using computer-generated randomization with the help of a researcher not participating in the study to either spinal morphine or transverse abdominus plane block (TAP) as a postoperative analgesic technique. To achieve blinding to intervention group among patients, drape was used to prevent women from visualizing performance of TAP block and assigning two data collector one for intraoperative and the other for postoperative period to achieve blinding to intervention group. Intraoperative care giver was not blinded to intervention group.

Study Interventions

In spinal morphine group spinal anesthesia was performed in sitting position under strict aseptic technique between L3-L4 interspace using tuffiers line as a landmark and 23 gauge spinal needle was used to administer 12.5 mg, 0.5% isobaric bupivacaine together with 100µg preservative free morphine. In TAP group bilateral TAP block was performed at end of surgery using 20ml of 0.25% bupivacaine in each side of facial plane. (Annex 10)

Study Outcomes

The primary outcome was time to first analgesic request; time to first analgesic request was recorded up on patient request. Secondary outcome were postoperative pain intensity, analgesic consumption, proportion of patients achieved adequate analgesia, adverse effect (pruritus, nausea, vomiting and sedation) and maternal satisfaction in analgesia quality. Postoperative pain intensity was measured by standardized numeric rating scale (NRS) at 2 hours, 6 hours, 12 hours and 24 hours postoperatively.

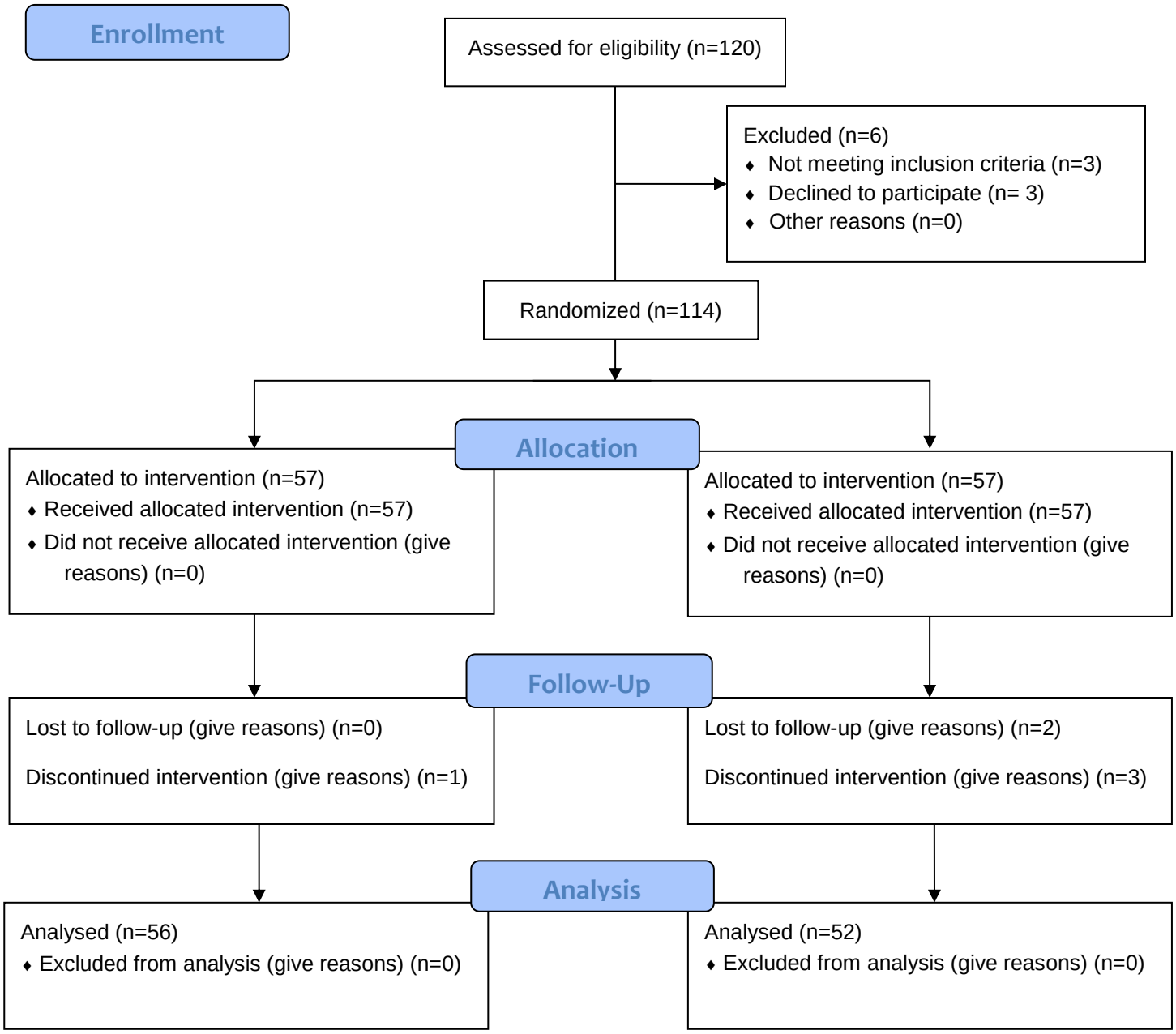

Figure 1: Consort flow diagram of patient enrolment

4.8 Data collection procedure

Data was collected by structured questioner from parturient and clinical chart of participant who were undergo CS. Information about the study benefit, harm and objective of the study prepared by English, translated to Amharic, and was explained to the study participant. Six trained data collectors and one supervisor were involved in data collection process.

During preoperative period

Preanesthetic evaluation was done on morning of surgery and eligibility criteria were checked before recruiting the study participants. Vital sign, organ function test, history and physical examination were revised .On arrival to the operating room parturient was premedicated with IV cimetidine (200mg), metoclopramide (10mg), dexamethasone (4mg) and ondasetrone 0.1mg/kg 30 minutes before induction of anesthesia, for prevention of aspiration, nausea vomiting and pruritus according to institutional protocol. Written informed consent was being obtained just before anesthesia.

Intraoperative period

After informed consent is obtained standard monitoring non-invasive blood pressure (NIBP), oxygen saturation (spo2), heart rate and rhythm, end tidal carbon dioxide and temperature was measured every five minute and recorded every ten minute. Then spinal anesthesia were administered between L3-L4 with 12.5mg of 0.5% heavy bupivacaine with 100µg preservative free morphine by using 24 gauge spinal needle for spinal morphine group, and spinal anesthesia with 12.5mg of 0.5% heavy bupivacaine and bilateral TAP block with 20ml, 0.25% bupivacaine after spinal anesthesia for TAP group at the end operation.

Postoperative period

During follow-up visits in the postoperative period, patients' blood pressure, heart rates, and pain score (using NRS) was assessed and managed according to protocol. After the parturient discharged from operation theater pain severity were assessed by using NRS at 2^{nd} 6^{th} 12^{th} and 24^{th} hours at rest and movement. If NRS score is above 3 points, the patient was managed as per our protocol **(annex 7)**. Tramadol used during postoperative period was converted to morphine equivalent dose using online conversion formula (http://clincalc.com/Opioids/). The time to first analgesic request and analgesic consumption were recorded from participant chart. Postoperative

adverse events such as nausea vomiting, purities and respiratory depression were recorded and managed according to the protocol. **(Annex 7&8)**

4.9 Data processing and analysis procedure

Data were checked, coded, entered, and analyzed by using SPSS version 22 software packages. The data were tested for normality by using Shapiro–Wilk and homogeneity of variance by Levene's test for continuous data. Numeric data was described in terms of mean ± SD for symmetric and median (Interquartile range) for asymmetric data. Comparison of numerical variables between study groups was done using unpaired student t- test and Manny Whitney U test for symmetric and asymmetric data respectively. Frequency and percentage were used to describe categorical variable and statistical difference between groups was tested by using Chi-square and fisher exact test according to the nature of data. Time to event variable was be analyzed by using Kaplan Meir survival function. Generalized estimating equations were used to model repeatedly assessed NRS pain score longitudinally to investigate interactive effects of intervention group and repeated time. Autoregressive Order 1 (AR1) structure of working correlation matrix was assumed and standard errors were used. The independent variables were follow-up time and intervention group. The main effects of follow-up time and intervention and the interaction of both follow-up time and intervention were assessed. P-value less than 0.05 was considered as statistically significant.

4.10 Data quality assurance

To assure the quality of data, training on the objectives and relevance of the study and brief orientation on the assessment tools was provided for data collector. To ensure quality of data, pre-test of the data collection tool (questioner) were tested on 5% of patients who were not be included in the main study during data collection. Each questioner was revised by the investigator for being complete and appropriate. The data collectors were instructed to write card number on the questionnaire during the data collection if further cross check is needed.

4.11 Ethical committee approval

Support letter was received from Dilla University College of medicine and health science and ethical clearance from institutional review board of Dilla and Hawassa hospital before start of the

study. The advantage and risk of the study were explained &written informed consent was obtained from each patient. Any modification in the study protocol was communicated to IRB. All ethics committee or IRB revised informed consent and materials given to participant. Participants who refuse to give consent and want to with draw from the study was not restricted to leave the study and reasons for withdrawal was documented.

4.12 Dissemination of Results

The result of this study will be presented to the department of anesthesia as part of MSc in advanced clinical anesthesia thesis. It will also be presented on annual research conference and it will send to local and international journals for publication.

5. Result

One hundred twenty patients were screened for this prospective, randomized, doubled-blind, controlled study. Of these, One hundred and fourteen patients were recruited and randomly assigned and received interventions (Fig. 1). Among them, three patients were excluded after randomization due to refusal for participation and three not meeting inclusion criteria. After allocation four patients were changed to general anesthesia, while two cases discharged from hospital during follow up. In total, One hundred and eight patients completed this study. Sociodemographic and baseline clinical variable comparison results indicated that no significant differences were detected between groups in age, body mass index, the duration of surgery and anesthesia except height and gestational age (Table 1).

Table 1: Socio demographic characteristics of patients who underwent elective cesarean section in HUCSH, Ethiopia July 01, 2019 to July, 2020

Variable	Spinal morphine (SM)	TAP	P-value
Age (years)	27.39±4.65	28.1±5.52	0.475
Height (m)	1.64±0.04	1.66±0.06	**0.049***
Weight(kg)	71.05±9.11	72.6±9.35	0.35
Body mass index	25.3±2.68	25.46±2.68	0.88
Gestational age (weeks)	38.7±0.62	38.5±0.5	**0.02***
Baseline heart rate	91.17±14.6	89.65±14.32	0.58
Baseline diastolic blood pressure(mmhg)	77.6±9.55	76.48±1.98	0.51
Baseline systolic blood pressure(mmhg)	129.78±16	127.65±11.3	0.43
Base line respiratory rate	20.4±8.03	18.7±1.4	0.15

Baseline spo2	98.53±1.26	97.25±10.9	0.386
NPO Time	7.75±1.48	8.3±0.82	0.019
Time taken to injection of spinal Anesthesia (second)	6.76±1.9	7.3±2.1	0.164
Parity			0.248
multipara	45(80.4)	46(88.56)	
Nulipara	11(19.6)	6(11.58)	
Ethnicity			0.2
Sidama	20(35.7)	22(42.3)	
Oromo	33(58.9)	23(44.2)	
0thers	3(5.4)	7(13.5)	
History of nausea			0.119
Yes	4(7.1)	0(0)	
no	52(92.9)	52(100)	
History of vomiting			0.119
Yes	4(7.1)	0(0.0)	
no	52(92.9)	50(100)	

TAP, transversus abdominis plane. HUCSH, hawasa university comprehensive and specialized hospital, Data are mean ± SD or number (%). * Significant difference between groups.

The perioperative hemodynamics status and variables related to anesthetic and surgical interventions

There was no statistical significant difference regarding the perioperative hemodynamic status like SBP,DBP,SPO2,RR and level of motor and sensory block duration of surgery between the groups with p-value of >.05 as shown in (table 2&3).

Table 2: perioperative variables related to anesthetic and surgical interventions who underwent elective caesarian section at Hawassa University Comprehensive Specialized Hospital, Hawassa, Ethiopia from July 01, 2019 to July, 2020.

Variable	Spinal morphine (SM)	TAP	p-value
Level of sensory			0.278
T4	54(96.4)	47(90.46)	
T5	0(0.0)	2(3.8)	
T6	2(3.6)	3(4.6)	
Level of motor			0.229
Grade (4)	0(0)	2(1.9)	
Grade(5)	56(100)	50(96.2)	
Nausea			0.83
Yes	14(25)	14(26.9)	
No	42(75)	38(73.1)	
Vomiting			0.115
Yes	3(5.4)	8(15.4)	
No	53(94.6)	44(84.6)	
Apgar	8.71±0.62	8.42±0.67	0.064
Intraoperative tramadol rescue dose (mg)	36.6 ±11.54	20±0.0	0.148
Duration of surgery	48.3±4.79	47.8±5.17	0.663
Duration of Anesthesia	122.14±5.94	123.6±13.25	0.441

T4&T5=Thoracic vertebra 4&5, SM=spinal morphine, TAP, transversus abdominis plane. HUCSH, hawasa university comprehensive and specialized hospital, Data are mean ± SD or number (%).

Table 3: Intraoperative hemodynamic variable of parturients underwent elective caesarian section at Hawassa University Comprehensive Specialized Hospital, Hawassa, Ethiopia from July 01, 2019 to July, 2020.

Variable	Spinal morphine (SM)	TAP	P-value
Systolic blood pressure before SA	130.4±16	128.3±10.09	0.429
Systolic blood pressure @3min	117.4±18.45	112.59±18.57	0.18
Systolic blood pressure@6min	110.6±17.02	110.5±17.07	0.99
Systolic blood pressure@15 min	107.4±17.3	109.6±15.09	0.484
Systolic blood pressure@ 20 min	105.6±16.46	107.9±15.09	0.459
Systolic blood pressure@ 25min	106.26±14.13	107.6±16.13	0.681
Systolic blood pressure@ 30 min	107.26±14.4	109.48±16.2	0.455
Systolic blood pressure@35min	108.5±14.4	113.7±16.0	0.78
Systolic blood pressure@40 min	112.10±15.17	112.07±25.45	0.99
Diastolic blood pressure before spinal Anesthesia	77.3±9.49	76.7±7.7	0.734
Diastolic blood pressure@3min	69.73±13.3	66.65±10.8	0.193
Diastolic blood pressure@6min	69.73±13.3	66.65±10.8	0.475
Diastolic blood pressure@15min	62.8±9.72	63.03±9.66	0,968
Diastolic blood pressure@20 min	60.4±10.3	62.6±9.8	0.259
Diastolic blood pressure@25min	62.6±10.59	63.01±11.19	0.871
Diastolic blood pressure@30 min	62.16±10.38	64.17±11.3	0.339
Diastolic blood pressure@35 min	64.4 ±10.47	65.7±10.79	0.514

Diastolic blood pressure@40min	65.4±10.68	67.39±10.79	0.342
Heart rate before SA	93.44±13.4	91.25±14.7	0.42
Heart rate after@ 3 min	91.14±10.8	87.17±14.11	0.103
Heart rate @6min	85.8±11.6	87.8±15.4	0.446
Heart rate @15 min	85.39±10.79	86.3±14.1	0.681
Heart rate@20min	84.91±12,56	85.36±15,45	0.876
Heart rate @25 min	83.3±11.8	83.3±11.8	0.428
Heart rate @30min	84.6±13.3	84.7±14.0	0.99
Heart rate@35 min	86.2±15.1	85.07±15.9	0.69
Heart rate @40min	84.63±12.96	84.01±14.4	0.99
Respiratory rate before SA	22.39±15.9	18.9±1,72	0.127
Respiratory rate @3min	19.17±2.07	18.6±1.69	0.127
Respiratory rate @6min	18.89 ±1.92	18.63±2.0	0.449
Respiratory rate @15 min	18.7±1.86	18.19±1.7	0.721
Respiratory rate @20 min	18.42±1.75	18.19±1.72	0.606
Respiratory rate @ 25	18.32±1.8	18.19±2.7	0.706
Respiratory rate @ 30	18.3±1.84	18.8±2.7	0.311
Respiratory rate @ 35 min	18.4±1.85	19.2±7.51	0.438
Respiratory rate @ 40 min	18.5±1.8	19.9±11.4	0.399

SM=spinal morphine, TAP, transversus abdominis plane, SA=spinal anesthesia

5.1 Time to first analgesic request

Time to first analgesic request was significantly shorter in TAP with a median (IQR) of 240 (180-390) minute vs 360 (270-480) minute in SM (figure 2). Cumulative proportion of patient requesting analgesia at time of 4h after surgery in the spinal morphine group was 20% compared to 62% in TAP group. Particularly the patient in the SM Group, median time: 360min, 95% CI: [332- 387] had significantly longer time to first analgesic request compared to TAP group median time: 240min 95% CI: [217 - 262] (p=0.004).

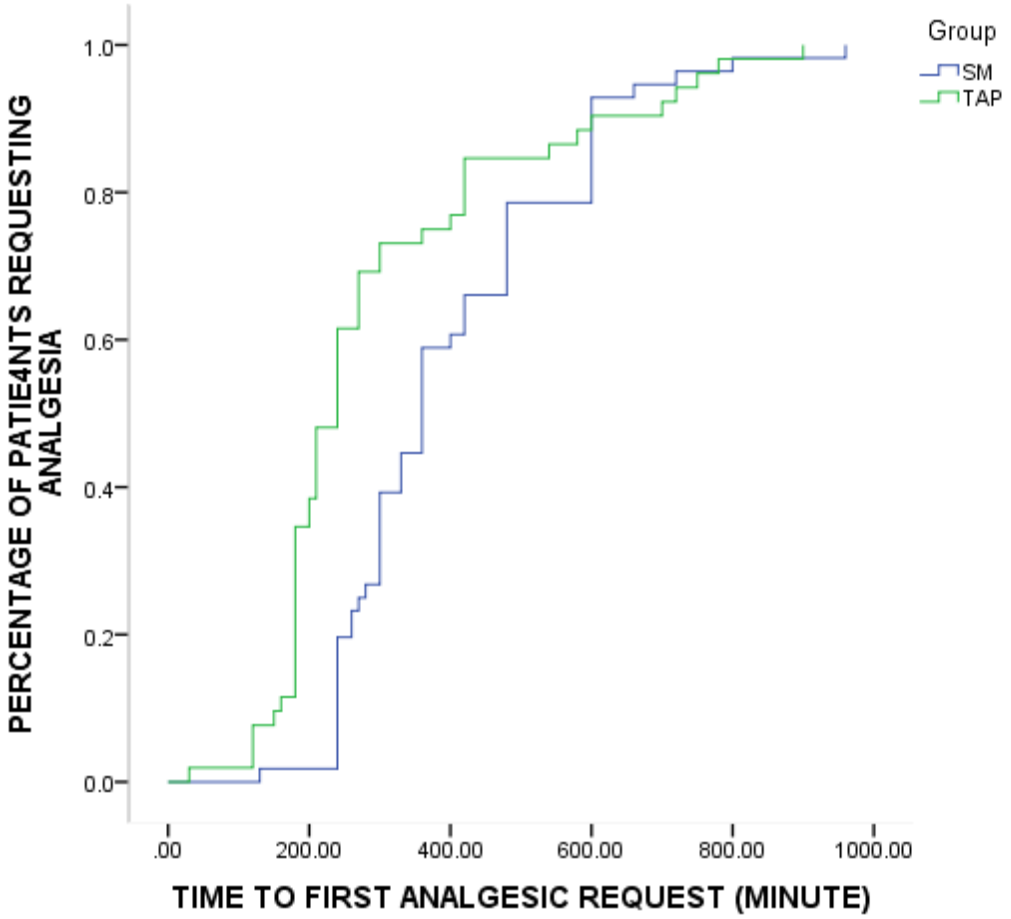

Fig 2: Kaplan–Meier curve depicting of the proportion of patients in each group over time who require supplemental analgesic (P 0.004, log-rank test). Spinal morphine; TAP transversus abdominis plane

5.2 Postoperative pain intensity

A Mann-Whitney U test was used to determine if there were differences in postoperative pain severity scores at different points between spinal morphine and transversus abdominius plane block. Postoperative pain intensity scores at different points of time between spinal morphine and transversus abdominius plane block were significantly different, as assessed by numerical pain rating scale.

Reported median (IQR) NRS pain score postoperatively at rest 2 hours 0(0-1) in Spinal morphine group and 2(1-2) in TAP group (p <0.001). Similarly, in the 6 hours, 12 hours and 24 hours postoperatively, median (IQR) NRS score was 1 (0-1) vs 3(2-4) (p < 0.001), 2 (1-3) vs 4(3-4) (p <0.001), and 3 (3-3) vs 4(3-4) (p <0.001) in the spinal morphine (SM) and TAP groups, respectively.

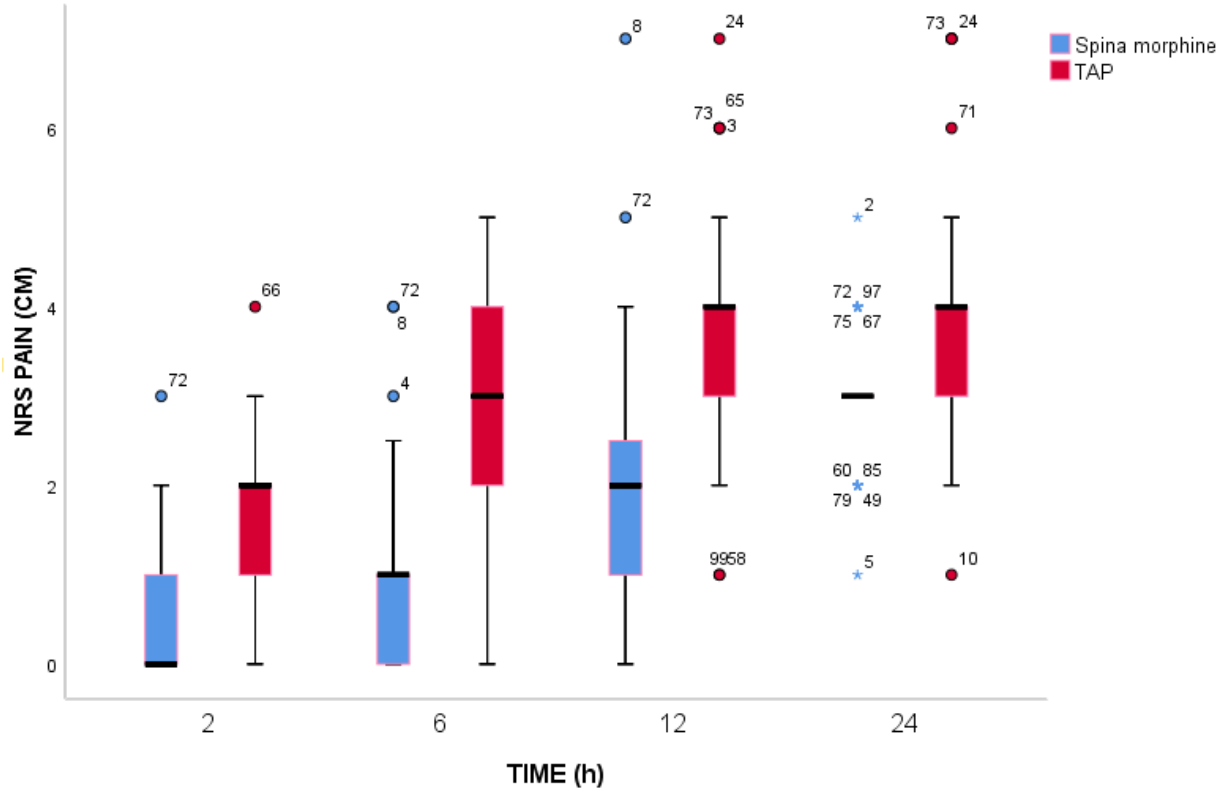

Fig 3: Postoperative pain scores at rest at different time point during 24 hours assessment period. SM, spinal morphine; TAP, transversus abdominis plane block

Median postoperative NRS score during movement at 2nd hour, 6th hour, 12th hour and 24th hour were 0.5(0-1) vs 2(1-3) (p <0.001), 1(0-1) vs 3(2-4) (p <0.001), 2(2-3) vs 4(3-5) (p <0.001) and 3(3-4) vs 4(3-5) (p <0.001) in the spinal morphine (SM) and TAP groups, respectively.

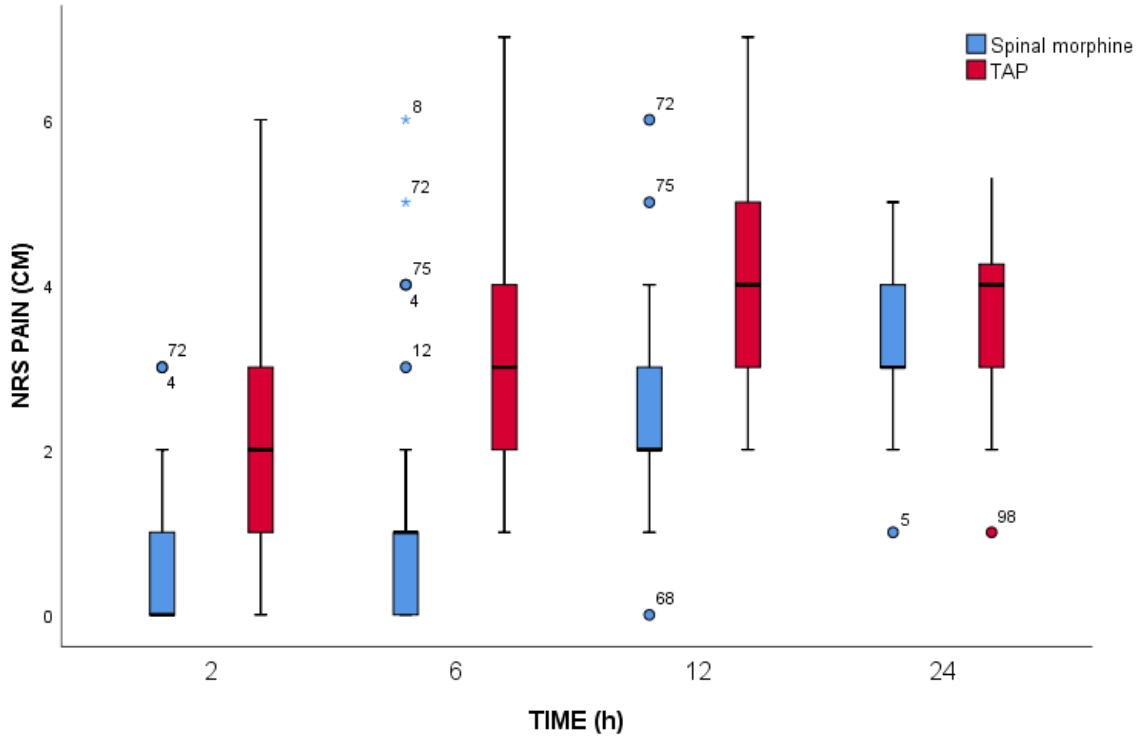

Fig 4: Postoperative pain scores with movement at different time point during 24 hours assessment period. SM, spinal morphine; TAP, transversus abdominis plane block

Group and repeated measure Interaction

After adjustment of NRS pain score at rest for repeated measurement, generalized estimating equation model show NRS score were 0.9 unit lower in spinal morphine (SM) group than TAP group during the first 24 hour postoperative period in NRS pain scores at rest (β = −0.9, 95% Confidence Interval (CI) = −1.3- −0.5, Wald's $\chi 2$=20.8, p<0.001).

GEE indicated that there was a statistically significant group and repeated measure Interaction at 6thhours and 12thhours (β = −0.827, 95% Confidence Interval (CI) = −1.3- −0.33, Wald's $\chi 2$=10.9, p=0.001 and β = −0.769, 95% Confidence Interval (CI) = −1.2- −0.31, Wald's $\chi 2$=11, p=0.001 respectively)

Repeated measure

There was statistically significant effects of repeated measurement in the NRS score at rest 2nd hours (β =−2.4, 95% CI=−2.78– −2.01, Wald's χ2=168, p<0.001 6th hours postoperatively (β =−1.3, 95% CI=−1.7,-0.9, Wald's χ2=41.7, p<0.001) in the GEE model.

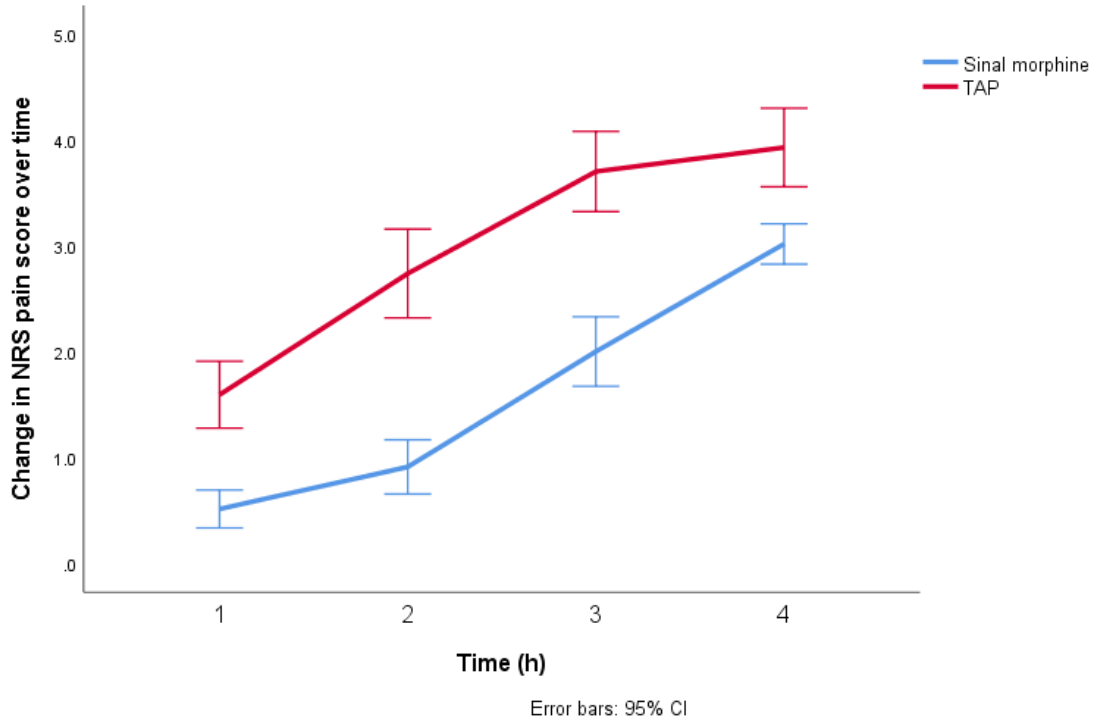

Fig 5: Change in postoperative numeric rating (NRS) pain score at rest during 24 hours postoperative period.

Intervention group and repeated measurement Interaction

After adjustment of NRS pain score during movement for repeated measurement, generalized estimating equation model show NRS score were 0.74 unit lower in spinal morphine (SM) group than TAP group during the first 24 hour postoperative period (β = −0.74, 95% Confidence Interval (CI) = −1.13- −0.34, Wald's χ2=13.2, p<0.001).

The GEE model indicated that there was a statistically significant intervention group and repeated measurement interaction during movement NRS pain score at 2nd hours (β =−0.88, 95% CI = −1.3- −0.42, Wald's χ2=14.06, p<0.001), 6th hours (β = −1.42, 95% CI = −1.9- −0.9, Wald's χ2=33.00, p<0.001), and 12th hours (β =−1.19, 95% CI = −1.63- −0.75, Wald's χ2=28.08, p<0.001).

Repeated measurement

There were statistically significant effects of repeated measurement on pain intensity (NRS) during movement at 2nd hours (β =−1.8, 95% CI=−2.2– −1.4, Wald's $\chi 2$=79.10, p<0.001) and 6th hours postoperatively (β =−0.75, 95% CI=−1.14-−0.35, Wald's $\chi 2$=13.8, p<0.001).

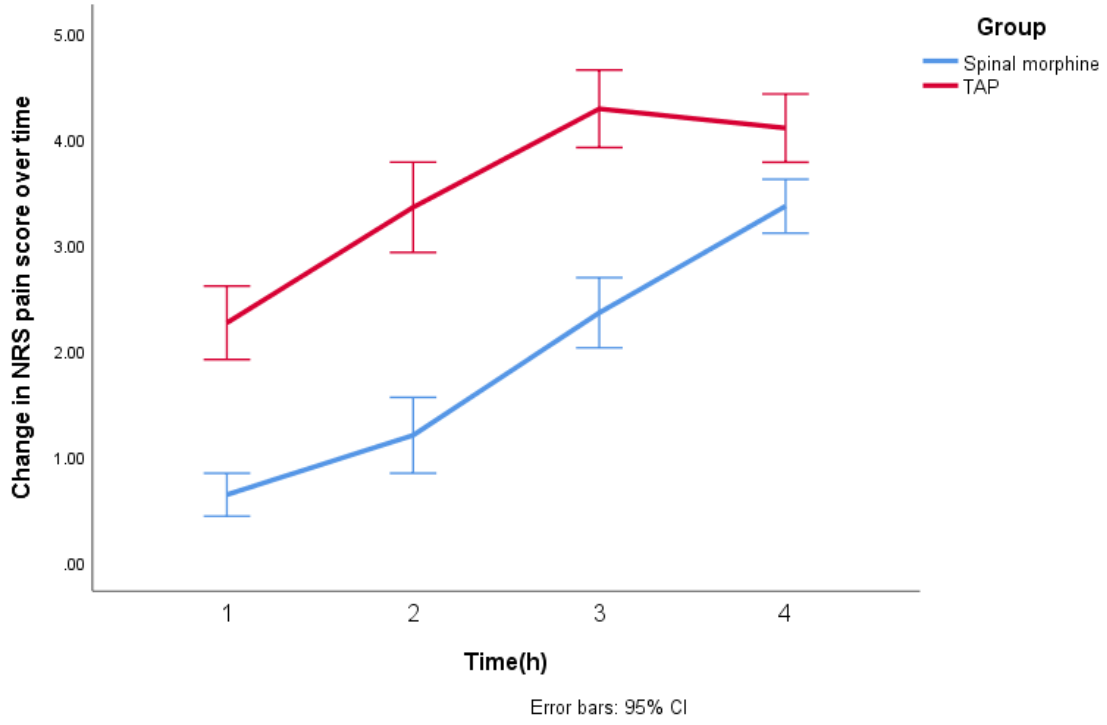

Fig 6: Change in postoperative numeric rating (NRS) pain score on movement during 24 hours postoperative period.

5.3 Postoperative analgesic consumption

In the immediate postoperative period (2 hours), median tramadol consumption was 0 ± (0) mg in Spinal morphine group and 12.5± (21.8) mg in TAP group (p <0.001). Similarly, in the 6 hours, 12 hours and 24 hours postoperatively, median tramadol consumption was 8.9± (23.5) mg vs 50.9± (40.2) mg (p < 0.001), 56.2± (36.2) mg vs 99.5± (40.9) mg (p <0.001), and 71.8± (37.2) vs 124.5± (55.8) mg (p <0.001) in the spinal morphine (SM) and TAP groups, respectively.

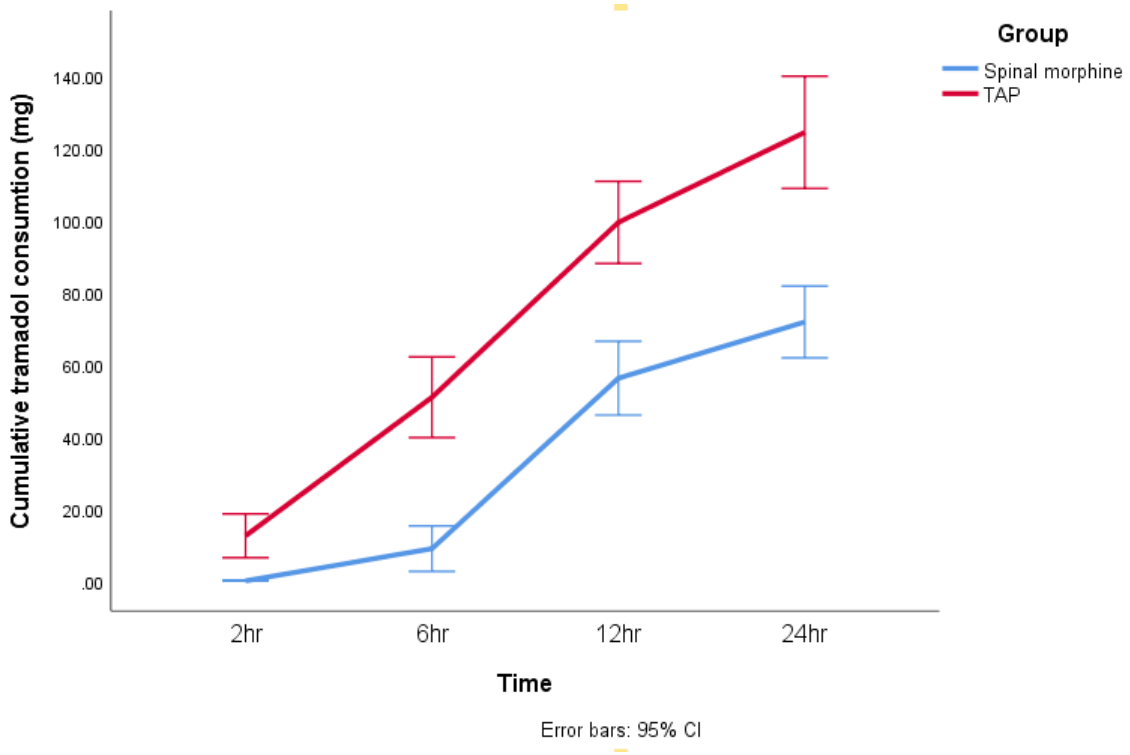

Fig 7: Postoperative cumulative tramadol consumption during the first 24 hours postoperatively

Morphine equivalent consumption

Twenty four hour median morphine consumption was reduced in spinal morphine group 0 (0-4) mg compared to TAP block group 4 (0-6) mg ($p<0.001$).

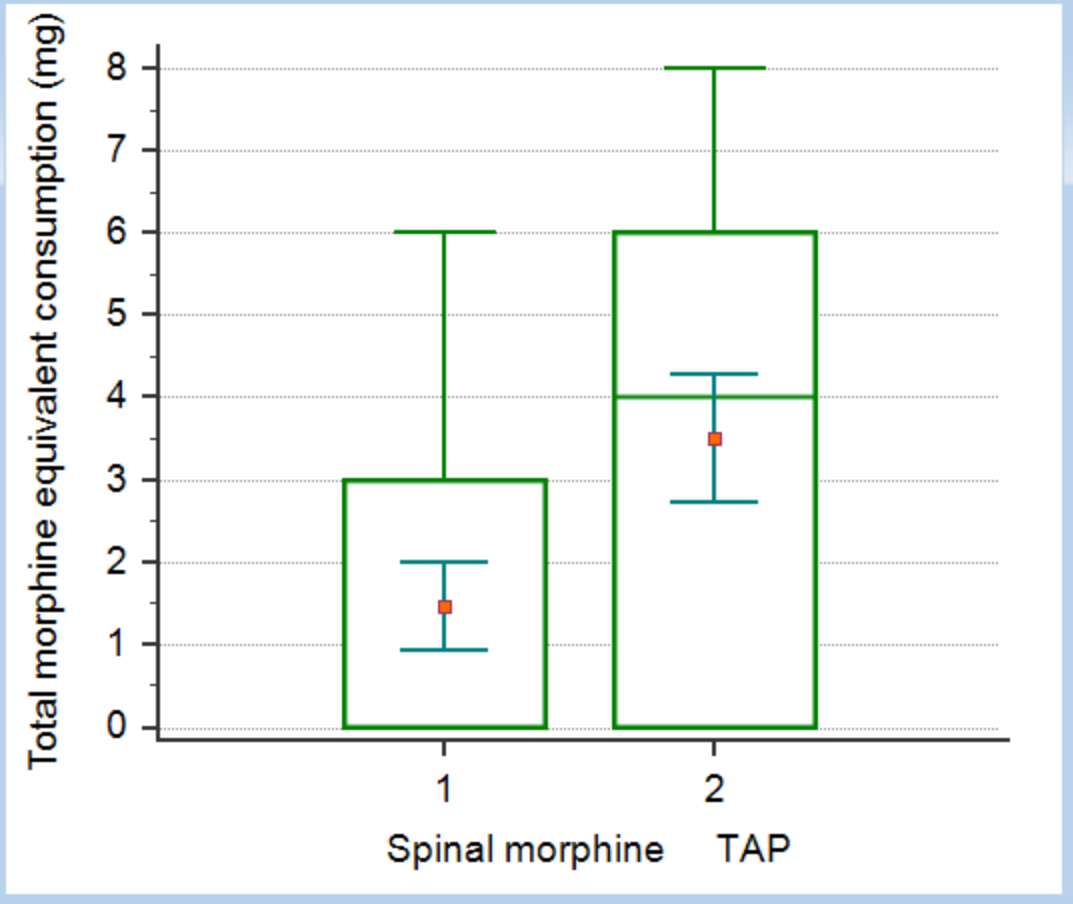

Fig 8: Total 24 hours morphine equivalent analgesic consumption

Adequacy of analgesia

At rest, 62.6% of patients in the spinal morphine group reported pain scores ≤ 3 compared with 37.4% in the TAP group. Spinal morphine group was significantly associated with adequate analgesia at rest (pain scores ≤ 3) compared to TAP group (OR: 1.96, 95% CI: 1.34-2.57, P <

0.001).

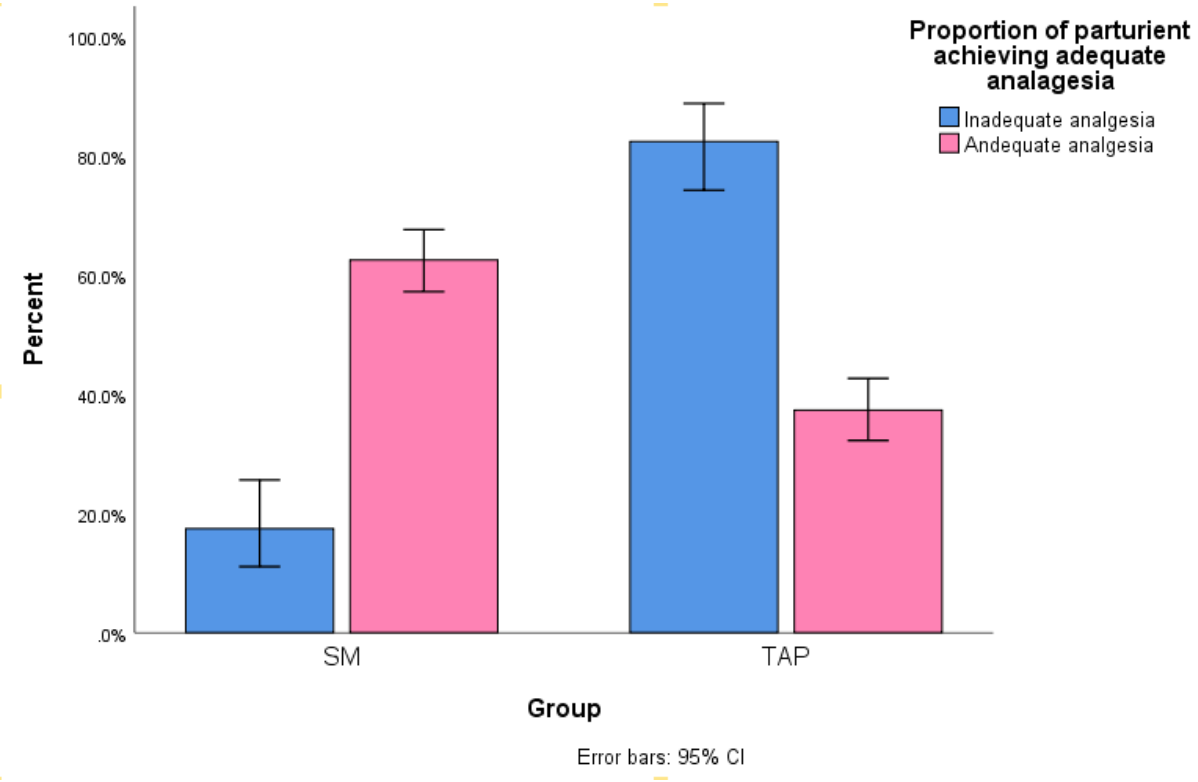

Fig 9: Proportion of patients achieving adequate analgesia at rest during 24 postoperative hours. SM, spinal morphine; TAP, transversus abdominis plane block

With movement, 65.8% of patients in the Spinal morphine group had pain scores ≤ 3 as opposed to 34.2% in the TAP group. Spinal morphine group was significantly associated with adequate analgesia during movement (pain scores ≤ 3) compared to TAP group (OR: 1.70, 95% CI: 1.14-2.25, P <0.001).

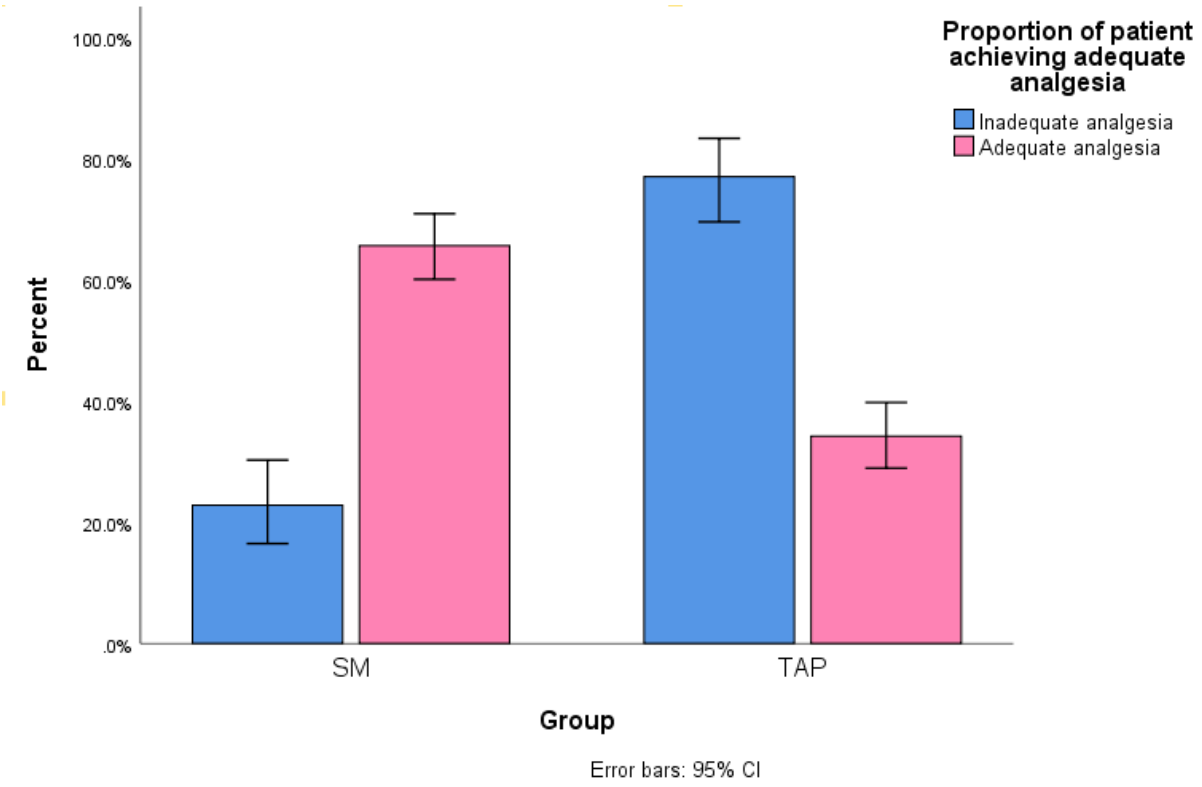

Fig 10: Proportion of patients achieving adequate analgesia on movement during 24 postoperative hours. SM, spinal morphine; TAP, transversus abdominis plane block

5.4 Postoperative complication and patient satisfaction

Side effects are reported in table (6). None of the patients in the study develop respiratory depression. Two patients from spinal morphine group were slightly sedated and one patient had also moderate purities but didn't require treatment. Majority of the mothers rated their satisfaction more highly satisfied in spinal morphine than the TAP group. There is a statistically significant difference regarding their postoperative satisfaction among the two groups. There was no statically significance difference in sedation, nausea, purities scores among two groups.

Table 4: postoperative complication and satisfaction of parturients underwent elective caesarian section at Hawassa University Comprehensive Specialized Hospital, Hawassa, Ethiopia from July 01, 2019 to July, 2020

Variable	Spinal morphine (SM)	TAP	p-value
Rammessy sedation score			0.49
Awake	54(96.4)	52(100)	
Slightly sedated	2(100)	0	
Post-operative nausea			0.496
No	46(82.1%)	46(88.5%)	
Mild	10(17.9%)	4(7.7%)	
moderate	0(0)	1(1.9%)	
severe	0(0)	1(1.9%)	
Pruritus			1.00
None	55(98.2%)	52(100%)	
Moderate	1(1.8%)	0(0)	
Satisfaction			**<0.001**
Highly satisfied *	45(19.6%)	14 (23.74	
Satisfied	11(19.6%)	36(69.2%)	
dissatisfied	0(0)	1(1.9%)	
Respiratory depression	0(0)	0(0)	

* Significant difference between

6. Discussion

Post cesarean section pain delay healing process and prolong recovery of the patient. Eisenach et al investigated that acute pain after delivery is a cause for persistent pain and depression, and it is difficult to deliver postoperative pain management which is adequate and suitable for both mother and child.(61, 62)

Studies have investigated the analgesic efficacy between spinal morphine compared with TAP block after cesarean section under spinal anesthesia. Our study found that spinal morphine provided better analgesic efficacy with prolonged time to first analgesic request, lower NRS pain score and less tramadol consumption compared to TAP group. Time to first analgesic request was significantly shorter in TAP with a median (IQR) of 240 (180-390) minute vs 360 (270-480) minute in SM. Kaplan-Meier estimate with the log-rank test revealed a p=0.004. Which is comparable with a randomized controlled trial conducted by Kanazi et al demonstrated that intrathecal morphine (ITM) provides better analgesia than does transverse abdominis plane block, with delayed median time (480 minute) to supplemental analgesia request, lower VAS pain scores, and less tramadol consumption after cesarean section. They explained their findings by the effectiveness of ITM to treat somatic and visceral pain arising from the wound and the uterus, respectively. Conversely, transverse abdominis plane block deals only with somatic pain.(43)

Contrary to our study, previous studies were investigated that the analgesic efficacy between spinal morphine and TAP their outcomes were time to first analgesic request, rescue medication need, and pain intensity and they did not found significant difference between the groups. This difference might be explained by they were using ultrasound for TAP block and using in addition to spinal morphine they were adding 5mcg fentanyl so it may effect on the prolonged effect on analgesia as well as increase the intensity of analgesia.(42, 63)

In our study we compared pain intensity by NRS at rest as well as on movement between the groups. Reported pain at rest and movement postoperative at 2 hours,6 hours, 12 hours and 24 hours in the spinal morphine group exhibited significantly lower NRS scores than TAP group (P <0.001). Similarly study conducted by McMorrow et al reveals that spinal morphine group had significantly lower VRS score than the TAP group. The median 24 hours pain scores at rest was

3 cm in spinal morphine group and 4 cm in TAP group compared to study by McMorrow et al median VRS score 10mm and 26.5mm at rest during the first 24 hours. The reason for the difference in pain intensity score between our study and this study are might be explained by the difference in tool used for pain score assessment, medication used and volume of local anesthetics used for both TAP and spinal anesthesia.(39)

We observed a significant difference in analgesic consumption between groups. There is less need of analgesia in SM group than TAP group. Twenty four hour median morphine equivalents consumption was reduced in spinal morphine group 0 (0-4) mg compared to TAP block group 4 (0-6) mg ($p<0.001$). Similar to our findings, Loane .et al found that the TAP block was associated with greater supplemental morphine equivalents requirements 7.5 mg (95% CI 4.8–10.2) than spinal morphine 2.7 mg (95% CI 1.0–4.3).(41)

Regarding post-operative complication (sedation, nausea &vomiting and purities) result between the two groups we didn't found clinically significant difference. In contrast, Ghassan et al found significantly high number of patient report postoperative nausea, vomiting and pruritus requiring treatment in spinal morphine group compared to TAP group. However, similar to our study sedation scores were comparable between groups and were consistently ≤ 2. None of the patients developed respiratory depression. The reason for discrepancy of the results may be explained by the difference in study protocol. In our study all patient received 4mg of ondasetrone before the procedure for prophylaxis of vomiting and purities. However, in their study there was no explanation about the preventive approach for postoperative nausea, vomiting and purities.(43)

Postoperative maternal satisfaction with quality of pain relief was significantly different between two intervention groups. Most of the patients in the spinal morphine group were highly satisfied with quality of pain control compared to TAP group. In contrary to our study previous studies shown maternal satisfaction was similar for both spinal morphine and TAP group.(42, 43, 63) The difference result with our study was explained by the content assessed for maternal satisfaction. In their study they assessed overall maternal satisfaction however, in our study we were assessed maternal satisfaction on quality of pain control that how satisfied the patient on their pain management. Respiratory depression has not been observed after intrathecal administration of morphine at doses of 0.1mg for CS, and was not seen in our study either.(42, 63)

Limitations of the study

The challenge in our study are, we didn't use ultrasound during TAP block because of lack of ultrasound for nerve block in our set up and also we didn't assessed rare complication secondary to TAP block like organ penetration and others**.** Another limitation of our study is that we did not assess the success rate or sensory distribution of the resulting block, because residual sensory block from spinal anesthesia may remain in the early post-operative period. Additionally, there is difficulty in adequately blinding intraoperative care giver and data collection. However, neither the patients nor postoperative data collector were aware of group allocation.

Conclusion

We conclude that preservative free 100µg Intrathecal morphine for cesarean section provides better postoperative analgesia, prolonged time to first analgesic request and less postoperative analgesic consumption than TAP block. No significant difference in postoperative complications like nausea, vomiting and pruritus between groups.

Recommendations

We recommend use of preservative free 100µg Intrathecal morphine for parturients undergo cesarean section under spinal anesthesia to prolong time to first analgesic request, for better post-operative analgesia, and to reduce analgesic consumption and their side effects.

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Registration: This study is registered on Pan African Clinical Trial Registry **(PACTR202002616299138)**

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Annex 1

INVESTIGATOR BROCHURE AND CASE REPORT FILE

Title: Analgesic Efficacy of spinal morphine in comparison with Bilateral Transversus Abdominis Plane Nerve Blocks after Cesarean section in parturient underwent Spinal Anesthesia: Randomized trial

Principal investigator: Fetiya Mohammed (Bsc)

Name of advisors

I. Bedru Jemal (BSc, MSc)

II. Engida Eyob (BSc, MSc)

The aim of this study is to compare the analgesic efficacy of spinal morphine and bilateral transversus abdominis plane nerve blocks after caesareans section under spinal anaesthesia for the first 24 post-operative hours.

Chemical Properties of Morphine

Morphine is a naturally occurring phenanthrene derivative. It is the standard drug against which all other opioids are compared. Morphine acts mainly on mu receptors to cause a wide variety of effects. Morphine is used to relieve pain. This is an effect of its action on the spinal cord to decrease the transmission of painful stimuli from body to brain, and its action within the brain itself. It can be taken for both acute pain and chronic pain. It is frequently used for pain from myocardial infarction and during labor. It can be given by mouth, by injection into a muscle, by injection under the skin, intravenously, injection spinal and epidural spaces. Maximum effect is reached after about 20 minutes when given intravenously and after 60 minutes when given by mouth, while duration of effect is 3–7 hours and when it administers through spinal its peak effect reached in 15 minutes. Long-acting formulations also exist. Morphine can be given into the epidural or subarachnoid space. This is to deliver the morphine close to one of its sites of

action, the spinal cord. It is thought that pain relief of long duration can be obtained with very low doses of morphine

Intrathecal Morphine

Opioids can be injected Intrathecal either as single agents (e.g. major abdominal surgery under general anesthesia integral to their effect or as an adjunct to local anesthetic, producing a better quality block and prolonged analgesia post operatively.

An opioid binding to its receptor in the spinal cord is to decrease, or turn off, a passing nociceptive signal. In addition, they modulate the pain pathway in the midbrain by influencing the descending pathways.

The clinical use of Intrathecal morphine is indicated during the peri-operative period for acute pain management. It is commonly used in cesarean section as single or added to the local anesthetics in spinal anesthesia.

Dosage for Intrathecal use 0.1mg-0.2mg is recommended for cesarean section.

Pharmacovigilance

Complication related to Intrathecal morphine administration are respiratory depression, purities, urinary retention, nausea and vomiting which was minimized by giving low concentration of the drug. There may be pain during injection of Intrathecal injection and it will treat by skin infiltration by 2ml of lidocaine 2% prior to Intrathecal injection.

The safety monitoring procedures are established in relation to informed consent and patient safety assuring sheet in the case report file. The safety of the patients in relation to complication, respiratory depression, purities, nausea vomiting, and urinary retention addressed in control and managing by protocol based on their severity scale.

The safety of the patients in relation to pain control also addressed in the pain control protocol of the patients in postoperative period that deals with management of pain by administering analgesic drugs according to the severity of pain.

Chemical Properties of Bupivacaine

Bupivacaine is an amino-amide type local anesthetic widely used for regional anesthesia and peripheral nerve block like femoral nerve block, sciatic nerve, cervical plexus block and for transverse abdominus plane. It has longer onset and duration of action in comparison to other local anesthetics.

All local anesthetics are membrane stabilizing drugs by inhibiting action potential propagation by blocking Na – K channels. They reversibly decrease the rate of depolarization and repolarization of excitable membranes like nociceptors.

Bupivacaine has similarity with other local anesthetic drugs i.e. the analgesic effectiveness is related to volume of the local anesthetic than the dose and concentration. The maximum safe concentration for bupivacaine to be administered for peripheral nerve block is 2mg/kg. The preparation of bupivacaine found in Ethiopia university hospital is 0.5% of bupivacaine, which is 5mg/ml.

The amount of local anesthetic injected for TAP block is according to the following

1) For TAP nerve block: the concentration or dose that injected was 0.6-0.75ml/kg of 0.25% bupivacaine.

The maximum safe dose for 0.25% bupivacaine is 4mg/kg since the concentration is reduced by half by diluting it with normal saline 0.9%. The injection was given before surgical incision is made.

Pharmacovigilance

The complication related to drug injection is local anesthetic toxicity and minimal bleeding on the injection site. Toxicity was prevented by giving the lower concentration of local anesthetic as mentioned above. The bleeding on the injection site was minimized by selecting experienced anesthetist in doing this block and also by manual compression on the injection site.

The safety monitoring procedures are established in relation to informed consent and patient safety assuring sheet in the case report file.

The safety of the patients in relation to pain control also addressed in the pain control protocol of the patients in postoperative period that deals with management of pain by administering

analgesic drugs according to the severity of pain. Since pain is an inevitable condition that can occur after the surgery, the drugs was administered by weighting the benefit of relieving the discomfort and risk of adverse effects of drugs like respiratory depression and nausea and vomiting. This thought is applied as a good clinical practice principle even for the patients not included to the study.

Transversus Abdominis Plane (Tap) Block

Anatomy

Innervation of the anterolateral abdominal wall arises from the anterior rami of spinal nerves T6 to L1.These includes the intercostal nerves (T7-T11), the subcostal nerve (T12), and the illiohypogastric and illioinguinal nerves (L1).

The anterior divisions of T6-T11 continue from the intercostal space to enter the abdominal wall between the internal oblique and transversus abdominis muscles until they reach the rectus abdominis, which they perforate and supply, ending as anterior cutaneous branches supplying the skin of the front of the abdomen. Midway in their course they pierce the external oblique muscle giving off the lateral cutaneous branch which divides into anterior and posterior branches that supply the external oblique muscle and latissimus dorsi respectively.

Indications

This block is indicated for any lower abdominal surgery including appendectomy, hernia repair, caesarean section, abdominal hysterectomy, and prostatectomy, Bilateral blocks can be given for midline incisions or laparoscopic surgery.

Contraindication

Like other peripheral nerve blocks, TAP block is contraindicated when there is Patient refusal, Local anaesthetic allergy, severe coagulation disorders and Local infection.

Block Technique

The point of entry for the blind TAP block is the lumbar triangle of Petit. This is situated between the lower costal margin and iliac crest. It is bound anteriorly by the external oblique muscle and posteriorly by the latissimus dorsi. This technique relies on feeling double pops as

the needle traverses the external oblique and internal oblique muscles. A blunt needle was used make the loss of resistance more appreciable. 20 to 30 ml local anesthetic (any local anesthetic concentration, this block relies on local anesthetic spread rather than concentration ,i.e. is volume dependent.

Complication

Intra hepatic injection and other complications include intraperitoneal injection, bowel hematoma, and transient femoral nerve palsy. Local anesthetic toxicity could also occur due to the large volumes required to perform this block especially if it was done bilaterally. As with any regional technique, careful aspiration was used to avoid intravascular injections.

Annex 2

Title:

Analgesic Efficacy of spinal morphine in comparison with TAP blocks after Cesarean section Under Spinal Anesthesia, HUCSH southern Ethiopia.

Name of Principal Investigator: Fetiha Mohammed (Bsc)

Name of advisors: -Bedru Jemal (BSc, MSc)

- Engida Eyob (BSc, MSc)

Name of the Organization: Dilla university referral hospital, College of Medicine and Health Sciences, Department of Anesthesia

Name of the Sponsor: Dilla University

Purpose of the Research Project

The aim of the study is to compare the analgesic efficacy Intrathecal morphine and transversus abdominis plane blocks for post-caesarean pain management delivery under spinal anesthesia.

This information sheet and consent form is prepared with the aim of explaining the research project. The main aim of the study is to compare analgesic efficacy of Intrathecal morphine and transversus abdominis plane block in parturient who underwent caesarean delivery in under spinal anaesthesia in Hawassa comprehensive and specialized hospital.

Procedure

I invite you to take part in our project to determine and identify effective preventive method of pain after cesarean delivery by reducing pain severity and opioid drug requirement. If you think that this research is worth participating, you will be asked to sign the consent form. Data collectors will ask you some 10 minutes question and take some data from your chart. If you are by any means reluctant to participate you will have the full right to withdraw.

All of your responses, your name and data taken from the chart are confidential by a coding system. The subjects will be selected by computer generated random number method for all

patients who underwent caesarean delivery via Pfannenstiel incision after the incision type confirmed, HUCSH.

Risk and discomfort

You might be asked some questions at the time when you are not comfortable post operation. So you might feel that this is not worth it. If you participate in this research you will be giving a valuable data for further intervention.

Incentive

There is no incentive or payment to be gained by taking part in this project. The information collected from this research project will be kept confidential and only accessed the researcher and research assistant only. This research project will be reviewed and approved by ethical committee of the DURH.

Confidentiality

Except the principal investigator, no one will have access to your collected data, name or anything taken from your chart. The data will be kept coded and locked with no labeling specifying you or anyone participating in the research.

Right to refuse

You will have the full right of refusing at or during the conduct of the research. You will not be benefited from or injured in any way by refusing to participate in the research. You can re-join the research at any time you feel comfortable. If you do not want to participate with this study, this will not have positive or negative impact on the postoperative pain control quality during your stay here in our hospital

Whom to contact

This research project will be received and approved by Ethical Committee and Department of Anaesthesia in DURH.

If you have any question, contact any of the following individuals and you may ask at any time you want:

1. Fetiha Mohammed- principal investigator

Department of anaesthesia, Dilla University

Tel: +251 921895794

2. Bedru jemal – advisor

Department of anaesthesia, Dilla University

Tel: +251 924415702

3. Engida Eyob – advisor

Department of anaesthesia, Dilla University

Tel:

Annex 3: Informed consents

Data collectors will read the Following Paragraph for the Selected Person:

"To conduct our study, I would like to ask you some question which may take about 10 minutes in three different times. As your participation is very important to the outcome of the study, we kindly request you to give us your sincere and truthful answer. All the information that you and other patients are going to provide us will remain confidential and you don't need to mention your name."

Are you willing to participate in the interview? Yes - continue), No - (thank & stop here)

Signature -_____ Date _____

Signature of the interviewer certifying that consent has been obtained verbally.

Questionnaire

It is prepared to collect data on " to comparison Intrathecal morphine with transversus abdominis plane nerve blocks under spinal anaesthesia after caesarean delivery for the first 24 postoperative hours, in Hawassa University Hospital, southern Ethiopia, 2019."

I. English version questionnaire

Dilla University College of medicine and health science department of anaesthesia

Questionnaire identification number_____

Greeting

Hello, I am_____. I am conducting in research for fulfilment of Master of Science in Dilla University Department of Anaesthesia. I would like to ask you a few questions about experiences of your surgical caesarean pain.

The purpose of this questionnaire is to gather information about "post-operative efficacy of Intrathecal morphine and transversus abdominis plane nerve blocks after caesarean section" under spinal anaesthesia. The research will be beneficial to those who need caesarean section to

control their postoperative suffering from pain with less need of other analgesic drugs and reduced risk of postoperative nausea and vomiting side effects of systemic opioids.

We will ask you some questions, which will take few minutes in three different times. The answer to those questions is confidential. We will not write your name in the questionnaire.

You can refuse to respond to any of the questions and you can interrupt at any point in the interview. Do I have your permission to continue?

1. **If yes, continue to the next page 2. If no, skip to the next participant**

Informed consent Certified by

Interviewer: Code _____Name_____ signature_____

Date of interview _____Time started _____ Time completed_____

Result of interview: 1. Completed 2. Respondent not available 3. Refused 4. Partially completed

Supervisor (Checked): Name _____ Signature _____Date_____

Guide line for the interviewer

For selected patients introduce yourself as coming from HUCSH after greeting the person you meet first. Then explain the purpose of the study for the respondent by saying that:

The reason why I came here is to ask you few questions about experiences of your surgical caesarean pain. The purpose of this study is to gather information about efficacy Intrathecal morphine and transversus abdominis plane nerve blocks after caesarean delivery in Hawassa university comprehensive specialized hospital forward some recommendation to concerned bodies that will help to improve postoperative pain management after caesarean delivery.

Annex 4:

የመረጃ እና የስምምነት ቅጽ

የምርምሩ/የጥናቱ ርዕስ

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mGb!Ã

ይህ የመረጃ እና የስምምነት ውል ቅፅ የተዘጋጀው እርስዎ ተሳታፊ እንዲሆኑ ስለተጋበዙበት በምርምር ቡድኑ ¾T>"H@¨<" Ø"ƒ u}SKŸ} SÓKÝ uSeÖƒ ′¨<:: ¾²=I U`U` ª" ›LT ukÊ ØÑ" ¾T>¨MÆ □X"„‹" ŸkÊ ØÑ"¨< u%EL LK<ƒ 24 c¯ƒ ¾JÉ leKƒ ISU" K¥¬gS ¾T>c^ eû"M V`ò" □ X" yT‰NSvRS xBì¸nS Pl@N ¾'`{ TÅ"²'" ²È wnƒ TØ"~ ¾U`U` u<É'< ›vLƒ uG<K}— ÉÓ] udÃ"e Te}` ¾›"e,¶Á }S^m }T]:-

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Annex- 5:

Case report file / Data collection tool

Section.1**: Questions on socio-economic and demographic characteristics of patients**

S.NO	Question	Possible responses	Code
01	Age (in year)	……	
02	Weigh (in kg)	……..	
03	Height (in meter)	……	
04	Body mass index (in kg/m2)	.....	
05	Residency of mothers		
06	Parity	1 Multiparous 2 Nulliparous	
07	ethincity	1. sidama 2. oromo 3. gedio 4. other	
08	Gestational age	1 2	

Section .2 Questions during Preoperative period

		response	Code
No	Questions		
07	Base line heart rate		
08	Base line blood pressure (mmhg)		
09	Respiratory rate before giving of spinal aneasthesia		

010	Spo2 before spinal aneasthesia		
011	History of nausea before giving of spinal aneasthesia		
012	Hx of vomiting		

S. No.		Response
013	For How long the patient fast (NPO) time	……. local time
	Does patient have hx of drug (opioid)allergy	
	Does patient have hx of local anesthetics allergy	
	Does the patient take intravenous fluid before starting spinal anesthesia	

Section .3.**Peri operative Question related to anesthetic and surgical interventions**

No	Questions	Response
	Vital sign before giving spinal anesthesia	BP:_____mmhg PR:_____bpm Sao2___% RR-----bpm
	Time of spinal injection	……..minutes
	Morhipne 0.1mg	1Yes 2 no
	Time of bilateral TAP block	……..minutes
	Bupivacaine0.5%(2.5ml)Isobaric	1 yes 2 no

	Level of sensory block	1=T4 2=T5 3=T6
	Level of motor blocks	1=Grade1 2=grade2 3=grade3 4=grade 4 5=grade5 6=grade 6
	Does patient have nausea	
	Does patient experience vomiting	Yes No
	If patient complain nausea how is severity	0 = no 1=mild 2=moderate 3=severe
	Does the patient complain itching	(0)-none, (1)-mild, (sometimes, slight itching), (2)-moderate,(persistent or intermittent itching not disturbing sleep) and (3)-severe (irritative itching disturbing sleep
	Does patient complain of sleepy	1Yes 2 no
	Apgar score of the fetus	
	For How long the duration of Duration of anesthesia stays	…….minutes

Section. 4 **Intraoperative hemodynamics parameter**

V/S	Before SA	**After SA give**	**6min**	**15 minutes**	**20 minutes**	**25 minutes**	**30 minutes**	**35 minutes**	**40 minutes**

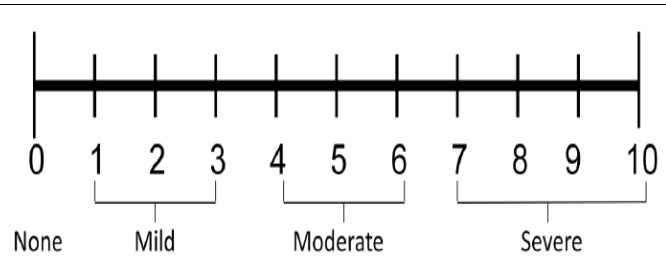
	given	**n 3min**							
SBP(mmhg)									
DBP(mmhg)									
MAP9mmhg)									
HR9beat/minute)									
RR(breath /minute)									
SPO2(%)									

Section 5. **Values of hemodynamic parameter on post-operative periods after surgery**

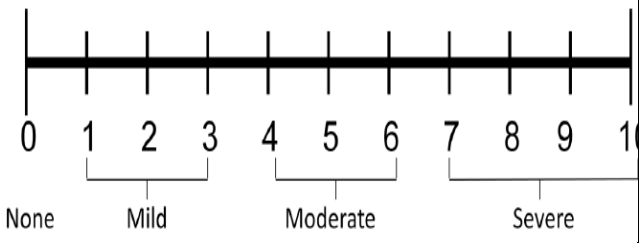
S.NO	Time (in hour)	Parameter	Value
301	At 2 hour of post-operative period	HR	……bpm
		SBP	……. mmhg
		DBP	……. mmhg
302	After 6 hour of post-operative period	HR	……. bpm
		SBP	…….mmhg
		DBP	……mmhg
303	After 12 hour of post-operative period	HR	……bpm
		SBP	……mmhg
		DBP	……mmhg
304	After 24 hours of post-operative period	HR	……..bpm
		SBP	……mmhg
		DBP	……mmhg

Section .6: **Questions on Severity of pain after 2 hours, at rest**

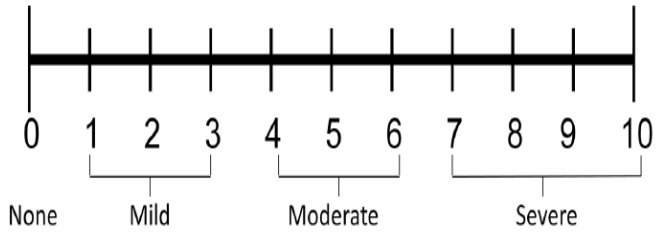
S.NO	Question	Possible answers	Code

401	Numerical pain score		
402	Amount of tramadol given	…. . ….mg iv	

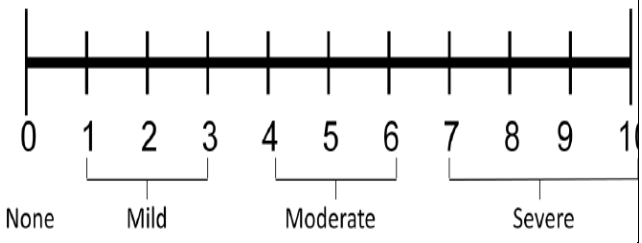
Section .7**:** **Questions on Severity of pain after 2 hours on movement/coughing**

S.NO	Question	Possible response	Code
501	Numerical rating pain scale		
502	Amount of tramadol given	……mg iv	

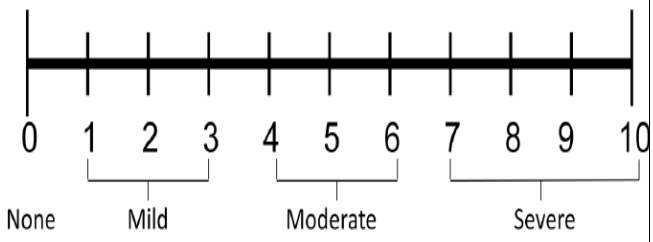
Section 8.: **Questions on Severity of pain after 6 hours at rest**

S.NO	Question	Possible response	Code
601	Numerical rating pain scale		
602	Amount of tramadol given	…….mg IV	

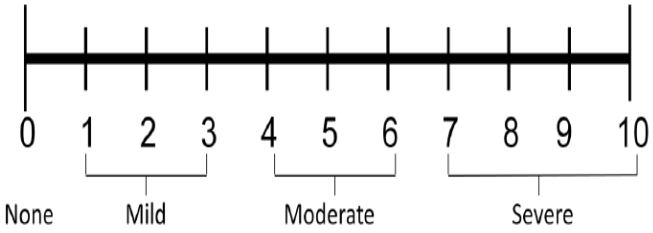
Section .9**: Questions on Severity of pain after6 hours on movement/coughing**

S.NO	Question	Possible response	Code
701	Numerical rating pain scale		
702	Amount of tramadol given	……mg iv	

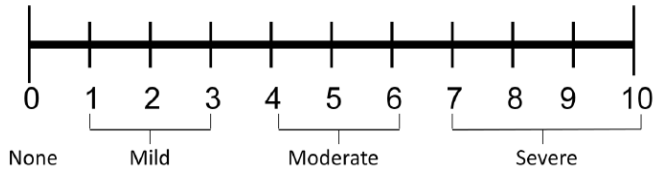
Section 10**: questions on severity of pain after12 hours, at rest**

S.NO	Question	Possible response	Code
801	Numerical rating pain scale		
802	Amount of tramadol given	…….mg iv	

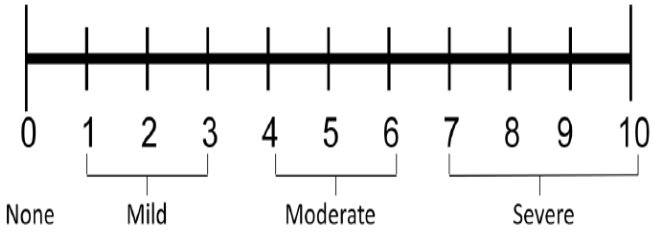
Section 11**: Question on severity of pain after 12 hour on movement/ coughing**

S.NO	Question	Possible response	Code
901	Numerical rating pain scale		
902	Amount of tramadol given	…….mg iv	

Section 12**: question on severity of pain after 24 hours, at rest**

S.NO	Question	Possible response	Code
1001	Numerical rating pain scale		
1002	Amount of tramadol given	……mg iv	

Section 13**: question on severity of pain after 24 hours on movement/coughing**

S.NO	Question	Possible answers	Code
1101	Numerical rating pain score		
1102	Amount of tramadol given	…….mg iv	

Section 14: **Postoperative Analgesic Data**

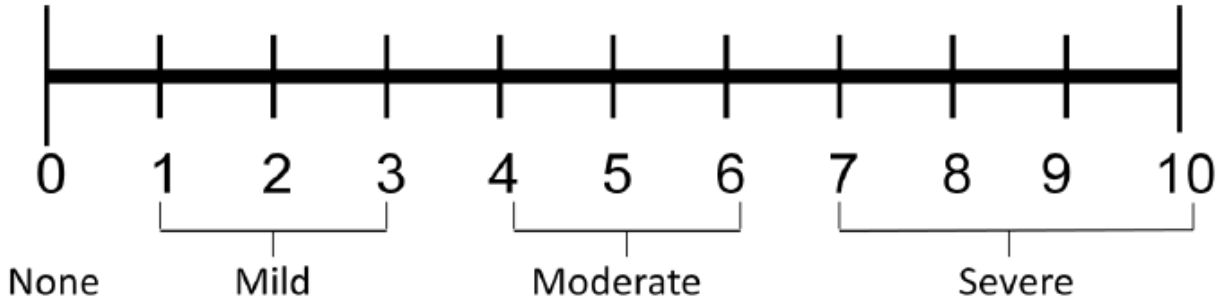
S.NO	Question	Possible response	Code
1301	Time to first analgesic request (hours)	……min/hour	
1302	Number of Tramadol doses received 0–12 hours	Tramadol……mg	
	Number of oral diclofenac doses received 24 hours	Diclofenac ……mg	
	Number of opioid given in 24 post-operative hours	Other ……mg	
	Duration in minutes till initial analgesic requirement after the patient arrived in the ward	……pm/am {time per 24 hr/date/month/ETH. year}	
	Analgesic required time	……pm/am {time per 24 hr/date/month/ETH. year	
	Duration	…….minutes/hour	
	Total and type of analgesic consumption with 24 hrs after patient arrive in the ward is	Diclofenac……mg Tramadol……mg Morphine ……mg Others…	

Section 15: Post-operative incidences

	Sedation	0 paralayed 1 awake 2 lightly sedated 3 follows simple commands 4 responds to non-painful stimuli 5 responds only to painful stimuli 6 unresponsive to painful stimuli	
	Nausea	0 no 1 Mild 2 moderate 3 severe	
	Pruritus	(0)-none, (1)-mild, (sometimes, slight itching), (2)-moderate,(persistent or intermittent itching not disturbing sleep) and (3)-severe (irritative itching disturbing sleep	
	Satisfaction scores	1 Highly satisfied 2 Satisfied 3Dissatisfied	

Annex 6: Numerical rating scale to measure severity of pain

The verbal numeric analogue scale (VNRS)



A. The scale will be taken 4 times within the first 24 hours. The patient will be asked one of the following questions:

    a) What number on a 0 to 10 scale would you give your pain right now?

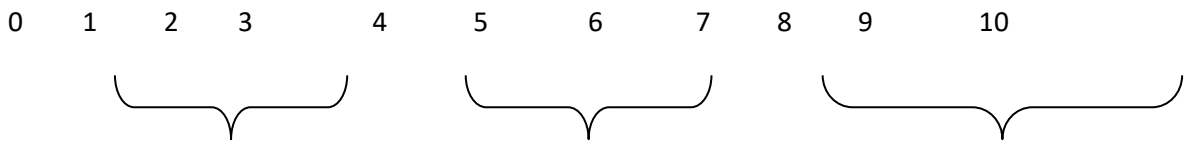
B. When the explanation suggested above is not sufficient for the patient, further explanation or conceptualization of the scale will be done:

0 = No Pain

1-3 = Mild Pain (nagging, annoying, interfering little with ADLs)

4–6 = Moderate Pain (interferes significantly with ADLs)

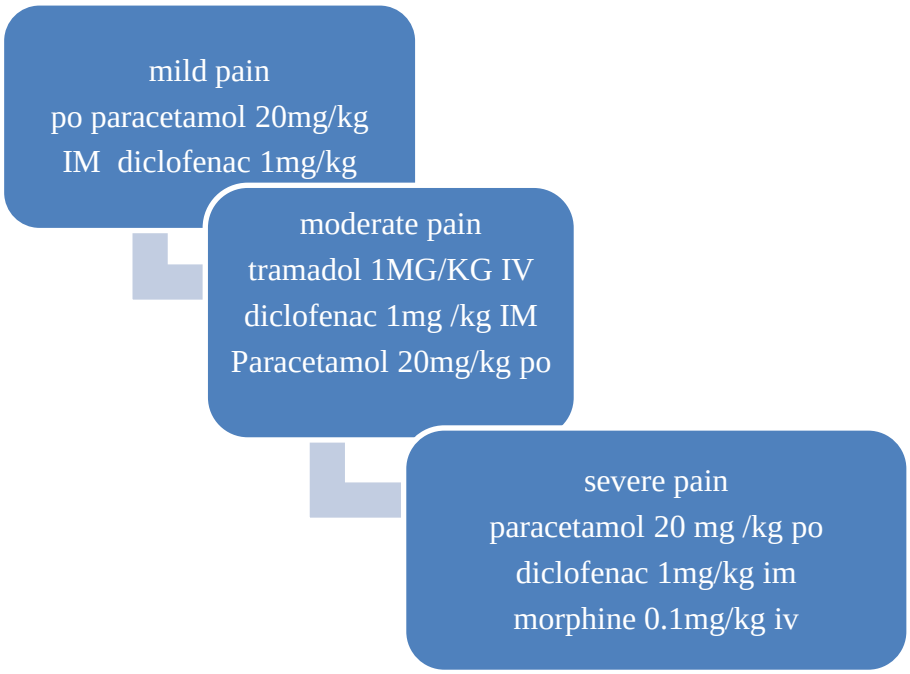
7-10 Severe Pain (disabling; unable to perform ADL



1. ይህ መለኪያ በመጀመሪያዉ 24 ሰአት 4 ጊዜ የሚወሰድ ሲሆን.
    i. በሽተኛዉ የሚጠየቃቸዉ ጥያቄዎች
        1. አሁን የሚሰማዎትን ህመም በየትኛዉ ቁጥር ይወክሉታል ;
        2. ከዜሮ እስከ አስር ካሉት ቁጥሮች አሁን የሚሰማዎትን ህመም የትኛዉ ቁጥር ይገልፀዋል
2. ከላይ የተሰጠዉ ማብራሪያ በቂ ሳይሆን ሲቀር፣ ለበሽተኛዉ የበለጠ መረጃ መስጠት አስፈላጊ ሆኖ ይገኛል
    a. 0- ምንም ህመም የለም
    b. 1-3 - ትንሽ ህመም አለ
    c. 4-6 - መካከለኛ ህመም አለ
    d. 7-10 - ከባድ ህመም አለ

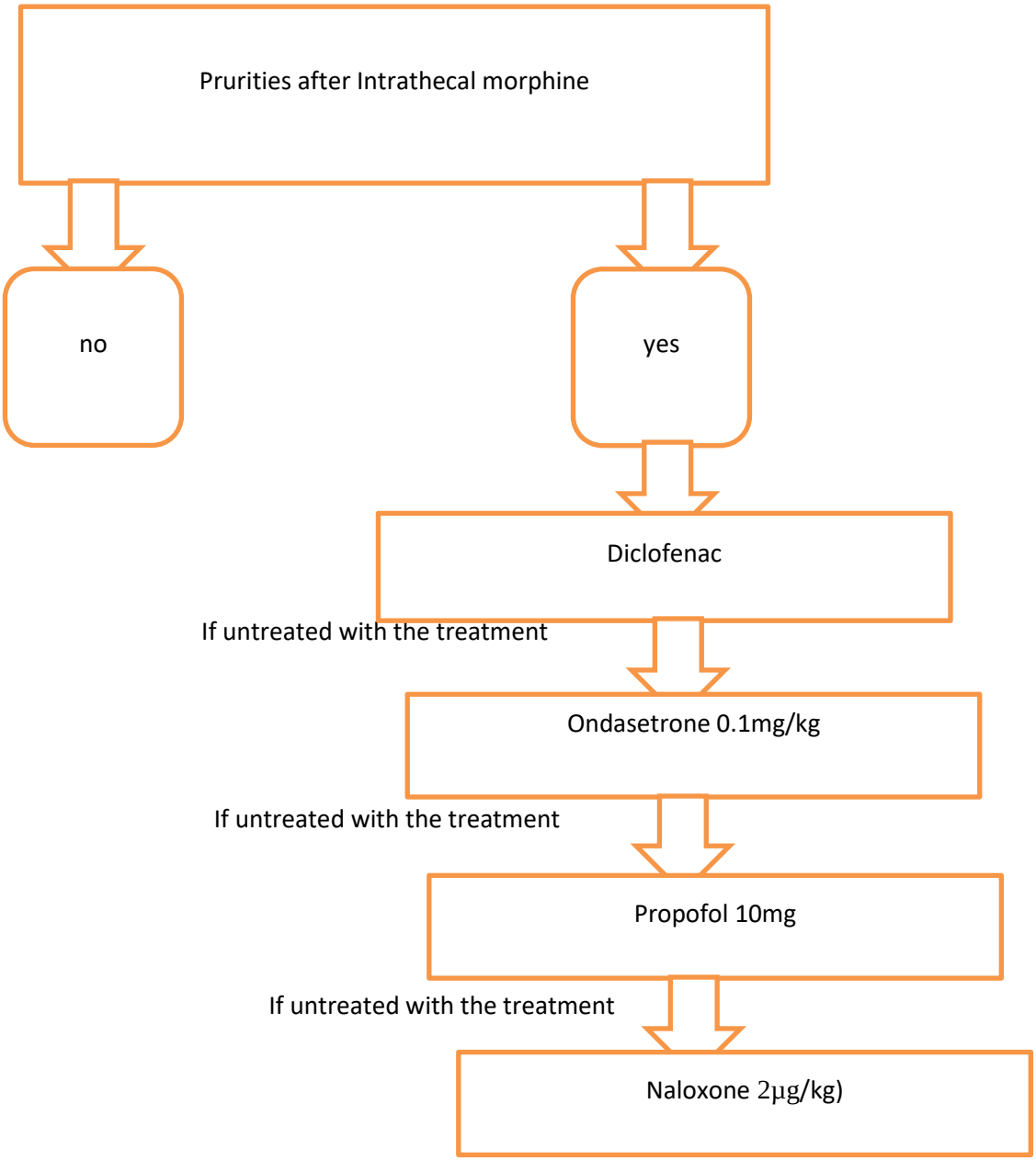
Annex 7:

Patient pain management protocol



Annex 8:

Pruritus management protocol



Annex 9:

Respiratory depression management protocol

Event	Intervention
If respiratory rate less than 10 breath /minute	Treat with 100% oxygen by face mask
Not responded With Above intervention and spo2 is less than 90 %	Treat with continuous positive airway pressure ventilation
Still not managed	Give naloxone in addition to the above management

Annex 10:

Standard Operating Procedure (SOP)

In both Dilla and Hawassa university hospital One day prior to day of surgery a staff member who is not involved in this study perform preoperative assessment, screened for the study, take informed consent and assign the patient randomly to either of two groups. On the same day, a night before day of surgery (midnight) intravenous fluid was started and preemptive oral paracetamol (1gram) was given for all both groups.

On day of surgery when they arrive at the waiting room all patients was asked necessary information and premedicated with dexamethasone (8mg) and cimetidine (400mg), ondansetron (4mg). Standard monitoring will be applied to the patient and baseline vital signs blood pressure, Heart rate, respiratory rate and pulse oximetry values was taken and recorded.

As part of the fluid resuscitation 10ml /kg of isotonic normal saline fluid to the patient of both groups before giving spinal anesthesia and co loading. In addition, all patient should get the same spinal anesthesia protocol was applied in both groups.

Intrathecal morphine administration

In spinal morphine group 0.1mg of preservative free morphine was prepared and simultaneously patient was positioned on operating table and under strict aseptic technique local infiltration of the entry point using 5ml (40mg) off 2% plain lidocaine was done. Spinal anesthesia was performed by responsible anesthetist between L3-L4 interspace by using tuffers line as a landmark with a 25 gauge spinal needle then after the free flow of cerebrospinal fluid (CSF) 2.5 ml of 0.5% isobaric bupivacaine (12.5 mg) together with 0.1mg preservative free morphine. Immediately after patient was made on supine position, pillow was inserted under the right hip to prevent aortocaval compression. The level of block was checked (alcohol drips for autonomic, pinprick for sensory & bromage scale for motor) and surgery started after a sensory level of T6.

TAP BLOCK

In TAP group after spinal anesthesia then the patient immediately put on supine position which is similar with the above procedure in in terms of spinal anesthesia injection but without morphine.

After completion of surgery nerve block was performed by one of the BSc anesthetist who is experienced and he has been managing many cesarean section and used TAP block for post-operative pain management as protocol with multimodal analgesia in obstetric by using a standard landmark technique bilaterally. 0.25% bupivacaine solution prepared by using 0.9% normal saline for dilution by the investigator.

Landmark

TAP block:

Anterior superior iliac crest, latissimus dorsi muscle, and external oblique muscle

Technique – single injection

The patient will lie in supine position.

The skin will be prepared with 0.5% chlorhexidine in 70% alcohol. Wait until the skin is dry.

Then identify identified the lumbar triangle of Petit as an access point to the neurofascial plane This triangle is bounded posteriorly by the latissimus dorsi muscle, anteriorly by the external oblique, and inferiorly by the iliac crest. Then a 23G blunted needle was advanced perpendicular to skin.

As the external oblique muscle is pierced, a characteristic ‘click’ or ‘pop’ is felt and as the needle is advanced further a second ‘click’ is felt as the internal oblique muscle is pierced then after care full aspiration 20ml of 0.25% bupivacaine in injected in the facial plane.

The same procedure will be performed at the contra lateral side

Post-operatively blood pressure, HR, and arterial saturation were observed. Nausea and vomiting grade is also assessed using the standard NRS score. Pain severity was also assessed using the

standard numerical rating scale. If NRS score is above 3 points, 1mg/kg IM diclofenac injected along with 20mg/kg PO paracetamol. If this is inadequate for pain relief within 30 minutes, an additional 1mg/kg IV tramadol will be added. If this is ineffective within 30 min, additional 0.1mg/kg IV morphine will be administered. Postoperative nausea/vomiting also asked and treating depend on the severity and other Intrathecal morphine related postoperative side effect and spinal anesthesia related complication will be managed and follow-up will goes up to 24 postoperative hours.

Preparation

Before start of operating list check before the start of the operating list, the following items, and equipment must be checked. Patients MUST NOT enter the OR until these are checked. Any problems should be recorded and reported back to Fetiha Mohammed DO NOT PROCEED IF ITEMS IN BOLD ARE NOT WORKING/NOT AVAILABLE

BEFORE START OF OPERATING LIST		
ANAESTHETIC MACHINE CHECK – are these working?		
Full anesthetic machine check by responsible anesthetist		
Oxygen supply		
Circuit leak check		
Ventilator check (if applicable)		
MONITORING – are these working?		
Pulse oximetery		
ECG		
Blood pressure		
Capnography (if applicable)		

AIRWAY EQUIPMENT – are these available?		
Face mask		

Oropharyngeal airway		
ETT – 5-7 sizes		
LMA (if appropriate)		
Bugie or Stylet (if needed)		
DRUGS 1 –are these emergency drugs drawn up?		
Adrenaline 10mcg/m		
Atropine		
Drugs 2 – are these induction drugs prepared?		
Thiopental/Propofol/Ketamine		
Suxamethonium		
Vecronium / Pancuronium		
Drugs 3 - are these analgesic drugs prepared		
Paracetamol		
Diclofenac		
Fentanyl		
Pethidine		
Drugs 4 – Is the antiemetic prophylaxis prepared		
Metoclopramide		
Drug 5-bupivacaine, lidocaine and spinal set is checked and prepared		

Annex 11:

Code: _____

S.No	Tools checked	Yes	No	Data entry
1	Are the Inclusion criteria /exclusion criteria done appropriately			
2	Informed consent issues sheet given and understood with the patient?			
3	Is the consent sheet signed?			
4	Was randomization done appropriately?			
5	Is all analgesic drugs prepared for postoperative period?			
6	Were all preparation steps for SOP fulfilled?			
7	Was the SOP followed strictly			

Data accuracy check sheet

Code: _____

S.No.	Tools	Yes	No
1	Are all questions on Sociodemographic data filed appropriately?		
2	Are all questions on intraoperative period data filled appropriately?		
3	Are all questions on postoperative period data filled appropriately?		
4	Was the postoperative analgesic drugs filled with appropriate type of drug and dose		

Analgesic rescuing administration sheet

S.No	Severity of pain	Tramadol Given	
		Yes	No
1	Moderate pain		
2	Severe pain		

Declaration

I, the undersigned, declare that this thesis proposal is my original work, has not been presented, in this or any other university and that all sources of materials used for the thesis proposal have been fully acknowledged.

Name_____ Signature _____Date _____

Adviser I

Name_____ Signature _____Date_____

Adviser II

Name_____ Signature _____Date _____