ADDIS ABABA UNIVERSITY

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DEPARTMENT OF ANESTHESIA

TITLE: EFFECTIVENESS BETWEEN PERINEURAL AND INTRAVENOUS DEXAMETHASONE AS AN ADJUVANT TO BUPIVACAINE ON TRANSVERSUS ABDOMINIS PLANE BLOCK FOR POST CESAREAN DELIVERY PAIN CONTROL IN MAHATMA GANDHI AND ZEWDITU MEMORIAL HOSPITALS, ADDIS ABABA , A PROSPECTIVE COHORT STUDY

Investigator: Abebayehu Zemedkun (B.Sc.)

Advisors: wosenyeleh Admasu (M.Sc.)

Siryet Tesfaye (M.Sc.)

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Investigator: Abebayehu Zemedkun (MSC student)

Contact details: email- abe.z01n@gmail.com

Telephone: +251916658994 / +251900053426

Advisors:

1. Wosenyeleh Admasu (BSC, MSC in Clinical Anesthesia, Lecturer and Clinical Anesthetist)
2. Siryet Tesfaye (BSC, MSC in Clinical Anesthesia, Lecturer and Clinical Anesthetist)

Declaration

I, the undersigned, declare that this thesis is my original work in partial fulfillment of the requirements for the Master of Science degree in Anaesthesia. I understand that plagiarism will not be tolerated and all directly quoted material has been appropriately referenced

Name: _____

Signature: _____

Submission to MSc Tutor, Dept. of Anesthesia, Addis Ababa University.

Date of Submission: _____

This thesis work has been submitted for examination with my/our approval as Advisors and Tutors on the Master of Science degree in Anaesthesia

Name Signature

1. _____ _____

2. _____ _____

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Abstract

Back ground: Caesarean delivery (CD) has been one of the most frequently performed major surgical interventions, and causes severe postoperative pain. Abdominal field blocks like TAP block are mostly preferred as post-operative analgesia for this operation. Using different adjuvants like dexamethasone by different routes increases the quality and duration of block and maximizes patient satisfaction.

Objective: The objective of this study was to compare the analgesic effectiveness between perineural and intravenous dexamethasone as an adjuvant to bupivacaine on bilateral transversus abdominis plane block for post cesarean delivery pain control after SA.

Methodology: An institutional based prospective cohort study was conducted on 87 patients. Study participants were selected by systematic random sampling technique. Data collection methods include preoperative chart review, intraoperative observation and postoperative patient interview at 4^{th}, 6^{th}, 8^{th}, 12^{th} and 24^{th} hours. Sociodemographic variable were analyzed by ANOVA and chi square test. Kruskal Wallis with post hoc analysis was used to compare post-operative severity of pain score and cumulative analgesic consumption. Time to first analgesic request was analyzed using Kaplan Meier survival analysis with log rank. Categorical variable were analyzed by chi square.

Result: Time to first analgesic request was significantly longer in TAP-IVD and TAP-PD compared to TAP alone ($p < 0.05$). The postoperative NRS score at rest and on coughing were significantly lowered in TAP-PD and TAP-IVD group compared to TAP alone group ($p <0.05$).The total analgesic consumption in the first 24h was significantly lower in TAP-IVD and TAP-PD group compared to TAP alone group ($p < 0.05$).

Conclusion and recommendation: dexamethasone 8mg both intravenously and perineurally is effective adjuvant to bupivacaine on bilateral TAP block with prolonged time to first analgesic request, reduced severity of pain and total analgesic consumption. Therefore, TAP-PD and TAP-IVD are a valuable alternative to each other for post cesarean delivery pain control and we recommend use of perineural or intravenous dexamethasone as an adjuvant to bupivacaine on bilateral transversus abdominis plane block.

Key words: TAP block, intravenous dexamethasone, perineural dexamethasone

Acronyms and Abbreviation

AAU	Addis Ababa university
ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CD	Caesarean delivery
DBP	Diastolic Blood pressure
HR	Heart Rate
IQR	Inter Quartile Range
ML	Milliliters
Mg/kg	Milligram per Kilogram
Msc	Master of Science
NIBP	Non- Invasive Blood Pressure
NRS	Numerical Rating Scale
NSAID	Non Steroidal Anti Inflammatory Agents
PNB	Peripheral Nerve block
PONV	Post-operative Nausea and Vomiting
RCT	Randomized Control Trial
SBP	Systolic Blood Pressure
SPSS	Statistical Package for Social Sciences
TAP	Transversus Abdominis Plane Block
TAP-IVD	Transversus Abdominis Plane Block with Intravenous Dexamethasone
TAP-PD	Transversus Abdominis Plane Block with Perineural Dexamethasone
VAS	Visual Analogue Scale

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Chapter one: Introduction

1.1: Background information

Cesarean section is an operative technique by which a fetus is delivered through an abdominal and uterine incision. When adequately indicated it can prevent poor obstetric outcomes and be a life-saving procedure for both the mother and the fetus(1)

Cesarean section is the most commonly performed operation in the world. The WHO report shows the global average caesarean delivery (CD) rate increased from 12.4% to 18.6% in the year 1990-2014. The highest CD rate according to this report is Caribbean and Latin America (40.5%) followed by North America (32.3%). The lowest CD rates were observed in Asia (19.2%) and Africa 7.3% (2).

A national population based CD rate in Ethiopia was 0.6% with regional rates varying from 0.2% to 9%. The overall institutional rate was 18% with the highest rate (46%) in private sector and 15% in public sector (3,4)

Ethiopian demographic health survey found that the Addis Ababa CD rate was 22% which is higher than the WHO recommendations as treatments of pregnancy (4).

Obstructed labor is the commonest indications for CD accounting for 31% of total CD indication in Sub-Saharan countries followed by malpresentations (18%) and previous CS (14%) (5). A retrospective record review at Felegehiwot referral hospital, Bahirdar, Northwest Ethiopia showed Obstructed labor (30.7 %), fetal distress (15.9 %) and abnormal presentation (13.4 %) were the major obstetric indications for cesarean section (1)**.**

The technique of anesthesia for CD 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(6)

A study done in Brazil showed that the incidence of moderate-severe post cesarean delivery pain was 78%. Furthermore, preoperative anxiety increases the risk. Intrathecal morphine with Fentanyl added to bupivacaine was a protective factor against this pain (7).

Postoperative pain is often treated by peripheral nerve blocks, but block duration limits the effectiveness of a single injection. In an attempt to prolong block duration, different adjuvants (e.g. dexamethasone, clonidine, Dexmedetomidine, opioids, and epinephrine) have been added to local anesthetics. Currently, dexamethasone seems to be the most promising of these adjuvants, and recent systematic reviews have shown that perineural dexamethasone prolongs analgesia by approximately 8–10h compared with placebo(8)

The TAP block, which was first described by Rafi in 2001, involves injecting local anesthetic (LA) between the internal oblique muscle and transversus abdominis muscles to block nerve signal conduction and alleviate pain after abdominal surgery. In 2004, McDonnell et al. presented preliminary work on TAP block in cadavers and in healthy volunteers at the scientific meeting of the American Society of Anesthesiologists. Despite of technical simplicity the block with local anesthetic alone may not provide a sufficient duration of analgesia(9,10)**.**

The transversus abdominis plane (TAP) block is a regional anesthesia technique that provides analgesia to the parietal peritoneum as well as the skin and muscles of anterior abdominal wall. It mainly blocks nerve fibers arising from T7-L1 nerve roots, performed either by bind technique or ultrasound guided. A "double pop" resulted from the blunt needle passing through the fascial extensions of the abdominal wall muscles (external and internal obliques) within the floor of the triangle of Petit. All anatomical landmark-based approaches to the TAP make use of blunt-tipped needles to improve tactile sensitivity and appreciation for distinct "pop" sensations (10).

Dexamethasone is a synthetic glucocorticosteriod with minimal mineralocorticoid activity, utilized frequently in perioperative setting for alleviating of acute &chronic pain, prophylaxis against postoperative nausea and vomiting (PONV) and reduction of airway and cerebral edema (11).

Mechanism of action of glucocorticoids is not fully understood, however, the suggested theories include: Inhibition of production of inflammatory mediators (prostaglandin, bradykinin), inhibition of potassium channel‐mediated discharge of C‐fibers, preventing reduction of pain threshold which occurs in surgeries and reducing tissue swelling because of anti‐inflammatory effects therefore inhibit nerve compression by inflammatory tissue (12).

1.2: Statement of the problem

Pain is ranked highest among undesirable clinical outcomes associated with caesarean section. Some of the body responses to pain are straight muscles hypertonia and spasm, increase of oxygen expenditure and acid lactic production, which can stimulate autonomic nervous system and increase heart rate (HR) and cardiac output(13).

Pain management is crucially important in the postoperative period as it increases patient comfort and satisfaction (14). Caesarean delivery (CD) has been one of the most frequently performed major surgical interventions, and causes severe postoperative pain. Caesarean delivery (CD) and subsequent manipulation performed through Pfannenstiel incision is associated commonly with significant degree of pain in the postoperative period and up to 79% of women experience pain at the incision site that can last for up to 2 months (15).

Usually the pain experienced after CD becomes intense during sitting down and standing up, or walking. Increase in BMI, an increase in operating time, being a single women and general anesthesia were independent predictors of post caesarean pain intensity(16). Patients with more intense of acute postoperative pain on movement, preoperative depression, and longer surgical time had greater risk for chronic post surgical pain following surgery with rates ranging between 1 and 18 % (17).

The presence of higher intensity pain on the day 1 post cesarean delivery is the most commonly associated factor for chronic post cesarean section pain (CPCSP) (18).

Inadequate postoperative analgesia is one of the most common causes for poor patient satisfaction following caesarean section (15,19). Inadequate postoperative pain relief after Caesarean delivery (CD) can negatively impact ambulation, breastfeeding, even maternal bonding and leads to chronic pain syndromes and poor quality of life (20).

The provision of effective postoperative analgesia is a key to facilitate early mobilization of the mother, infant care, and prevention of postoperative morbidity. Improvement in postoperative analgesia may not only increase patient satisfaction but also diminish the duration of hospital stay and reduce the risk of complications (21,22).

The ideal form of postoperative analgesia is unknown, but the procedure is mostly carried out under spinal anaesthesia. Currently, opioids are commonly used for relief of postoperative pain after caesarean section, either by intrathecal administration prior to cesarean section or postoperative parenteral administration as a component of multimodal analgesia during the postoperative period (21,23).

Even if opioids are given via the spinal or systemic route, they are frequently associated with adverse effects such as nausea, vomiting, sedation, itching, and risk of delayed maternal respiratory depression, all of which reduce overall patient satisfaction (15,23). Additionally, these opioid-related adverse effects can produce other problems for newborns such as delayed initiation of breastfeeding and impairment of mother/infant bonding (15).

Intrathecal morphine, which is considered as the gold standard and epidural morphine are single-shot drugs for post cesarean pain management, providing long-lasting analgesia for 14 to 36 hours. But both are associated with increased side effects of nausea, vomiting, and pruritus and in higher dose increased fetal transfer has been seen and it requires experienced person and higher level of monitoring. Although continuous and patient-controlled epidural analgesia infusions have been used for post cesarean analgesia, their use decreases maternal mobility, complicates anticoagulation prophylaxis, increases nursing workload, and adds to cost and requires special circumstances (eg, women with chronic pain) (24).

Drugs like Non-steroidal anti inflammatory drugs (NSAID) and paracetamol can only supplement other modes of analgesia and are not sufficient on their own. Regional field blocks like Transversus Abdominis Plane (TAP) block and iliohypogastric ilioinguinal nerve blocks are gaining in popularity, especially after the advent of ultrasound in anesthesia. Wound infiltration catheters are also in vogue (25).

Continuous research is being done to identify the effect of various adjuvants in improving the quality and increase the duration of the local anesthetic action in different peripheral nerves and regional block techniques. The addition of adjuvant substances as Alpha-2 Adrenoreceptor agonists (clonidine, Dexmedetomidine), adrenaline, Tramadol, midazolam, ketamine, opioids, adenosine, non-steroidal anti-inflammatory and steroid to the local anesthetic drugs in TAP block and their efficiency have been studied and adjuvant to local anesthetics is an evolving and

exciting field of anesthesia practice with new technology promising to improve patient satisfaction and safety (26–30)

Dexamethasone has a long and efficient glucocorticoids structure with anti-inflammatory properties. When added to local anesthetics as an adjuvant in peripheral blocks, it increases the action time, prolong the analgesia time and contribute to the TAP block (31–33). Intravenous dexamethasone has also been shown to reduce pain at rest and with movement and opioid consumption after surgery (34).

To date, it is unclear whether the perineural administration confers advantages over the IV administration of this drug (35,36). So that the result of our study may be used as a base line data for further research, may show possible analgesic modalities for postoperative pain control in caesarean section patients and may provides alternative routes to enhance quality and duration of TAP block

1.3: Significance of the study

With dramatic rise in the rate of cesarean deliveries in the last two decades, post-operative pain management of this patients has become a major medical challenge(37).

An ideal method of pain relief after caesarean delivery should be cost effective, safe for the mother, require minimal monitoring and use drugs that are not secreted into breast milk. Many scholars have been studying to find the safest and effective way of interventions for post operative CD pain management and they suggest methods like opioid or local anesthetic skin infiltration, epidural analgesia, intrathecal or intravenous opioids and abdominal field blocks like TAP block.

Among the above listed ways of pain management, intravenous opioids, NSAIDs and regional nerve block are the main stay of treatment for post caesarean pain in our study area. Despite the use of opioids for analgesia is evidenced and widely practiced, concerns of side effects like pruritus, nausea, vomiting, sedation and respiratory depression are calling for medical attention. The other alternative is epidural analgesia, which is the most versatile regional analgesia technique for post caesarean pain, but it is yet not fully practiced in the study area as well as the country due to lack of equipment, lack of experienced expert and its technical invasiveness. Additionally it is associated with has risk of infection, catheter migration and may also limit movement because of risk of motor block (38).

Abdominal field blocks like TAP are the main stay of treatment for post caesarean pain because of opioid sparing effect, prolonged pain relief, technical simplicity and affordability (39). Studies have found that TAP blocks with local anesthetics only, offer no analgesic benefits in terms of post-operative analgesic consumption and severity of pain when compared to intrathecal morphine. Therefore, different adjuvants have been used to intensify the quality and increase the duration of action of local anaesthetics(37).

Dexamethasone is one of the additives and has been proved to be an effective adjuvant for extending the duration of sensory block, reduced total analgesic consumption and severity of pain when given perineurally and intravenously . However, there are conflicting reports about which of the two routes of administration is the best or if both exert an equivalent effect (40).

Dexamethasone is easily affordable, accessible, cheap and safe. So that, both intravenously and perineurally has been used as adjuvant to bupivacaine on TAP block in the study area to prolong duration of analgesia, decrease post-operative analgesic consumption and prevent PONV. Therefore, the choice between IV and perineural dexamethasone with regard to time to first analgesic request, duration of analgesia & post-operative analgesic drug consumption needs investigation for better practice of perioperative pain control and patient care. Additionally, many current literatures recommend effectiveness between these two routes on prolongation of TAP block needs investigation.

Prolonging duration of analgesia, decreasing post-operative severity of pain and total analgesic consumption has a paramount importance like decreasing hospital stay and associated costs, decreasing hospital acquired infections, allowing early mobilization, facilitating mother to fetal bonding, reducing thrombo-embolic events and increasing patient satisfaction.

Although both roots are said to be effective on PNB, as far as my search there is no study conducted on this title in our country and abroad. Furthermore, the result may be used as a base line data for further research, may show possible analgesic modalities for post CS pain control in resource limited settings like ours and provides alternative routes to enhance quality and duration of TAP block.

Chapter 2: Literature review

Delivery by caesarean section is rising from time to time in the world. Data from the United States show an increase in rate from 21% in 1996 to 32% in 2011. According to WHO reports, the rate has risen to 46% in China and 25% and above in many Asian, European and Latin American countries. Many deliveries are carried out in units with fewer infrastructures. This makes it more challenging to provide good pain control for these parturients (25).

Systemic or Neuraxial opioids are the mainstay for treating postoperative pain, as they are effective against both visceral and somatic components of pain. However, they are associated with a number of undesirable side effects such as nausea, vomiting, pruritus, constipation, and respiratory depressions. multi modal analgesia using systemic analgesics in combination with regional blocks are currently recommended(41).

A prospective cohort study conducted by Tarekegn F et al in Debretabor, Ethiopia showed that Bilateral TAP block provides lower postoperative severity of pain, reduced total postoperative Tramadol analgesics consumption and prolonged time for the first analgesic request after cesarean section under spinal anesthesia when it is used as multimodal analgesia(42).

Another prospective observational cohort study in Gondar evaluating the effectiveness of TAP block after abdominal surgery showed Transverse abdominis plan block is safe, reduces postoperative tramadol requirement and possibly the severity of pain in the first 24 hours (43)

Desale TK et al in Asmara, Eritrea demonstrated the effectiveness of TAP block after CS and showed VAS pain scores were significantly lower in the TAP block group at rest, deep breathing, intentional coughing, and mobilisation in all cases ($p < 0.05$). Morphine and Diclofenac consumption was significantly higher in the control group ($p < 0.001$) (44).

A systematic review and metanalysis evaluating the effectiveness of Transversus abdominis plane block for postoperative analgesia after cesarean delivery performed under spinal anaesthesia showed that TAP block reduced the mean 24 hr IV morphine consumption by 24mg. TAP block also reduced visual analogue scale pain scores by 0.8centimeter and decreased the incidence of opioid-related side effects(20).

2.1: Perineural dexamethasone

A RCT done in India on Comparison of dexamethasone and clonidine as an adjunct to bupivacaine in TAP block in patients undergoing lower segment caesarean section showed that the average VAS score in patients who received TAP with dexamethasone was (1.50) which is significantly lower than those who received clonidine (1.95) with P value of 0.0001. The duration of analgesia was 151 minutes longer in dexamethasone group. Furthermore, in majority of the patients (84%) who received clonidine with TAP, the analgesia was persisted for 2-4 hours. While in patients who received dexamethasone addition, the analgesia persisted for 6-8 hours in 37% (38).

Another randomized clinical comparative trial by Mamatha Raghukumar et al on the efficacy of adding Clonidine or Dexamethasone to Bupivacaine (0.5%) in prolonging the duration of post operative analgesia with ultrasound guided TAP block in cesarean delivery showed VAS scores were comparable in all the three groups (20ml of 0.125% Bupivacaine with Dexamethasone (4mg), Clonidine (25µg), Saline (2ml) on each side) in the first 12hr ($p>0.05$), it was higher in saline group in the next 36hrs. Time to first analgesic request was prolonged by 2hrs in all three groups. Tramadol requirement was significantly lower in the clonidine and dexamethasone group after 12hrs (37).

A meta-analysis on clinical analgesic efficacy of dexamethasone as a local anesthetic adjuvant for transversus abdominis plane (TAP) block showed that perineural dexamethasone prolonged the duration of LA effect in the TAP block [mean difference (MD): 2.98 h; 95% confidence interval (CI): 2.19 to 3.78] and reduced VAS scores at 2, 6 and 12 h postoperatively. Furthermore, the use of perineural dexamethasone was associated with less analgesic consumption and a lower incidence of nausea and vomiting [odds ratio: 0.28; 95% CI: 0.16 to 0.49] on the first day after surgery (45).

A study done by Fouad and his colleagues on the efficacy of preemptive dexamethasone added to bupivacaine in ultrasound guided TAP block for postoperative analgesia after inguinal herniorraphy showed that TAP with dexamethasone when compared to TAP alone showed significantly a lower VAS score at the postoperative 4 ,8, 12,16,and 20hrs and in all cases it was statistically significant. longer time till first opioids requirement , prolonged the duration of the

block, less requirement for opioids, increased patient satisfaction and decreased the incidence of nausea and vomiting also seen in TAP with dexamethasone group (46)

A RCT study done in Egypt on Effect of adding dexamethasone to bupivacaine on transversus abdominis plane block for abdominal hysterectomy showed, the pain VAS score was significantly lower at the postoperative 2 h (4.9 vs. 28.1, P=0.01), 4 h (12.2 vs. 31.1, P=0.01) and 12 h (15.7 vs. 25.4, P=0.02) when compared to TAP block with bupivacaine alone. Furthermore, time to first analgesic request (TFA) was significantly longer in the dexamethasone group (459.8 vs. 325.4 min, P=0.002), with lesser morphine requirements in the postoperative 48 h (4.9 vs. 21.2 mg, P=0.003) and lower incidence of nausea and vomiting (6 vs. 14, P=0.03) (47).

Another RCT in India showed TFA was significantly longer in patients who receive 8mg dexamethasone with ropivacaine for TAP block when compared to ropivacaine alone (5.92 ± 1.02 vs. 3.11 ± 0.82 h, P < 0.0001). They also had decreased Tramadol requirement postoperatively (100.00 ± 0.00 vs. 140.00 ± 50.26 mg, P = 0.046). The incidence of nausea and vomiting was also lower (82.86% vs. 97.14%, P = 0.02318) and the patient satisfaction with regard to pain relief was more with dexamethasone group (57.14% vs. 25.71%, P = 0.038) (48).

Another study evaluating the Adjuvant Effect of Dexamethasone to Ropivacaine in TAP block for Inguinal hernia repair and Spermatocelectomy could not show a statistically significant prolongation of analgesia, though there was a one point drop in pain score at 12 hours post block when dexamethasone was added to the block solution (49).

A double blinded trial by Cummings et al. also showed Dexamethasone prolongs analgesia from interscalene blocks using ropivacaine or bupivacaine. The effect was stronger with ropivacaine but block duration was longer with plain bupivacaine than ropivacaine. The combined effect of dexamethasone and either drug produced nearly the same 22 h of analgesia (50)

A prospective, randomized, double blinded controlled study done by yadav RK et al on the effectiveness of addition of neostigmine or dexamethasone to local anesthetic (Lidocaine) in providing perioperative analgesia for brachial plexus block showed the Duration of analgesia in dexamethasone group was 454min compared with neostigmine group 225 min, which is statistically significant. The mean VAS was significantly lower in dexamethasone group in 12 hours post-operatively (51).

Alarasn KA et al also found that dexamethasone fastens the onset of sensory and motor block and significantly increases the duration of analgesia in patients receiving low volume Supraclavicular brachial plexus block (52).

2.2: Intravenous (IV) dexamethasone and perineural versus intravenous dexamethasone

Intravenous (IV) dexamethasone has also been shown to reduce pain at rest and with movement and opioid consumption after surgery (34).

Dhanger, et al demonstrated the efficacy of low dose intravenous dexamethasone (2mg) in Prolongation of Analgesia in Supraclavicular Block and showed a significant prolongation in duration of analgesia and reduced analgesic request and better patient satisfaction when compared to placebo (53).

Currently there are many studies comparing the effectiveness of both perineural and intravenous dexamethasone as an adjuvant to peripheral nerve blocks

Zhao et al showed that the effects of perineural and intravenous dexamethasone were equivalent concerning the duration (mean difference 0.03 hrs, 95%CI -0.17 to 0.24). The two roots of administration did not show any significant difference in the incidence of PONV nor post op analgesic consumption at 24 hr (40).

A systematic review, metanalysis, meta regression and trial sequential analysis investigated the effects of co - administration of dexamethasone with peripheral nerve blocks, which included 9 low risk of bias RCTs (783 patients) and showed perineural dexamethasone prolonged peripheral nerve block duration of analgesia as compared with IV dexamethasone (54).

Another meta-analysis of thirteen randomized controlled trials comprising a total of 937 patients (intravenous: 464 patients; perineural: 473 patients) showed there was no difference in duration of analgesia between perineural and intravenous dexamethasone when using a dose of dexamethasone ≥8 mg as adjuvant to peripheral nerve block (SMD, 0.33 h; 95% CI, −0.11 to 0.77). Perineural dexamethasone had more benefits in terms of prolongation of motor block duration, decreasing pain score, reducing opioid consumption, and less postoperative nausea and vomiting(55).

A RCT done in Egypt showed both perineural and IV administration of dexamethasone improve the efficacy of lumbar plexus block by prolonging the duration of analgesia, enhancing onset action of local anesthetics, and reducing postoperative analgesic requirements without increasing the incidence of complications (56).

Route of dexamethasone administration did not impact on improved duration for interscalene brachial plexus block, but compared to intravenous dosing, perineural dexamethasone (8 mg) results in longer durations of sensorimotor block and postoperative analgesia for ultrasound-guided axillary block (57).

Another systematic review and meta-analysis was done on efficacy of perineural vs systemic dexamethasone to prolong analgesia after peripheral nerve block and it showed the duration of analgesia was significantly increased with perineural dexamethasone vs systemic dexamethasone by a mean difference of 3h [95% confidence interval (CI): 1.4-4.5h; P=0.0001]. Dexamethasone combined with bupivacaine, but not ropivacaine, slightly prolongs the duration of analgesia, without an impact on other pain-related outcomes (58).

So that, the aim of our study is to compare analgesic effectiveness between perineural and intravenous dexamethasone as an adjuvant to bupivacaine on bupivacaine for post cesarean delivery pain control

Research hypothesis

HO1: There is no statistically significant difference in time to first analgesic request between groups.

HA1: There is statistically significant difference in time to first analgesic request between groups.

HO2: There is no statistically significant difference in NRS between groups.

HA2: There is statistically significant difference in NRS between groups

HO3: There is no statistically significant difference in analgesic consumption between groups.

HA3: There is statistically significant difference in analgesic consumption between groups.

Chapter 3: Objectives

3.1: General objectives

To compare the effectiveness between perineural and intravenous dexamethasone as an adjuvant to bupivacaine on bilateral transversus abdominis plane block for post cesarean delivery pain control for mothers operated under spinal anesthesia in GANDHI and ZEWDITU memorial hospital from January to April 2019

3.2: Specific Objectives

-To compare the time elapsed before the first request of analgesia between the groups.

-To compare the severity of post-operative pain using NRS between the groups at rest

-To compare the severity of post-operative pain using NRS between the groups on coughing/movement.

-To compare total amount of Analgesic consumption between the groups.

Chapter four: Methodology

4.1 Study area: This study was conducted in Gandhi and Empress Zewditu Memorial Hospitals, the public hospitals in Addis Ababa, capital of Ethiopia.

Gandhi Memorial Hospital was established in 1958 G.C when it was called the only maternity hospital in Ethiopia. The hospital was named as Gandhi Memorial Hospital for the memory of Mahatma Gandhi. It is one of the governmental hospitals found in Addis Ababa. The Hospital primarily gives services for women and children. The Hospital provides Gynecologic, Obstetric and reproductive health services including Maternal and Child Health (MCH), infertility and sexual violence services. Currently, it is providing inpatient, outpatient services and emergency cases. The hospital has 110 beds, four operation theatre and average number of elective caesarian deliveries done at the hospital is three per day.

Zewditu Memorial Hospital is located in Kirkos sub city woreda 08. This hospital was built, owned and operated by the Seventh day Adventist Church, but was nationalized during the Derg regime in 1976. The hospital is named after Empress Zewditu, the cousin and predecessor on the throne of Emperor Haile Selassie. Today both hospitals are operated by Addis Ababa city administration Health bureau.

4.2: Study design and period

An institutional-based prospective cohort study was employed from January to April 2019

4.3: Population

4.3.1 Source population: all parturient who underwent elective caesarean delivery under spinal anesthesia and took TAP block with dexamethasone or alone in Gandhi and Zewditu Memorial Hospital

4.3.2 Study population: all parturient who underwent elective CS under spinal anesthesia and took TAP block with dexamethasone or alone in Gandhi and Zewditu memorial hospital during the study period

4.4 Study variables:

4.4.1 Dependent variable:

Time to first analgesic request, pain severity (measured by NRS score at rest and coughing/movement) and total post-operative analgesic consumption in 24 hours.

4.4.2 Independent variables:

Socio demographic characteristics: (age, weight, height and BMI), Duration of surgery, hemodynamic variables (Heart rate, blood pressure, MAP), parity, previous caesarean delivery, exposure status, years of experience of anesthesia provider and preoperative pain.

4.5 Operational definition

Postoperative pain: the presence of pain in the postoperative period will be defined as a pain score other than zero starting from recovery within 24 hours.

ASA physical status classification-see Annex 7

Numerical pain rating scale (NRS):

A valid pain assessment tool in which 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.

Evidence supports that there is a strong correlation between the verbally administered numerical rating scale (VNRS) and the Visual analogue scale (VAS). The overall equivalence of the measures was based on the regression analysis. The finding is that, agreement between them is almost the same as agreement between two VAS measurements taken 1 minute apart, and the nearly identical minimum clinically significant differences suggest that the NRS can be used to measure acute pain in clinical studies (59)

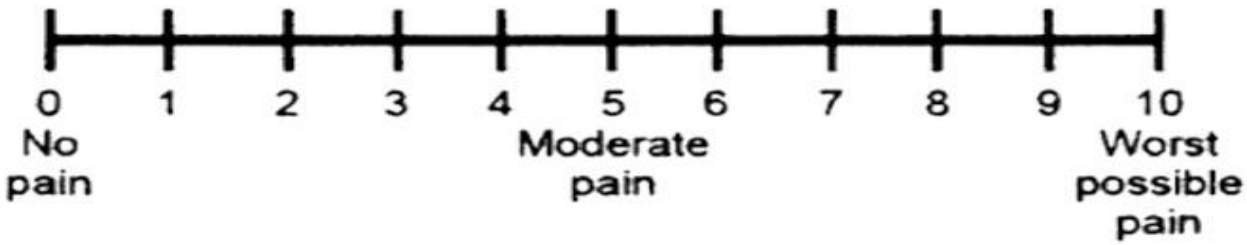


Figure1: Adopted from the National Initiative on Pain Control™ (NIPC™)

Time to first analgesia request: a time in minutes (hour) from the end of surgery to a first time analgesia (Diclofenac or tramadol or both) were given.

Total post-operative analgesia consumption: total dose and type of analgesic medication given in mg within the first 24 hour starting from admission to recovery room.

Right censored: defined as patient not requesting analgesia during study period.

TAP (tansversus abdominis plane block) alone group: parturients who took bilateral transversus abdominis plane block with 40 ml (20 ml each side) of 0.25% bupivacaine

TAP-IVD (Transversus abdominis plane with intravenous dexamethasone) group: parturients who took bilateral transversus abdominis plane block with 40 ml (20 ml each side) of 0.25% bupivacaine + 8mg dexamethasone intravenously concomitantly with the block

TAP-PD (transversus abdominis plane block with perineural dexamethasone): parturients who took bilateral transversus abdominis plane block with 40 ml (20 ml each side) of 0.25% bupivacaine + 8mg (4mg each side) dexamethasone added to the bupivacaine.

Exposed group: parturients who took TAP-IVD and TAP-PD

Non-exposed: parturients who took TAP alone

Post-operative nausea and vomiting: when a patients experience at least one episode of either nausea or vomiting within 24 hours

Shivering: in voluntary repetitive activity of skeletal muscle

Failed TAP block: when the NRS score is ≥ 4 at 4^{th} hour post procedure.

Lost follow up: any follow up followed for less than 24 hour for any reason.

Duration of surgery: time in minutes from skin incision to end of surgery.

4.6: Inclusion and exclusion criteria

4.6.1: Inclusion criteria

All ASA II parturients who underwent elective caesarean delivery under spinal anaesthesia.

4.6.2: Exclusion Criteria

Parturients with preeclampsia, eclampsia, history of medical illness, history of chronic opioid use, diabetes mellitus, patient refusal, use of other adjuvant, use of adjuvants for spinal anesthesia bleeding abnormality and patients with BMI>30kg/m2 were excluded.

4.7 Sample size and sampling technique

4.71 Sample size

The sample size was calculated from the data of the primary outcome in a preceding pilot study using all outcome variables. The outcome measure for this study were time to first analgesic request, numeric rating scale (NRS) score and mean total analgesic consumption between groups over 24 hours. Time to first analgesic request was used to estimate the sample size because it gave us the largest sample size. The observed mean time to first analgesic request from the pilot study was μ1= 5.4 ±1.78 μ2=6.2±1.095 μ3= 6.8±1.75 SD pooled= 1.57. A priori power analysis for a one-way ANOVA with 3 groups was conducted in G*Power (using version 3.1.9.2) to determine sample size using an alpha = 0.05, a power of 0.80. In order to ensure a minimum of 78 patients needed, an additional 9 patients (≈10 %) were added as attrition rate. The results of that pilot study were not included in the present analysis, and none of the patients from the pilot study were included in the present study.

4.7.2: Sampling technique

The two hospitals were selected conveniently because, the block is mainly performed by Msc in anesthesia students and these 2 hospitals are the only hospitals which are site for Msc in anesthesia programme for gynecology and obstetrics attachment. So, TAP with dexamethasone and TAP alone is mainly practiced in these two hospitals. Then, proportional allocation of sample was implemented in selected two governmental hospitals in Addis Ababa, Ethiopia, in order to compare analgesic effectiveness between perineural and intravenous dexamethasone as adjuvant to bupivacaine for post cesarean delivery pain control under spinal anesthesia. From situational analysis about 130 patients are estimated to take TAP block with dexamethasone or alone during the study period in the two hospitals. Proportional allocation to size (PAS) were determined from these 130 patients, 87 participants were recruited with the probability of about 66%. By considering the consecutive TAP block with dexamethasone or alone, data collection was made on 2 patients for every 3 patients who underwent elective CS under spinal anesthesia

and took TAP block with dexamethasone and alone. From number 1 to 3, one number was selected by lottery method which was used for exclusion for consecutive patient in all groups until the required sample size is reached.

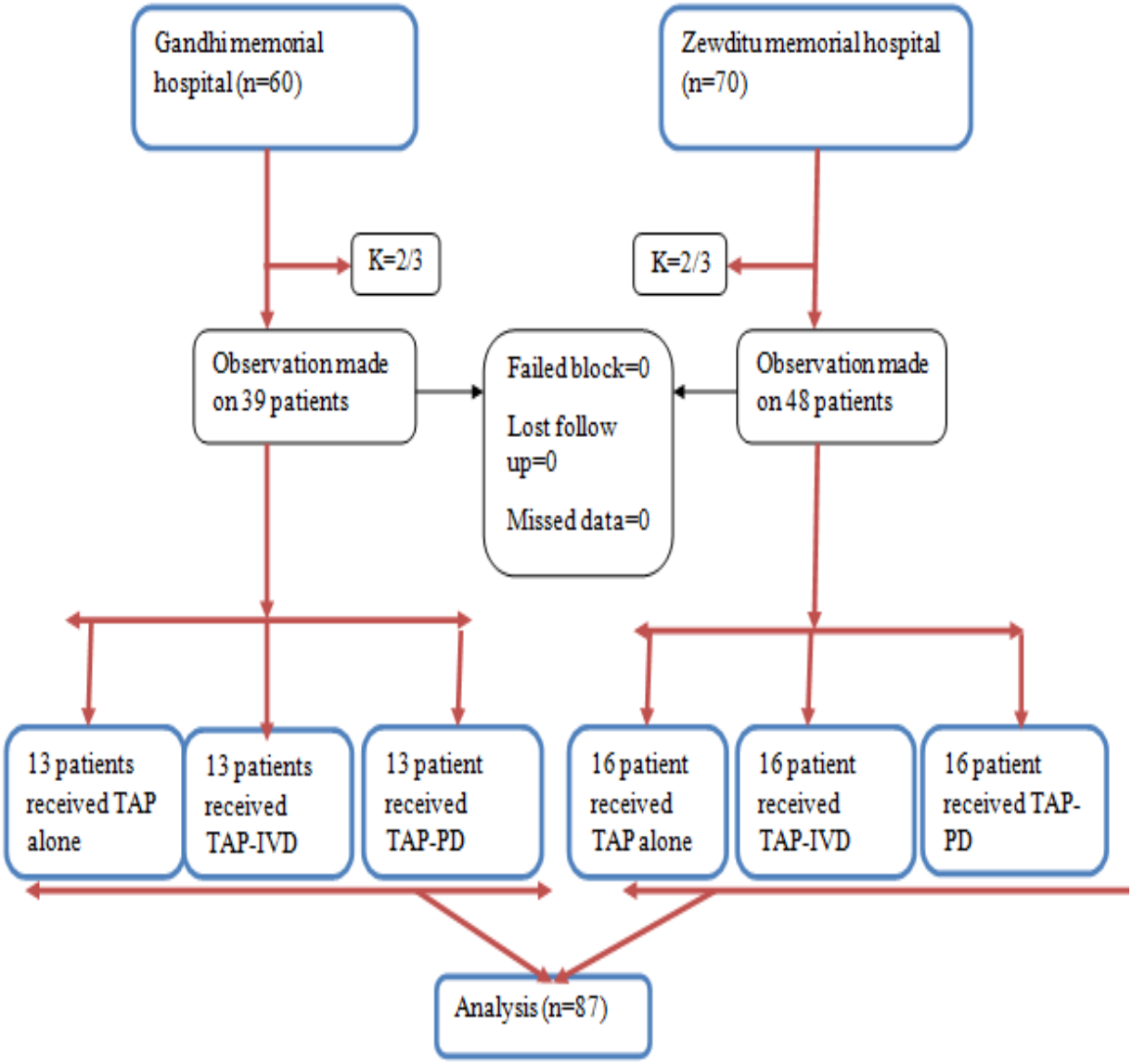


Figure 1: proportional allocation and enrollment chart of patients who underwent elective cesarean section in Gandhi and zewditu memorial hospital, Addis Ababa, 2018/19

Exposed: TAP-IVD and TAP-PD

Non-exposed: TAP alone

4.8. Data Collection Procedures

Before data collection, training was given for data collectors with a brief short lecture about NRS scoring system and practical session when appropriate. Data was collected using pretested questionnaires. All patients scheduled for elective CS who fulfill inclusion criteria and volunteer to take part in the study was thoroughly assessed before surgery by history taking, and chart review following informed consent. On the morning of the surgery data collector instructed the patient on how to self-report pain using the eleven point NRS score 0 to 10.

On arrival of the patients to the operative theater, and after application of the routine hospital monitoring protocol, HR, noninvasive blood pressure, and SPO2 has been recorded before institution of spinal anesthesia, then all patient received spinal anesthesia between L3-L4 level with 2-3 ml of 0.5% bupivacaine (according to the height of the patient) using 25 or 26-Gauge spinal needle based on the responsible anesthetists preference. After this, all patients were repositioned in supine position and level of sensory block was assessed and tested by pinprick sensation. Then, the necessary Intraoperative data was recorded

In both study hospital Msc anesthesia trainee have periodic rotation and they are well exposed for regional anesthesia for postoperative pain management as a part of multimodal analgesia at the end of surgery, most of Msc anesthetists or Msc students give regional anesthesia for postoperative pain management. In study hospital postoperative pain management for CS are done by either by bilateral TAP block with bupivacaine alone (40 ml (20ml each side), 0.25%), with IV dexamethasone (8mg) or perineural dexamethasone (8 mg) depending the decision of anesthetist in charge. The block was performed by using a standard land mark technique immediately after skin closure.

TAP alone, TAP-IVD and TAP-PD

Under aseptic technique, after identifying lumbar triangle of Petit as an access point to the neurofascial plane, TAP block has been performed by Msc anesthesia trainee or staff Msc on duty with the patient lying in supine position. This triangle is bounded posteriorly by the

latissimus dorsi muscle, anteriorly by the external oblique, and inferiorly by the iliac crest. Following aseptic preparation of the skin, 22G blunted needle was advanced perpendicular to skin 2cm above anterior superior iliac spine in triangle of petit, as the external oblique muscle is pierced a characteristic 'click' or 'pop' was felt and as the needle was advanced further a second 'click' was felt as the internal oblique muscle is pierced then after care full aspiration 20ml of 0.25% bupivacaine (for one side) was injected in the facial plane.

Eight (8) mg Dexamethasone was given either mixed with bupivacaine or IV immediately when the block is performed (for TAP-PD and TAP-IVD respectively).

The same procedure has been performed at the contra lateral side and the patients were transferred to the obstetric recovery ward after the procedure

After the block there was a close observation by responsible anesthetist for any complication, and then patients were transferred to PACU then to maternity ward. Often if TAP block was performed the responsible gynecologist and obstetrician or the resident wrote the pain management as PRN basis for ward nurses. There is continuous follow up by the responsible nurses in the ward. Hemodynamic parameters (HR, SPO2 and BP) and any analgesic or other medication given will be documented with dose and time.

The pain management practice of both hospitals was as per WHO post-operative pain management guideline i.e mild pain (NSAIDs, mainly Diclofenac), moderate pain (NSAIDs (Diclofenac) +week opioid (tramadol)) and severe pain ((NSAIDs (Diclofenac) +week opiods mainly tramadol + any available strong opioids).

Postoperative pain was assessed in all groups using a NRS score. The scale consists of horizontal lines ranging from 0 (no pain) to 10 (worst imaginable pain). Patients were asked to report their pain based on 11 point NRS score. The pain intensity was rated as no pain (NRS: 0), mild (NRS: 1–3), moderate (NRS: 4–6), and severe (NRS: 7–10). The first NRS score was recorded at 4^{th} hr of the procedure and then at 6^{th} , 8^{th} , 12^{th} and 24^{th} hr. The pain score was assessed during a quiet breathing period or at rest (static NRS) and after voluntary cough/ movement (dynamic NRS). The time to the first request and total analgesic consumption of each patient was recorded from the chart. At the times of pain evaluation, the heart rate, the mean arterial blood pressure, respiratory rate, SPO2 and analgesic requirement was assessed. Any postoperative adverse

events such as nausea, vomiting and shivering were recorded and informed for the clinicians on duty for treatment

4.9 Data quality control

To assure the reliability and validity of the data, questionnaire was pretested along the pilot study before the actual data collection. Training and orientation about the objectives and relevance of the study, each items included in the study tools and the whole process of data collection were provided for data collectors and supervisors. Consent was obtained from the patients. During data collection, regular supervision and follow were undertaken. The supervisor has checked each questionnaire daily with further cross check by principal investigator for completeness and consistency of data. Data clean up and crosschecking of missing data was done by multiple imputation method before analysis on SPSS.

4.10 Data analysis and interpretation

Data were entered and analyzed by SPSS V 20. The data were tested for normality using histogram and Shapiro–Wilk normality test and homogeneity of variance by Levene's test for normally distributed. Normally distributed and continuous data were analyzed using one way analysis of variance (ANOVA) with post hoc analysis for multiple tests and non-normally distributed data were analyzed using kuruska-walih H rank test with pairwise comparison (post hoc). Time to first analgesic request was analyzed using Life table, log rank Kaplan–Meier survival curves.

The comparisons of categorical variable were analyzed using Pearson chi-square test or Fisher's exact test. Data were presented as mean ±SD for normally distributed, median ± IQR (25th–75th percentile) and mean rank for non normally distributed data (decision was made by visual inspection of box plot) and categorical data were presented as numbers and frequencies (percentages). P-values <0.05 were considered statistically significant.

4.11 Ethical consideration

Ethical clearance was obtained from the department ethical clearance committee before the start of the study. Official support letter was written to the Hospitals and permission for data collection were sought from the responsible authorities. The purposes and the importance of the study were explained and verbal as well as written informed consent was obtained from each

participant. Confidentiality was maintained at all levels of the study by avoiding identifiers and using codes to identify patients. The participant's involvement in the study were on a voluntary basis, participants who are not willing to participate in the study and those who wish to quit their participation at any stage were informed and allowed to do so without any restrictions.

4.12 Dissemination plan

The research will be presented for the entire department of anesthesia staff. It will also be presented at the annual research conference. The research will be submitted to reputable journals for publication.

CHAPTER FIVE: RESULTS

5.1 Demographic and perioperative Characteristics

Eighty seven (87) patients participated in this study based on whether they received TAP-IVD (transversus abdominis plane block with intravenous dexamethasone) or TAP-PD (transversus abdominis plane block with perineural dexamethasone) at the end of surgery for postoperative analgesia as exposed group and those with TAP (transversus abdominis plane block) alone during postoperative period as control group. There was no significant difference among the three groups with regard to age, BMI, operation duration, Parity, indication for surgery, baseline MAP and HR (p value > 0.05). Previous cesarean section scar was the commonest indication for CS but there is no statistical difference between three groups as depicted in Table 1.

Table 1socio demographic and perioperative characteristics of patients who underwent elective cesarean section in Gandhi and zewditu memorial hospital, Addis Ababa,2018/19

	TAP alone	TAP-IVD	TAP - PD	P-Value
Age(year)	29.3±4.2	29.7±4	29.5±4.5	0.951
BMI(kg/m2)	26±1.2	25.8±1.2	26±1.2	0.745
Duration of surgery (min)	50±11.6	47.6±9.7	48.8±10.6	0.692
Parity				0.810
• Nulliparous (n, %)	10 (11.5%)	10 (11.5%)	8 (9.2%)	
• Multiparous (n, %)	19 (21.8%)	19 (21.8%)	21 (24.1)	
Previous cesarean section				
• Yes (n, %)	16 (18.4%)	15 (17.2)	19 (21.8%)	0.872
• No (n, %)	13 (14.9%)	14 (16.1)	10 (11.5%)	
Indications				0.885
• Previous CS scar (n, %)	16 (18.4%)	15 (17.2)	19 (21.8%)	
• Big baby (n, %)	7 (8%)	10 (11.5%)	6 (6.9%)	
• Malpresentations (n, %)	4 (4.6%)	3 (3.4%)	3 (3.4%)	
• Others (n, %)	2 (2.3%)	1 (1.1%)	1 (1.1%)	
Experience				
• year 1 Msc student	2 (2.3%))	0 (0%)	0 (0%)	0.193
• year 2 Msc student	26 (29.9)	27 (31%)	25(28.7%)	
• Msc	1 (1.1%)	2 (2.3%))	4 (4.6%)	
Baseline MAP	95 ±1.8	94.9±1.8	94.6±1.9	0.679
Baseline HR	88.2±1.8	88.6±2.4	89±1.9	0.306

Value are presented as: Mean± SD, Number (%), One way ANOVA test, chi-square test and $p<0.05$ is statistically significant.

5.2 Comparison of time to first analgesia request

Kaplan-Meier curve for the first analgesic request with the patient not receiving any analgesics after 24 h censored to the right presented in figure 2

TAP-PD and TAP-IVD groups had a median time to first analgesic request of 9 hr (95% CI, 8-10) and 7.5h (95% CI, 6.5-8.5) respectively, which were longer than the TAP alone group 5hr (95% CI, 4.4-5.6). A log rank test revealed that the survival distributions for the three groups were statistically significantly different, χ^2 (2) = 19.789, $p < .0005$.

Pairwise log rank comparisons with a Bonferroni correction shows there was a statistically significant difference in survival distributions for TAP –IVD vs TAP alone, $\chi^2(1) = 9.39$, $p = .002$, and TAP-PD vs TAP alone, $\chi^2(1) = 15.705$, $p < .0005$. However, the survival distributions for TAP-PD vs TAP –IVD were not statistically significantly different, χ^2 (1) = 1.427, $p = .235$

Life table shows cumulative proportion of patient not requesting analgesia within 6hr after admission to recovery in TAP alone group was 28% compared to 73% and 83% in TAP-IVD and TAP-PD group respectively.

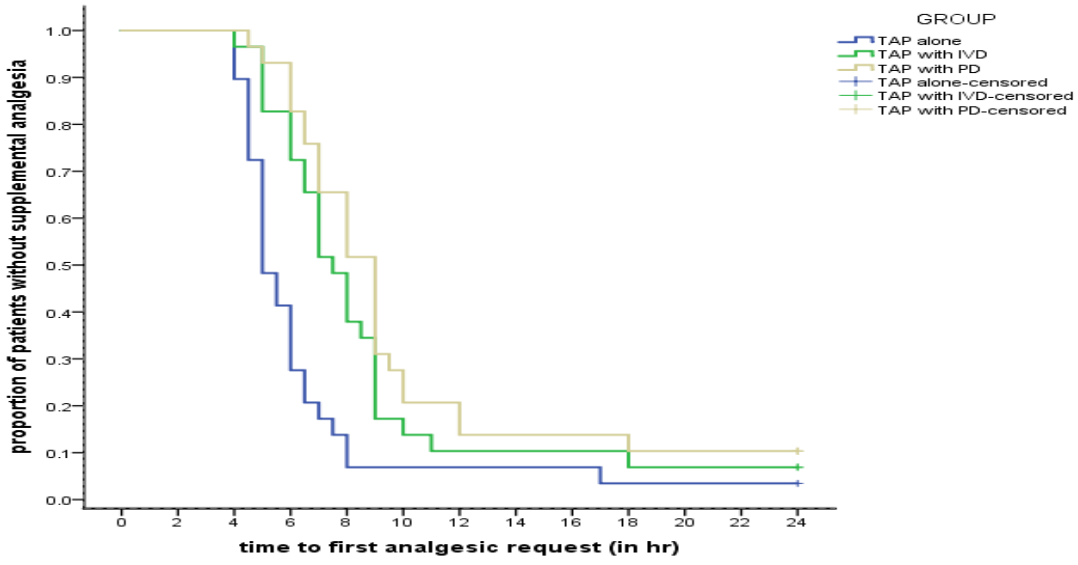
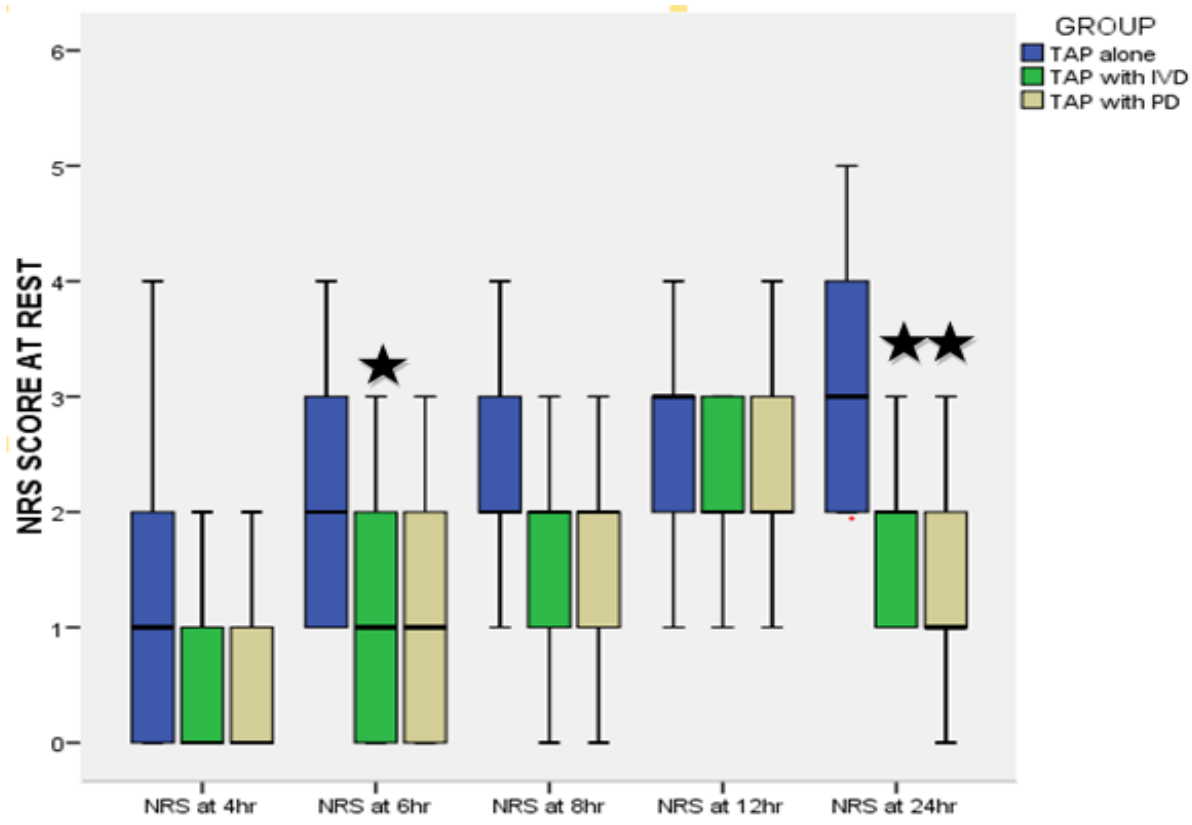


Figure 2 Kaplan Meier survival plot for time to first analgesic request of participants after TAP alone, TAP-IVD and TAP-PD in Gandhi and Zewditu memorial hospitals, Addis Ababa, 2018/19.

5.3 Comparison of Postoperative Numeric Pain Rating scale at Rest and coughing

A Kruskal-Wallis test was conducted to determine if there were differences in NRS score between the groups: TAP alone (n=29), TAP-IVD (n=29), TAP-PD (n=29) and it revealed that the difference in NRS scores was not statistically significant at 4^{th}, 8^{th} and 12^{th} hours (p>0.05) between three groups at rest. The mean ranks of NRS scores were statistically significantly different between groups at 6^{th} ($\chi 2$ (2) = 17.5, p< 0 .0001) and 24th hr ($\chi 2$ (2) = 39.7, p < 0 .0001). Subsequently, post hoc analysis was made and it revealed statistically significant differences in NRS scores between TAP- PD (mean rank = 35.47) and TAP alone (mean rank = 59.48) (p = .001) and TAP-IVD (mean rank=37.05) and TAP alone (p = .001) groups at 6^{th} hr at rest, but not between TAP- PD and TAP- IVD groups. Additionally, post hoc analysis revealed a statistically significant difference between TAP- PD and TAP alone, TAP- PD and TAP-IVD and TAP- IVD and TAP alone with adjusted *p value*= 0.014, 0.0001 and 0.002 respectively at 24^{th} at rest.

NRS scores of TAP-PD group were lower than TAP-IVD at all time during 24 hour at rest but, these were not statistically significant except at 24^{th} hour with adjusted p value of <0.0001

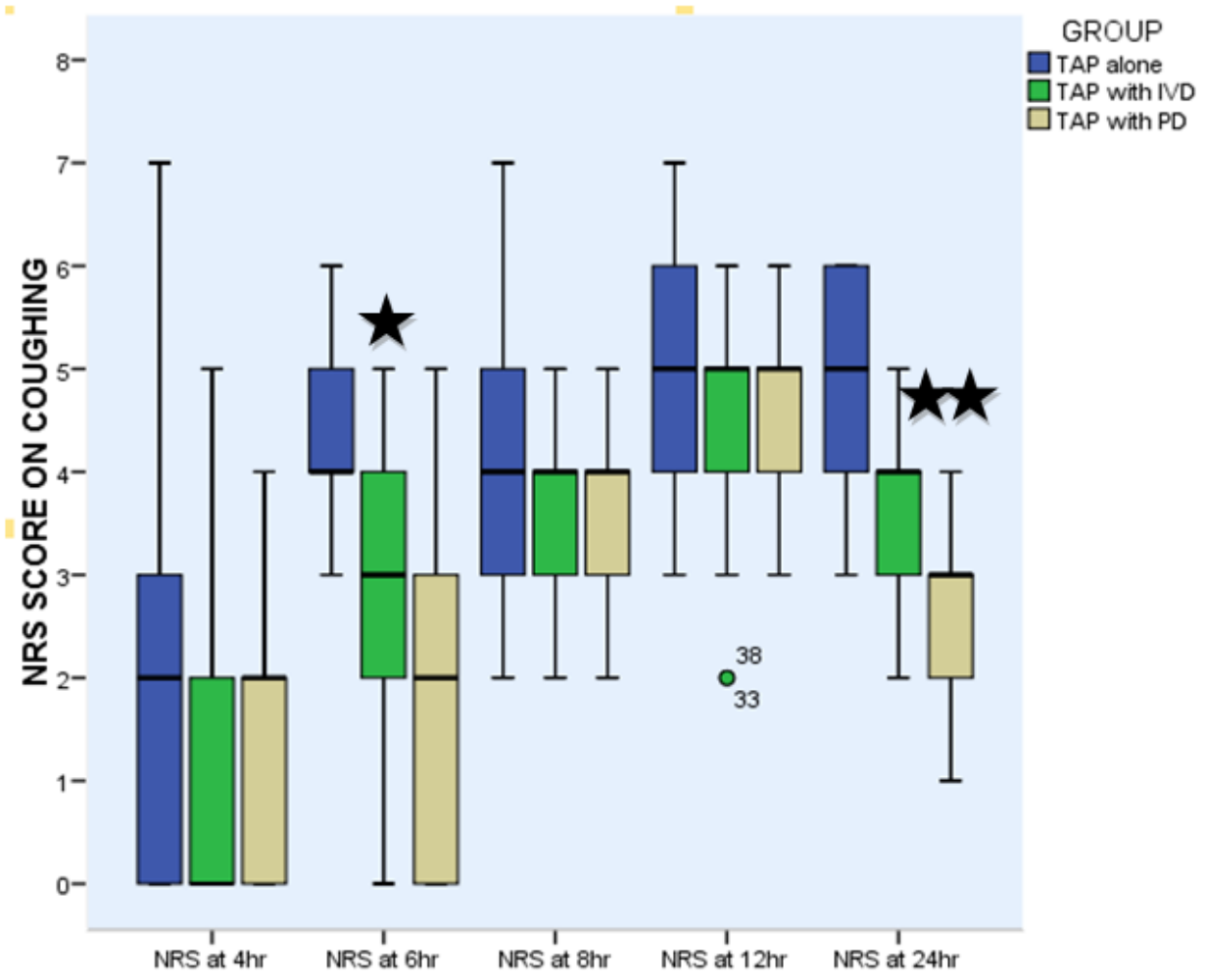


★p<0.05 compared to TAP alone, ★★ p <0.05 between the three groups

Figure 3Comparison of postoperative pain of participants using 11 point NRS score (0-10) at rest in Gandhi and Zewditu memorial hospitals, Addis Ababa, 2018/19.

The Kruskal Wallis test revealed that the median NRS score were not significant at 4th, 8th and 12th hours (p>0.05) between three groups at coughing. The NRS score were significantly different between the groups at 6th ($\chi 2$ (2) = 31.04, p < .0001) and 24th hr ($\chi 2$ (2) = 36.36, p < .0001) post -operatively on coughing. Post hoc analysis shows significant reduction in NRS score between TAP-PD and TAP alone, TAP-IVD and TAP alone at 6th hour on coughing with adjusted p value<0.0001 in both cases, but not between TAP-PD and TAP- IVD groups(p>0.05). Significant difference in NRS score was also seen in all pairwise comparison groups at 24th hour on coughing.

NRS scores of TAP-PD group were lower than TAP-IVD at all time during 24 hour but, these were not statistically significant except at 24th hour with adjusted p value of <0.0001



★p<0.05 compared to TAP alone, ★★ p <0.05 between the three groups

Figure 4 Comparison of postoperative pain of participants using 11 point NRS score (0-10) on coughing in Gandhi and Zewditu memorial hospitals, Addis Ababa, 2018/19

5.4 Comparison of cumulative analgesia consumption between groups

A Kruskal-Wallis test revealed total tramadol and Diclofenac consumption were significantly different between groups $\chi 2$ (2) = 25.06, p < .0001 and $\chi 2$ (2) = 19.93, p =, 0001 respectively. Pairwise comparison (Post hoc analysis) shows significant difference in median total tramadol consumption between TAP-PD (median = 50) vs TAP alone (median=100) (p<0.0001) and TAP-IVD (median=50) vs TAP alone (p<0.0001) but not between TAP- PD and TAP- IVD groups (p=1). It also showed significant reduction in median (IQR) total Diclofenac consumption between TAP-PD (75(0-75)) vs TAP alone (75 (75-150)) (p<0.0001) and TAP-IVD (75(75)) vs TAP alone (P<0.0001) but not between TAP- PD and TAP- IVD groups (p=0.186).

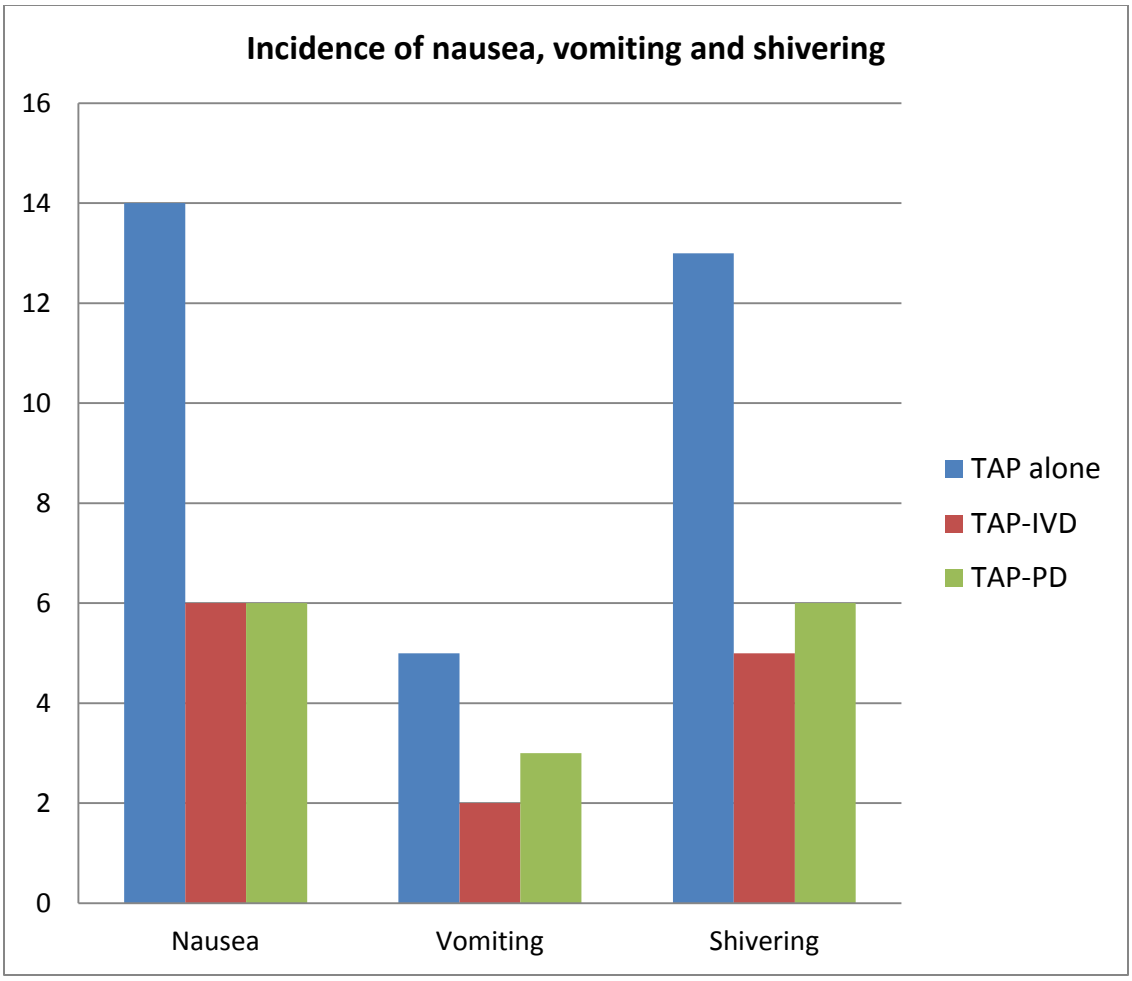
Table 2 Cumulative analgesic consumption of participants after TAP alone, TAP-IVD and TAP-PD in Gandhi and Zewditu memorial hospitals, Addis Ababa, 2018/19.

	TAP alone	TAP-IVD	TAP- PD	P-Value
Cumulative analgesic consumption				
• Total tramadol in mg	100(100-150)	50 (0-100)$^{+}$	50 (0-100)$^{+}$	<0.0001
• Total Diclofenac in mg	75 (75-150)	75(75)$^{+}$	75(0-75)$^{+}$	<0.0001

$^{+}p< 0.05$ compared to TAP lone group, Value are presented as median (IQR), Kruskal-Wallis test with pairwise comparison

5.5 Incidence of postoperative complications

The incidence of nausea over 24 hours was 30%. The proportions of patients with nausea was higher (48%) In TAP alone group compared to TAP-IVD (20.7%) and TAP-PD (20.7%) group, X^2 (2, N=87) =7.021, p= 0.03, $\varphi_{c= 0.28}$. But not between TAP-IVD and TAP-PD groups. The rate of vomiting was comparable in all the three groups X^2 (2, N=87) =1.58, p=0.453. The incidence of post operative shivering was (27.5%). The proportion of post-operative shivering was lower in TAP-PD (18.5%) and TAP-IVD (17.2%) when compared to TAP alone (44.8%) , X^2=3.867, p=0.038, $\varphi_{c=0.28.}$



Data are absolute number of patients (Chi-Square Test)

Figure 5 incidence of post operative nausea, vomiting and shivering of participants after TAP alone, TAP-IVD and TAP-PD in Gandhi and Zewditu memorial hospitals, Addis Ababa, 2018/19.

CHAPTER SIX: DISCUSSION

In our study, TAP-PD and TAP-IVD significantly decreased postoperative pain, reduced total analgesic consumption and prolonged the median time to first analgesic request in postoperative period after elective cesarean section under spinal anesthesia.

We found that TAP-PD and TAP-IVD provide comparable level of median time to first analgesic request 9hr (95% CI, 8.023-9.977) and 7.5h (95% CI, 6.511-8.489) (p=) respectively which were significantly higher than TAP alone 5hr (95% CI, 4.414-5.586) with p value of < .0005.

This was comparable with the previous RCT on 104 patients by Falia MD et al on comparison of dexamethasone and clonidine as an adjuvant to bupivacaine in TAP block for CS ,which showed about 90% of the perineural dexamethasone with TAP group requested analgesia within 10 hr of post operative period (37). Similar to our finding, another RCT by Fouad et al evaluating efficacy dexamethasone added to bupivacaine in ultrasound guided transversus abdominis plane block showed that time to first analgesic request (TFA) was significantly longer in the dexamethasone group when compared to control (TAP alone) group (438.2 ± 24.95 min vs. 272.04 ± 37.51 min, P=0.002) (46). This finding was also supported by *Zhao et al* (40) which evaluated the effectiveness of Perineural versus intravenous dexamethasone as an adjuvant in peripheral nerve block and showed the effect of perineural and intravenous dexamethasone was equivalent concerning duration of analgesia.

In agreement with our finding *Uma Datt Sharma*(60) also studied the effectiveness of perineural dexamethasone as adjuvant to ropivacaine on transversus abdominis plane block showed that the dexamethasone group showed statistically significant prolongation in time to first analgesic request when compared to the control (TAP alone) group with a median time of (547.5 vs 387.5, p<0.001.

A prospective cohort study by *Molla Y* and his colleagues in Gondar, Ethiopia also evaluated the effectiveness of transversus abdominis plane block after abdominal surgery and showed the median (IQR) time to first analgesic request for TAP block was 360(500) minutes, which was comparable with our finding(43).

In accordance with our finding prospective RCT by *Ammar and Mahmoud* assessing effect of adding dexamethasone to bupivacaine on transversus abdominis plane block for abdominal hysterectomy showed TFA was significantly longer in the dexamethasone group when compared to placebo (459.8 vs. 325.4 min, P=0.002) (47). Furthermore, another study also showed perineural and intravenous dexamethasone has equivalent analgesic benefits and similar safety profiles when used an adjuvant to peripheral nerve block (61). *Rosenfeld et al* (35) also showed only there was a mean 1.3 hr difference between intravenous and perineural dexamethasone in terms of time to first analgesic request, which is comparable with our study which showed only median 1.5 hr difference.

In contrary to our finding *Heesen et al* that there was 241(95% CI ,87-394) minute prolongation in TFA in perineural dexamethasone when compared to intravenous dexamethasone in peripheral nerve blocks(54). This discrepancy could be due to a difference I study design, variability in population and surgical procedures (their study included upper and lower extremity blocks). Additionally, another study also showed significant difference between the perineural and intravenous dexamethasone when used as adjuvant for axillary block ($p<0.001$)(57). This difference can be strongly explained by addition of 5mcg/ml adrenaline, 1% Lidocaine with bupivacaine and difference in surgical procedure and the block.

Our study showed statistically significant differences in NRS scores between TAP- PD and TAP alone ($p<0.05$) and TAP-IVD and TAP alone ($p<0.05$) groups at 6^{th} and 24^{th} hr at rest and on coughing. There was no statistically significant difference in NRS score between TAP-PD and TAP- IVD group at all time during 24 hours except at 24^{th} hour with adjusted p value of <0.0001. This is in line with a study by *Mamatha Raghukumar et al*(37) which showed a higher VAS score in TAP alone and lower VAS score in TAP with perineural dexamethasone groups at 24^{th} hour post operatively after cesarean delivery.

Our finding was also comparable with a study by *Abdelhamid et al* (56) who investigated the efficacy and safety of dexamethasone an adjuvant to local anesthetics in lumbar plexus block and showed a statistically significant lower VAS score at 24^{th} hr between intravenous 5 (0-50) and perineural dexamethasone 0 (0-50) when compared to bupivacaine alone 40(0-90) group ($p<0.05$). similarly, another study in Ireland by *Szucs et al* (62) also showed preoperatively administered 0.1mg/kg dexamethasone intravenously showed superior analgesic profile at 6^{th} hr

when compared with placebo with NRS score of 0.8±1.3 vs 3.9 ±2.9 (p =0.0004). In agreement with our finding *Kertalov A* et also studied the effect of adding dexamethasone as a ropivacaine adjuvant in ultrasound guided transversus abdominis plane block showed that the there is a statistically significant difference in median VAS score between TAP with perineural dexamethasone and TAP alone group at 6^{th} (1 vs 2, p<0.001) and 24^{th} hours (1 vs 2, p<0.001) respectively (63)

In contrast to our study a study by *Fouad et al* revealed that there was no difference in VAS score between TAP-alone and TAP with perineural dexamethasone group at 24^{th} hr both at rest and movement after inguinal herniorraphy (46). This can be due to difference in surgical procedure, design and follow up interval. Furthermore, another study in Egypt showed addition of dexamethasone to bupivacaine for transversus abdominis plane block significantly decreased VAS score at 2hr (4.9 vs. 28.1, P=0.01),4hr (12.2 vs. 31.1, P=0.01) and 12hr (15.7 vs. 25.4, P=0.02) but not at 24^{th} hr (p=0.41)(47). This can be due to different dose of bupivacaine (they used 20ml only) and difference in population and study design

Robert Wegner and his colleagues in Texas evaluated the effect of 8mg dexamethasone to ropivacaine in TAP block for inguinal hernia repair and Spermatocelectomy and showed that there is no difference in pain severity between TAP with dexamethasone and TAP alone groups within 24 and 48 hrs post procedure (p>0.05) (49). Again this discrepancy could be due to difference in population, study design, local anesthetic used (ropivacaine vs bupivacaine).

Our study found a significantly reduced post-operative analgesic consumption (tramadol and Diclofenac) in both dexamethasone groups when compared to the control (TAP alone) group.

In agreement with our find a RCT by *Sachdeva and Sinha* on 70 patients also investigated the effect of dexamethasone as additive to Ropivacaine on ultrasound-Guided Transversus abdominis plane block in Cesarean Section, and showed decreased tramadol requirement postoperatively in dexamethasone when compared to the non dexamethasone group (100.00 ± 0.00 vs. 140.00 ± 50.26 mg, P = 0.046) (48)

.

Ammar and mahmoud (47) also studied the effect of adding dexamethasone to bupivacaine on TAP block for abdominal hysterectomy and showed that the total post operative 24 hr morphine consumption was significantly reduced in dexamethasone group 19.2 (8.1-24.2) vs 4.1(1.7-6.2) p=0.01. This was comparable with our finding when an opioid conversion factor of morphine to tramadol is applied (1:10). *Zhao et al.* also showed the two routes of administration (intravenous and perineural) did not show any significant difference in post op analgesic consumption(40).

Small dose intravenous dexamethasone (2mg) significantly reduced post-operative rescue tramadol requirement when compared to placebo group 38.00 ± 20.5mg vs 173.33 ± 34.07 respectively ($p<0.05$) over 24 hr and this is in-line with our finding even if there is a difference in dose of dexamethasone (53).

Desale et al (44) in Asmara, Eritrea conducted a randomized control trial on effectiveness Transversus abdominis plane block after Caesarean section in an area with limited resources showed the mean ± SD Diclofenac consumption was 87.21 ± 51.20. This was comparable with our finding which showed a total Diclofenac consumption of 75 (75-150) in TAP alone group.

In contrast to our finding, one systematic review and metanalysis evaluating effectiveness of perineural vs intravenous dexamethasone group showed that perineural dexamethasone patients consumed slightly less oral opioids at 24 hours than IV dexamethasone patients (p=0.029) (64). This difference can be due to difference in study design, variability in doses of dexamethasone doses, difference in pain management protocol and differences in surgical procedures.

A prospective cohort study by *Molla Y* and his colleagues in Gondar, Ethiopia also evaluated the effectiveness of transversus abdominis plane block after abdominal surgery and showed the median (IQR) total tramadol consumption was 38 (50) mg, which found a lower requirement than our finding, 100(100-150) mg (43). This discrepancy could be due to they include all emergency and elective abdominal surgery patient under general and spinal anesthesia; they used long acting opioid (pethidine) intra-operatively. Similarly, *Uma Datt Sharma* (60) also studied the effectiveness of perineural dexamethasone as adjuvant to ropivacaine on transversus abdominis plane block after spinal anesthesia showed that there was decrement in total tramadol consumption in 24 hour when compared to control group (223.33± 56.83 vs 293.33 ± 25.7, $p<0.001$) but, this result is by much higher than our finding, 50 (0-100) vs100(100-150). This

could difference could be justified by difference in population, difference in study design, difference in sample size and surgical procedure (hernia repair vs cesarean section).

Our study showed Incidence of nausea and shivering was significantly lower in the two dexamethasone groups when compared to the non dexamethasone group. This was comparable with a previous study showing significantly lower incidence of nausea in TAP with perineural dexamethasone group when compared to TAP alone(46). This finding is also in agreement with a study showing lower incidence of shivering in patients pretreated with dexamethasone (65)

Limitation

The current study has certain limitations, including the inability to use ultrasound-guided TAP block, lack of control over the confounding factor like incision size, dexamethasone and bupivacaine dose/kg, and participation of different anesthetist and surgeon. Shorter duration of postoperative follow up and Limited availability of similar studies for comparison were some of the limitations of our study

Strength

Comparable study groups in terms of socio demographic distribution, perioperative factors that affect study outcome and the same surgical procedure so that the difference observed may be due to exposure factors.

CHAPTER SEVEN: CONCLUSION AND RECOMMENDATION

7.1 Conclusion

Based on the finding of this study we concluded that, dexamethasone 8mg both intravenously and perineurally is effective adjuvant to bupivacaine on bilateral transversus abdominis plane block for post cesarean delivery pain control with both routes, prolonged time to first analgesic request, reduced total analgesic dose requirements. Perineural dexamethasone was effective in decreasing severity of pain at 24^{th} hr post operatively. We therefore conclude that two routes are a valuable alternative to each other for post cesarean delivery pain control.

7.2 Recommendation

Anesthetists: We recommend the alternative use of perineural or intravenous dexamethasone as an adjuvant to bupivacaine on bilateral transversus abdominis plane block for post cesarean delivery pain control after spinal anesthesia

Researcher: Further randomized control trial with adequate follow up period addressing postoperative complication study is recommended.

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Annex 1: Information sheet to get permission for the research

Introduction

This information sheet is prepared to explain the research project that you are asked to join by a research investigators.

The research team includes Msc students, two senior advisors from AAU and two nurses for data collection from Gandhi and Empress Zewditu Memorial Hospital.

Name of Principal investigator: - Abebayehu zemedkun

Advisor's name: - Mr.:- wosenyeleh Admasu

Ms.:- Siryet tesfaye

Name of sponsor: - AAU

Name of organization: - AAU, college of Health sciences, anesthesia department

This information sheet is prepared by the above mentioned investigator.

Risk

There is no any risk or harm that you will face by participating in this research. Any personal information recorded will not be copied and transferred to other bodies. No need of writing participants' name but by a code. Every piece of information will be kept confidentially.

Benefits

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 by the researcher and research assistant only. This research project will be reviewed and approved by ethical committee of the department. If you want to know more information, you can contact the committee through the address below.

1. Abebayehu Zemedkun - principal investigator
   Department of anaesthesia, Addis Ababa University
   Tel: 0900053426
2. Wosenyeleh Admasu – advisor
   Department of anaesthesia, Addis Ababa University
   Tel: 0911104940
3. Siryet tesfaye – advisor
   Department of anaesthesia, Addis Ababa University
   Tel:

Annex 2: 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 five 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 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 "comparison of the analgesic effectiveness of perineural and intravenous dexamethasone as adjuvant to bupivacaine on transversus abdominis plane block after caesarean delivery for the mothers operated under SA in mahatma gandi and zewditu memorial hospital from January to April 1019

I. English version questionnaire

Department of Anaesthesia College of Medicine and Health Sciences, AAU

Questionnaire identification number_____

Greeting

Hello, I am_____. I am working in the research team of Addis Ababa 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 "analgesic effectiveness between perineural and intravenous dexamethasone as adjuvant to bupivacaine on bilateral transversus abdominis plane block after caesarean delivery ". The research will be beneficial to those who undergone caesarean section to control their postoperative suffering from pain with less need of other analgesic drugs and reduced risk of postoperative nausea and vomiting and side effects of 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 AAU 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 analgesic effectiveness between perineural and intravenous dexamethasone as adjuvant to bupivacaine on bilateral transversus abdominis plane block after caesarean delivery in mahatma gandi and zewditu memorial hospital and forward some recommendation to concerned bodies that will help to improve postoperative pain management after caesarean delivery.

□መ□□ቅ □ቃት

ጤና ይስጥልኝ

እኔ ----------□ባላለሁ፡፡ በአዲስ አበባዮኒቨርሲቲ አንስቴዥዮያ ትምህርት □አል ውስ□ እ□ሰራሁ እቸኛለሁ፡፡ በቀዶ ጥገና ከወለዱ በኋላ ስለሚሰማዎት የሆድ ቁስለት ህመም የተወሰኑ ጥያቄዎችን ልጠይቅዎት □□ልፉለሁ፡፡

የዚህ መጠይቅ ዋና አላማ ቀዶ ጥገና ከተሰራሎት በኋላ የሚከሰት የሆድ ቁስለት ህመም ለማስታገሽ በባለሙያዎች ስለሚሰራው የማደንዘዣ አይነት በትክክል የሆድ ህመም ስቃይን ማስወገድ አለማስወገዱን ለማወቅ ነው፡፡

በዚህ ጥናት በመሳተፍዎ የሚደርስብዎ ምንም አይነት የጎላ ጉዳት የሌለ ሲሆን ለግልዎ □ሚ□ኙት ጥቅማጥቅም አይኖርም ነገር ግን የምርምሩ ውጤት ለወደፊቱ ቀዶ ጥገና

ለሚሰራላቸዉ ታካሚዎች □ሆት ቁስለት የህመም ስቃይን ለማስታገስ እና ሌሎች ማስታገሻ መዳህኒቶችን አላስፈላጊነት ለመቀነስ ከነዚህ መዳህኒቶች ጋር ተያይዘው የሚከሰቱ እንደ ማቅለሽለሽ □ እና ማስታወ□□መሳሰሉ ተጓዳኝው□ቶችን ለመቀነስ ነው። በጥናቱ ውስጥ ጥቂት ደቂቃዎችን የሚወስዱ ጥያቄዎችን በአምስት የተለያዩ ግዚያት□ እንጠይቀዎታለን።

በጥናቱ ላይ ስምምነትዎን መፃፍ የማያስፈልግ እና የሚሰጡትን ምላሾች ሁሉ በሚስጥር እንደሚያዙ ልንገልፅልዎት እንወዳለን።በጥናቱ ላይ መሳተፍ ካልፈለጉ አለመሳተፍ □ እንዲሁም መሳተፍ ጀምረው ማቋረጥ ቢፈልጉ ያለምንም ቅድመ ሁኔታ□ ማቋረጥ ይችላሉ። ነገር ግን □□እርሶ ለጥያቄዎቹ የሚሰጡትን ትክክለኛ ምላሽ ለጥናቱ ጥሩ የሆኑ የህመም ማስታገሻ ዘዴዎችን ለመምረጥ ይረዳናል።

ለመሳተአ □ቃ□ኛ ነዎት ?

ለመሳተአ □ቃ□ኛ ከሆኑ ወደ ሚቀጥለው ገፅ ይለፉ ለመሳተፍ ፈቃደኛ ካልሆኑ አመስግነውእ□ህ ላ□ □ቁሙ።

Annex:-3: Case report file / Data collection tool

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

S.NO	Question	Possible responses	code
101	Age (in year)	……	
102	Weigh (in kg)	…….....	
103	Height (in meter)	……	
104	Body mass index (in kg/m2)	.....	
105	Parity	1. Nulliparous 2. Multi parous	
106	Number of previous caesarean section	1. 0 2. 1 3. 2 4. 3 and above	
107	Does the patient have previous uterine incision for non cesarean surgery?	1. Yes 2. No If yes specify_____	
109	Does the patient has preexisting medical problem	1. Yes 2. No If yes specify _____	

Section 2: Data during preoperative period

Ser. number	Question	Response	Code
201	Base line Heart rate	____bpm	
202	Base line Blood pressure	_____mmhg	
203	Base line RR & spo2	_____br/m &_____%	
204	Diagnosis	_____	

Section 3: Questions related to spinal anesthesia and surgery.

S. No.	Parameter	Values	code
301	Duration of surgery	…….. Minutes	
302	Type of uterine incision	1. transverse 2. vertical	Code
304	Experience of the surgeon	1. R2 2. R3 3. R4 4. Senior	
305	Type of post op pain management groups	1. Tap alone 2. Tap with IV dexamethasone 3.TAP with perineural dexamethasone	
306	Year of Experience of anesthetist	1.Msc Y1 2. Msc Y2 3. Msc	

Section 4: Values of hemodynamic parameter on post-operative periods after surgery

S.NO	Time (in hour)	Parameter	Value	Code
401	At 4 hour of post-operative period	HR	…… bpm	
		SBP	…….mmhg	
		DBP	…….mmhg	
402	After 6 hour of post-operative period	HR	…….bpm	
		SBP	……..mmhg	
		DBP	……mmhg	
403	After 8 hour of post-operative period	HR	……bpm	
		SBP	……mmhg	

		DBP	……mmhg	
404	After 12 hours of post-operative period	HR	……...bpm	
		SBP	……mmhg	
		DBP	……mmhg	
405	At 24 hour of post-operative period	HR	……. bpm	
		SBP	……. mmhg	
		DBP	……. mmhg	

Section 5: questions related to severity of pain and analgesic consumption

401. Severity of pain on NRS postoperatively Severity of pain on movement/coughing type and dose of analgesics given

At 4 hr. _____ _____ _____

At 6 hrs. _____ _____ _____

At 8 hrs. _____ _____ _____

At 12hrs. _____ _____ _____

At 24 hrs. _____ _____ _____

Section 6: question about over all experience of post-operative pain in the past 48 post-operative hours

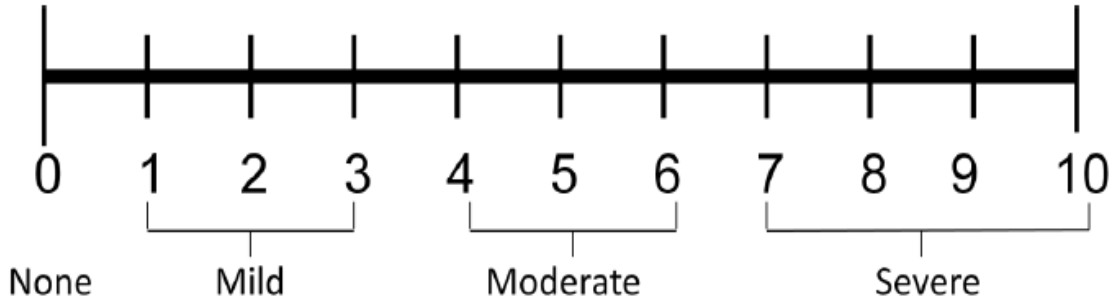
S.NO	Question	Possible response	Code
1301	Time before the first request of further analgesia	……min/hour	
1302	Total amount of opioid given in the last 24 hours o Opioid o Non opioid	 ----------mg ----------mg	

Section 7: Complications during the post-operative period

Type of complication	Score	Remark
Nausea	1.yes 2. no	
Vomiting	1. Yes 2. No	
shivering	1. Yes 2. no	
Others (specify)		

Section 8: numerical rating scale to measure severity of pain

The numeric analogue scale (NRS)



a) The scale will be taken 10 (5 at rest and 5 on coughing/movement) times within the first 24 hours. The patient will be asked one of the following questions:

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

- 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 ADLs)

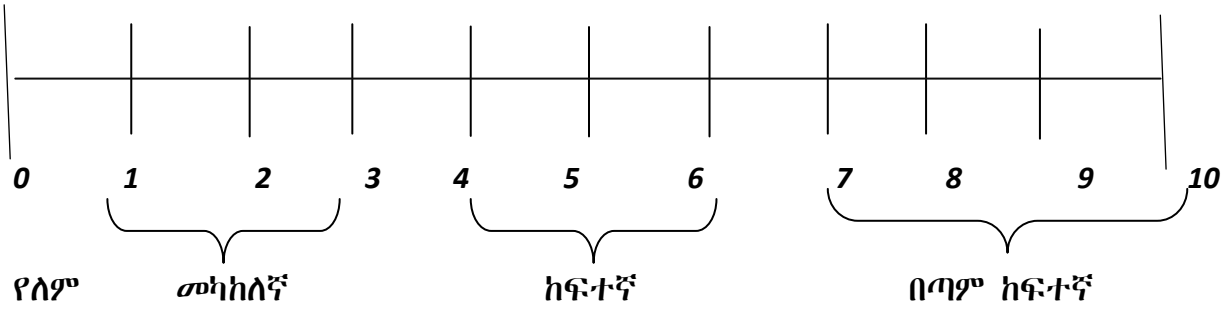
- ✓ Duration in minutes till initial analgesic requirement after the patient arrived in the ward

A. Arrived at _____pm/am {time per 24hr/date/month/ETH. year}

B. Analgesic required time _____PM/AM {time per24hr/date/month/ETH. year}

C. Duration _____

<u>አማርኛ ትርጉም</u>



መለኪያዉ በ 24 ሰአት ዉስጥ 10 ጊዜ የ ሚለካ ሲሆን ታካሚዎች የሚሰማቸዉ የህመም መጠን በየ 6 ሰአት ልዩነት እንዲያሳዩን እንጠይቃለን

ታካሚዎች የሚከተሉትን ጥያቄዎች ይጠየቃሉ፤-
ሀ . አሁን ከተገለጹት ቁጥሮች ማለትም (0-10) ባሉት ዉስጥ የእርስዎ የህመም መጠን ስንት ላይ ነው
ለ. ከላይ የተገለጸዉ በቂ ካልሆነ ተጨማሪ ማብራሪያ ይሰጦታል ፡
0 **ህመም የለም**
1-3 **መካከለኛ ህመም (መነጫነጭ፣መረበሽ፣ወ.ዘ.ተ)**
4-6 **ከፍተኛ ህመም (ከ ህመሙ በተያያዘ ስራን በ አግባቡ አለመስራት)**
7-10 **በጣም ከፍተኛ ህመም (እለታዊ ትግባራትን ማከናወን አለመቻል**

Annex -4: Data accuracy check sheet

<u>Code</u>: _____

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

Annex-5: Standard operating procedure /SOP/

Those patients who fulfill the standard of practice should be recruited to the study.

Step 1: Elective cesarean delivery performed under spinal anesthesia

Step 2: Following closure of the skin using antiseptic solution skin will be prepared at the area TAP block

Landmark to perform TAP block

Mid clavicular line, anterior superior iliac spine and triangle of petit are the main landmarks for the TAP block. Triangle of petit is formed laterally by latissimus dorsi, anteriorly by external oblique muscle, inferiorly by superior boarder of anterior superior iliac crest. 2 cm above the anterior superior iliac crest in mid clavicular line should be marked.

Technique – TAP alone, TAP-IVD and TAP-PD

Under aseptic technique, after identifying lumbar triangle of Petit as an access point to the neurofascial plane, TAP block should be performed by dominant hand by putting non dominant

hand fingers 2 cm above the anterior superior iliac spine in the triangle of petit. 22G blunted needle (to feel the pop sounds) should be advanced perpendicular to skin, as the external oblique muscle is pierced a characteristic ‘click’ or ‘pop’ should be felt and as the needle was advanced further a second ‘click’ was felt as the internal oblique muscle is pierced then after care full aspiration 20ml of 0.25% bupivacaine (for one side) needs to be injected in the facial plane.

Eight (8) mg Dexamethasone should be given either mixed with bupivacaine or IV immediately when the block is performed (for TAP-PD and TAP-IVD respectively).

The same procedure should be performed at the contra lateral side

Annex 6: Classification of Obesity based on BMI.

BMI(kg/m2)	Description
<18.5	Underweight
18.5–24.9	Normal
25–29.9	Overweight
30–34.9	Obesity (class I)
35–39.9	Obesity (class II)
≥40	Morbid obesity (class III)
≥50	Super obesity
≥60	Super -super obesity

Adopted from Paul G. Barash clinical anesthesia 7th edition.

Annex 7: America n Society of Anesthesiologists (ASA) physical status classification of patients

ASA PS Classification	Definition	Examples, including, but not limited to:
ASA I	A normal healthy patient	Healthy, non-smoking, no or minimal alcohol use
ASA II	A patient with mild systemic disease	Mild diseases only without substantive functional limitations. Examples include (but not limited to): current smoker, social alcohol drinker, pregnancy, obesity (30<BMI<40), well-controlled DM/HTN, mild lung disease
ASA III	A patient with severe systemic disease	Substantive functional limitations; One or more moderate to severe diseases. Examples include (but not limited to): poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, ESRD undergoing regularly scheduled dialysis, premature infant PCA < 60 weeks, history (>3 months) of MI, CVA, TIA, or CAD/stents.
ASA IV	A patient with severe systemic disease that is a constant threat to life	Examples include (but not limited to): recent (<3 months) MI, CVA, TIA, or CAD/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, sepsis, DIC, ARD or ESRD not undergoing regularly scheduled dialysis
ASA V	A moribund patient who is not expected to survive without the operation	Examples include (but not limited to): ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organ/system dysfunction
ASA VI	A declared brain-dead patient whose organs are being removed for donor purposes	

Adopted from: ASA physical status classification last approved by the ASA House of Delegates on October 15, 2014