
# POST-OPERATIVE ANALGESIC EFFECT OF CAUDAL NEOSTIGMINE ADDED TO BUPIVACAINE AS COMPARED WITH CAUDAL BUPIVACAINE ALONE FOR PEDIATRIC ELECTIVE INFRA UMBILICAL SURGERY AT TIKUR ANBESA SPECIALIZED HOSPITAL.

**THESIS TO BE SUBMITTED TO DEPARTMENT OF ANESTHESIA, SCHOOL OF MEDICINE, COLLEGE OF HEALTH SCIENCE, ADDIS ABABA UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR MASTER OF SCIENCE IN ANESTHESIA.**

**BY: YITAYAL GUADIE**

**JUNE, 2020 G.C**

**ADDIS ABABA, ETHIOPIA**

**ADDIS ABABA UNIVERSITY**

**COLLEGE OF HEALTH SCIENCE**

**SCHOOL OF MEDICINE**

**DEPARTMENT OF ANESTHESIA**

# ASSESSMENT OF POSTOPERATIVE ANALGESIC EFFECT OF CAUDAL NEOSTIGMINE ADDED TO BUPIVACAINE FOR PEDIATRIC ELECTIVE INFRA UMBILICAL SURGERY.

**PRINCIPAL INVESTIGETOR: YITAYAL GUADIE (BSc, MSc student in anesthesia)**

**E- mail:guadyitu@gmail.com**

**Advisers:**

**1 .Wosenyeleh Admasu (BSc, MSc in ACA, Lecturer, Ass prof)**

**2. Senait Awoke (BSc, MSc in ACA, Lecturer)**

**JUNE, 2020 G.C**

**ADDISS ABABA, ETHIOPIA**

# Declaration

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

Student name: Yitayal Guadie

Date _____ 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 Anesthesia.

| Name of approval advisors | Date | Signature |
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| 2._____ | _____ | _____ |

## Acknowledgement

I would like thank to Addis Ababa University, Collage Health Science and department of anesthesia for adding the research program in the curriculum that will lay the foundation for my future career development and academic engagement on research**.**

I also would like to express my heartfelt gratitude to my advisers: Wosenyeleh Admasu and Senait Awoke for their unreserved guidance and constructive suggestions from the stage to develop thesis.

I would like also to extend my appreciation to Amanu Gashaw and, my friends and others those who had helped me a lot in giving additional advice.

Finally I would like to say thank to my data collectors and study participants.

## Acronyms

| | |
|---|---|
| AIDS | Acquired Immune Deficiency Syndromes |
| ASA | American Society of Anesthesiologist |
| BAG | Bupivacaine Alone Group |
| BNG | Bupivacaine Neostigmine Group |
| BP | Blood Pressure |
| CB | Caudal Block |
| CNS | Central Nerve System |
| FLACC | Face Legs Activity Cray Consolable |
| FMOH | Federal Ministry of Health |
| HIV | Human Immunodeficiency Virus |
| Hr | Hour |
| HR | Heart Rate |
| IQR | Inter Quartile Range |
| M | Median |
| NRS | Numerical Rating Scale |
| OPS | Objective Pain Scale |
| PACU | Post Anesthesia Care Unit |
| PCM | Paracetamol |
| PONV | Postoperative Nausea and Vomiting |
| POP | Postoperative Pain |
| PSIS | Posterior Superior Iliac Spine |

| | |
|---|---|
| SD | Standard Deviation |
| SPSS | Statistical Package for Social Science |
| TASH | Tikur Anbesa Specialized Hospital |
| VS | Vital Sign |
| WHO | World Health Organization |

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# ABSTRACT

**Background:** Caudal epidural block is one of the most commonly used, popular, safe and easy regional anesthetic techniques to be performed in children undergoing infra-umbilical surgeries. The main disadvantage of single-shot caudal anesthesia is the short duration of action. Neostigmine is one of adjuvant with local anesthetic agents to improve the efficiency and quality to prolong the duration of analgesia after surgery.

**Objective:** To assess the effect of adding neostigmine to bupivacaine on post-operative analgesia in pediatric patient during infra umbilical surgery at Tikur Anbesa specialized hospital from November1, 2019 to January 30, 2020 G.C.

**Methodology:** Hospital based Prospective cohort study was conducted among 68 children's, whose aged is between 1-12 years, American Association of Anesthesiologists I & II undergoing elective infra umbilical surgery received caudal bupivacaine alone or bupivacaine with neostigmine. A systemic random sampling technique was used to select study participants. Postoperative severity of pain, time to request and total analgesic consumption was evaluated up to 24 hours after the operation. Based on the normality assumption, the analysis was done by independent sample t- test, a chi-square test and Mann–Whitney *U*-test. A p-value <0.05 was considered as statistically significant.

**Result:** In this study the median duration of postoperative analgesia in neostigmine group was 644 min while it was 322.5 min in bupivacaine alone group with statistically significant difference. With p-value <0.0001. Median postoperative pain severity was being statistically significant difference at $4^{th}$, $8^{th}$, $12^{th}$ and $24^{th}$ hour with p-value of <0.05 but it was statistically insignificant at arrival, $1^{st}$ and $2^{nd}$ hour. Median post-operative analgesic consumption in mg within 24 h neostigmine group was 250 and bupivacaine alone group was 750 statistically significant with p-value of <0.0001.

**Conclusion and Recommendation:** Caudal neostigmine with bupivacaine provides effective post-operative analgesia in pediatrics undergoing infra-umbilical surgeries. Based on this we recommend that neostigmine in the dose of 2μg/kg added to caudal bupivacaine is safe and with less or no side effect statistically significant.



**Key words**: Caudal block, bupivacaine, neostigmine, analgesic effect, infra umbilical surgery.

# 1. CHAPTER ONE: INTRODUCTION

## 1.1 Background

Based on an international association study pain is unpleasant sensory and emotional experience associated with actual or potential tissue damage (1).

The history of pediatric regional anesthesia is followed after the introduction of adults, which occurred after the discovery of the local anesthetic properties of cocaine in the eye by Koller in1884. Caudal block was first described in 1933 by Campbell and today it has become one of the most popular regional analgesic technique (2).

Caudal epidural anesthesia initially came from developing countries in 1967, Fortuna reported a series of 170 patients between the ages of 1-12 years who received caudal epidural anesthesia for surgical procedures below umbilical surgeries (3). Caudal block is useful for infra-umbilical surgery interventions in children for providing pain relief intra and post operatively and also to reduce intraoperative inhalational or opioid agent consumption .Caudal analgesia technique is the most popular and frequently used for postoperative analgesia in children (4).

Caudal epidural block technique can be performed under general anesthesia in the prone or lateral decubitus position. The first step is to identify the sacral hiatus and the caudal area is cleaned with iodine or alcohol containing solution, which is allowed to dry. Drawing an equilateral triangle by connecting the two posterior superior iliac spines (PSIS) usually locates the sacral hiatus at the apex and using sterile technique, the caudal epidural space is entered using a short 23 or 22 needle -gauge at 45- degree angle to the skin (5).

The main disadvantage of caudal administration of bupivacaine alone has a short duration of action (120 -150 min). There is a concern regarding the use of caudal catheters to administer repeated doses or infusions of local anesthetic due to the risk of infection (6). Being Premature newborn and infants are high risk of perioperative respiratory depression due to immature state of CNS when using caudal block analgesia (7).

There are several attempts to prolong the analgesic effects by combining a local anesthetic drug with additives to improve the efficacy of the CB in children(8). Caudal opioids have some adverse effect like nausea, vomiting, pruritus, urinary retention and respiratory depression (7).Likewise,

administration of α2 agonists produces hypotension, bradycardia and sedation (7). Because of these side effects such adjuncts may not be appropriate for pediatric surgeries (9).

Neostigmine acts by inhibiting the breakdown of acetylcholine in endogenous neurotransmitter by producing analgesia when given in a central neuraxial route .It produces intra and postoperative analgesia by inhibiting the breakdown of acetylcholine at muscarinic receptors in the dorsal horn of spinal cord .Unlike caudal opioids , respiratory depration and pruritus are not countered with the administration of neostigmine (10).Being a qua-ternary amine, it does not cross blood brain - barrier (11).

## 1.2 Statement of the problem

Based on an international association study report, pain is widely under-treated that may have psychological, economic and social adverse effects .It also increase the burden on patients' families ,quality of life in the society , unemployment and mental health. Post-operative pain can lead to delayed recovery and increased hospital stay (12).

According to WHO report 80% of people in worldwide do not receive adequate treatment for pain based on that only one in four patients had adequate relief of POP (13).

Infants and children pain express often goes unrecognized, even neglected because they cannot express it and also optimum pain relief is a big challenge because it is difficult to differentiate restlessness or crying due to pain from that of hunger or fear (14).

Even though improved pain management procedures during the past forty years, pain remains a global problem for hospitalized patients. According to study showed that in Azerbaijan ,the prevalence of pain was 86% and almost 40% had moderate-to-severe pain in hospitalized children (15).

Study conducted in USA on pediatric patients, the experience of pain is common among children undergoing surgery out of 48 children about 46% of them reported severe pain (16). A prior similar study conducted in Canada reported that the majority of children experiencing intensive pain after surgery, even when receiving analgesics (17).

A study done in USA in all pediatric patients the prevalence of moderate to severe in hospital pain was 27%. Teenagers and infants experienced higher prevalence rates of moderate to severe pain (38% and 32% respectively) than children 17%, in addition, patients admitted to medical services had much lower rates of moderate to severe pain (13%) than those admitted to surgical services 44% (18).In another study conducted in USA by Eland found that only 25% of them were given relief for their pain; 40% of these children experienced medium to severe pain. Although this problem has been repeatedly documented, inadequate postoperative pain management for children is still reported in recent studies(19).

A study done in London reported by Mather and Mackie is probably typical of practice in many units (75 % of children were in pain on the day of surgery, 13% of them in severe pain; on the first

day after operation 17% were in severe pain (20) .The providing of anesthesia and analgesia is seen as a low priority in comparison with the treatment of diseases such as malaria, tuberculosis and HIV/AIDS (21).

Infants and Children's are often more sensitive to adverse effects of medication due to immature of many systems including the renal, hepatic and central nervous systems (22).

Pain after surgery is usually most severe in the first 24–72 h but may persist for several days or weeks. A significant number of children still suffer from moderate to severe pain in the postoperative period (23).Untreated acute pain is the major cause of chronic pain with a reduction in quality of life.

In Ethiopia, a study conducted by the Ethiopian Public Health Association in 2005 showed that health care providers believe that pain was under-treated due to nonstandard practice, absence of medications ,poor knowledge and attitude among professionals (24).

In Ethiopia, intra and postoperative analgesia is commonly achieved by the use of suppository paracetamol (PCM). In order to provide adequate analgesia with fewer side effects and complications, alternative analgesia or analgesic technique is required like, peripheral, central blocks and neuraxial anesthesia can be used as an alternative method to providing perioperative analgesia (25). To avoid the above mention problem, many additives have been used to improve the quality and prolong of post-operative analgesic effectiveness of CB without increasing the total dose of local anesthesia (26). But there is an inter-individual variability in the response to additives. To solve this problem, ideal adjuvants that can be used with bupivacaine for stable intraoperative conditions and prolonging the postoperative analgesia with minimal side effects are being investigated.

Neostigmine acts by inhibiting the breakdown of acetylcholine the endogenous neurotransmitter there by producing infra and postoperative analgesia when given with a central the neuraxial route in response to alpha(2)-adrenergic analgesia lead the evaluation of cholinergic receptor at the mechanism of endogenous analgesia (8).Neostigmine used as an additive to bupivacaine to prolong analgesia but its analgesic efficacy and safety has not been extensively studied (27).

Therefore, this study was conducted to evaluate the effect of adding neostigmine to bupivacaine for the prevention of postoperative pain in pediatric patients undergoing infra- umbilical surgeries.

## 1.3 Significance of the study

Several attempts are made to prolong the analgesic effects of CB by combining a local anesthetic drug with other additives variable results in children, none of them is out of side effects. Unfortunately, a number of potential side-effects are associated with the use of caudal epidural opioids like nausea, vomiting, pruritus, urinary retention and potentially serious risk of respiratory depression (8).Therefore, alternative methods of prolonging caudal analgesia invalidated yet. But it is wise to use easily available, low cost, equally potent with less complication drug in a simple and inexpensive manner by using a single caudally administered drug for most of the postoperative period.

In Ethiopia setting, there is single published data effectiveness of caudal block using bupivacaine with neostigmine for pediatric lower extremity orthopedic hospital .But there is differ in the surgical site (type), the hospital set up, inter variability of pain dermatome level and time is too long compared to our study. The cost of neostigmine is relatively low, easily available that makes routine use is reasonable in all hospitals in Ethiopia. Such studies in the resource-limited area can improve pain management and patient comfort.

Generally, this study gives the effect of adding neostigmine with bupivacaine for caudal block to provide postoperative analgesia, necessary information on the technique for all undergoing infra - umbilical surgeries, complications and side effect which may be used as a baseline for future research studies.

# 2 CHAPTER TWO: LITERATURE REVIEW

In the review of caudal analgesia in children, it was suggested that caudal epidural block can be used effectively in pediatrics to provide both intraoperative anesthesia and post-operative analgesia for infra-umbilical surgeries (28).

A recent study was done at Institute of child health Faisalabad in Pakistan 2018 by Mohsin Riaz Askri etal on 60 children were included . BAG 1ml/kg of 0.25% caudal bupivacaine and BNG 1ml/kg of 0.25% caudal bupivacaine with 2µg/kg neostigmine given. The result of mean duration post-operative analgesia was 6.70±2.12 h vs 11.97±3.80 h in BAG and BNG respectively (29).

A study done at Trakya University of Medical Faculty in Turkey 2003 by Dilek Memis etal on 45 children. BAG received 0.25% bupivacaine 0.5 ml/ kg and BNG received 0.25% bupivacaine 0.5 ml/kg with 1µg/kg neostigmine. The duration of postoperative pain relief did not differ between the two groups; 15.40 ± 10.97 h vs 15.45 ± 10.99 h respectively P -value > 0.05 (30).

A prospective RCT done at King Hussein Medical Center in Amman, Jordan, Arab West Asia 2015 conducted by Dr Emil Batarseh on 134 children of ASAI and ASA II. Children were randomly assigned into four groups to receive a caudal administration of 0.25% plain bupivacaine 0.5ml/kg (BAGI, n= 33) For the following three groups, bupivacaine was mixed with neostigmine in the following manner 1.5µg/kg neostigmine (BNG II, n= 34), 3µg/kg neostigmine (BNG III, n= 33) and 6µg/kg neostigmine (BNG IV, n= 34), with a total caudal volume of 1ml/kg administered in all groups after induction of general anesthesia. Mean duration of postoperative analgesia result was 4.7 h ± 1.9h in BG I but it was 16.35h ±4.5 h,16.8h ±5.15 h and 16.65 h± 4.4h in BNG II, III and IV, respectively ($P<0.05$) . Post-operative pain severity is statically significant at $4^{th}$, 8th, 12th and 24 hour while it is insignificant at arrival, at $1^{st}$ hour and $2^{nd}$ hour though they had used different doses with the p-value of <0.05. Mean postoperative paracetamol consumption was 41.9mg/kg in group I, 12.8mg/kg,14.1 mg/kg and 11.4mg/kg in groups II, III and IV, respectively ($P<0.05$), during the first 24 postoperative hours (31).

Y.K. Batra etal study done in 2003 on 120 ASA I children for elective hypnopedia correction surgery. They used neostigmine as adjuvant to bupivacaine to find it's efficacy in providing post op analgesia in these children. Adequate dose of caudal bupivacaine with neostigmine increase the

duration of postoperative analgesia. However, they found that higher doses of neostigmine caused vomiting in some patients (32).

A prospective randomized double blind study done in India 2004 by Dr Rajesh Mahajan etal on 80 boys aged two to eight years scheduled for surgical repair of hypnopedia were allocated randomly to one of four groups (n = 20 each) and received only caudal 0.25% plain bupivacaine 0.5 ml/kg (BG I) or 0.25% plain bupivacaine 0.5 ml/kg with neostigmine (BNG II-IV) in doses of 2, 3 and 4 µg/ kg respectively. The duration of postoperative analgesia in BG I (5.1 ± 2.3 hr.) was significantly shorter than in the other three BNG (II -16.6 ± 4.9 hr.; III -17.2 ± 5.5 hr.; IV -17.0 ± 5.8 h and post-operative total analgesia consumption was BG (697.6 ± 240.7 mg) than in the groups receiving caudal neostigmine (II -248.0 ± 178.4; III -270.2 ± 180.8 and IV -230.6 ± 166.9 mg) P -value < 0.05 (33).

A prospective double blind study done in India 2005 by Dr Rudra A on 40 children ASAI, aged 5–10 years. Caudal block produced by BAG 0.25% bupivacaine 1ml/kg and BNG 0.25% bupivacaine 1ml/kg with 2 µg/kg neostigmine. They found that the mean time to first rescue analgesia was 7.6±5.4 hours in the study group while it was 19.0±4.2 hours in control group. Statistically a significant difference ($p<0.001$) was observed in both the groups .Emesis was not significantly different in both groups (34).

A Study done at CSM Medical University, Lucknow by Dr Kaushal in 2008 on 90 children of ASA I or II undergoing infra-umbilical surgeries. The mean ± SD, first rescue analgesic times were 6.05±2.04 h, 11.5±3.42h, and 16.86 ± 4.92 h in the BG alone, BNG 2 µg/kg and BNG 5µg/kg groups, respectively. Postoperative nausea and vomiting occurred in 6.7%, 16.7% and 33.3% patients in caudal BG, BNG 2µg/kg and BNG 5µg/kg, respectively ($p<0.05$) (35).

A comparative study conducted by Sunanda Maji in 2013 on 50 children of ASAI and II, aged between 2 to 8 years, undergoing infra-umbilical surgeries. Bupivacaine alone group 0.125% 1ml/kg and bupivacaine with neostigmine group 2µg/kg,the Mean ± SD duration of post-operative analgesia was 6.1 ± 1.7 h vs 11.4 ±0.97 h in BAG and BNG respectively (36).

A prospective RCT study done in India 2017 on 60 children by Kannan Santhanakrishnan etal, in pediatrics received a caudal injection of 0.25% BAG and 0.25% BNG 0.5ml/kg with 2µg/kg . The

mean duration of post-operative analgesia was 14.6 h in the BNG compared to BAG 4.3 h. There was no incidence of nausea and vomiting in both groups (37).

A resent Prospective research done at Sheri Kashmir Institute of Medical Sciences in India 2017 conducted by Dr Tahira Akhter etal on 100 children, ASAI of either sex in aged one to five years for elective infra- umbilical surgical procedures to receive caudal injection of either 1ml/kg of 0.25% bupivacaine with saline 0.2ml/kg in BAG or 2µg/Kg neostigmine with 1ml/kg of 0.25% bupivacaine in BNG. The mean duration of analgesia in BG was 4.16±1.687 h while in BNG was 11.87±3.502 h. Postoperative pain severity scale is statistically significant at 4$^{th}$, 8th, 12th and 24$^{th}$ hour with p-value of <0.01 and it is statistically insignificant at arrival and 1$^{st}$ hour with a p-value of 0.059 and 0.004 respectively (38).

Another recent Prospective RCT study done in India 2018 conducted by Manjit George etal on 40 ASA1 children aged 2-6 years, in to BAG and BNG. The mean duration of post-operative analgesia was prolonged in BNG 15.16 h than BG alone 6.52 h. There was no incidence of nausea and vomiting in both groups (39).

Study was done in India 2007 by Bhardwaj, etal 120 children ASA I aged 1-12 years undergoing elective urethroplasty for hypnopedia in to BAG 0.75ml/kg bupivacaine, and BNG1, BNG2, BNG3, (2, 3, and 4µg/Kg 0.75ml/kg bupivacaine with neostigmine respectively). Pain assessment tool was used OPS and NRS .The mean duration of postoperative pain relief did not differ among the BAG and BN groups (p-value <0.05 was significant) (40).

A comparative study was done by Fyneface-Ogan S etal in Nigeria, between caudal BAG and BNG for postoperative analgesia in which 66 children aged 1-6 years, of ASAI or II posted for elective unilateral herniotomy under general anesthesia without premedication were studied. The Mean duration of post-operative analgesia in patients who received mixture of BNG was significantly longer, 7.7 ± 1 h compared to the group which received only plain BG, 4.77 ± 0,8h ($p < 0.001$) (41).

Research conducted at Muhimbili University of Health and Allied Sciences in Dar Es Salaam Tanzania, on 2013 showed that duration of analgesia bupivacaine alone was (8.2±2.1) h (42).

A study done in Egypt 2002 conducted by Dr Mohamed Abdulatif on 60 children, ASA I, aged 2–10 years, undergoing hypnopedia repair surgery. Children were allocated randomly into three

groups (n=20) to receive a caudal injection of either 0.25% bupivacaine1mL/kg, with or without neostigmine 2µg/kg, or neostigmine2µg/kg in normal saline 1mL/kg. Recovery to first rescue analgesic times were (mean ± SD) 22.8 ±2.9 h, 8.1±5.9h and5.2±2. h1in bupivacaine/neostigmine, bupivacaine and neostigmine groups respectively (P<0.001) (43).

A recent study done in Egypt 2017 at Tanta University hospital on 105 children aged 1-6 years scheduled for inguinal hernia repair were randomly allocated into three groups. CB was performed with 0.25% bupivacaine (0.75 ml/kg) 1 ml saline, dexamethasone (0.1 mg/kg) in 1 ml saline and neostigmine (2µg/kg) in 1 ml saline were added in BG, BDG and BNG respectively. The duration of postoperative analgesia was prolonged in BDG (8.68± 1.685hr) and BNG (13.2± 3.3) as compared to BG (4.9 ± 1,05hr), (185.0–265.9) and (425.7–568.0) respectively (P < 0.05). Postoperative nausea and vomiting was insignificantly different among the three groups (44).

A recent study conducted in Egypt 2018 by El-Miseery etal Tanta University on 70 children undergoing congenital inguinal hernia repair in BNG received 0.25% of bupivacaine with neostigmine 2 µg/kg and BAG received 0.25% of bupivacaine alone caudally. Post-operative pain score, total analgesia consumption statistically significantly lower BNG than BAG P-value <0.05.There was no statistically significant deference between both groups incidence of postoperative vomiting p-value <0.05 (45).

A study done in Ethiopia 2014 by Mr Getu Ataro conducted on 86 children aged 1-12 years undergoing lower extremity orthopedic surgeries 43 children in BAG received 1 ml/kg of 0.25% bupivacaine and the other 43 in BNG received 1 ml/kg of 0.25% bupivacaine with 2.5 µg/kg neostigmine caudally. Mean duration of pain score variation was not differ at 30 min ,$1^{st}$ ,$2^{nd}$ ,$4^{th}$ ,$8^{th}$ ,$12^{th}$ and $24^{th}$ hour. The mean analgesia duration in BAG was 5.8 ± 2.3 h and 8.7 ± 5.3 hrs. In BNG (p=0.003). The PONV incidence was observed in BG (4.6%) and BNG (13.9%) which is not statistically significant (p>0.05) across the group (46).

## 2.2 Hypothesis Testing

**HO1**: -there is no significant different in severity of post-operative pain in bupivacaine alone and neostigmine with bupivacaine group by FLACC scale / NRS.

**HA1**: -there is significant different in severity of post-operative pain in bupivacaine alone and neostigmine with bupivacaine group FLACC scale / NRS.

**HO2**: - there is no significant different in time to first analgesic request in bupivacaine alone and neostigmine with bupivacaine group in h /min.

**HA2**: - there is significant different in time to first analgesic request in bupivacaine alone and neostigmine with bupivacaine group in h /min.

**HO3**: -there is no significant different for the total analgesic consumption in mg the first 24 hours in bupivacaine alone and neostigmine with bupivacaine group.

**HA3**: -there is significant different for the total analgesic consumption in mg the first 24 hours in bupivacaine alone and neostigmine with bupivacaine group.

## 2.3. Conceptual frame work

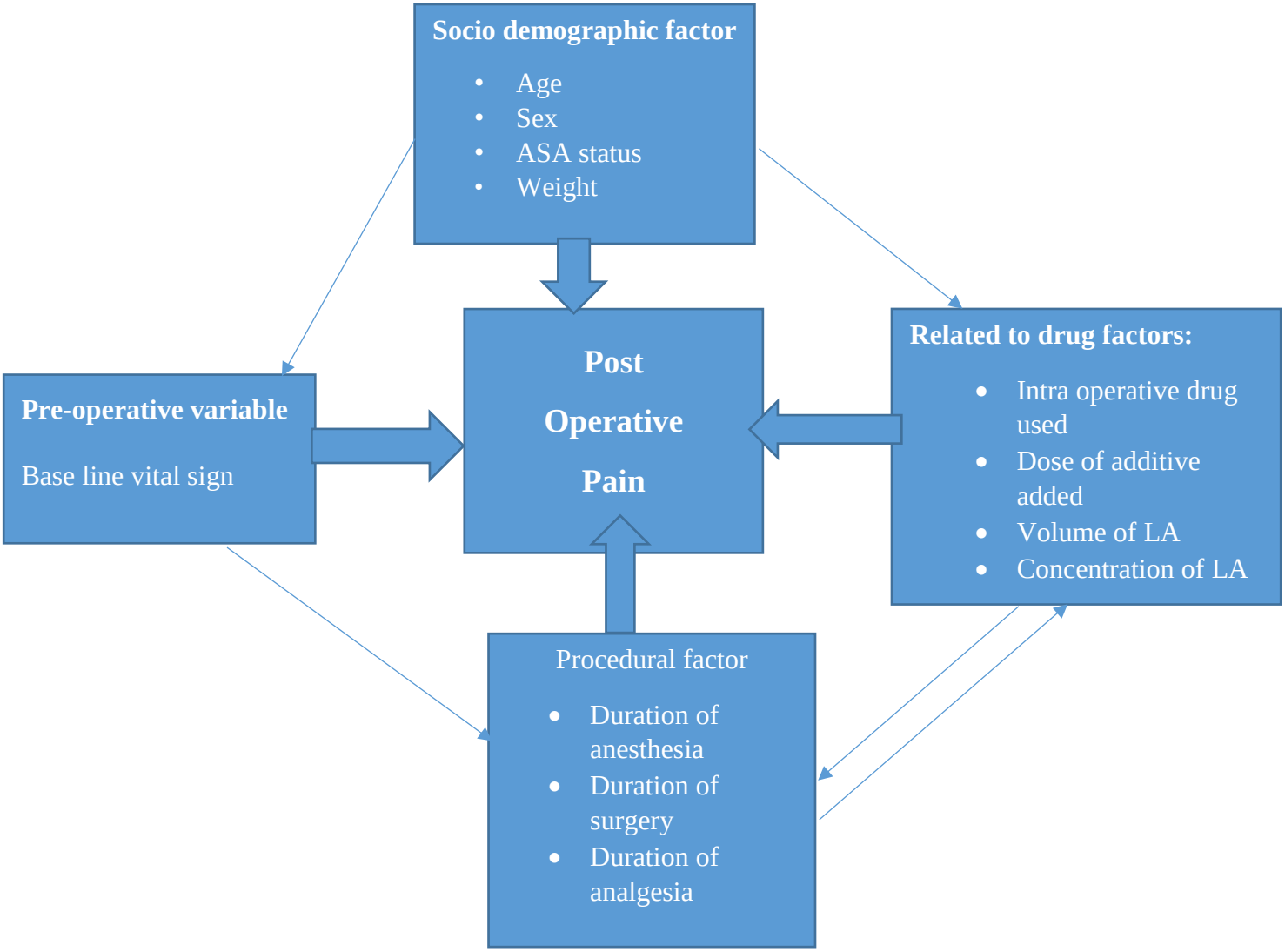


Figure 1 : Conceptual frame work in pediatric patients for infra umbilical surgery at Tikur Anbesa specialized hospital from November 1, 2019G.C to January 30, 2020 G.C.

# CHAPTER THREE -OBJECTIVE

## General objectives

To assess post-operative analgesic effect of adding caudal neostigmine with bupivacaine in pediatric patients for infra umbilical surgery at Tikur Anbesa specialized hospital from November 1, 2019G.C to January 30, 2020 G.C.

## Specific objective

1. To compare the duration of analgesia between bupivacaine alone and neostigmine added groups in h /minutes.
2. To compare the post-operative pain severity between bupivacaine alone and neostigmine added groups by FLACC / NRS.
3. To compare the total analgesia consumption between bupivacaine alone and neostigmine added groups in the first 24 hours.

# 4 CHAPTER FOUR: METHODOLOGY

## 4.1 Study Area and period

The study was conducted at Tikur Anbesa specialized hospital which is located in Addis Ababa, Ethiopia. Tikur Anbesa specialized hospital is multi-specialist tertiary care teaching hospital in Ethiopia, opened since 1972 and in 1998 transferred to school by FMOH since then it became a university teaching and largest referral hospital in a country. TASH is now the main teaching hospital for clinical and preclinical training in most disciplines. It is also an institution where specialized clinical services that are not available in other public or private institutions are rendered to the whole nation. It has 1 Blood bank, about 700 beds, it has about 15 operation theatre and more than 900 health professionals in different specialties dedicated to providing health care services and the various departments residents under specialty training in the school of medicine also provide patient care in the hospital. The hospital can perform a total adult surgery of 700 per month and pediatrics surgery per month 70.The study was conducted from November 1, 2019 G.C to January 30, 2020 G.C.

## 4.2 Study design

Hospital based Prospective cohort study design was employed from November 1, 2019 G.C to January 30, 2020G.C.

## 4.3 Population

### 4.3.1 Source of population

All pediatric elective surgical patients scheduled for infra umbilical procedures at Tikur Anbesa specialized hospital.

### 4.3.2 Study population

All pediatric elective surgical patients scheduled for infra umbilical procedures in the study data collection period who was undergo operation under general anesthesia with caudal bupivacaine with neostigmine or caudal bupivacaine alone and those who fulfill inclusion criteria was included in the study.

### 4.3.3 Study unit

Individual patient involved in the study

## 4.4 Eligibility criteria

### 4.4.1 Inclusive criteria

Pediatrics who received caudal neostigmine or bupivacaine

ASA status I and II

Pediatric patients age from 1-12years

### 4.4.2 Exclusive criteria

Failed caudal block

Day case surgery

Additive drugs used during caudal analgesia other than neostigmine

Dose other than 1ml/kg bupivacaine and 2 µg /kg neostigmine

## 4.5 Sampling technique and sample size determination

### 4.5.1 Sample size determination

Comparison of mean with equal sample size for two independent sample size formula of two independent cohort based on mean duration of postoperative analgesia among the group where n1=sample for bupivacaine alone group, n2=sample for neostigmine with bupivacaine group. Z alpha =0.05, which is 1.96, power = 80%, which is 0.84.Sample size calculation has been used to literature review from previous study on 2014 in Ethiopia, showed that the mean duration of postoperative analgesia was 5.8 ± 2.3h vs 8.7 ± 5.3h bupivacaine alone and neostigmine with bupivacaine group respectively in the first postoperative day (46).

$$n = \frac{(S1)^2 + (S2)^2 (a+b)^2}{(X1 - X2)^2}$$

Where n = the sample size in each of the groups.

X 1 = Sample mean duration of post-operative analgesia in neostigmine with bupivacaine group.

X 2 = Sample mean duration of post-operative analgesia in bupivacaine alone group.

X 1- X 2 = the difference the investigator wishes to detect

$(S1)^2$ = Sample variance in bupivacaine alone group.

$(S2)^2$ = Sample variance in neostigmine with bupivacaine group.

a = conventional multiplier for alpha =0.05, which is 1.96.

b = conventional multiplier for power = 0.80 which is 0.84.

Substituting for this variables yields.

$$n = \frac{(2.3)^2 + (5.3^2) \times (1.96 + 0.84)^2}{(8.7-5.8)^2}$$

$$n = \frac{261.6992}{8.41} = \mathbf{31}$$

using 1:1 ratio between groups and adding 10% contingency, sample size become n1= n2=34 children in each group. Based on the mean duration of analgesia outcome variable, a total of 68 pediatric patients involved in the study.

### 4.5.2 Sample technique

A systematic random sampling technique was used to select study participants on the daily operation schedule list. Based on the average values of the previous surgery per 3 months on the logbook, 204 pediatrics patients were operated who took caudal analgesia for elective infra umbilical surgery. The sampling interval k was determined by using the formula: k=N/n; where, n = total sample size, N = population per 3 months.

Therefore, the sampling interval was 3 and the first study participant (random start) was selected by using lottery method after which data collector recruit 1patient for every 3 consecutive patients' undergoing infra umbilical surgery grouping based on whether the received caudal bupivacaine alone or bupivacaine with neostigmine till the required sample size was achieved.

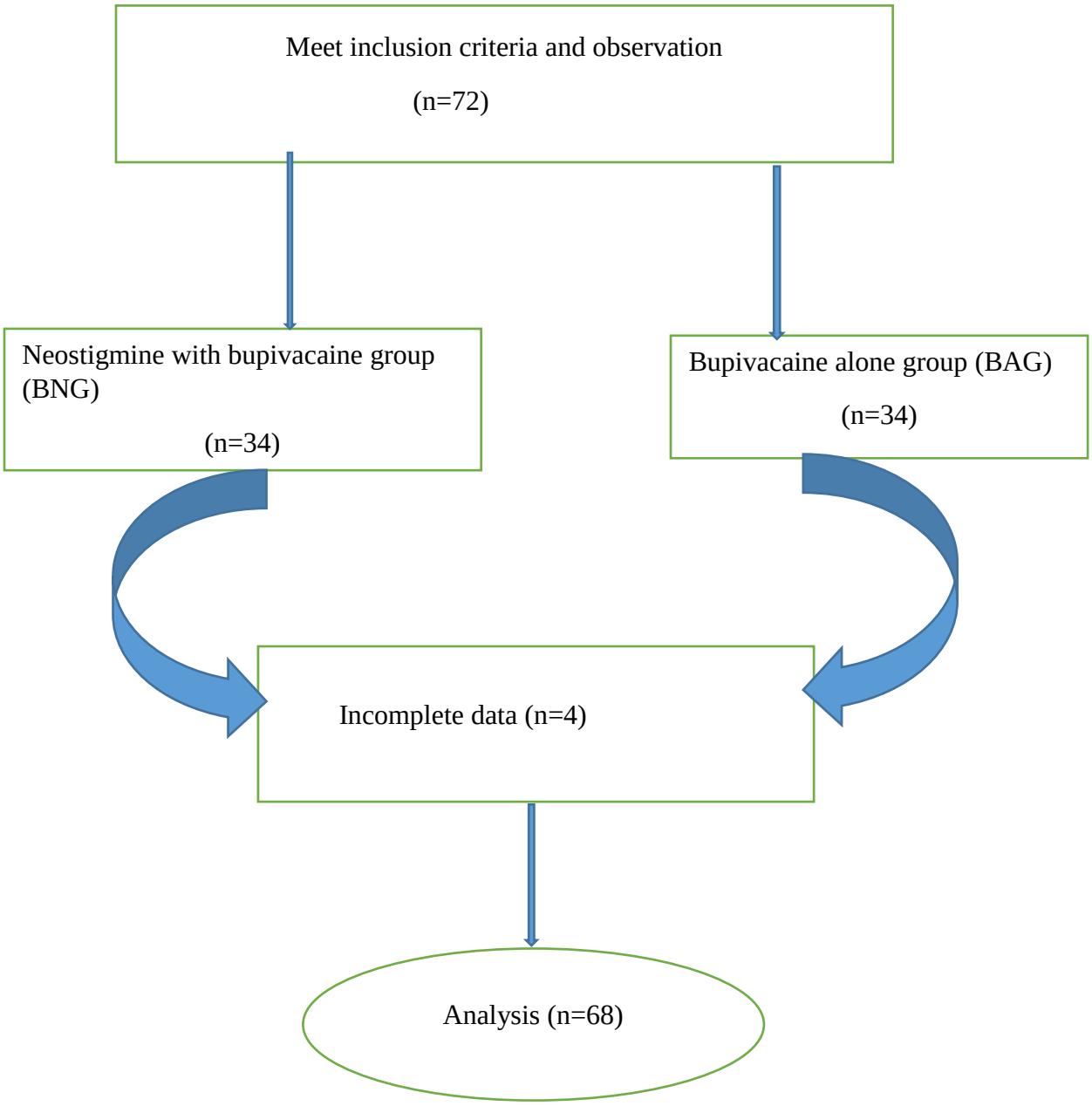


Figure 2: Enrollment chart for elective pediatrics patients scheduled at Tikur Anbesa specialized hospital from November 1, 2019G.C to January 30, 2020 G.C.

## 4.6 Study variable

### 4.6.1 Dependent variable

Duration of analgesia in minutes

Severity of postoperative pain by FLACC scale / NRS

Total number of analgesics consumption in 24 hrs.

### 4.6.2 Independent variable

**Socio demographic variable**

Age

Sex

Weight

**ASA physical status**

ASA I, II

**Pre-operative variable**

Baseline vital sign

**Intraoperative variable**

Type of surgery

Vital sign before and after skin incision

Duration of surgery

Duration of anesthesia

## 4.7 Operational Definition

**Duration of anesthesia:** The time from pre oxygenation to patients get a response to verbal command was notified by anesthesia record sheet in time minutes.

**Duration of surgery:** Time interval in minutes between skin incision and closure.

**Failed caudal anesthesia:** an increase in BP and HR greater than 20% from the base line response to skin incision.

**Post-operative nausea and vomiting:** when a patient experiences at least one episode of either nausea or vomiting within 24 hours.

**Postoperative pain**: the presence of pain in the postoperative period was defined as a patient complaining pain and assessment of pain score other than zero within 24 hours.

**Time to first analgesia request:** Initial time in which patients need pain treatment post operatively.

**Total analgesia consumption:** the type and dose in mg of analgesic drugs given to the patient within 24h post operatively.

**FLACC scale:** is a measurement scale used to assess postoperative pain for children between age two months to seven years or for individual that are unable to communicate their pain going to score in PACU and wards.

In patients who are asleep: observe for 5 minutes or longer, Observe body and legs uncovered. If

Possible, re position the patient, touch the body and assess for tenseness and tone.

In patients who are awake: observe for 1 to 5 minutes or longer, Observe legs and body

Uncovered. Re position patient or observe activity. Assess body for tenseness and tone. Initiate

Consoling interventions if needed. Each category is scored on the 0-2 scale, which results in a total score of 0-10 (See ANNEX II).

The scale is scored between ranges of 0-10 with 0 representing no pain.

The scale has 5 criteria which are each assigned a score of 0, 1 or 2.

**Interpreting the Behavioral Score**

0: Relaxed and comfortable

1-3: Mild discomfort

4-6: Moderate pain

7-10: severe discomfort or pain or both and study effectiveness was evaluated based on FLACC pain scores pediatrics aged 1-7years. FLACC pain score has been reported to be reliability and validity score for evaluation of pain assessment tools (47).

**NRS**: is a valid pain intensity assessment tool in pediatrics age > 7 years that involves asking a patient to rate his or her pain from 0-10 (11-point scale) with the understanding that 0 is equal to no pain and 10 equal to the worst possible pain (48).

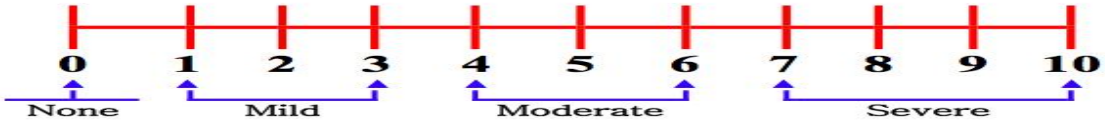


Figure 3 : NRS pain assessment tool Adopted from the National Initiative on Pain Control™ (NIPC™).

### 4.8 Data collection methods

Pediatric patients who were scheduled for elective infra- umbilical surgery who fulfill inclusion criteria and parents' consent to take part in the study was instructed on how data collector use to assess pain in the morning of operation day.

Induction of anesthesia was selected by anesthesiology resident student, MSc anesthesia student, MSc anesthetists done with Propofol, thiopental, ketamine and maintenance with halothane or isoflurane. None invasive baseline vital sign (blood pressure and heart rate) was measured and documented.

Patient monitoring attached ECG, noninvasive blood pressure, pulse oximeter, precordial stethoscope and time to start induction was documented. IV line was secured for drugs and fluids administration, dextrose10%, Na Cl 0.9% (4-2-1 regime) was given as maintenance during the operation. Caudal block was done with bupivacaine (0.25%) alone 1ml/kg or bupivacaine 0.25% of (1ml/kg) with neostigmine (2µg /kg). There was variability of anesthesia in using caudal neostigmine and bupivacaine alone. We used that advantage to group patient in bupivacaine alone and bupivacaine neostigmine group in TASH.

Caudal block was done left lateral decubitus position and performed by MSc anesthesia students, anesthesiology resident student, MSc anesthetists and another anesthetist was maintained

ventilated the child. Pre incision parameters (blood pressure and heart rate) was measured 5 minutes after the block just before skin incision.

After skin incision parameters (BP&HR) was measured 5 minutes later, then hemodynamic parameters was measured and documented. Ability to reduce inhalational concentration without increase in parameters by >20 points (blood pressure by >20mmhg, heart rate by >20 beats/minute) caudal block was considered successful (44) .If the parameters increased by more than 20 points caudal block was considered unsuccessful and those children were given IV analgesia for intraoperative and postoperative analgesia.

In the postoperative time patients was transferred to PACU and to ward when they recover from anesthesia. Patient was observed by trained nurses and pain was managed based on patient complain. Either FLACC/ NRS pain score was assessed & measured at arrival, $1^{st}$, $2^{nd}$, $4^{th}$, $8^{th}$, $12^{th}$ and $24^{th}$ hour after end of surgery, time to first analgesia request and total analgesia consumption in 24 hrs. In addition, adverse effects such as post-operative nausea and vomiting, motor block, urinary retention and sedation was documented when it is reported within 24 hours.

Structure d questionnaires and check lists were prepared in English which includes socio demographic data, preoperative vital signs, ASA classification, duration of anesthesia, duration of surgery, and dose of analgesia if given, total volume of drug, dose of additive, dose of local anesthesia and post operatively severity of pain, duration of analgesia, rescue analgesic consumption and adverse effects was monitored for 24hours.

Data collection was done using check lists and structured questionnaires. Intraoperative data was collected from anesthesia sheet by one Anesthetists while postoperative data was collected by two nurses after getting training with pain assessment tool, measured and supervisor supervise the completeness of the data daily and further checking by principal investigator.

## 4.9 Data Quality Control and assurance

To assure the reliability and validity of the data, questionnaires was pretested on 5% of the total sample size before actual data collection. Training, orientation about the objectives and relevance of the study, each items included in the study tools and the whole process of data collection was provided for data collectors and supervisors. Written informed consent was obtained from the parents. Data completeness and consistency was checked daily by supervisor and further cross

check by principal investigator. Incomplete data was not entered in to the data base and data clean up and cross-checking was done by using SPSS before analysis.

## 4.10 Data Processing and Analysis

Data was checked manually for completeness then coded and entered in to SPSS version 26 computer program for analysis.

Descriptive statistics was used to summarize data, tables and figures to display the result. Continuous variables were expressed as mean ± SD for normally distribute data and median ± IQR for skewed data.

Shapiro Wilk test was used to test normality while homogeneity of variance was assessed by using Levene's test for equality of variance. Frequency and cross tabulation were conducted to describe relevant variables in relation to the outcome variables and after checking for the normality assumption.

Analysis of the data was done by using independent sample t test to compare the means of two independent samples which was used for comparing baseline continuous variables.

Chi-square test was used to analyze categorical variables.

Mann-Whitney *U*-test was used to analyzed ordinal and non-normally distributed variables , with a power of 95% confidence level .In this study, a p -value <0.05 was considered as statistically significant.

## 4.11 Ethical consideration

Ethical clearance was obtained from anesthesia department ethical clearance committee before the start of the study. Get permission from TASH clinical director office after submission of official letter. The importance of the study explained and written informed consent was obtained from each participant relative by the data collector. Confidentiality was maintained at all levels of the study by avoiding identifiers and using codes to identify patients. Participant's involvement in the study was on voluntary bases, participants who was not willing to participate in the study & those who wish to quit their participation at any stage was informed to do so without any restriction.

## 4.12 Dissemination plan

The result of this study will be submitted to Addis Ababa University College of health science school of medicine department of Anesthesia. After the research is presented for the entire department of anesthesia staff. It will be also presented at the annual National conference of Ethiopian Anesthetists Association (EAA) research conference and lastly it will be submitted to journals for publication.

# 5 CHAPTER FIVE: RESULT

A total of sixty eight pediatric patients (34 patients in each group) were analyzed whether they received caudal block with additive of neostigmine or bupivacaine alone group after induction of anesthesia.

## 5.1 Socio demographic and preoperative patient characteristic

The Socio demographic patient characteristics were comparable for all patient in the two groups. But there is no statistically significant difference between the two groups p- value >0.05**(Table 1).**

Table 1 : Socio demographic and preoperative patient characteristic between BN & BA groups in pediatric elective infra-umbilical surgery at TASH. From November 1, 2019 G.C to January 30, 2020 G.C

| **Variables** | **Bupivacaine alone group (n=34)** | **Bupivacaine with neostigmine group (n=34)** | **P-value** |
|---|---|---|---|
| **Sex** | | | |
| Male n (%) | 21(61.8 %) | 27(79.4 %) | 0.11 |
| Female n (%) | 13(38.2 %) | 7(20.6 %) | |
| **Age(years)** * | 4 (2-5.25) | 3(2-6) | 0.941 |
| **Wight(kg)** * | 14(10-19.25) | 4.5(10-20) | 0.711 |
| **ASA Status** | | | |
| ASAI n (%) | 26(76.5 %) | 27(79.4 %) | |
| ASAII n (%) | 8(23.5 %) | 7 (20.6 %) | 0.77 |
| **Type of surgery** | | | |
| Urogenital n (%) | 12 (35.5 %) | 19 (55.9 %) | |
| GI/Lower abdominal n (%) | 22 (64.7 %) | 13 (38.2 %) | 0.17 |
| Calf venous malformation n (%) | 0 (0%) | 2 (5.9 %) | |
| Duration of surgery (min ) * | 135 (90-176.25 ) | 120(87.5-162.5 ) | 0.449 |
| Duration of anesthesia (min) * | 152.5 (103.75-188.75 ) | 130 (100-176.25 ) | 0.332 |
| **Induction agent** | | | |
| Thiopental | 13(38.2%) | 14(42.2%) | |
| Propofol | 8(23. 5%) | 10(29.4) | 0.722 |

| | | |
|---|---|---|
| Ketamine | 13(38.2%) | 10(29.4%) |

**NB :** BN=bupivacaine with neostigmine added, BA= bupivacaine alone, *= M(IQR) =median (Inter-quartile range), n%= number (proportion), chi-square (x2)–test and Mann -Whitney U test was used, p-value < 0.05 is significant.

## 5.2 Hemodynamic response before and after caudal anesthesia between two groups

There was no statistically significant difference in baseline vital sign, before, after skin incision, immediately at arrival and 60 minutes in hemodynamic response (PR and MAP) between two groups with P-value >0.05 **(Table 2).**

Table 2: Hemodynamic response before and after caudal analgesia between BN & BA groups in pediatrics elective infra-umbilical surgery at TASH .From November 1, 2019GC - January 30, 2020 GC.

| **Variables** | **Bupivacaine alone group (n=34)** | **Bupivacaine with neostigmine group(n=34)** | **P-value** |
|---|---|---|---|
| Base line pulse rate** | 124.91±15.927 | 121.91±22.28 | 0.525 |
| Base line MAP * | 69 (63-82) | 72.5 (64.75-80) | 0.956 |
| **Vital sign before skin incision** | | | |
| Pulse rate** | 126.18±17.02 | 122.82±21.67 | 0.481 |
| Mean arterial pressure* | 71(63-82) | 70 (64-79) | 0.703 |
| **Vital sign after skin incision** | | | |
| Pulse rate* | 124 (109.75-133.5) | 124(115.5-130) | 0.636 |
| Mean arterial pressure* | 67.5 (60-80) | 64 (60-72) | 0.141 |
| **Vital sign immediately at arrival (PACU)** | | | |
| Pulse rate** | 115.97±9.22 | 112.88±10.06 | 0.192 |
| Mean arterial pressure * | 66(60.75 -72) | 65.5(60-67.5) | 0.619 |
| **Vital sign within 60 min** | | | |
| Pulse rate ** | 114.65±8.339 | 115.65±9.764 | 0.532 |

| | | | |
|---|---|---|---|
| Mean arterial pressure * | 73(66.5-80.5) | 70(66-78.5) | 0.507 |

**NB**: BN=bupivacaine with neostigmine added, BA= bupivacaine alone,**= mean ±SD, *= =median(Inter-quartile range), PR= Pulse rate in beat per minute, MAP = mean arterial blood pressure in mmhg, Independent sample t-test for normal distributed data and Mann -Whitney U test for non-parametric test was used, p-value < 0.05 is significant.

## 5.3 Comparison of postoperative pain severity by FLACC/NRS pain rating scale between two groups.

The median FLACC/NRS score were comparable immediately at PACU, 1st and 2nd hour post operatively between bupivacaine alone and neostigmine with bupivacaine groups with statistically insignificant difference (p- value of >0.05).But the median FLACC/NRS were lower in neostigmine with bupivacaine group at 4th, 8th, 12th and 24th hour post operatively with statistically significant (p-value of <0.05) **Table 3.**

Table 3: Comparison of postoperative pain severity by FLACC/NRS pain rating scale between BN & BA groups in pediatrics elective infra-umbilical surgery at TASH .From November 1, 2019 GC - January 30, 2020 GC.

| **Variable * pain FLACC/NRS Score** | Bupivacaine alone group (n=34) | Bupivacaine with neostigmine group(n=34) | P-value |
|---|---|---|---|
| **Immediately postoperatively** | 1(0-1) | 1(0-1.25) | 0.747 |
| **1st h post Postoperatively** | 1(0-1) | 0(0-1) | 0.209 |
| **2nd h post-operatively** | 1(0-2) | 0(0-1) | 0.159 |
| **4th h post-operatively** | 3(2-3) | 2(1-2.25) | 0.001* |
| **8th h post-operatively** | 3(2-4.25) | 2(1-3) | <0.0001* |
| **12th h post –operatively** | 4(4-5) | 3(2-3) | <0.0001* |
| **24th h post-operatively** | 5(3.75-5) | 3(2-3) | <0.0001* |

**NB: BN=bupivacaine with neostigmine, BA= bupivacaine alone, * = M =median (Inter-quartile range),*= statistically significant, Mann -Whitney U test was used, p-value < 0.05 is significant.**

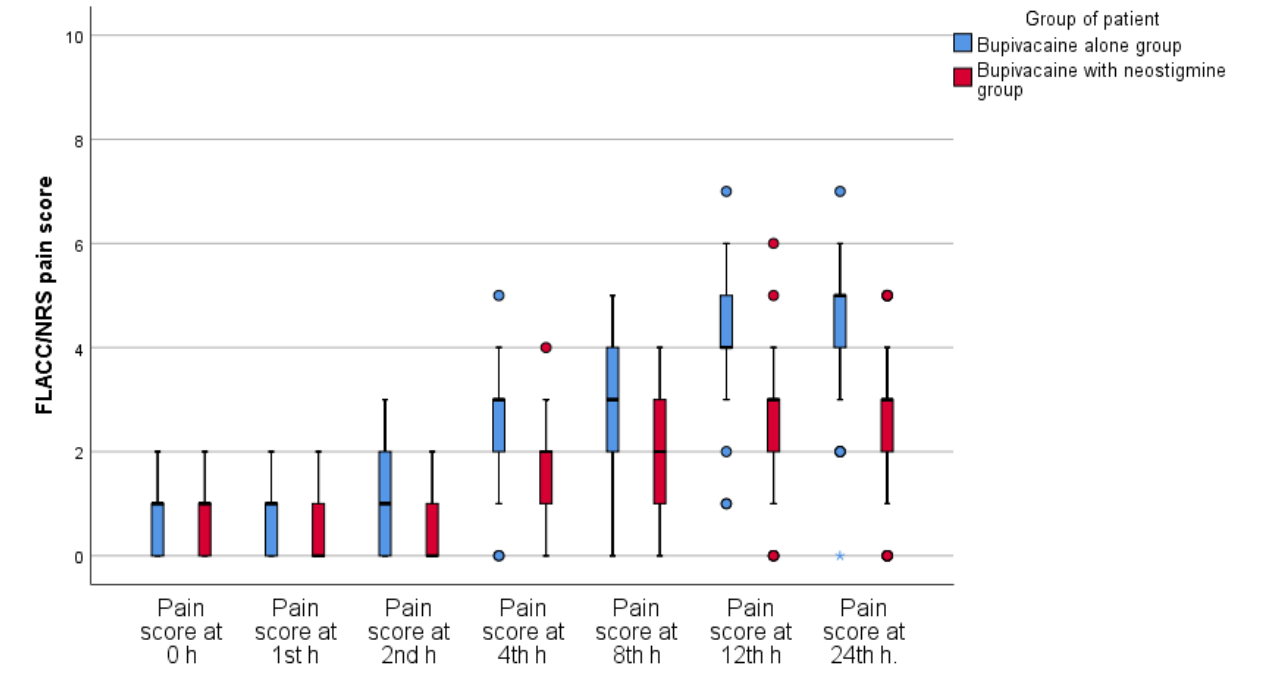


Figure 4: Comparison of postoperative pain severity using 11 points FLACC/NRS (0-10) score between BN & BA groups in pediatrics elective infra-umbilical surgery at TASH .From November 1, 2019 GC - January 30, 2020 GC.

## 5.4 Comparison of time to first analgesia request, total dose of analgesic consumption in mg 24 h, Proportion of pt. need analgesia in 24h n (%) & number of analgesic request in 24h between two groups.

The result for time to first analgesia request found that neostigmine with bupivacaine group prolongs the analgesia duration than in bupivacaine alone group with statistically significant (p-value <0.05 (Table 4).

Total dose of analgesic consumption paracetamol in mg within the first 24 h in neostigmine with bupivacaine group median were less used than bupivacaine alone group which is statistically significant (p-value <0.05).

The number of analgesic request in 24 h median compared in neostigmine with bupivacaine group were less number request than bupivacaine alone group with statistically significant (p- value <0.05).

Table4:Comparison of time to first analgesia request, total dose of analgesic Consumption in mg 24 h & number of analgesic request in 24h between BN &BA groups in pediatrics elective infra-umbilical surgery at TASH .From November 1, 2019 GC - January 30, 2020 GC**.**

| Variables * | Bupivacaine alone group (n=34) | Bupivacaine within neostigmine (n=34) | p-value |
|---|---|---|---|
| Time to first analgesic request minutes | 322.5(242.5-375) | 644(450-1440) | <0.0001* |
| Total dose of analgesia Paracetamol consumption in mg 24 h | 750(500-750) | 250(0-500) | <0.0001* |
| Number of analgesic request in 24h | 3(3-4) | 1.5(0-2) | <0.0001* |
| Proportion of pt. need analgesia in 24h n (%) | 34(100%) | 23(67.6%) | <0.0001* |

NB: *= statistically significant, * =median or inter-quartile range, chi-square (x2) test and Mann -Whitney U test was used, p-value < 0.05 is significant.

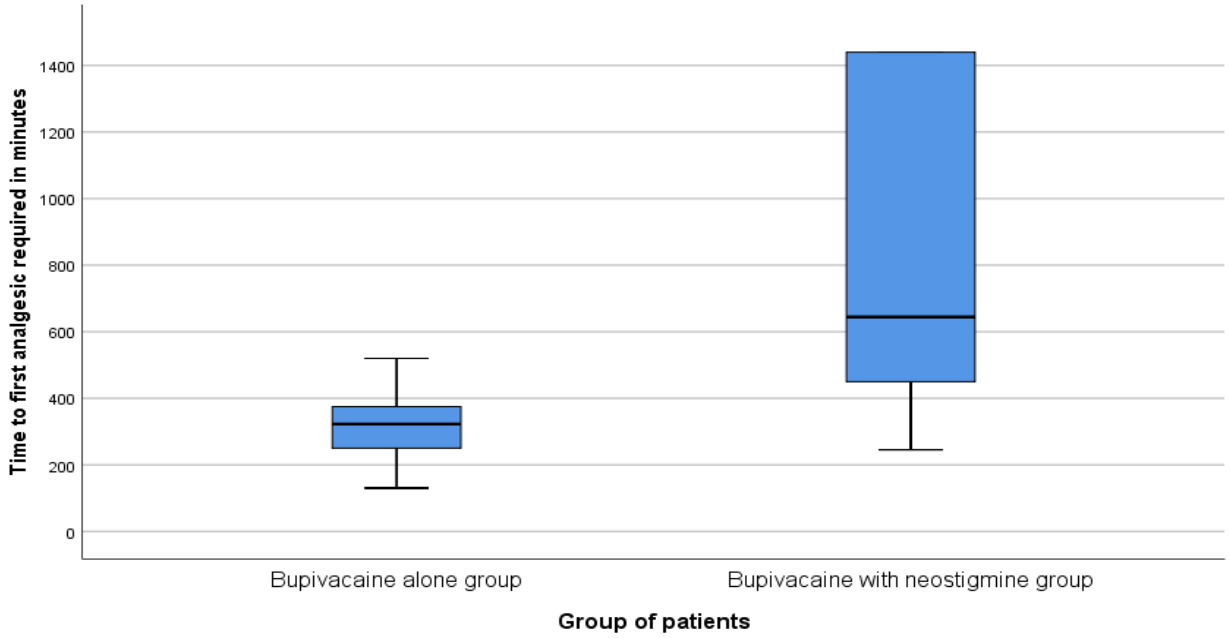


**Figure 5 :** Comparison of time to first analgesia request between BN and BA groups within 24 hours in minutes groups in pediatrics elective infra-umbilical surgery at TASH .From November 1, 2019 GC -January 30, 2020 GC.

## 5.5 Incidence of post-operative complication between two groups

The incidence of post-operative nausea and vomiting over 24 hours is 2.9% in both groups. But statistically insignificant difference between two groups with and also the other complication like motor/leg weakness, sedation and urinary retention statistically insignificant difference between the two groups with (p-value >0.05).

**Table 5 : Incidence of post-operative nausea & vomiting over 24 hour complication between two groups BN & BA groups in pediatrics elective infra-umbilical surgery at TASH. From November 1, 2019GC -January 30, 2020 GC.**

| **Post-operative complication Within 24 h (n= %)** | Bupivacaine alone group(n=34) | Bupivacaine with neostigmine group (n=34) | P-value |
|---|---|---|---|
| **Nausea and vomiting (n %)** | 1(1.45%) | 1 (1.45%) | 1.00 |
| Motor/leg weakness (n %) | 0 | 0 | |
| Sedation (n %) | 0 | 0 | |
| Urinary retention (n %) | 0 | 0 | |

**NB: (n= %) = number (proportion), Bupivacaine alone group (BA), Bupivacaine with neostigmine group (BN), chi-square (x2)–test was used with p-value <0.05 is significant**.

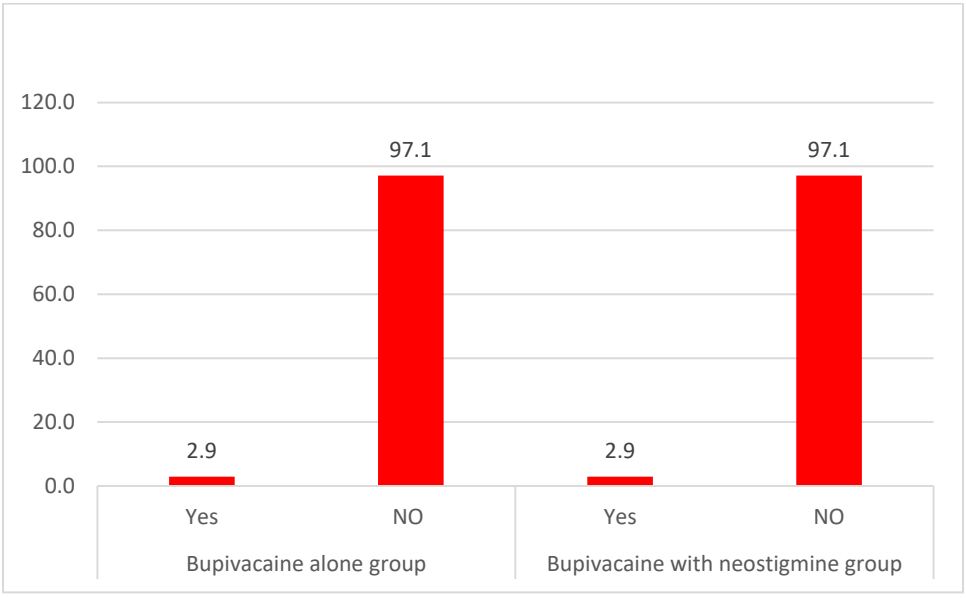


Figure 6 : Incidence of post-operative nausea & vomiting over 24 hour complication between two groups BN & BA groups in pediatrics elective infra-umbilical surgery at TASH .From November 1, 2019 GC - January 30, 2020 GC.

# 6 CHAPTRER SIX: DISCUSSION

In our study the Socio demographic characteristic of age, Wight, gender, ASA status, duration of surgery and duration of anesthesia were comparable in both groups and hemodynamic parameters vital sign like base line, before and after skin incision by mean or median (blood pressure & heart rate) .There was no statistically significant differences between the two groups (p-value>0.05) which is similar with the study conducted in Turkey by Dilek Memis and in India Dr Tahira Akhter etal (30, 38).

In our study the median pain score at $4^{th}$,$8^{th}$ ,$12^{th}$ and $24^{th}$ postoperative hour in the neostigmine with bupivacaine compared to bupivacaine alone groups was statistically significant with p -value <0.05 but there was statistically insignificant immediately at PACU,$1^{st}$ and $2^{nd}$ postoperative hour between the two groups .

In this study neostigmine with bupivacaine group statistically significant decrease the median postoperative pain severity, reduced total analgesic consumption and prolong time to first analgesic request in postoperative period compared to bupivacaine alone group after in pediatrics elective infra-umbilical surgeries.

In this study, the result with median duration of postoperative analgesia was 322.5 minutes vs 644 minutes in bupivacaine alone group and neostigmine with bupivacaine group postoperative respectively (P-value<0.05). This finding is similar with the study done in Pakistan by Mohsin Riaz etal showed that the mean duration of postoperative pain relief in BNG was 11.97±3.80 h and BAG was 6.70±2.12 h statistically significant difference with p-value <0. 001 (29).

This study has also similar finding with the studies which was conducted in India by Dr Rudra A etal, Sunanda Maji etal, Kannan Santhanakrishnan etal, Dr Tahira Akhter etal which showed that the duration of analgesia for neostigmine with bupivacaine vs bupivacaine alone group was ( 19.0±4.2 h vs7.6±5.4 h, 11.4 ±0.97h vs 6.1 ± 1.7 h , 14.6 vs 4.3 h, 11.87±3.502h vs 4.16±1.687 h) with statistically significant in neostigmine with bupivacaine and bupivacaine alone group respectively (34, 36-38).

Our study also shows comparable result with study done by S Fyneface -Ogan etal in Nigeria 2014 on comparison of caudal bupivacaine and neostigmine to relief postoperative pain in children

showed that the mean post-operative duration of analgesia was 4.77 ± 0.8 vs 7.7 ± 1 h in bupivacaine alone group and neostigmine with bupivacaine group respectively (41).

In this study also align with study done in Egypt by El-Miseery etal 2018 compression of caudal bupivacaine alone and neostigmine with bupivacaine group duration of postoperative analgesia was statistically significant between two groups with p-value of <0.05 (45).

In contrast to this study, research done in Turkey by Dilek Memis etal showed that the mean duration of postoperative pain relief did not differ bupivacaine alone group was 15.40 ± 10.97 h and neostigmine with bupivacaine group was 15.45 ± 10.99 with (P-value > 0.05) (30).This might be due to the administration of small dose neostigmine with bupivacaine (1µg /kg of neostigmine mixed with 0.5 ml/kg 0.25 % bupivacaine) compared to in our study.

In opposing to our study, research conducted in India by Bhardwaj N etal on 2007 didn't show that the deference median duration of postoperative analgesia, in bupivacaine alone and three different doses neostigmine with bupivacaine groups. Median postoperative time to first analgesic request was 540 min vs 450min in bupivacaine alone group and neostigmine with bupivacaine group respectively (p-value < 0.05) (40).This might be due to administer small dose and volume of the local anesthetic which may affect the effect of adjuvant drugs and differ pain management practice in the study set up compared to in this study.

In this study, the median post-operative pain severity assessed by FLACC/NRS scale between two groups at $4^{th}$, $8^{th}$, $12^{th}$ and $24^{th}$ hours after surgery with p-value of <0.05.But it is statistically insignificant at arrival (PACU), $1^{st}$ and $2^{nd}$ h.

This finding was similar with the result done by Dr Emil Batarseh 2015 in Arab West Asia which showed that post-operative pain severity is statistically significant at $4^{th}$,$8^{th}$,$12^{th}$ and $24^{th}$ hour with the p-value of <0.05 while it was insignificant at arrival, $1^{st}$ and $2^{nd}$ hour (31) .

This result comparable with study conducted in Kashmir, India by Dr Tahira Akhter etal 2019 generalized that postoperative pain severity scale was statically significant at $4^{th}$, $8^{th}$ , $12^{th}$ and $24^{th}$ hour with p-value of <0.01.But it was statistically insignificant at arrival and $1^{st}$ hour with p-value of 0.059 and 0.004 respectively (38).

In this study also comparable with a study done in Egypt by El-Miseery etal 2018 showed that postoperative pain severity scale was statistically significant at $4^{th}$,$6^{th}$ ,$12^{th}$,and $24^{th}$ h with the p-value <0.05 . It was not statistically significant at $1^{st}$ and $2^{nd}$ h with p-value <0.05 (45).

In contrast to this study, research conducted by Dilek Memis in Turkey which states no pain severity difference between the two groups (30). This might be due to the use of small dose neostigmine lower than our study Nurses variability about pain perception and expectation to pain score recorded at a time the caudal analgesia wear off or not.

Another study conducted in India by Bhardwaj N etal which showed that ,there was no mean duration post-operative pain severity between the two groups which is incomparable with our study finding (40) .This might be due to the use of different pain assessment tools and According to the study done by Getu Ataro showed that mean duration of pain severity statistically insignificant at 30 min ,$1^{st}$ ,$2^{nd}$ ,$4^{th}$ ,$8^{th}$ ,$12^{th}$ and $24^{th}$ hour with p- value of >0.05.This might be due to difference pin assessment tools and type of surgery (46) .

In this study, the median post-operative analgesia consumption in mg within 24 h in neostigmine group was 250 and bupivacaine alone group was 750 statistically significant with p-value of <0.0001.

This finding is in line with study done in India by Dr Rajesh Mahajan etal post-operative total analgesia consumption bupivacaine alone group was (697.6 ± 240.7 mg) compared to in neostigmine with bupivacaine groups were (II -248.0 ± 178.4, III -270.2 ± 180.8 and IV -230.6 ± 166.9 mg) with P -value < 0.05 (33).

Another study conducted in Arab West Asia by Dr Emil Batarseh(31) and in Egypt by El-Miseery etal (45) post-operative total analgesia consumption lower in neostigmine with bupivacaine group than bupivacaine alone group in 24 hour with p-value <0.05.

Another study conducted by Dilek Memis etal in Turkey conclude that there was no statistically significant postoperative analgesic consumption between two groups which is incomparable to our study (30) .The likely explanation for this reason may be due they have used small dose of neostigmine (1ug/kg) in the study group.

According to the result of this study, postoperative nausea and vomiting was too low in bupivacaine alone and neostigmine with bupivacaine groups respectively, which is statistically insignificant between the two groups (p-value>0.05).This finding is related with the study which was conducted by Dr. Rudra A etal (34) , Kannan Santhanakrishnan etal(37), Manjit George etal (49) and El-Miseery etal (45) those conclude postoperative nausea and vomiting was not significantly different between the two groups.

In contrast with our study, research conducted by Y.K. Batra etal (32) and D Kaushal (35)in India which found that postoperative nausea and vomiting was statistically significant. The possible reason may be due to they had used higher dose of neostigmine

Another Study conducted in Ethiopia by Getu Ataro (46) summarized that postoperative nausea and vomiting are statistically insignificant (p-value >0.05), but the percentage postoperative nausea and vomiting in neostigmine with bupivacaine group is higher compared to our study. This might be due to higher dose of neostigmine administration in their study.

## 6.1 Limitation of the study

Variability in the performance of the caudal block technique since different anesthetist involved.
Inability assign similar surgeons for the procedures.

## 6.2 Strength of the study

The strength of this study participants were homogeneous between the two groups.

# 7 CHAPTER SEVEN: CONCLUSION AND RECOMMENDATION

## 7.1 Conclusion

Caudal analgesia using neostigmine added with bupivacaine (2µg/kg) is increased the duration of post-operative analgesia for pediatric elective infra umbilical surgical procedure without any significant side effects.

## 7.2 Recommendation

We recommend that use of additive neostigmine with bupivacaine for caudal analgesia undergoing infra-umbilical pediatrics surgeries to prolong post-operative analgesic effectiveness.

We also recommend additional randomized controlled study

# 8. References


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# 9. ANNEXES

## Annex I: Questionnaire

### Addis Ababa University,
### College of Health Sciences
### Department of Anesthesia

**Prospective Cohort Study**: Post-operative analgesic effect of caudal neostigmine added to bupivacaine as compared with caudal bupivacaine alone for pediatric elective patients undergoing infra umbilical Surgery at Tikur Anbesa Specialized Hospital Addis Ababa, Ethiopia.

**Instruction: For each of the questions, please circle the number of alternative(s) that fit the response or fill the blank space provided.**

**I, Socio Demographic Data**

**Date……year……**

| **Card number:** | **Bed number:** | | **Code** |
|---|---|---|---|
| **Serial no** | **Questions** | **Response** | |
| **101** | **Age** | **……years** | |
| **102** | **Sex** | **1,Male 2,Female** | |
| **103** | **Wight** | **……..Kg** | |
| **104** | **ASA** | **1,ASA I 2,ASAII** | |

**Section II: Data during pre and intraoperative period**

| **S,No** | Questions | Response | **Code** |
|---|---|---|---|
| **201** | Diagnosis | | |
| **202** | Type of procedure | | |
| **203** | Baseline heart rate | ……..BPM | |
| **204** | Baseline blood pressure | ……./……..mmhg | |
| **205** | Baseline Spo2 | ..…… …. % | |

| | | | |
|---|---|---|---|
| **206** | Vital sign before skin incision | BP……./…….mmhg<br>PR…….BPM<br>Spo2……% | |
| **207** | Induction time | | |
| **208** | Induction agent | 1,Thiopental<br>2,Propofol<br>3,Ketamine | |
| **209** | Does the patient receive analgesia during induction | 1 ,yes<br>2, no | |
| **210** | If yes specify type ,dose, time | ……(mg) | |
| **211** | Caudal block; | Time performed<br>……<br>Bupivacaine0.25%<br>dose…….……(mg) | |
| **212** | Dose of neostigmine added | …….(µg) | |
| **213** | Incision time | ……..……..<br>AM/PM h /min | |
| **214** | Vital sign after skin incision | BP……/…….mmhg<br>PR……..BPM<br>Spo2…… % | |
| **215** | Additional intraoperative analgesia given | 1) yes 2) no | |
| **216** | If yes specify the type,time,doseof of the drug given | ……mg | |
| **217** | Duration of surgery | …….min | |

| | | | |
|---|---|---|---|
| | | | |
| **218** | Duration of anesthesia | …….min | |

**Section III: Post-Operative Observation Vital sign at recovery room**

| Vital sign | ImedatellyAt arrival(PACU**)** | 60 min |
|---|---|---|
| PR | | |
| BP | | |
| Spo2 | | |
| FLACC/NRS score | | |
| Analgesia given type & dose (mg) | | |

**SECTION IV POST OPRATIVE OBSERVATION**

| **S no** | **Flow up time** | **2nd h Post op** | **4th h Post op** | **8th h Post op** | **12th h Post op** | **24th h post op** |
|---|---|---|---|---|---|---|
| **301** | **FLACC/NRS Score** | | | | | |
| **302** | **Analgesia given Type and dose in (mg)** | | | | | |

**303.** Arrived at PACU ……PM/AM (time per 24hr/date/month/E.C)

**302**. First analgesic required time …….PM/AM (timeper24hr/date/month/E.C)

**303**. Number of analgesic request ……

**304**. Total and type of analgesic consumption within 24 hours after the patient arrived in recovery/ward……

**Section V: Complications observed**

**401.** Does the patient have nausea within the first 24 hours of surgery? 1. YES 2. NO

**402.** Does the patient develop vomiting within first 24 hours of surgery? 1. YES 2. NO

**403**. Does the patient develop motor/leg weakness within first 24 hours of surgery?

1. YES 2. NO

**404**. Does the patient develop sedation within first 24 hours of surgery? 1. YES 2. NO

**405**. Does the patient develop urine retention within first 24 hours of surgery? 1. YES 2. NO

**406**. If "Yes" for above question does the patient catheterized? 1. YES 2. NO

**407.** Does the patient develop any other complication within 24 hours of surgery? 1. YES 2. NO

**408**. If 'YES 'for above question then please list down the complication……

## Annex II Pain assessment tools

### FLACC Scale

Behavioral observation pain rating scale

| SCORING | | | |
|---|---|---|---|
| **CATEGORIES** | **0** | **1** | **2** |
| FACE | No particular expression or smile | Occasional grimace or frown, withdrawn, disinterested. | Frequent to constant quivering chin, clenched jaw. |
| LEGS | Normal position or relaxed. | Uneasy, restless, tense | Kicking or legs drawn up. |
| ACTIVITY | Lying quietly, normal position moves easily | Squirming, shifting back and forth, tense | Arched, rigid or jerking. |
| CRY | No cry, (awake or asleep) | Moans or whimpers; occasional complaint | Crying steadily, screams or sobs, frequent complaints |
| CONSOLABILITY | Content, relaxed | Reassured by occasional touching hugging or being talked to, distracted | Difficulty to console or comfort |
| Each of the five categories faces (A), legs (L), Activity (A), Cry(c), Consoliablity (C) is scored from 0-2, which results in a total score between 0-10. | | | |

Each category is scored on the 0–2 scale, which results in a total score of 0–10.

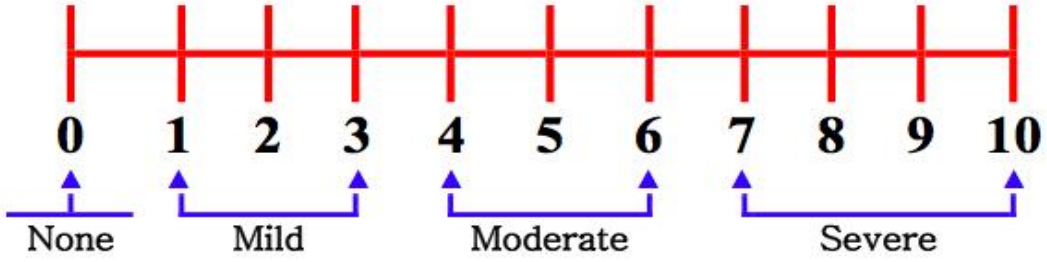
**0:** Relaxed and comfortable

**1–3:** Mild discomfort

**4 –6:** Moderate pain

**7–10:** Severe discomfort or pain or both

**Annex III: Numerical rating scale**



Annex IV: Data accuracy check list

| S.no | Tools | Yes | No |
|---|---|---|---|
| 1 | Are the inclusive /exclusive criteria done appropriately? | | |
| 2 | Are all questions socio demographic data filed appropriately? | | |
| 3 | Are all the questions on preoperative period data filled appropriately? | | |
| 4 | Are all the questions intraoperatively data filled appropriately? | | |
| 5 | Did the postoperative analgesic drugs filled with appropriate type of drug, time and dose? | | |
| 6 | Are all questions pain score followed strictly? | | |
| 7 | Are all incidence of complication data filled appropriately? | | |

## Annex V: ASA status

**ASA physical status classification:** The modern classification system consists of six categories, as described below

| ASA classification | Description |
|---|---|
| ASA I | Normal healthy patient. |
| ASA II | Patient with mild systemic diseases |
| ASA III | Patient with severe systemic diseases. |
| ASA IV | Patient with severe systemic diseases that is a constant threat to life. |
| ASA V | Moribund patient who is not expected to survive without the operation. |
| ASA VI | A declared brain dead patient whose organs are being removed for donor purposes |

**Adopted from Morgan and Mikhail 5th edition.**

## Annex VI: Information sheet

**Title of the Research Project:** To assess postoperative analgesic efficacy of caudal neostigmine added to bupivacaine for elective pediatric patients infra umbilical surgery from October, 1, 2019 G.C to January, 30, 2020 G.C at Tikur Anbesa Specialized hospital, Ethiopia.

**Name of the principal investigator: Yitayal Guadie**

**Name of the organization:** Addis Ababa University, Collage of Health Science, School of medicine, department of anesthesia.

**Name of the sponsor:** Addis Ababa University

**Introduction** : The main concern of this information was prepared with the aim of assessing the effect of adding neostigmine to bupivacaine on duration of a caudal block for prevention of post-operative pain during pediatric infra umbilical surgery at TASH. The research group includes the principal investigator, three data collectors and two advisers from AAU.

**Purpose of the Research project**: The main concern of this study to assess the effect of adding neostigmine to bupivacaine on duration of a caudal block for prevention of post-operative pain during pediatric infra umbilical surgery at TASH. The finding of this study is expected to be used by decision makers, FMOH, EAA, Department of Anesthesia and Health Practitioners.

**Procedure:** This study including all elective pediatric patients undergoing for infra umbilical surgery during the study period. They have been selected as part of the study participants whose parents are willing to participate in this study and willing to have consent. Anyone can have refused to participate during study.

**Benefits, Risk or Discomfort**

There will be no direct benefit to study participants, but they will be monitoring and follow for 24 hours. The result of this study will be used for further improvement of the service. There will no risk of participating in this study.

**Confidentiality:** The information collected from the study subjects will be keep confidential and stored in the file, without their name by assigning a code number to each.

**Right to refusal or withdraw**

Study subjects will have full right to refuse from participating in this research.

**Person to contact**

For any questions or concerns you can contact the principal investigator using the following addresses:

Name: Yitayal Guadie

Phone: +251918745577

E-mail: guadyitu@gmail.com

**Annex VII: study subjects consent form**

## Addis Ababa University

## College of Health Sciences

## School of medicine

## Department of Anesthesia

**Prospective Cohort Study, Post-Operative Analgesic Efficacy of Caudal Neostigmine Added to Bupivacaine for Pediatric Infra Umbilical Surgery in TASH, From October, 1, 2019G.C to January 30, 2020G.C**

Hello! My name is _____ I am of the members of the research team and I am here to ask you some questions and to collect some important information from your chart. If you are willing to participate in this research on postoperative analgesic efficacy of caudal neostigmine added to bupivacaine. So you are kindly requested to your child to participate on this study. I obtained the child name from the list of operation for surgery. Participation is voluntary. We strictly keep confidentiality. This observation will for 24 hours. Therefore, we kindly request your child to participate in the observation? I understood about the objectives of the research and the roles I will have in the research. I have agreed to participate in the research. **A**) **Agree B**) **Disagree**

If agrees, the observation will be started.

**Annex VIII Amharic Version: የጥናቱ ተሳታፊ ለመሆን የስምምነት ቅፅ**

# አዲስ አበባ ዩኒቨርስቲ

# ጤና ሳይንስ ኮሌጅ

# አንስቴዝያ ት/ት ክፍል

የተከበራችሁ የጥናቱ ተካፋይ ዎላጆች/የቅርብ ዘመዶች

ጤና ይስጥልን፡ስሜ----------ይባላል በአዲስ አበባ ዩኒቨርስቲ፣ጤና ምርምር ስር ተሳታፊ ነኝ ፈቃደኛ ከሆኑ ልጆዎን በጥናቱ ለማሳተፍ ፈልገን ነበር ስሙን ከቀዶ ህክምና ተራ አግኝተን ነዉ የማንኛውም ግለሰብ ስም አይመዘገብም እንዲሁም ሀሳቡ ብቻውን ይፋ እንዲዎጣ አይደረግም:: ሙሉ በሙሉ በሚስጥር የተጠበቀ ነው ።ይህ ጥናት ቀዶ ህክምና ለሚደረግላቸዉ ህፃናት ከጠቅላላ አንስቴዝያ በኋላ ከቀዶ ህክምናው በፊት የሚሰጠው(caudal anesthesia) ላይ የሚሰጥ በመዳኒቶች (bupivacaine ብቻውን ና bupivacaine ከ neostigmine ሲቀላቀል ) ለህመም ማሰታግሻ ለምን ያክልጊዜ እንደሚቆያ ለማዎቅ በጥቁር አንበሳ ልዩ የማስተማሪያ ሆስፒታል ህዳር አንድ እስክ የጥር ሰላሳ ድረስ ከእንብረት በታች ባለዉ የሰውነት ክፍል ለቀዶ ህክምና የሚመጡ እዲሜያቸው ከ አንድ እስክ አስራሁለት ያሉ ህፃናትን ለሃያ አራት ሰአት ወደፊት፣የህመም መጠን፣የመስታገሻ የሚጠይቁበትን ጊዜ ፣ምን ያህል የማሰታግሻ መድሀኒት በሃያ አራት ሰአት እነድተጠቀሙ እንዲሁም የማስታዎክ፣የማሰተኛት እግር አለመታዘዝ መኖር መከታተል ሲሆን ልጅዎን ለማሳተፍ የእርስዎን ፍቃድ ግድ የለውም መሳተፍ በፍላጎት ብቻ ነው።ስለዚህ ስምምነትዎን በአክብሮት እንጠይቃለን። የጥናቱን አላማ እንደሁም የኔን ሃለፊነት ተረድቻለሁ ሰለዚህ ልጄ እንዲሳተፍ

ሀ) ፈቅጀለሁ ለ) አልፈቅድም

ከፈቀደ /ች ክትትሉ ይጀመራል።

## Appendix I: English Version of Numeric Rating scale (NRS)

The scale will be taken 6 times within the first 24 hours. Patients will be asked to rate their pain will be assessed and recorded at 0 min (immediately on acceptance of patient at recovery room) and 0-1, 1-2,2-4,4-8,8-12,12-24 hours post-operatively.

The patient has been asked one of the following questions:

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)

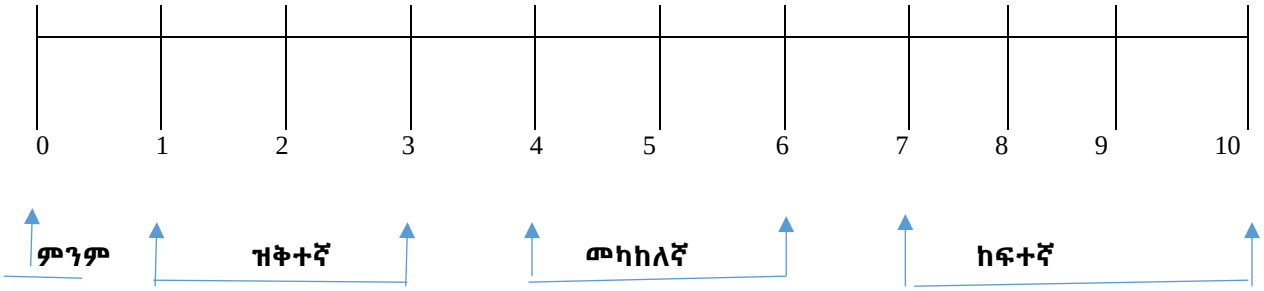
## Appendix II: አጣርኛ ትርጉም በቁጥር አምሳያ መለኪያ (NRS)

ይህ መለኪያ በመጀመሪያዉ 24 ሰአት 6 ጊዜ የሚወሰድ ሲሆን

ሀ) በሽተኛዉ የሚጠየቃቸዉ ጥያቄዎች

1.አሁን የሚሰማዎትን ህመም በየትኛዉ ቁጥር ይወክሉታል

2. ከዜሮ እስክ አስር ካሉት ቁጥሮች አሁን የሚሰማዎትን ህመም የትኛዉ ቁጥር ይገልፀዋል




ለ) ከላይ የተሰጠዉማብራሪያ በቂ ሳይሆን ሲቀር፣ለበሽተኛዉ የበለጠ መረጃ መስጠት አስፈላጊ ሆኖ ይገኛል

0- ምንም ህመም የለም

1-3 - ትንሽ ህመም አለ

4-6 - መካከለኛ ህመም አለ

7-10 - ከባድ ህመም አለ