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A COMPARATIVE STUDY ON POSTOPERATIVE ANALGESIC EFFECTIVENESS OF CAUDAL MORPHINE ADDED TO BUPIVACAINE IN COMPARISON WITH BUPIVACAINE ALONE FOR ELECTIVE PEDIATRIC UNDERGOING BELOW UMBILICAL SURGERY AT MINILIK II HOSPITAL, ADDIS ABABA, ETHIOPIA 2017/18

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JUNE, 2018

ADDIS ABABA, ETHIOPIA

Declaration

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

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Date of Submission: _____

This thesis work has been submitted for examination with my/our approval as Advisors and Tutors on the MSc in Advanced Clinical Anesthesia course

Name Signature

1. _____

2. _____

3. _____

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Abstract

Introduction: One of the most commonly used regional anesthetic techniques in pediatric surgeries is the caudal epidural block. Its main disadvantage remains the short duration of action. Hence, different additives have been used. The use of additives drug caudal anesthesia have increased in last decade by 58%. Uses of opioids additive has decreased from 36% to 18% due to high incidence of complications but other studies show that opioids prolong analgesia with minimum side effect; morphine is one of the opioid used additives used.

Objective: To compare the effectiveness of combination of bupivacaine with morphine and bupivacaine alone injected into the caudal space for relief of postoperative pain in pediatric undergoing below umbilical Surgery at Minilik II hospital from December – April 2017/2018.

Methods: The total of 60 pediatric patients from age 2-12 were participated in the study as standards of ASA I and II who underwent below umbilical surgery. After induction of general anesthesia, 30 children in Group-B received 1 ml/kg of 0.25% bupivacaine alone and the other 30 in Group-BM received 1 ml/kg of 0.25% bupivacaine with 20mic/kg morphine caudally. Demographic data, hemodynamic data before and after caudal, ASA status, duration of general anesthesia, duration of surgery, episode of post-operative nausea and vomiting (PONV) and pain score were recorded. Analgesic duration was defined as time from caudal injection to first rescue analgesic administration. Mann-Whitney test to compare median values and chi-square test and Fisher exact test for nominal data were used. A value “ $P < 0.05$ ” was considered as statistically significant.

Results: The median analgesic duration in Group-B was 360(495-338) minutes and 910(1200-705) minutes in Group-BM ($p < 0.001$). The PONV incidence was observed in Group-B 6 (20%) and Group- BM 8 (26.7%) and respiratory depression 1 (3.3%) and itching within Group-BM 2(6.7%) but not statistically significant difference across the groups ($p > 0.05$).

Conclusion and Recommendation: In routine clinical practice, addition of morphine to caudally administered bupivacaine prolongs analgesic duration without significant difference in postoperative complications.

Keywords: Caudal epidural block; Analgesia; Bupivacaine; Morphine; Postoperative

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List of Abbreviations

ASA - American Society of Anesthesiologist

CEB- Caudal Epidural Block

ECG - Electrocardiogram

FLACC - Face, Leg, Activity, Cry, Consolability Scale

IRB- Institutional Review Board

NSAID - Non Steroidal Ant inflammatory Drugs

PONV- Postoperative Nausea and Vomiting

PACU –Post Anesthesia Care Unit

SBP- Systolic Blood Pressure

PONV- Post Operative Nausea and Vomiting

SPSS - Statistical Package for Social Science

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CHAPTER ONE: INTRODUCTION

1.1 BACKGROUND

Pain is a highly unpleasant sensory and emotional experience further complicated in children by their inability to express and react (1). Various pharmacological agents and analgesic delivery systems have been employed to avoid under-treatment of pain in children (2). Caudal Epidural Block (CEB), which is technically easier in pediatrics than adults, can be used as a modality of treating pain due to below umbilical surgeries (3, 4).

Caudal block was first described in 1933 by Campbell, and it has become one of the most popular regional analgesic techniques today (5). Under general anesthesia caudal epidural block can be performed in the prone or lateral decubitus position. The first step is to identify the sacral hiatus and the caudal area is cleaned with an 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-gauge needle(6).

General anesthesia will often be required in addition to caudal block. This is due to the fact that pediatric patients do not generally tolerate surgery under regional anesthesia alone (7). The advantages of combined caudal block with general anesthesia is to reduce intraoperative inhalational or opioid agent consumption but also to obtain efficient postoperative analgesia for pediatric patients undergoing inguinal hernia, circumcision, hypospadias repair , orchidopexy, lower abdominal surgeries, superficial operations such as skin grafting, perineal procedures, and lower limb surgery(7) .

The main disadvantage of caudal anesthesia is the relatively short duration of action, even with the use of long-acting local anesthetics such as bupivacaine (8). 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. To improve the duration of action and quality of analgesia of a single shot caudal block with bupivacaine, various additives have been used, for example, opioids, neostigmine, and clonidine, with their associated side-effects (9) .Although addition of caudal opioids has been shown to provide sustained analgesia, their use can result in troublesome side-effects; including the potentially serious risk of respiratory depression (10).

1.2 STATEMENT OF THE PROBLEM

Pain management as one of the important components of balanced anesthesia is usually undertreated or neglected by many anesthetic providers in pediatric patients. This is due to the belief that children do not feel pain or they do not respond to pain to the same degree as adults (11, 12). This was proven otherwise by different studies confirming that children do feel pain and they respond to pain in the same degree as adult (13). In Ethiopia intraoperative and postoperative analgesia is commonly achieved by the use of suppository paracetamol (PCM).

Alternative analgesia or analgesic technique is required in order to provide adequate analgesia with less side effects and complications in pediatric patients. Peripheral and central blocks can be used as alternative method of providing perioperative analgesia.

Caudal anesthesia is widely used technique for providing regional anesthesia and analgesia in children undergoing below umbilical and lower limb surgeries and prolong its effect wide range of additives have been used in combination with local anesthetics to promote analgesia (14).

The use of additives drug caudal anesthesia have increased in last decade by 58% specially with ketamine 38% and clonidine 42%, whereas uses of opioids additive has decreased from 36% to 18% due to high incidence of complications(15). But various studies have reported the use of caudal morphine along with local anesthetic prolonged duration and the intensity of analgesia provided by it, still remains unparalleled provides analgesia with minimal side effects (16, 17, and 18).

The studies done in different countries are more depend on their own sociodemographic and different setups. So it's better to conduct research in our country than adopted the result of other studies that more different from our country in sociodemographic and setup.

Up to my search there were no studies conducted in regards to the interested title in Ethiopia so far. Thus the present study was aimed to analyze the effectiveness of two groups of drugs by comparing the duration of postoperative analgesic efficacy and side-effects of single-dose among pediatric patients undergoing below umbilical surgery.

Undertaking such studies in resource limited area can improve pain treatment and patient comfort by counteracting the effect of high patients to nurse ratio. On the other hand, it will open the gate to bring quality education and used as a baseline for further research activities.

1.3 SIGNIFICANT OF THE STUDY

Pain management is very important during and after surgery for both children and adults. Perioperative pain management by the use of opioids in Ethiopia is feared by many anesthetic providers because of the associated side effect. Because of this children have been denied medications during surgical interventions so as to avoid the side effect.

Caudal block in children is one of the most popular regional blocks which use different additives in order to increase duration of postoperative analgesia for children undergoing below umbilical surgeries. In Ethiopia even if caudal anesthesia is one of routinely done procedure there is a few published or documented data are available about the use of additive for caudal block in children. The introduction or adaptation of additive caudal block will become a good alternative analgesic technique in children undergoing below umbilicus surgeries.

The study will give some information on the analgesic efficacy and side effects of a combination of morphine with bupivacaine with bupivacaine alone in children undergoing lower umbilical procedures.

CHAPTER TWO: LITERATURE REVIEW

Pain management is a very important component of anesthetic management in pediatric and general population. The provision of adequate analgesia is necessary during and after any surgery and it is all more important in children who have long been under-medicated with narcotics for pain relief (11). When compared to adult children do feel pain at the same intensity as adults, but their response to pain is by crying, increase in heart rate and change in facial expression it's important that they receive the same care to alleviate pain(19).

Pediatrics response to analgesics varies according to age, site of surgery and additives given together with the local anesthetic agent, side effects are often unpredictable (20). There have been a number of recent advances that have allowed improvements in pain management in children. Regional anesthetic techniques have become one of the routine interventions in children and infants (21).

The most frequently used regional anesthetic technique are caudal and lumbar epidural blocks, ilioinguinal, iliohypogastric and penile nerve blocks, among those technique the most preferred pediatrics regional anesthetic technique is epidural block with a caudal approach. Indications for caudal block include anesthesia and analgesia below the umbilicus in pediatrics (22).

Caudal analgesia in combination with general anesthesia may affect the circulatory hemodynamic due to sympatholytic vasodilating effects where by lower body vascular resistance is reduced .A success or failure of caudal block can be determined by the hemodynamic changes following skin incision. Maintained or reduced value as compared to values before incision indicates a successful blocks. During surgery, adequate analgesia was defined by hemodynamic stability, as indicated by the absence of an increase in HR or SBP of more than 20% compared with baseline values obtained just before the surgical incision (23).

Pharmacologic Considerations for Caudal Epidural analgesia in Children

Drugs which are commonly used for caudal block includes, Lidocaine1%, Bupivacaine 0.25%, levobupivacaine, and ropivacaine. Bupivacaine is an amide local anesthetic with a slow onset and long duration of action (24, 25). Bupivacaine has a longer duration of action than lidocaine, is used more often and remains a commonly administered local anesthetic for single-dose caudal blocks. levobupivacaine and ropivacaine are also used because they have fewer side effects as compared to bupivacaine (26).

Research conducted at Muhimbili University of Health and Allied Sciences in Dar Es Salaam Tanzania, in 2013 by Angela Paul Muhozya show that duration of analgesia bupivacaine alone (8.2 ± 2.1) hr(27) .

Adjuvant to local anesthetics doses are;-

Additives to local anesthetic agents are very important because they improve the quality of the block intraoperatively, decrease the degree of motor block, increase the duration of action of the block, Lower the concentration of local anesthetics and have less Cardiovascular side effects compared to local anesthetics (28) . All adjuvant should be preservative free. There are different types of additives that can be used opioid and non opioid. Non opioids adjuvant includes ketamine, neostigmine and midazolam.

Epidural opioids when given together with local anesthetic agent enhance and prolong analgesia. Opioids and non opioids adjuvants may be combined in order to increase the analgesic effect and reduce side effects. Luz studied the effect of combined clonidine 1mg/kg, morphine 30mcg/kg with local anesthetic effect which showed better results compared to when only one adjuvant is added(29).

The study conducted in Hebrew University, Jerusalem, Israel show that caudal anesthesia supplemented with low dose morphine provides a longer duration of analgesia without significant side-effects in children undergoing renal surgery (30).

Research done by Robert D et al 138 case report show that caudal morphine in a large group of relatively young pediatric patients demonstrates its usefulness as a means of providing effective postoperative pain control. At the same time the clinician should be aware of the increased incidence of respiratory depression in patients under 1 yr of age, especially those patients that have received supplemental intravenous narcotics or have been dosed with caudal morphine via "high" caudal catheters (31).

The study done in India in 2004 by MK Arora et al. show that caudal analgesic using a combination of low dose morphine(0.03mg/kg) with bupivacaine offer a prolong duration of analgesia after pediatric urogenital, general surgical and orthopedic procedure lasting up to 26 hours without any significant increase in side effect (32) .

Comparative study done Egypt show that the addition of dexmedetomidine to local anesthetic bupivacaine for single dose caudal analgesia produced longer postoperative analgesia with fewer side-effects in children undergoing lower abdominal surgery when compared with morphine, with better emergence from anesthesia and hemodynamic stability (33).

2.2 HYPOTHESIS

Ho1: -There is no statistically significant difference in duration analgesia post-operative in bupivacaine group alone and morphine added group

HA1: - There is statistically significant difference in duration analgesia post-operative in bupivacaine group alone and morphine added group

H02:- There is no statistically significant difference in pain severity between two groups

HA2:- There is statistically significant difference in pain severity between two groups.

HO3: -There is no association between in complications between bupivacaine group alone and morphine added group

HA3: - There is association between in complications between bupivacaine group alone and morphine added group

2.3 Conceptual frame work

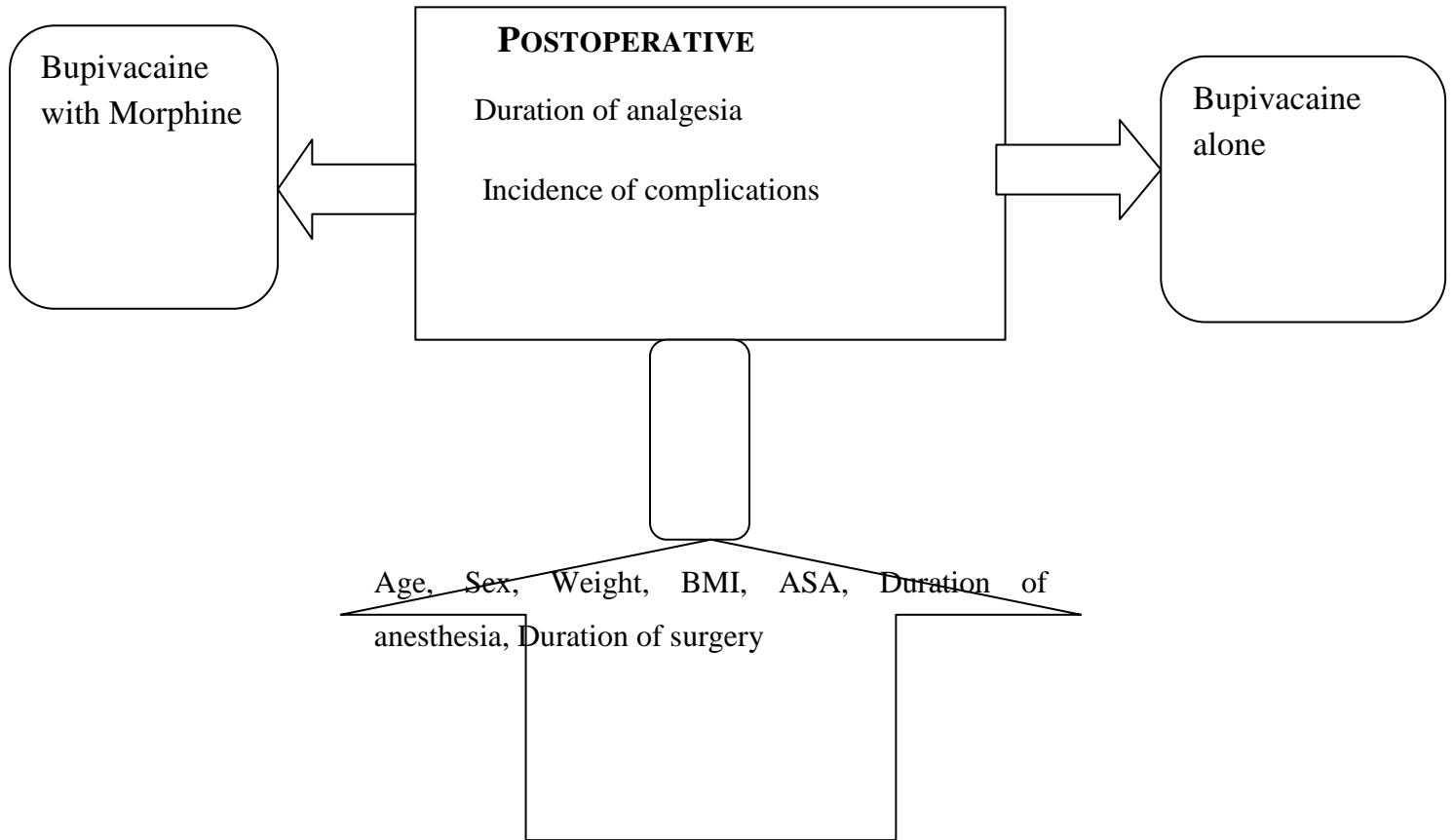


Figure 1 Conceptual frame work

CHAPTER THREE: - OBJECTIVES

3.1 General objective

To compare the effectiveness of combination of bupivacaine with morphine and bupivacaine alone injected into the caudal space for relief of postoperative pain in children undergoing below umbilical Surgery at Minilik II Hospital Addis Ababa Ethiopia from December, 1 –April, 30 2017/2018.

3.2 Specific objectives

- I). To compare the incidence of postoperative pain severity relief provided by adding morphine to bupivacaine with bupivacaine alone into caudal block
- II). To compare postoperative first analgesia request provided by adding morphine to bupivacaine with bupivacaine alone into caudal block
- III). To compare the side effects of adding morphine to bupivacaine with bupivacaine alone

CHAPTER FOUR: - METHODOLOGY

4.1 Study Area and period

The study was conducted at Minilik II Hospital is one of Addis Ababa university affiliated referral hospital in Addis Ababa Ethiopia. Minilik II hospital provides high quality comprehensive health services to patients from all over the region for around 1.6 million people per year. The hospital offer services with different specialty such as; medicine, general surgery, chest, eye, urology, trauma and orthopedic and pediatric. Also has in patients and outpatient department. The hospital has three major functional operation theaters and one recovery room. A study was conducted from December 1, 2017 to April 30, 2018.

4.2 Study design

Institutional based prospective cohort study design was employed for 24 hour.

4.3 Population

4.3.1 Source Population

All pediatric patients who admitted for below umbilical procedures at Minilik II hospital

4.3.2 Study Population

All pediatric patients schedule for below umbilical surgery under general anesthesia at Minilik II hospital during study period that fulfills the inclusion criteria.

4.4 Sampling Technique and Sample Size Determination

4.4. 1. Sample size determination

Two independent sample size formula based on the mean difference of time to first analgesia request among two groups were used to calculate sample size for each group. Having no previous study done in the study area, result adopted from literature has been used to calculate sample size based on the outcome variable. The study done in African countries show that (9.9 ± 1.2) hr in Egyptian (33) and (8.20 ± 2.1) hr in Tanzania (27).

$$n_1 = \frac{(\sigma_1^2 + \sigma_2^2)(Z_{\alpha/2} + Z_{\beta})^2}{(\mu_1 - \mu_2)^2}$$

When; n1- a group of bupivacaine alone,

n2- a group of bupivacaine with morphine,

$$\Delta = \mu_1 - \mu_2$$

Z=Z equal to 1.96,

$1 - \beta$ = the power of function 90% = 1.28,

σ_1 = Standard Deviation of bupivacaine alone,

σ_2 = Standard Deviation of morphine with bupivacaine,

μ_1 = Mean of bupivacaine alone and

μ_2 = Mean of morphine with bupivacaine.

$$n = (1.96 + 1.28)^2 (2.4^2 + 1.2^2) / (9.9 - 8.2)^2 = 27$$

$$n_1 = n_2 = 27$$

Using 1:1 ratio between groups and when 10 % of contingency is included for dropouts, total sample of 60 patients or 30 patients per group was required, based on the outcome variables and to get the largest sample size, a total of 60 pediatric patients was involve in the study.

4.4.2 Sampling technique: Systematic random sampling technique was used to select study participants on daily operation schedule list. Depending upon average values of the previous surgery per 5 months on the log book, 112 patients were operated on pediatric who take caudal anesthesia for elective below umbilical surgery. The sampling interval k was determined using the formula: $k = N/n$; where, n = total sample size, N = population per 5 months. Therefore, the sampling interval was 2 and the first study participant (random start) was selected using lottery method after which data collector recruit 1 patient for every 2 consecutive patients undergoes below umbilical surgery grouping based on whether they received caudal bupivacaine alone or bupivacaine with morphine till the required sample size is saturated.

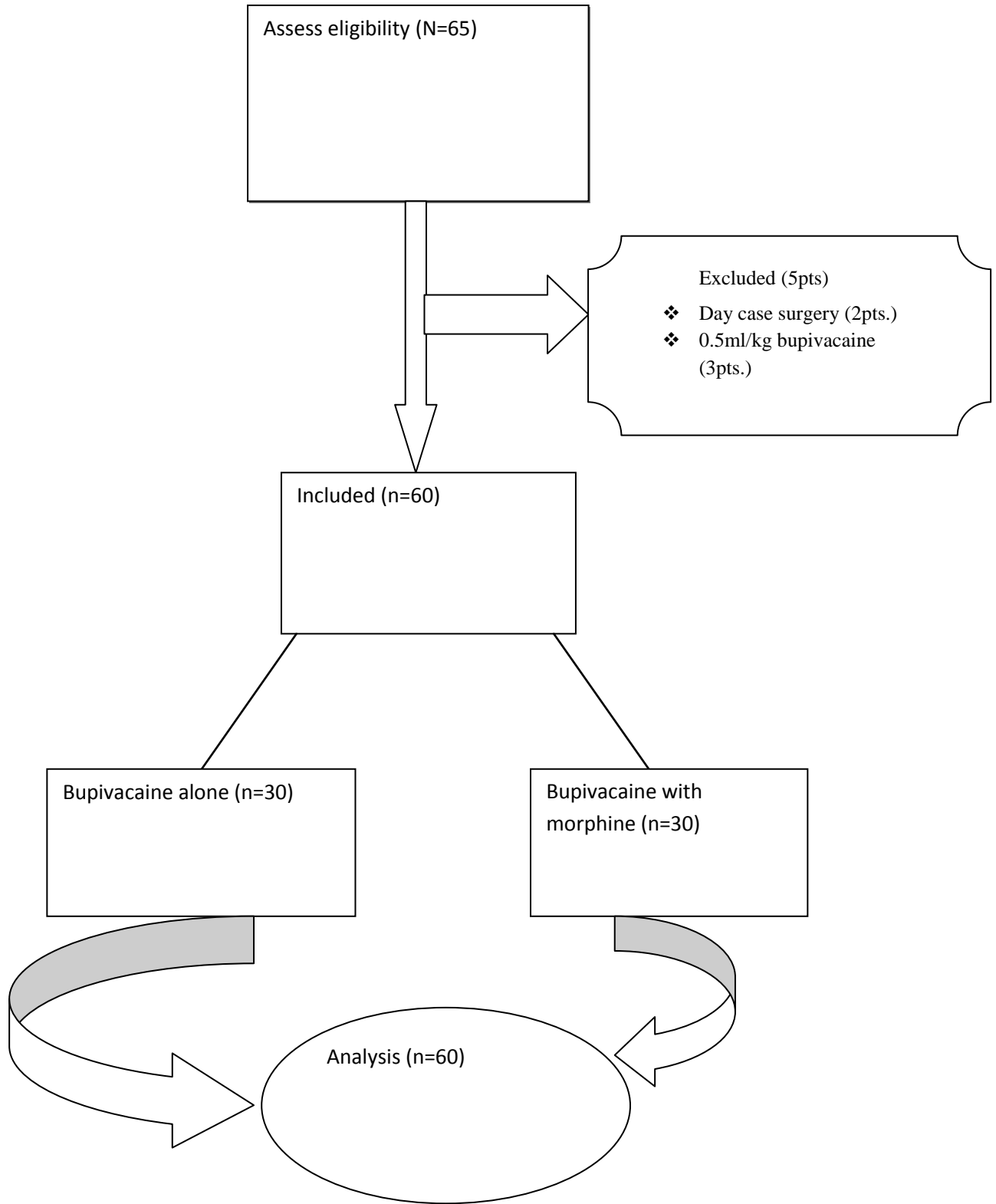


Figure 2. Enrollment chart for elective pediatrics patients scheduled at Minilik II hospital Addis Ababa, Ethiopia, from December – April 2017/18

4.5 Eligibility criteria

4.5.1 Inclusion criteria

- Patients who received caudal anesthesia
- ASA status I and II
- pediatric age between 2 and 12

4.5.2 Exclusion criteria

- Day case surgery
- failed caudal anesthesia
- Patients take addition anti pain perioperative
- Additive drugs used during caudal anesthesia other than morphine

Patients who fulfilled the inclusion criteria were divided into two groups based on exposure status

Group (BM):30 patients received 0.25% bupivacaine 1ml/kg + 0.02 mg/kg morphine added-exposed group

Group (BA):30 patients received 0.25% bupivacaine 1ml/kg alone –unexposed group since bupivacaine is commonly used in caudal block.

4.6 Study variables

4.6.1 Dependent variables

- Duration of analgesia
- Incidence of complications (postoperative nausea and vomiting, respiratory depression)

4.6.2 Independent variables

- Age
- Sex
- Weight
- BMI
- ASA status

- Vital sign
- Duration of anesthesia
- Duration of surgery
- Bupivacaine alone
- Morphine with bupivacaine

4.7 Operational Definition

ASA physical status classification

The modern classification system consists of six categories, as described below.

ASA 1 Normal healthy patient

ASA 2 Patients with mild systemic disease

ASA 3 Patients with severe systemic disease

ASA 4 Patients with severe systemic disease that is a constant threat to life

ASA 5 Moribund patients who are not expected to survive without the operation

ASA 6 A declared brain-dead patient who organs are being removed for donor purposes

Adequate analgesia: - defined as less than 20% or no increment of blood pressure, heart rate or respiratory rate in response to surgical manipulation

Day case:- Patient discharge after surgery to their home on a day of surgery

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

Duration of analgesia: - time interval in minutes between caudal injections to first rescue analgesic administration

Failed caudal anesthesia:- increment more than 20% of blood pressure, heart rate or respiratory rate in response to surgical manipulation

FLACC scale - After recovery from anesthesia FLACC scale used to assess postoperative pain in PACU and wards.

FLACC Scale

Behavioral observation pain score rating scale

Categories	Scoring		
	0	1	2
Face	No particular expression or smile ; disinterested	Occasional grimace or frown, withdrawn	Frequent to constant frown, clenched jaw, quivering chin
Legs	No position or relaxed	Uneasy, restless, tense	Arched , or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid, or jerking
Cry	No crying (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaint
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or talking to, Distractable	Difficult to console or comfort
Each of the five categories (F)Face; (L)Legs; (A)Activity; (C)Cry; (C)Consolability is scored from 0-2, which results in a total score between 0and 10			

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

- 0: relaxed and comfortable

- 1–3: mild discomfort
- 4 –6: moderate pain
- 7–10: severe discomfort or pain or both (41).

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

Respiratory depression- when Spo2 <93% and respond to supplementation of oxygen without requirement of naloxane or respirator rate is <10.

Time to first analgesia request: time from caudal injection to first rescue analgesic administration

4.8 Data Collection Tools

The checklist was prepared in English which includes socio demographic data, perioperative data, severity of pain, first analgesic request time, analgesic consumption and adverse effects. Pediatric patients scheduled for elective below umbilical surgery that fulfills inclusion criteria and parents' consent to take part in the study was instructed on how data collector uses to assess pain in the morning of operation day. Induction of anesthesia was done with Propofol or ketamine and maintenance with halothane or isoflurane. Baseline vital sign (blood pressure and heart rate) were measured and documented.

Patient monitoring included ECG, noninvasive blood pressure, pulse oximeter, precordial stethoscope and time to start induction was documented. IV line was secured for drugs and fluids administration, dextrose 10% NaCl 0.9% (4-2-1 regime) was given as maintenance during the operation. Atropine 0.02mg/kg was given for children based on anesthetist wish. Caudal block was done with bupivacaine alone 1ml/kg or bupivacaine (1ml/kg) with morphine (0.02mg/kg). Caudal was done left lateral position and performed by different hospital anesthetists and Msc anesthesia students. Pre incision parameters (blood pressure and heart rate) were measured 10 minutes after the block just before skin incision. Post incision parameters (BP&HR) were measured 5 minutes after skin incision. Inhalational concentration was reduced from 1.5% to 1% 10 minutes after incision, then hemodynamic parameters 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. 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. Postoperative after recovery from anesthesia FLACC scale was used to assess postoperative pain in the recovery room and wards on age of patient a FLACC score of 4 or greater indicated pain those children were given rescue analgesia. Patient was observed by trained nurses & pain score was documented on arrival to recovery room, 1st hour, 2nd hour, 4th hour, 6th hour, 12th hour and 24th hour after end of surgery. First analgesia request as well as total analgesia consumption and adverse effects such as post-operative nausea and vomiting, itching, motor block and respiratory depression was documented when it is reported within 24 hours.

Intraoperative data was collected by two anesthetists while postoperative data was collected by four nurses after getting training and the principal investigator supervise the completeness of the data weekly.

4.9 Data Analysis and Interpretation

Data was entered into entered into Epi-info 7 and exported to SPSS Version 20 for analysis. Shapiro Wilk test were used to test for distributions of data while homogeneity of variance were assessed using Levene's test for equality of variance. Median (Interquartile range) for asymmetric numeric variables. Comparison of numerical variables between study groups were done using Manny Whitney test for asymmetric variable. Chi square and fisher's exact test used to compare categorical variables. Frequency and percentage were used to describe categorical variable and statistical difference between groups were tested using Chi square. A p value <0.05 with power of 95% considered statistically significant.

4.10 Data Quality Control

Collected data were checked for completeness, accuracy and clarity. Incomplete data were not entered a data base prepared on Epi-info. Data clean up and cross-checking was done before analysis on SPSS. Supervision was done during data collection by principal investigator and M.Sc. anesthesia students.

4.11 Ethical consideration

Ethical clearance was obtained from the university ethical clearance committee before the start of the study. The importance of the study was explained & verbal 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 were 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 results of the study will be presented to the department of anesthesia as part of M.Sc. in advanced clinical anesthesia thesis, communicated through annual students and staff research conference, annual National conference of Ethiopian Anesthetists Association (EAA) and will be sent to journals for publishing.

CHAPTER FIVE: RESULT

5.1 Socio-demographic characteristics

Sixty pediatric patients were analyzed based on whether they received caudal block with additive of morphine or bupivacaine alone after induction of anesthesia for analgesia supplementation for intra operative and postoperative period.

Majority of study participants were male about 81.67 % (Table 1).

Table 1: Demographic and peri operative characteristics of pediatric patients at Minilik II hospital December – April 2017/18 Addis Ababa, Ethiopia

Variables	Bupivacaine alone group (n=30)	Bupivacaine with Morphine group (n=30)
Age #	6(3-8)	4(3-6)
Sex (Male/Female)	23/7	26/4
Weight #	17(14-23)	15(12-18)
BMI #	22(19-24)	23(19-25)
ASA (I/II)	26/4	27/3
Type of surgery		
Urogenital, n (%)	23(76.7%)	22(73.3%)
GI surgery, n (%)	7(23%)	8(26.7%)
Duration of surgery #	48(35-55)	50(50-82)
Duration of anesthesia #	52(40-60)	53(50-82)
Hint # = median(interquartilerange), n (%)-number(proportion)		

5.2 Preoperative, before skin incision and after skin incision Vital Sign between two groups

As regards the vital sign preoperative, before skin incision and after skin incision the recorded mean arterial pressure and pulse rate showed no statistically significant difference between the two groups p value >0.05 (Table 2).

Table 2 vital sign pre operative, before skin incision and after skin incision at Minilik II hospital Addis Ababa, Ethiopia from December – April 2017/18

Vital sign #	Bupivacaine alone group (n=30)	Bupivacaine with Morphine group (n=30)	P value
Baseline pulse rate (beat/minute)	127(115-130)	117(102-130)	0.157
Baseline mean arterial pressure (mmhg)	65(61-68)	69(63-72)	0.290
Before skin incision vital sign			
Pulse rate (beat/minute)	120(114-123)	122(110-130)	0.727
Mean arterial pressure (mmhg)	75(72-79)	75(70-78)	0.542
After skin incision vital sign			
Pulse rate (beat/minute)	112(107-119)	106(100-117)	0.057
Mean arterial (mmhg)	70(66-73)	67(60-72)	0.065
Hint # = median(interquartilerange)			

5.3 Comparison of Postoperative Pain Severity by FLACC between two groups

Manny Whitney test showed that there is statistically significant difference in pain score severity by FLACC between two groups (4, 6, 12, and 24)hour after the surgery with p value of <0.001 (Table 3).

Table 3. Comparison of postoperative pain severity using FLACC at Minilik II hospital Addis Ababa, Ethiopia, December – April 2017/18

Pain score postoperatively #	Bupivacaine alone group (n=30)	Bupivacaine with Morphine (n=30)	P _{value}
Immediately postoperatively	0(0-0)	0(0-0)	1.000
1 st hour postoperatively	0(0-0)	0(0-0)	1.000
2 nd hour postoperatively	1(1-2)	1(1-2)	0.277
4 th hour postoperatively	3(2-3)	1(1-2)	<0.001*
6 th hour postoperatively	5(3-6)	1(1-2)	<0.001*
12 th hour postoperatively	5(5-5)	3(2-4)	<0.001*
24 th hour postoperatively	5(4-5)	4(4-4)	<0.001*

Hint # = median(interquartilerange), * statistically significant

5.4 Comparison of Time to First Analgesia Request between Groups

As regards the total duration of postoperative analgesia as indicated by the FLACC score when it becomes 4 or greater, there was a statistically difference between group BA 360(495-337.50) and group BM 910(1200-705) with p_{value} <001 (Table 4).

Table 4. Comparison of time to first analgesia request in minutes between two groups at Minilik II hospital Addis Ababa, Ethiopia, December – April 2017/18

	Bupivacaine group (n=30)	Bupivacaine with Morphine group (n=30)	P _{value}
Time to first analgesia request median (IQR) in minutes	360(338-495)	910 (705-1200)	<0.001*

Hint –IQR InterQuartile Range, * statistically significant

5.5 Incidence of postoperative complications two between groups

The incidence of complication in recovery room and ward after recovery was as follow : six patients of group BA had nausea and vomiting ,whereas in group BM eight patients had nausea and vomiting , one patient respiratory depression and two patients had itching. The other complications like hypotension and bradycardia not recorded but no statistically significant difference between two groups with p value >0.05 (Table 5).

Table5. Postoperative complication within 24hour within two groups at Minilik II hospital Addis Ababa Ethiopia, from December – April 2017/18.

Postoperative complications within 24hours n (%)	Bupivacaine alone group (n=30)	Bupivacaine with morphine group (n=30)	P value
Nausea and vomiting, n (%)	6(20%)	8(26.3%)	0.754
Respiratory depression, n (%)	0(0%)	1(3.3%)	1.00
Itching, n (%)	0(0%)	2(6.7%)	0.492

n (%) - number (proportion)

CHAPTER SIX

6.1 DISCUSSION

Pain after surgery is common and the relief of acute pain has been inadequate in most places. The situation is worse in children, since they have long been denied or under medicated for acute pain (11). Caudal block provides excellent analgesia during surgery as well as during postoperative period following infra umbilical surgeries in children (23). Caudal epidural analgesia is a widely used technique for providing regional anesthesia and analgesia in children undergoing below umbilical surgeries and to prolong its effect wide range of additives have been used in combination with local anesthetics (35).

Various adjuncts are added morphine was one of the first additives used in 1981. Since then more studies have been conducted to prove its efficacy. Morphine placed in epidural space may undergo into epidural fat, systemic circulation, or may diffuse across the dura into cerebrospinal fluid (CSF). It produces analgesia by acting on mu, kappa and delta receptors (42).

In the present study, we found that the addition of low dose morphine 0.02 mg/ kg body weight to 0.25% bupivacaine (1 ml/kg body weight) significantly improved the quality as well as the duration of analgesia after below umbilical surgical procedure in children aged between 2-12 years. The done by fernades et al showed that duration of pain relief was significantly longer using morphine with bupivacaine range from 610-2195 min and 245-515min with bupivacaine alone group with statistically difference with p value >0.001.

Our study also shows comparable result with study done in India by Mahesh K. et al in 2005 on comparison of caudal bupivacaine and morphine for relief of post operative pain in children showed that the duration of analgesia was range from 5-12 hours in bupivacaine group and range 12-26 hours in morphine mixed with bupivacaine group. In our study result was duration analgesia range from 240- 660 minutes in unexposed group and range 420 – 1560 minutes in exposed group post operative. The likely explanation for the similarity between two studies is the block was given with similar dose.

The study done by Fernades et al. showed that the duration of analgesia post operative was range from 610-2195 min in exposed group and 245-515min in unexposed group. Contrary our finding is due to the dose of morphine they used (0.05mg/kg).

Our finding shows the overall incidence of nausea and vomiting in both group after surgery in the first 24 hours was 21.7%. This proportion is less high in the exposed group with incidence of 26.7% compared to 20% in the unexposed group. Though there is a proportion difference, there is no statistical difference between two groups with regard to decreasing the incidence of nausea and vomiting in the first 24 hours ($p > 0.05$). These shows compare figures to study done by Mahesh k. Arora et al postoperative nausea vomiting over all 18.75% in bupivacaine alone group was 15% and 22.50% in morphine group but on respiratory depression in across the groups but in our study we found that 3.3% in morphine group. Other study showed that PONV increase with the parallel with dose of morphine M CESUR et al in 2007 done on the effect of reduction of the caudal morphine doses on quality of postoperative analgesia in dose of 0.01mg/kg,0.015mg/kg and 0.03mg/kg the incidence of nausea and vomiting was 13.3 %, 20 %and 46.7% respectively but no respiratory depression across the groups.

In our study effectiveness was evaluated based on FLACC for Pain scores. The FLACC has been tested, and its validity and interpreter reliability were established in 1997 (40). Von Baeyer et al. (41) found that the FLACC has moderate concurrent validity with the Faces Pain Scale and good validity with Visual Analog Scale for Pain. They noted that the FLACC is highly recommended for use in studies since it has excellent evidence of reliability, validity and responsiveness.

In our study demonstrate the median (interquartile) pain score by FLACC at (4, 6, 12 and 24) hour after surgery higher in unexposed group than exposed group with P value <0.001 . The result of this study is in line with study done by Fernades et al (2012), FLACC Pain score at (6,12 and 24) after surgery higher in group Bupivacaine Alone than group Bupivacaine Morphine with P value <0.05 .

6.2 Limitation of the Study

The main limitations of this study were:

Inabilities to assess urinary retention as many of our study patients were catheterized. Lack of randomization and control. Variability in the performance of the caudal block since different anesthetists were involved. Most of our studies we used for comparison were randomized control trial.

6.3 Strength of the study

The strength of our study participants were homogenous between the two groups.

CHAPTER SEVEN: CONCLUSION AND RECOMMENDATION

7.1 CONCLUSION

We conclude that morphine added to bupivacaine in caudal block increased the duration of postoperative analgesia. Provided stable hemodynamic and minimal side effects in pediatric patients. Besides, using morphine with bupivacaine decreases the number of doses of rescue analgesic required in the first postoperative day without significant complications. So it can be termed as a suitable additive for caudal block in children.

7.2 Recommendation

We recommend that a use of additive morphine for caudal block for pediatric patient is an effective for post-operative analgesia.

We also recommend additional randomized controlled study.

References

1. Barbara G. Melamed, et al. Influence of time and type of preparation children adjustment for surgery. *Journal of pediatric psychology* 2013; 1: 31-37.
2. *Dalens BJ*. Regional anesthesia in children. *In: Miller RD (Ed.). Anesthesia, 5th ed.* Philadelphia: Churchill Livingstone; 2000: 1549–85.
3. Wong SY, Li JY, Chen C, Tseng CH, Liou SC, et al. Caudal epidural block for minor gynecologic procedures in outpatient surgery. *Chang Gung Med J* 2004; 27: 116-121.
4. Alice E, Vinit GW Caudal Epidural Anesthesia for pediatric patients: A safe, reliable and effective method in developing country. *Update Anaesthesia* 2003; 17:15-19.
5. Brown TCK. History of pediatric regional anesthesia. Australia: Blackwell Publishing Ltd; 2012; 3-9.
6. Bainbridge, W et al .Pediatric Epidural and caudal analgesia and anesthesia in children; 2009:14:3
7. Hudson-Goodman P, Martin J. Beneficial effects of the combined techniques of caudal and general anesthesia in the pediatric patient: two case reports..*CR*1992 Nov;3(4):183-563
8. Cook B, Doyle E. The use of additives to local anaesthetic solutions for caudal epidural blockade. *Pediatric Anaesth* 1996; 6: 353–9
9. Abdulatif M, El-Sanabary M. Caudal neostigmine, bupivacaine and their combination for postoperative pain management after hypospadias surgery in children. *Anesth Analg* 2002; 95: 1215–8
10. *Batra YK, Arya VK, Mahajan R, Chari P*. Dose response study of caudal neostigmine for postoperative analgesia in pediatric patients undergoing genitourinary surgery. *Paediatr Anaesth* 2003; 13: 515–21
11. Scheter NL, Allen DA, Hanson K. Status of paediatric pain control: A comparison of hospital analgesia usage in children and adult. *paediatrics* 1986;77:11-15

- 12 . McCaffery M, Han L. Undertreatment of acute pain with narcotics. *American Journal of Nursing* 1976; 76: 1586-1591.
13. Lloyd-Thomas AR. Pain management in paediatric patients. *Br J Anaesth.* 1990;64(1):85-104.
14. Peutrell JM et al. *Regional anesthesia for babies and children* .Oxford: oxford university press.1997; 187-233.
15. Menzies R. et al. A Survey of pediatric caudal extra dural anesthesia practice .*paedia AnAesth.* 2009; 19:829-36.
16. Jensen BH. Caudal block for post operative pain relief in children after genital operations. A comparison between bupivacaine and morphine. *Acta Anaesthesiol Scand* 1981; 25: 373-375.
17. Krane EJ, Jacobson LE, Lynn AM, et al. Caudal morphine for post operative analgesia in children : A comparison with caudal bupivacaine and intravenous morphine. *Anesth Analg* 1987; 66:647-653.
18. Valley RD, Bailey AG. Caudal morphine for post operative analgesia in infants and children : A report of 138 cases. *Anesth Analg* 1991; 72:120-124.
19. Beyer JE, DeGood DE, Ashley LC, Russel GA. Patterns of post-operative analgesic use with adults and children following cardiac surgery. *Pain* 1983; 17: 17-81
20. . Khairat Mohd, Yasir, G. A. Mir Effect of Age, Adrenaline and Operation Site on Duration of Caudal Analgesia in Paediatric Patients vol 5 ,no 2, April-june 2003
21. Ross AK, Eck JB, Tobias JD. Paediatric regional anaesthesia: Beyond the caudal. *Anesth Analg.* 2000; 91:16-26.
22. Miller RD, Fleisher LA, Johns RA, et al. *Miller's Anaesthesia*. Houston: Elsevier, 2005; 1732-1734
23. Hong JY, Ahn S, Kil HK. Changes of dorsalis pedis artery flow pattern after caudal block in children: observational study using a duplex sonography. 2011 Feb; 21(2):116-20
24. Murat I, Delleur MM, Montay G, Saint-Maurice C. Bupivacaine pharmacokinetic during continuous epidural anesthesia in children (abst). *Anesthesiology* 1986;65:A425

25. Mazoit JX, Denson DD, Ahmad R, Samii K. Pharmacokinetics of bupivacaine in infants after caudal anesthesia (abst). *Anesthesiology* 1986;65:A431.
26. Silvani P, Camporesi A, Agostino MR, Salvo I. Caudal anesthesia in pediatrics: An update. *Minerva Anesthesiol.* 2006;72:453–9.
27. Angela paul muhozya. caudal block for pain relief in children undergoing perineal and lower abdominal surgeries . Muhimbili national hospital dar es salaam, Muhimbili University of Health and Allied Sciences July, 2013.
28. Marri SR. Adjuvants agents in regional anaesthesia. *Anaesthesia and Intensive care Medicine.* 2009.10;11
29. Luz G, Innerhofer P, Oswald E, Salner E, Hager J, Sparr H. Comparison of clonidine 1mg/kg with morphine 30 mg/ kg for post-operative caudal analgesia in children. *Eur J Anaesth* 1999; 16: 42-627
30. Boris Chertin et al. Use of Caudal Analgesia Supplemented with Low Dose of Morphine in Children Who Undergo Renal Surgery. *Current urology.* 2015;9:132-37
31. Robert D. Valley, MD, and Ann G. Bailey, MD. Caudal Morphine for Postoperative Analgesia in Infants and Children: A Report of 138 Cases. *Anesth Analc* 1991;72:120-4
32. Mahesh k. Arora et al. Comparison of caudal bupivacaine and morphine for relief of post op pain in children *Anesthesia Intensive Care* 2005; 3: 1
33. El Shamaa and Ibrahim: A comparative study of the effect of caudal dexmedetomidine versus morphine added to bupivacaine in pediatric infra-umbilical surgery. *Saudi Journal of Anesthesia.* 2014; 8(2).
34. Peutrell JM, Mather SJ. *Regional anesthesia for babies and children.* Oxford: oxford university press 1997; 187-233.
35. Krane EJ, Jacobson LE, Taylor DC. Caudal epidural morphine in children : A comparison of three doses. *Anaesthesiology* 1988; 69:A763.
36. Karl HW, Tyler DC, Krane EJ. Respiratory depression after low dose caudal morphine. *Can J Anaesth* 1996; 43 (10): 1065-1067.
37. Mayhew JF, Brodsky RC, Blakey D, Petersen W: Low-dose caudal morphine for postoperative analgesia

in infants and children: a report of 500 cases. *J Clin Anesth* 1995; 7:640–642.

38. Cesur M, Alici HA, Erdem AF, Yapanoglu T, Silbir F: Effects of reduction of the caudal morphine dose in paediatric circumcision on quality of postoperative analgesia and morphine-related side-effects. *Anaesth Intensive Care* 2007;35:743–747.

39. Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S: The FLACC: a behavioral scale for scoring postoperative pain in young children. *Pediatr Nurs* 1997; 23:293–297.

40. Von Baeyer CL, Soagryd LJ: Systematic review of observational (behavioural) measures of pain for children and adolescents age 3 to 18 years. *Pain* 2007; 127:140–150.

41. Sandra Merkel M, RN, Terri Voepel-Lewis, MS, RN, and Shobha Malviya, MD, . The FLACC: A behavioral scale for scoring postoperative pain in young children. *Pediatric Nursing*. 1997;23(3):293-7.

42. Fernandez ML, Pires KC et al. Caudal morphine or clonidine or supplemented with morphine plus clonidine in children undergoing infraumbilicus urologic and genital procedures : A prospective randomized and double-blind study *J Anesthesia* .2012 ;26:213-8[**pubmed**]

Annex

Annex I: - INFORMED CONSENT

My name is..... I am anesthesia provider. We are doing study on caudal block (CEB) .I am going to give you information and invite your child to be part of this research. You do not have to decide today whether or not your child will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

The study procedure: I the principal investigator (Zewdie) will give you the explanation of the study. The anesthetist who will administer the anesthetic may also collect and record data on my behalf. He/ she will also be in position of explaining further procedures for you. Your identity will be protected with utmost confidentiality during the study and only the initials and your medical registration number will be used to identify you.

I _____ have understood the explanation of this study.

I have allowed my child to participate in this study and understand that whether or not my child participates, the care he/she receive will not be compromised in any way whatsoever.

I also understand that I may choose to withdraw my child from the study at any stage without any penalty.

Signature: _____

Patient (Parent or guardian): _____

Anesthetist _____

Date _____

Annex II- Questionnaire

Addis Ababa University, College of Health Sciences Department of Anesthesia

Prospective Cohort Study, Comparison of Postoperative analgesic Effectiveness of Bupivacaine with Morphine to bupivacaine alone Caudally In Pediatric Patients undergoing below umbilical Surgery at Minilik II Hospital, Addis Ababa Ethiopia

Section I: Socio Demographic Data

Card number:		Bed no.	Code
Serial no.	Question	response	
101	AGE		
102	WEIGHT		
103	BMI		
104	ASA I/II	1. ASA I 2. ASA II	
105	SEX M/F	1. Male 2. Female	

Section II: Data during pre and intraoperative period

S. NO.	Question	RESPONSE	CODE
201	Diagnosis	
202	Procedure:	
203	Base line heart rateBPM	
204	Baseline blood pressure/.....(.....)mmhg	
205	Mean arterial pressure		
206	Baseline spo2		
207	Dose the patient take Analgesic	1. yes 2.no	
208	If yes for the above question, what was the drug? specify the dose?		
209	Premedication drugs (mg)		
210	Induction agents		
211	Induction time		
212	Time of caudal block		
213	Time taken to perform block		
214	Drug used for caudal block?		
215	Maintenance anesthesia used		
216	Vital sign before skin incision?	BP:...../.....(.....)mmhg PR:.....bpm Spo2.....	
217	Vital sign after skin incision?	BP:...../.....(.....)mmhg PR:.....bpm Spo2.....	

218	Duration of surgery		
219	Duration of anesthesia		

Section III Post-Operative Observation Vital sign at recovery room

<u>Vital sign</u>	<u>At Arrival</u>	<u>20min</u>	<u>40min</u>	<u>60min</u>
<u>PR</u>				
<u>BP</u>				
<u>SPO2</u>				
<u>FLACC/NRS SCORE</u>				
<u>Analgesia given (dose in mg)</u>				

SECTION IV POST OPERATIVE OBSERVATION

S.no	Follow up time	0 hr	1 st hr post op	2 nd hr post op	4 th hr post op	6 th hr post op	12 th hr post op	24 th hr post op
301	FLACC/NRS SCORE							
302	Analgesia given Type and mg							

303) First Analgesic required time _____ PM/AM (time per 24hr/date/month/E.C)

304) Duration till first analgesic request _____

305) 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 leg weakness within first 24 hours of surgery? 1. YES 2. NO

404) Does the patient develop respiratory depression 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.....