A STUDY OF THE EFFECT OF CAUDAL EPIDURAL NEOSTIGMINE FOR RELIEF OF POST OPERATIVE PAIN IN CHILDREN UNDERGOING LOWER ABDOMINAL GENERAL SURGICAL PROCEDURES.

Dissertation submitted for M.D. Degree Examination

Branch X - Anaesthesiology

THANJAVUR MEDICAL COLLEGE,
THE TAMILNADU DR MGR MEDICAL UNIVERSITY,
Chennai – Tamilnadu.
MARCH – 2008.

CERTIFICATE

This is to certify that this dissertation entitled

"A study of the effect of caudal epidural neostigmine for relief of post operative pain in children undergoing lower abdominal general surgical procedures."

is a bonafide record of the work done by Dr.s.kannan under my supervision and guidance in the department of Anaesthesiology at Government Raja Mirasudhar Hospital of Thanjavur medical college, Thanjavur during the period of his post graduate study from May 2005 to March 2008 for the partial fulfillment of M.D.(Branch X - Anaesthesiology) degree.

Professor and Head of Department,
Department of Anaesthesiology,
Thanjavur medical college,
Thanjavur.

The Dean,
Thanjavur medical college,
Thanjavur.

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INTRODUCTION

Pain has become the fifth vital sign and is now a critical focus of the patient. The relief of pain has always been part of anaesthesiologist's role. In the immediate post operative period and extending beyond post anaesthesia care unit. There is also increasing evidence that optimal pain management can impact outcome beyond the intra operative period. Alleviation of post operative pain may continue to improve clinical outcomes, hasten recovery, facilitate early mobilization and return to daily living.

The treatment and alleviation of pain is a basic human right. Children suffer pain in the same way as adults though they may be unable to describe the pain or their subjective experiences. Unfortunately even when their pain is obvious children frequently receive no treatment or inadequate treatment.

PAIN is a perception that is far more complex than simple transmission of information along nerve pathways to brain.

It consists of component of transmission of pain sensation, a component of processing and evaluation by higher centers of brain and a component of reaction to sensation.

The response to PAIN in children consists of behavioral, psychological and social changes. The cognitive ability, child's trust of caregivers and previous painful experiences will influence this response.

The manner in which the family reacts to the stress of a child's pain will also influence the response to pain. Appropriate pain management is of great importance when dealing with children, because the way the child is treated may influence the way he/she deals with pain for rest of his /her life.

Untreated Pain can lead to physiologic complications, psychological distress, and personality changes in developing children, family disruption, interruption of hospital routine and prolongation of hospitalization with resultant increased costs. In addition social withdrawal, temper tantrums and demanding behaviour are also seen in these children. Children withdraw from their environment and stop participating in interpersonal interactions.

Various pharmacological agents and analgesic delivery systems have been employed to avoid under treatment of pain in children. Many children will withdraw or deny their pain in an attempt to avoid yet another terrifying and painful experience-the intramuscular injection or "shot".

Genito urinary surgery is generally associated with considerable pain of long duration.

Caudal extradural block with bupivacaine ensures satisfactory analgesia in the initial post operative period only, and becomes ineffective once the block wears off.

Various methods have been devised to extend the duration of regional analgesia with local anaesthetics. Like placement of a catheter and using adjuvants like, clonidine, tramadol, ketamine and opioids.The placement of a catheter posses an inherent risk of

infection and delays mobilization.

The use of ketamine, clonidine and opioids is limited because of potential side effects such as sedation, respiratory depression, nausea and vomiting.

The role of neostigmine as an analgesic administered by the extra dural route is now well established in children and adults. Co administration of caudal neostigmine in a dosage of 2µg/kg with bupivacaine or ropivacaine has been found to prolong analgesia without any adverse effect.

Extra dural neostigmine (1, 2 or 4µg/kg) with local anaesthetic has been found to produce a dose independent analgesic effect in adult patients without increasing the incidence of adverse effects.

AIM OF THE STUDY

A study of the effect of caudal epidural neostigmine for relief of post operative pain in children undergoing lower abdominal general surgical procedures.

ANATOMY OF THE CAUDAL EPIDURAL SPACE

SACRAL HIATUS

It is a bony defect, triangular in shape and situated at the lower end of the sacrum just above the sacrococcygeal junction. The hiatus results from non-fusion of the 5th sacral and at times 4th sacral vertebral arches. It appears as an inverted U or V; the large bony processes on each side are called the cornua. The sacral cornua are in fact the embryological remains of the inferior articular processes of the 5th sacral vertebrae. The hiatus is covered by the sacrococcygeal membrane formed by the superficial and deep fibers of sacrococcygeal ligaments and is attached laterally to sacral cornua.

The sacrococcygeal membrane is actually a continuation of ligamentum flavum. The sacrum is cartilaginous in neonates and infants**,** and its ossification is completed between 25 to 30 years of age. At increasing age, the sacrococcygeal angle increases, thus closing sacral hiatus and therefore making caudal anaesthetic more difficult. This is especially true after the age of 7 years**.**

SACRAL CANAL AND THE CAUDAL EPIDURAL SPACE

The sacral canal is a caudal extension of the spinal canal. The spinal canal contains the last spinal nerve roots, which forms the cauda equina and also the filum terminale that anchors spinal cord to coccyx and sacrococcygeal ligament. The dural sac projects upto S3 - S4 level at birth, reaching the adult level of S2 during second year of life.

The caudal epidural space in a neonate is filled with epidural fat, which has a

gelatinous spongy appearance with distinct spaces between the fat globules and very few connective tissue fibers. This facilitates uniform and rapid spread of the local anaesthetic solutions. Between 6 to 7 years of age, the epidural fat gets denser and is surrounded by fibrous strands, thus reducing uniform spread of local anaesthetic solutions. The epidural space is richly vascularised and the veins are without valves; thus an inadvertent intravascular injection can lead to instantaneous systemic toxicity.

Caudal anaesthesia requires identification of the sacral hiatus. The sacrococcygeal ligament overlying the sacral hiatus lies between the sacral cornu. To facilitate locating the cornu, the posterior superior iliac spine should be located and by using the line between them as one side of an equilateral triangle, the location of sacral hiatus approximated. After the sacral hiatus is identified the index and middle finger of the palpating hand are placed on the sacral cornu, and the caudal needle is inserted at an angle of approximately 45 degrees to the sacrum. While advancing the needle, a decrease in resistance to needle insertion should be appreciated as the needle enters the caudal space. The needle is advanced until bone is contracted and then slightly withdrawn, and the needle is redirected so that the angle of insertion relative to the skin surface is decreased. In male patients this angle is almost parallel to the coronal plane, in female patients, a slightly steeper angle (15 degree) is necessary. During redirection of the needle and after loss of resistance again encountered, the needle is advanced approximately 1 to 2 cm into the caudal canal.

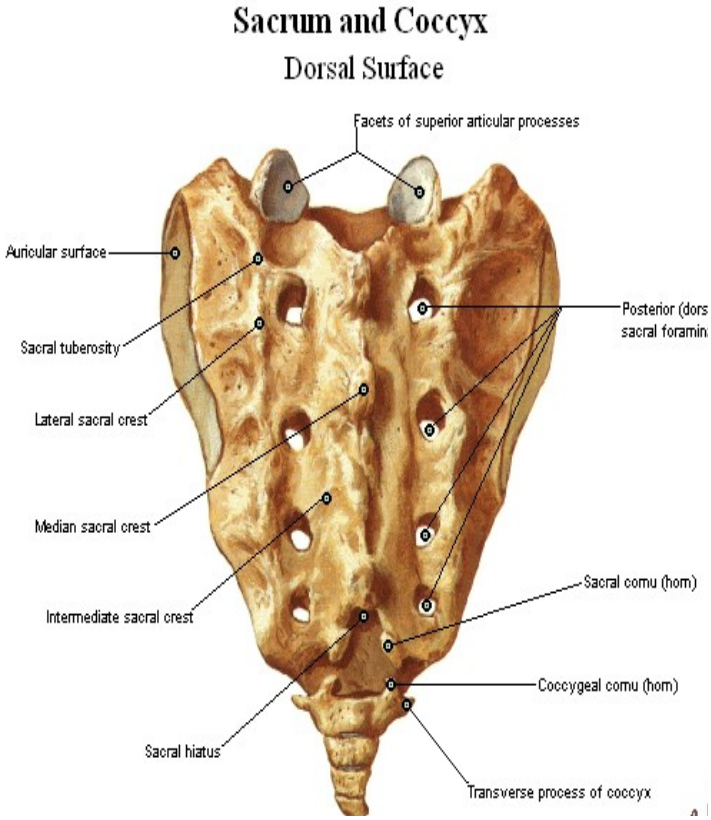

Sacrum and Coccyx
Dorsal Surface
Facets of superior articular processes
Auricular surface
Sacral tuberosity
Lateral sacral crest
Median sacral crest
Intermediate sacral crest
Sacral hiatus
Posterior (dors
sacral foramin
Sacral cornu (horn)
Coccygeal cornu (horn)
Transverse process of coccyx

FIG -1

COMPLICATIONS OF CAUDAL ANAESTHESIA

Intravascular or intraosseous injection:-This may lead to grand mal seizure and cardio respiratory arrest.

Dural puncture: Extreme care must be taken to avoid this as a total spinal block will occur if a dose for a caudal block is injected into the subarachnoid space.

Perforation of the rectum: While simple needle puncture is not important, contamination of the needle is extremely dangerous if it is then inserted into the epidural space.

Sepsis: This should be very rare occurrence if strict aseptic procedures are followed

Urinary retention: This is not uncommon and temporary catheterization may be required

Subcutaneous injection: This should be obvious as the drug is injected

Hematoma:

Absent or patchy block:

PHARMOCOLOGY OF BUPIVACAINE

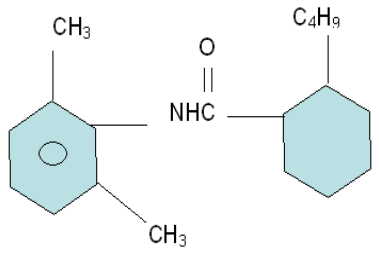
The pharmacology of local anaesthetics is generally the same in children as it is in adults. There are differences like

1. Increased volume of distribution
2. Decreased protein binding of local anaesthetics
3. Enzyme immaturity

Decreased protein binding of local anaesthetics and enzyme immaturity can lead to systemic toxicity of local anaesthetics with high protein affinity.

Caudal injections of bupivacaine are now routinely used in children undergoing lower abdominal and urogenital surgery to provide intraoperative and postoperative analgesia.

BUPIVACAINE



It is an amide local anaesthetic characterized as pipecoloxylidides. Addition of a butyl group to the piperidine nitrogen of mepivacaine results in Bupivacaine. It is a chiral drug because of possession of asymmetric carbon atom.

It was first synthesized in Sweden by **EKENSTAM** and his colleagues in 1957 and used clinically by **L.J.TELIVUO** in 1963. Its molecular weight is 288.

MECHANISM OF ACTION

It prevents transmission of nerve impulses by inhibiting passage of sodium ions through ion selective sodium channels in nerve membranes. They do not alter the resting transmembrane potential or threshold potential.

PHARMACOKINETICS

It is a weak base that has pk value above physiologic pH. At pH 7.4 only 15% exists in nonionised form. Absorption depends on the site of injection, dosage and use of epinephrine. Lung is capable of extracting bupivacaine from circulation, which will limit concentration of drug that reaches systemic circulation. This first pass pulmonary extraction is dose dependent suggesting that it becomes saturated rapidly.

pk	:	8.1
Protein Binding	:	95%
Lipid solubility	:	28

Volume of distribution	:	73 litre
Clearance of drug from plasma	:	0.471 lit/min
Elimination half life	:	210 min (3.5 hours)
Onset time	:	5 -7 min
$t_{½}\alpha$	:	2.7 min
$t_{½}\beta$	:	28 min

METABOLISM

Slowest metabolism among amide local anaesthetics. It undergoes aromatic hydroxylation, N- dealkylation, amide hydrolysis and conjugation. Only the N-desbutyl bupivacaine has been measured in blood or urine after epidural or spinal anaesthesia. Alpha-1 acid glycoprotein is the most important protein-binding site of bupivacaine.

SIDE EFFECTS

Bupivacaine is more cardio toxic than equieffective doses of Lignocaine. This is manifested by severe ventricular arrhythmias and myocardial depression. Bupivacaine blocks cardiac Na+ channels rapidly during systole and dissociates more slowly during diastole, so that a significant fraction of Na+ channels remain blocked at the end of the diastole. Thus the block by Bupivacaine is cumulative and substantially greater.

CLINICAL USE

Onset of anaesthesia and duration of action are long. Its tendency to provide more

sensory than motor block has made it popular for providing postoperative analgesia. Used mainly for

- Infiltration anaesthesia
- Field block anaesthesia
- Nerve block anaesthesia
- Spinal anaesthesia
- Epidural anaesthesia

RECOMMENDED DOSE

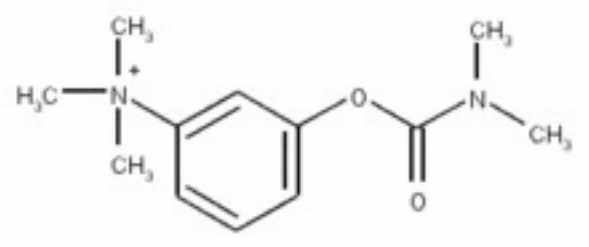
Bupivacaine without epinephrine – 2.5 mg/Kg

Bupivacaine with epinephrine – 3 mg/Kg

TOXIC PLASMA CONCENTRATION THRESHOLD

- 2 µg / ml

PHARMOCOLOGY OF NEOSTIGMINE METHYL SULPHATE



Acschlimam and Reinert synthesized neostigmine methyl sulphate in 1931.Anti curare action were discovered by Pal in 1900.

It prevents normal hydrolysis of Acetyl choline and so allows it to accumulate at neuro muscular junction. It is a standard antagonist to d-tudocurarine or other non depolarizing muscle relaxants.

PHARMACOLOGICAL ACTIONS

CNS:

By inhibiting normal hydrolysis of acetyl choline at the sites at which it is released,neostigmine raises the concentration and duration of action of acetyl choline. Neuraxial neostigmine is known to produce analgesia in animals, human volunteers and patients with pain.

Neuraxial administration of neostigmine inhibits breakdown of the endogenous spinal neurotransmitter acetyl choline, which has been shown to produce analgesia.

The analgesic effect is thought to be mediated via spinal muscarinic (M1) receptors A dose response study of caudal neostigmine has proved its efficacy and safety in paediatric patients. Dose dependant analgesia has been observed with caudal neostigmine in the range of 20-50µg/kg.

A single caudal injection of neostigmine 2µg/kg when added to bupivacaine 0.25% or ropivacaine 0.2% has been found to provide an extended duration of post operative analgesia.(~ 20-22 hrs), and reduced the need for supplementary analgesics in children undergoing genitourinary surgery.

Respiratory depression, sedation and pruritis ascribed to the use of caudal opioids are not encountered with caudal neostigmine.

Furthermore in contrast to clonidine its use with local anaesthetics is not associated with significant haemodynamic changes.

This is attributed to ability of neostigmine to counteract the sympathetic block of spinal bupivacaine on the sympathetic nervous system,

There by blunting the hypotension induced by neuraxial local anaesthetics and clonidine.

The main adverse effects reported with the use of neuraxial neostigmine are nausea and vomiting.

Although the incidence has been reported to be significantly higher with the intra thecal route, use of extradural neostigmine in adults and children has been found to be

associated with a lower incidence of nausea and vomiting.. It does not cross the blood brain barrier as it is a quaternary ammonium compound and hence no action on central nervous system when given intravenously.

ANS:

On autonomic nervous system it has both muscarinic and nicotinic actions. Nicotinic actions at the level of autonomic ganglia and skeletal muscle. muscarinic receptors present at lacrimal,salivary and gastric gland. Bronchial, gastro intestinal, and bladder Smooth muscle cells and SA and AV nodes of the heart.

CVS:

Peripheral vagal stimulation will cause bradycardia, cardiac dysrrhythmias and cardiac arrest may follow with large doses.

RS:

Increases secretion of tracheo bronchial tree and produces broncho constriction.

SMOOTH MUSCLE:

Increases peristalsis, miosis, prevents constipation and atony of urinary bladder.

DOSE:

0.04-0.08 mg/kg for reversal of non depolarizing blockade. 2µg-4µg /kg caudally along with local anaesthetics.

METABOLISM:

A small portion is excreted by glomerular filtration via kidneys and similar portion is destroyed in liver.

SIDE EFFECTS:

Restlessness, weakness, muscular twitching, dysarthria, pinpoint pupils, nystagmus, sweating, increased salivation, nausea ,vomiting, abdominal colic, urination and sudden cardiac arrest due to rapid administration.

CALCULATION OF THE VOLUME OF LOCAL ANAESTHETIC FOR CAUDAL ANAESTHESIA

Many formulas based on weight, age and number of spinal segments to be blocked and the parameter ’D’ (Distance from C7 to sacral Hiatus) have been used to determine the dose of local anaesthetic required.

SPIEGEL et al (6) described a formula to calculate the total volume of Bupivacaine (V) depending on the distance separating the sacral hiatus from the spinous process of the 7^{th} cervical vertebra as follows

$$V = 4 + (D-15)/2$$

V-Volume of local anaesthetic

D- Distance from C7 to sacral Hiatus

BROMAGE PR et al (8) proposed a formula to determine the volume of local anaesthetics to be injected into the caudal epidural space depending on the age of the patient and per spinal segment.

V = 0.106 + (0.075 X Age in years)

V-Volume of local anaesthestic

TAKASAKI M et al (9) suggested a calculation depending on the weight of the patient in kg.

V = 0.056 ml X Body weight (in kg) X number of spinal segments to be blocked.

SCHULTE – STEINBERG examined the statistical influence of age, weight and height on caudal dose requirements before puberty. He found that the pattern of spread was highly predictable in children. The relationship between age and dose requirements was strictly linear = 0.1 ml / segment / year of age.

V is volume in ml of 1% lignocaine or 0.25% bupivacaine.

In practice, however, it is easier to use the formula describes by **ARMITAGE EN et al (10)**

LUMBOSACRAL	0.5 ml/kg
THORACOLUMBAR	1 ml/Kg
MIDTHORACIC	1.25 ml/Kg

Of 0.25% bupivacaine.

Armitage formula was used in this study. This formula is easy to use, reliable and safe in children.

ASSESSMENT OF PAIN IN CHILDREN

Children present problems of assessment of pain when compared with adults because of their lower level of verbal fluency and the likelihood that varied development levels alter their understanding of questions or tests. Hence assessment of pain proved difficult in children. Assessment and management are interrelated. Unfortunately validated totally acceptable tools for measuring pain in children are not available. Various methods are available as per **Brown TCK. (11)**

1. Physiological measurements
2. Self report techniques
3. Behavioural assessment

PHYSIOLOGICAL MEASUREMENTS

Changes in pulse, blood pressure and respiration reflect autonomic arousal. Autonomic responses to pain and their measurement form an important aspect of certain pain scales. Metabolic changes cause release of catecholamine, growth hormone, glucagons, cortisol, aldosterone and beta-endorphins, which have been documented in

infants and children following

noxious stimulation. Only plasma cortisol has been shown to correlate with behavioural responses to noxious stimuli.

SELF REPORT TECHNIQUES

As described by **Manuksela et al, (12)** these are the best indicators of a child's subjective experience. Various methods have been used:

(a) **VISUAL ANALOGUE SCALE (13)**

The accepted method of measurement of pain in adults is acceptable and provides reproducible results in children down to an age of five years. VAS using a 10 cm length scale marked "no pain" at one to "worst pain possible" at the other end. The child is asked to identify a point on the scale, which corresponds to his pain. The point is measured from the left hand end and reported in mm from 0 to 100 or in cm from 0 to 10. A score of less than 4 is no pain, less than 6 implies tolerable pain and more than 6 means he needs medication.

(b) **OUCHER SCALE (14)**

It is a variant of the faces scale and is designed to measure pain intensity in children aged 3 to 12 years. The scale is displayed in a poster format. It consists of a vertical numerical scale (0 to 100) on the left and six photographs of children in varying degrees of pain positioned vertically to the right. This scale is based on mimic, vocalization and irritability. Characteristics of increasing pain are:

(1) Distortion of face such as lowering of the brow, broadening of the nasal root, angular and squarish mouth, tightly closed eyes and tightening of the jaw.

(2) Vocalization, changing from sobbing or groaning to cry.

(C) WONG – BAKER FACES PAIN RATING SCALE (15)

It is recommended for persons of age three and more. It contains six different faces of expression varying from a happy to sad mood. The patient has to be explained that each face is for a person who feels happy because he has no pain (hurt) or sad because he has some or a lot of pain. Ask the patient to choose the face that best describes how he is feeling.

A similar scale was designed by **Daiva Bieri et al (16)** to assess pain in the Children's Hospital, University of Helsinki. This scale was based on mimic, vocalization, movements or rigidity of the limbs and the body, response to handling and irritability together with the measured cardioventilatory parameters.

BEHAVIOURAL ASSESSMENT

This method of assessment relies on observation of behaviour and is more useful in the pre-school age group of children. They score the behaviour, which represent the reaction to pain and scores are allotted according to the degree of alteration of a particular behaviour .The behavioural score include vocal behaviour such as cry, scream, verbally expressed pain and anxiety and nonverbal behaviour such as muscle rigidity, torso movements, leg movements, facial expression.

(1) **THE PBRS:** Pain behaviours rating scale and Children's Hospital of Eastern Ontario pain scale - **CHEOPS (58)** are the two such scales. The observation in these scales can have an observer bias.

(2)**THE OBJECTIVE PAIN SCALE:** This measures pain as a physiological variable, blood pressure along with behavioral changes. This has been shown to be a sensitive and reliable tool in evaluating postoperative pain in children who are not able to verbally comment upon their pain experience. This takes into account the systolic blood pressure, cry and it's response to love and care, movement, agitation and verbal evaluation as described by **Hannallah RS. (18)**

TABLE -1: OBJECTIVE PAIN SCALE

TLC - TOUCH, LOVE AND CARE

–TABLE-II MODIFIED ALDRETE'S SCORE

TABLE III: RAMSAY SEDATION SCORE

Six point sedation score was assigned as follows

SCORE	CLINICAL DESCRIPTION
I	**Anxious, Agitated**
II	**Cooperative, Oriented, Tranquil**
III	**Responds only to verbal commands**
IV	**Asleep with brisk response to light stimulation**
V	**Asleep with sluggish response to stimulation**

VI	**Asleep without response to stimulation**

MATERIALS AND METHODS

The study population consisted of 60ASA I and II Children in the age group of 2 years to 8 years admitted to undergo elective lower abdominal general surgical procedure at our hospital.

Exclusion criteria consisted of local infection in the caudal region, bleeding diathesis, preexisting neurological or spinal diseases and congenital anomaly of the lower back. The study was approved by the institutional ethics committee.

A written consent was obtained from the parents after they were informed about the procedure to be performed, to give postoperative analgesia to their child.

All Children were kept fasting (NPO for 6 hours) and unpremedicated. They were received by an anaesthesiologist inside the operating room half an hour before surgery.

Thereafter, baseline cardio respiratory parameters such as pulse rate, systolic blood pressure, ECG, respiratory rate and (SpO_2) were recorded and monitored continuously until extubation.

Anaesthesia was induced by inhalation of halothane at increasing concentrations in N_2O and oxygen mixture. Intravenous line secured after achieving adequate depth of anaesthesia.

Thiopentone was used as the induction agent.Orotracheal intubation was performed with an appropriate size uncuffed endotracheal tube. No opioids or benzodiazepines were used intraoperatively.

Under controlled ventilation, muscle relaxation was maintained with atracurium. The patients were placed in left lateral position with hips and knees flexed.

The children were allocated into two groups of each 30 patients

Group B: 0.25% bupivacaine alone

Group BN. 0.25% bupivacaine with 2µg/kg neostigmine

The dosage of local anaesthetic injected into the caudal space was calculated according to the **ARMITAGE** formula.

A 22G hypodermic needle was inserted in the hiatus at 45° angle to the skin. Once the sacrococcygeal membrane was penetrated and loss of resistance obtained, the angle of the needle was changed and directed up the canal for further 0.5 cm. The injection was made after gentle aspiration to rule out any intrathecal and intravascular placement.

General anaesthesia was maintained with halothane and 60% nitrous oxide in 40% oxygen.

The surgical incision was made 20 min after administering caudal block during which time the children were surgically prepared and draped. Adequate caudal analgesia was defined as haemodynamic stability as indicated by absence of increase in heart rate and systolic BP of more than 15% compared with basal values obtained just before surgical incision with halothane concentration maintained at 1%.

If systolic BP >15% increase occurred analgesia was considered inadequate and

rescue opioids fentanyl given at the dosage of 2µg/kg.Intraoperative fluid management was taken care by using **HOLIDAY AND SEGAR** formula.

postoperatively the Children were shifted to the recovery room for continuous monitoring. Postoperative sedation score was done using **RAMSAY SCALE** every one hour for first 6 hours and then every 2 hours

The recovery was assessed using **Modified Aldrete Score** the children were shifted to a dedicated postoperative ward where monitoring of respiratory rate, (SpO_2), pulse rate and systolic blood pressure were continued. The quality of analgesia was assessed hourly for first 6 hours and then every 2 hours.

The intensity of pain was measured using the **Objective Pain Scale Score** devised by **Hannallah RS.** Each parameter was awarded a score of 0-2 accordingly. The sum total of the awarded score was taken at each time interval. A log was kept at the bedside for noting the occurrence of possible complications including, hypotension, urinary retention, nausea and vomiting.

Patients were administered rescue analgesia with syrup paracetamol 10 mg/Kg on evidence of pain that is if the OPS reached a value of 5. The time of first analgesia (TFA) was calculated from the time of injection of the drug in the epidural space to the time when OPS reached 5.

Respiratory depression was defined as decrease of (SpO_2) < 93% or a decrease in RR < 10 /min. Excessive sedation was defined as a **RAMSAY SEDATION SCORE** of V or VI.

Urinary retention was defined as inability to void urine for a period of at least 8 hours.

Caudal block and monitoring of scores for pain, nausea and vomiting and sedation were performed by anaesthesiologists blinded to the study allocations.

OBSERVATION AND ANALYSIS

Sixty patients posted for elective lower abdominal general surgical procedure who were admitted in the Department of paediatric surgery, RAJA MIRASUDHAR HOSPITAL, THANJAVUR MEDICAL COLLEGE of physical status ASA I and II were taken up for the study. They were randomly divided into two groups of 30 patients each to receive caudal block as mentioned below.

One group (group BN) received a mixture of Bupivacaine 0.25% and neostigmine at 2μg/kg, 20 minutes before surgery. Other group (group B) received 0.25% Bupivacaine alone 20 minutes before surgery. The patients were assessed by a blinded observer in the postoperative period.

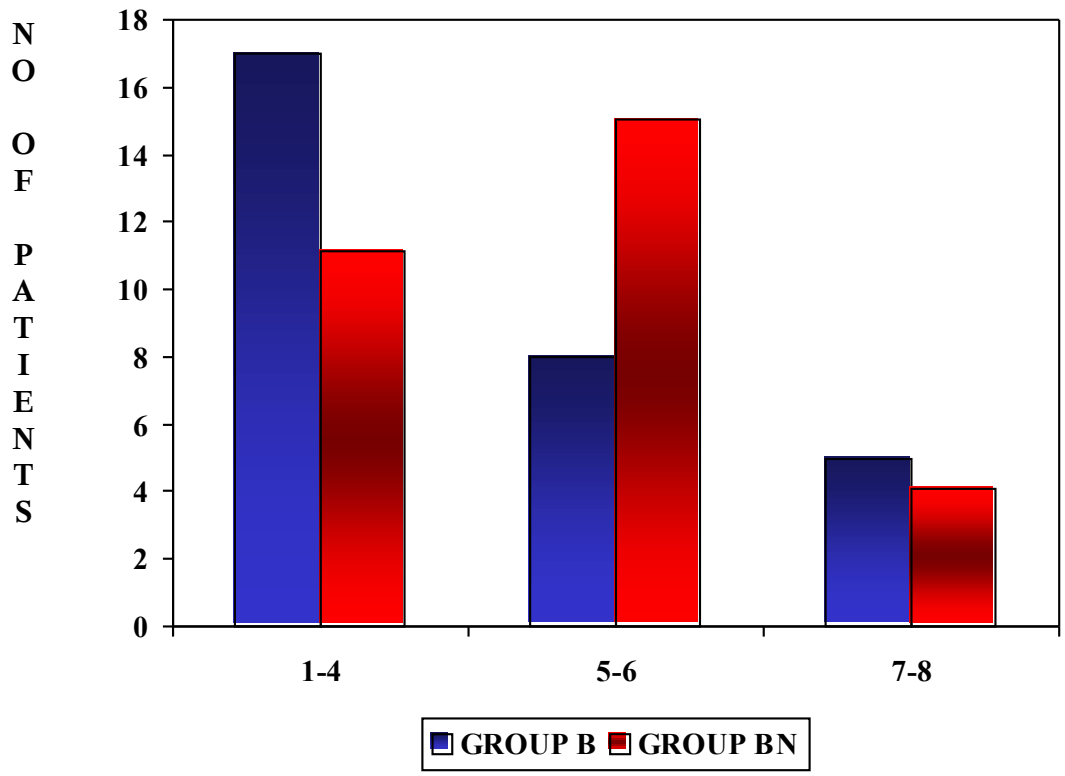
AGE AND SEX DISTRIBUTION

The age distribution in both groups ranged from 2 – 8 years .The age and sex distribution is as follows

From this table it is clear that the number of children in 24-48, 48-72, and 72-96 month interval are not much different between the two groups. This shows age was not a confounding factor.

AGE DISTRIBUTION

FIG -2



In this bar diagram, the horizontal axis represents age in years and vertical axis represents the number of patients. Although there are more children in the (1-4yrs) in B group the distribution among the two study group is almost the same.

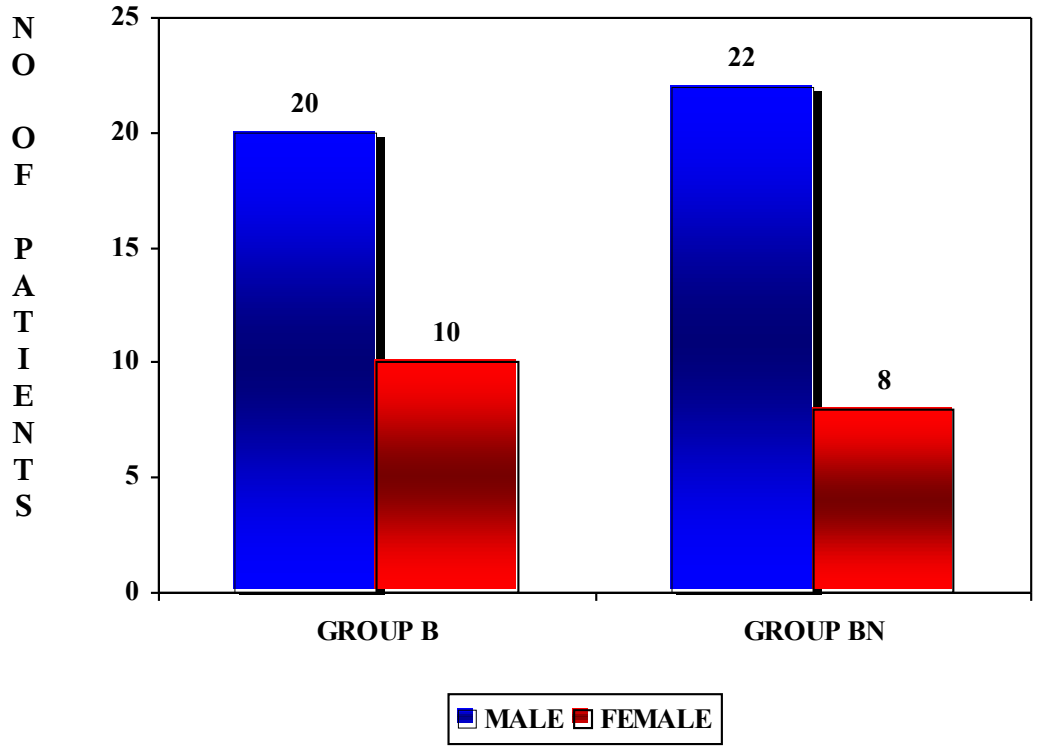
AGE IN YRS AGE BN

	Frequency	Percent	Valid percent	Cumulative percent
Valid <4	11	36.7	36.7	36.7
5-6	15	50	50	86.7
7-8	4	13.3	13.3	100
Total	30	100	100	

AGE B

	Frequency	Percent	Valid percent	Cumulative percent
Valid <4	17	56.7	56.7	56.7
5-6	8	26.7	26.7	83.3
7-8	5	16.7	16.7	100
Total	30	100	100	

SEX DISTRIBUTION
FIG -3



In group B 66.7% are male and 33.3% are female and in group BN 73.3% are male and 26.7 % are female. The sex distribution in both the group is also not much different. Hence there is no bias in the age and sex distribution .

SEX B

	Frequency	Percent	Valid percent	Cumulative percent
Valid				
Male	20	66.7	66.7	66.7
Female	10	33.3	33.3	100
Total	30	100	100	

SEX BN

	Frequency	Percent	Valid percent	Cumulative percent
Valid				
Male	22	73.3	73.3	73.3
Female	8	26.7	26.7	100
Total	30	100	100	

TYPES OF SURGICAL PROCEDURES

The various surgical procedures performed are shown below

SURGICAL PROCEDURES	GROUP B	GROUP BN
Herniotomy	**15**	**15**
PV sac ligation	**8**	**5**
Hypospadias	**7**	**10**
Total	**30**	**30**

From this table it is clear that the type of surgical procedures between the two groups is not much different. Hence there is no bias in the type of surgical procedures.

DURATION OF ANALGESIA

Duration of analgesia in group B (0.25% bupivacaine) range from 3. to 5 hours with a mean duration of 4.3 hours.

In group BN (0.25 % Bupivacaine + 2 µg/Kg Neostigmine) the duration of analgesia ranged from 10 to 16 hours with a mean duration of 14.6 hours.

DURATION OF ANALGESIA	GROUP B	GROUP BN
Range	**3-5**	**10-16**
Mean	**4.3**	**14.6**
Standard Deviation	**0.75**	**1.52**

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DURATION OF ANALGESIA

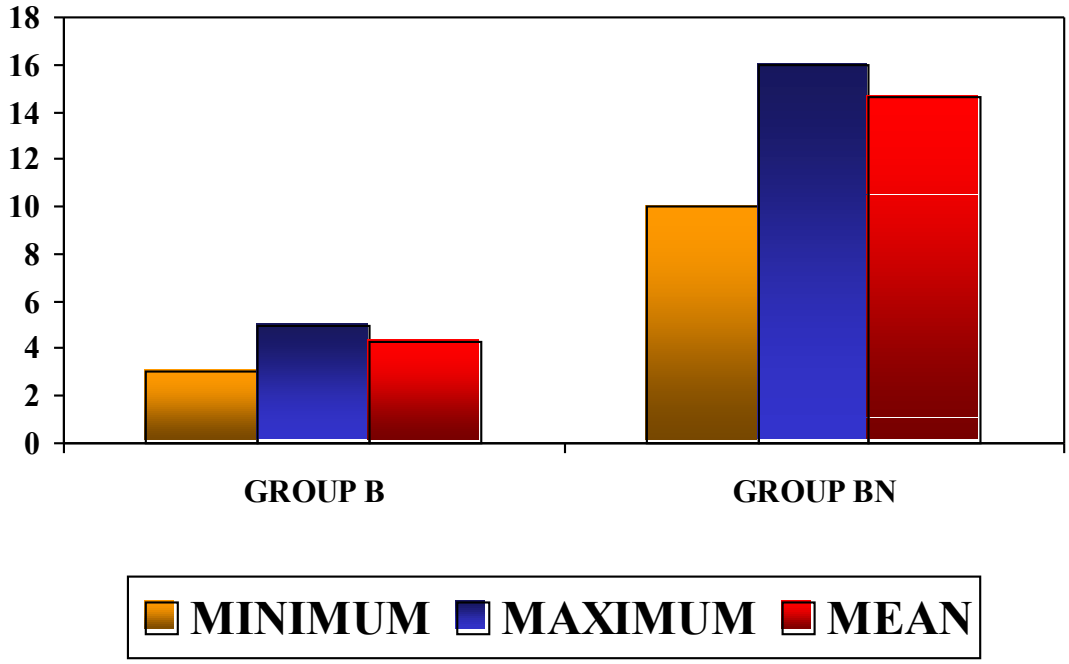

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FIG -4

The mean duration of analgesia in group BN is 14.6 hours, whereas in group B it is only about 4.3 hours. This means that group BN has got extended duration of analgesia when compared with group B.

This duration of analgesia is also statistically significant as detected by using One sample T test by which the probability value is less than 0.05 (P value < 0.0005). This P value means that it is highly significant.

SIDE EFFECTS

NAUSEA AND VOMITING

One patient in group B had nausea and vomiting (3.3%) when compared with two patients in group BN (6.6 %).

There was no significant difference in the incidence of urinary retention between the two groups.

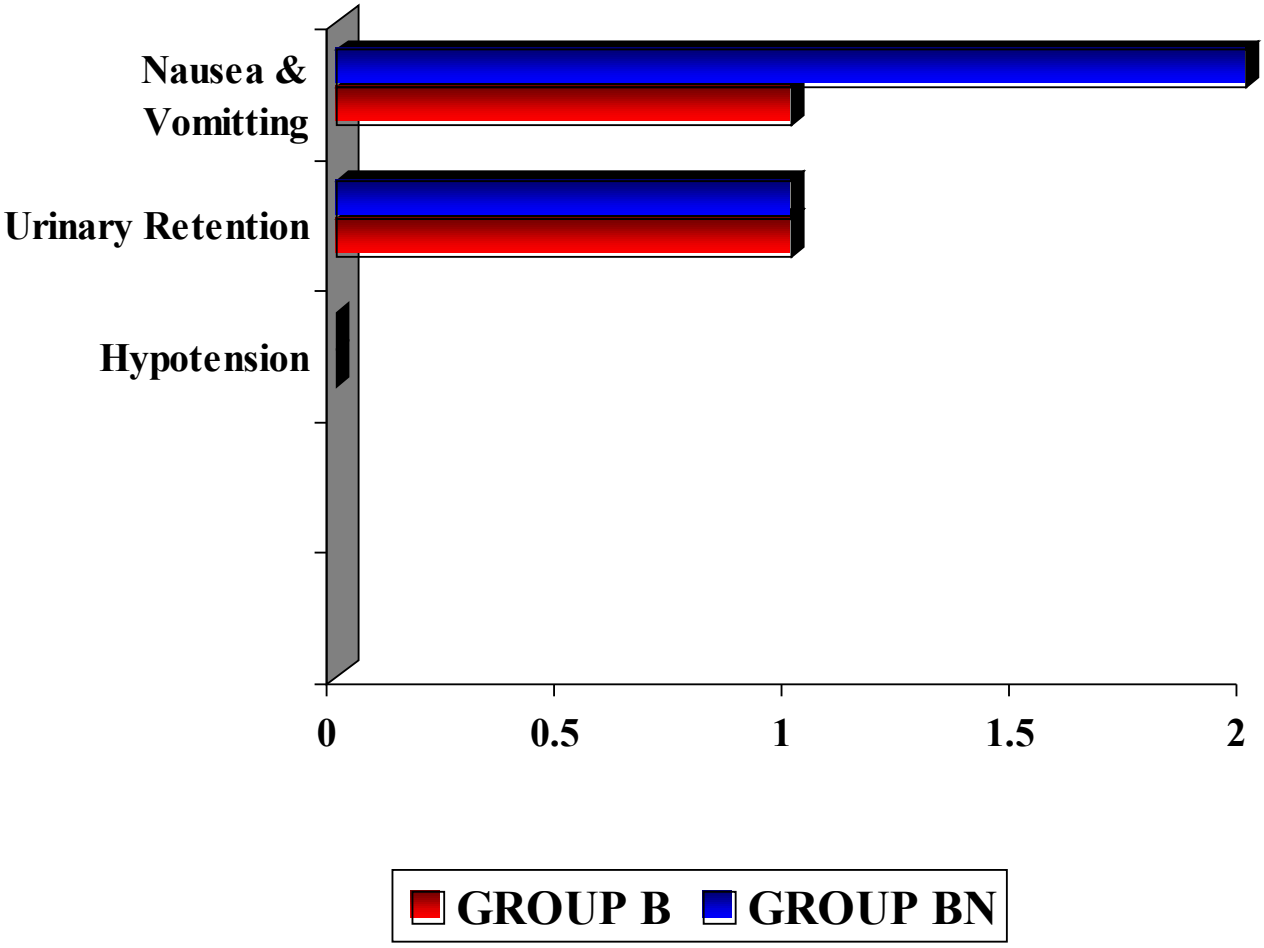
No side effects like hypotension, respiratory depression or apnea was seen in any patient. Overall side effects did not differ between the two groups.

SIDE EFFECTS

Side effects	Group B	Group BN
Nausea and vomiting	**1**	**2**
Urinary retention	**1**	**1**
Hypotension	**0**	**0**

FIG -6

SIDE EFFECTS



STATISTICS

DURATION OF ANALGESIA B

	Frequency	Percent	Valid percent	Cumulative percent
Valid 3	5	16.7	16.7	16.7
4	11	36.7	36.7	53.3
5	14	46.7	46.7	100
Total	13	100	100	

AGE B SEX B Cross tabulation

Count

	SEX B		TOTAL
	MALE	FEMALE	
AGE GROUP B <4	11	6	17
5-6	5	3	8
7-8	4	1	5
Total	20	10	30

AGE BN SEX BN Cross tabulation

Count

	SEX BN		TOTAL
	MALE	FEMALE	
AGE GROUP BN <4	9	2	11
5-6	11	4	15
7-8	2	2	4

Total	22	8	30

FREQUENCIES

Statistics

		Gp B Analgesia	Gp BN Analgesia	Wt Gp B	Wt Gp BN	Age Gp B	Age Gp BN
N	**Valid**	30	30	30	30	30	30
	Missing	0	0	0	0	0	0
Mean		4.3	14.6	21.33	23.87	4.43	5
Median		4	15	24	26	4	5
Std.Deviation		0.75	1.52	5.79	4.76	1.85	1.6

T-Test One sample statistics

	N	Mean	Std.Deviation	Std.error mean
Gp BN Analgesia	**30**	**14.6**	**1.52**	**0.28**
Gp B Analgesia	**30**	**4.3**	**0.75**	**0.14**

Here the mean time in the BN group (14.6 hrs) is higher than the group B(4.3).When we take the mean value of B group as test value and compare it with BN group the difference in the mean observed is statistically significant P<0.0005) with a 99% CI 0f 9.53 to 11.07.

One sample T Test

	Test Value=4.3					
	t	**Df**	**Sig .(2-tailed)**	**Mean difference**	**99% Confidence interval of the difference**	
					Lower	**Upper**
Gp BN Analgesia	**37.061**	**29**	**.000**	**10.30**	**9.53**	**11.07**

ABOUT ONE SAMPLE T TEST

The one sample T test procedure test whether the mean of a single variable differs from a specified constant.

A low significant value typically below 0.05 indicates that there is a significant difference between the test value and the observed mean. (Sig 2 tailed-4th column)

If the confidence interval for the mean difference does not contain the zero, this also indicates that the difference is significant. (99% CI Between 9.53-11.07 there is no

zero hence the difference observed is significant)

(If the significant value is high and the confidence interval for the mean difference contain zero then you can’t conclude that there is a significant difference between the test value and the observed mean)This is not the case in this study hence the result observed is significant.

Conclusion: The duration of analgesia of BN group is higher (14.6hrs) when compared to the B group (4.3 hrs) and the difference is also statistically significant ($P<0.0005$).

REVIEW OF LITERATURE

Caudal block is a simple and safe technique, which can be routinely adopted in children. This provides effective intraoperative and postoperative analgesia for almost all types of interventions on the lower part of the abdomen and the lower limbs, especially in the neonates, infants and certain high risk children as per the experience of **ARMITAGE EN AND ARTHUR DS.**

The success rate was found to be 94.5% as per the experience of **ARMANDO FORTUNA (22)**

Caudal anaesthesia is usually but not always combined with a light general anaesthesia with halothane followed by isoflurane either at the beginning or, sometimes, at the end of surgical procedure. **DALENS B, HASNAOUI A (23)**

The timing of caudal block placement in relation to surgery does not affect duration of post operative analgesia in paediatric ambulatory patients as evidenced by **RICE LJ, PUDIMAT MA, and HANNALLAH RS (24)**

HANNALLAH RSet al(25) conducted a study in children in the age group of 18 months to 12 years scheduled for orchiopexy to evaluate the effectiveness of caudal analgesia and compared it with local nerve blocks. They found that both caudal as well as Ilioinguinal / Iliohypogastric nerve blocks administered following inhaled anaesthesia for orchiopexy are safe and equally effective in controlling post operative pain of children.

GUNTER et al(27) conducted a study on 122 children aged 1 to 8 years scheduled for out patient inguinal herniorhaphy who were randomized to receive in a double blind fashion caudal anaesthetic with bupivacaine in one of the six concentrations (0.125%, 0.15%, 0.175%, 0.2% and 0.25%). After incision a programmed reduction in inspired halothane resulted, if tolerated by the subject. Although all concentrations were effective for combined general caudal anaesthesia in children, they concluded that 0.175% bupivacaine offers the best combination of effectiveness, rapid recovery and discharge for paediatric surgical outpatients without any motor blockade.

In another study by **WOLF AR et al (28)** on 114 infants and children of age 6 months to 10 years, undergoing elective superficial lower abdominal or genital surgery to find the optimum concentration of bupivacaine for caudal analgesia, concluded that 0.125% bupivacaine with 1 in 200,000 adrenaline provided equipotent analgesia and significantly less motor blockade than 0.25% bupivacaine.

Eisenach et al (41) demonstrated that acetylcholine has intrinsic analgesic properties, and that the concentration of acetylcholine in CSF is increased during painful electrical stimulation. They further suggested that enhanced amounts of acetylcholine released from preganglionic sympathetic neurons after spinal neostigmine administration may

counteract the sympatholytic actions of local anaesthetics or α_2-agonists (reducing the degree of hypotension) and add a synergistic antinociceptive effect to spinal α_2-agonists.

Abdullatif and EL-Sanabary (45) - A study in the children compared three groups to determine the effectiveness of neostigmine 2µg/kg as a caudal analgesic for hypospadiasis repair, either alone or in combination with bupivacaine.The combination of bupivacaine and neostigmine provided superior analgesia to either of the other two groups and mean duration of 22..8 hrs compared with 8.1 hrs in the bupivacaine plain group and 5.2hrs in the neostigmine plain group.

Batra YK, et al (47) evaluated for the first time the efficacy of a varying dose of caudal neostigmine for postoperative analgesia in children undergoing genitourinary surgery.

studied 120 children age group of 2-8 years scheduled for surgical repair of hypospadias under general anaesthesia:Caudal neostigmine in the dose range of 20-50 µg.kg(-1) provides dose dependent analgesia. However, dose exceeding 30 µg.kg(-1) is associated with a higher incidence of nausea and vomiting.

Ping-Heng Tan, **et al (56)** investigated the value of Intrathecal bupivacaine with morphine or neostigmine for postoperative analgesia after total knee replacement surgery

Sixty patients scheduled for elective total knee replacement under spinal anaesthesia were randomly divided into three equal groups which received intrathecal 0.5%

hyperbaric bupivacaine 15 mg with either normal saline 0.5 mL, neostigmine 50 μg, or morphine 300 μg.. Overall satisfaction rates were better in the neostigmine group than in the morphine and saline groups (P <0.05). Intrathecal neostigmine 50 μg produced postoperative analgesia lasting about seven hours with fewer side effects and better satisfaction ratings than intrathecal morphine 300 μg. **Rajesh Mahajan**,**et al (5)** evaluate the analgesic efficacy and duration of varying doses of caudal neostigmine with plain bupivacaine and its side effects in children undergoing genito-urinary surgery. In a randomized double-blind prospective study 80 boys aged two to eight years scheduled for surgical repair of hypospadias were allocated randomly to one of four groups (n = 20 each) and received either only caudal 0.25% plain bupivacaine 0.5 mL·kg^{-1} (Group I) or 0.25% plain bupivacaine 0.5 mL·kg^{-1} with neostigmine (Groups II–IV) in doses of 2, 3 and 4 μg·kg^{-1} respectively. The duration of postoperative analgesia in Group I (5.1 ± 2.3 hr) was significantly shorter than in the other three groups (II –16.6 ± 4.9 hr; III – 17.2 ± 5.5 hr; IV – 17.0 ± 5.8 hr; P < 0.05). Total analgesic (paracetamol) consumption was significantly more in Group I (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 < 0.05). Groups II, III and IV were comparable with regards to duration of postoperative analgesia and total analgesic consumption (P > 0.05). Incidence of nausea and vomiting were comparable in all four groups. No significant alteration in vital signs or any other adverse effects were observed. Caudal neostigmine (2, 3 and 4 μg·kg^{-1}) with bupivacaine produces a dose-independent analgesic effect (≈16–17 hr) in children as compared to

those receiving caudal bupivacaine alone (approximately five hours) and a reduction in postoperative rescue analgesic consumption without increasing the incidence of adverse effects.

Rudra A.et al (57) examined the analgesic efficacy of caudal administration of bupivacaine or a mixture of bupivacaine-neostigmine in 40 children (ASAI), undergoing inguinal herniotomy or orchidopexy. They were randomly allocated into two groups (n=20), to receive a caudal injection

of either 0.25% bupivacaine with or without neostigmine 2 µgkg-1. Time to first analgesic administration (paracetamol suppository) was longer ($p<0.05$) in the bupivacaine-neostigmine than in the other group. Side effects such

as emesis was not significantly different between the two groups. We conclude that a single caudal co-administration of the two drugs is associated with extended duration of postoperative analgesia.

Lauretti et al (46) Studied Epidural neostigmine (1, 2, or 4 microg/kg) in lidocaine produced a dose-independent analgesic effect (approximately 8 h) compared to the control group (approximately 3.5 h), and a reduction in postoperative rescue analgesic consumption without increasing the incidence of adverse effects.

Mahajan,**et al(5)** in their study evaluate the Caudal neostigmine (2, 3 and 4 $\mu g \cdot kg^{-1}$) with bupivacaine produces a dose-independent analgesic effect (≈16–17 hr) in children as compared to those receiving caudal bupivacaine alone (approximately five hours) and

a reduction in postoperative rescue analgesic consumption without increasing the incidence of adverse effects.

DISCUSSION

The present study demonstrated that caudal neostigmine in a dose of 2 µg/kg co-administered with bupivacaine 0.25% markedly prolonged postoperative analgesia and reduced the need for oral paracetamol in children undergoing lower abdominal surgeries.

The study conducted by **Mahajan (5)** and coworkers which reported a mean duration of 16.6 ± 4.9 hours, was well correlated with our study. The mean duration of postoperative analgesia in our study Group BN is (14.6 hours). This value is statistically significant as detected by one sample T- Test by which the probability value is less than 0.05 ($P < 0.0005$), which means that it is highly significant. In the present study, we have confirmed the analgesic efficacy of caudal neostigmine when co-administered with bupivacaine.

The neuraxial administration of neostigmine is known to produce analgesia in animals, human volunteers and patients with acute postoperative and chronic pain. Spinal delivery of the cholinesterase inhibitor neostigmine inhibits the breakdown of the endogenous spinal neurotransmitter acetylcholine which has been shown to produce analgesia. **Eisenach et al (40)**

Neuraxial administration of neostigmine increases the concentration of acetylcholine in cerebrospinal fluid and produces antinociception in animals which is blocked by the intrathecal administration of a muscarinic antagonist. The analgesic effect is thought to be mediated via spinal muscarinic M_1 receptors and supraspinal muscarinic

M_1 and M_2 and nicotinic cholinergic receptors.

Various investigators have reported a dose-independent effect of the neuraxial administration of neostigmine on postoperative pain relief and analgesic requirements. In pregnant patients **Krukowski *et al.* (32)** have demonstrated that varying doses of intrathecal (10, 30 and 100 µg) provided dose independent analgesia lasting approximately ten hours in all three groups.

Similarly **Lauretti *et al.* (39)** have shown dose independent analgesia in patients undergoing vaginal hysterectomy in a dose range of 25 to 75 µg intrathecal neostigmine. The same authors have also demonstrated dose independent analgesia with the combination of 20 mg intrathecal bupivacaine plus 85 mg epidural lidocaine with neostigmine (1, 2 or 4 $\mu g \cdot kg^{-1}$) in patients undergoing knee surgery **Lauretti *et al.* (38).**

The lowest dose of neostigmine may have maximally potentiated the analgesic effect of caudal bupivacaine, making higher doses of caudal neostigmine no more effective. Considering the lack of efficacy of neostigmine alone in doses < 10 $\mu g \cdot kg^{-1}$, **Batra YK, et al (47)**. It is not surprising that lower doses combined with bupivacaine may have uniformly potentiated the effect of caudal bupivacaine.

Although the use of neuraxial neostigmine has been associated with gastrointestinal side effects such as nausea and vomiting, these were encountered very minimally in the present study. **Lauretti *et al* (46)** and **Roelants *et al.* (62)** have also

reported the extradural administration of neostigmine to be devoid of these undesirable side effects. Further, these side effects have been found to be statistically insignificant **(Abdullatif and EL-Sanabary(45)**- and independent of the dose of neuraxial neostigmine **Lauretti *et al* (46)** . The use of caudal bupivacaine alone has been found to be associated with nausea and vomiting to the extent of 25 to 45%, **Wolf AR, (63)** an incidence similar to that seen with caudal morphine, fentanyl and tramadol. **SenelAC (59),Krane EJ, (60) ,Gaitini LA(61)** It seems that caudal neostigmine in such low doses contributes minimally to nausea and vomiting.

Caudal neostigmine is effective as a sole analgesic with duration of analgesia comparable to that reported with caudal bupivacaine 0.25%. **Abdullatif and EL-Sanabary(45).** In line with the findings of the present study, co-administration of neostigmine with bupivacaine significantly extended the duration of postoperative analgesia.

The duration of analgesia in Group BN ranged from 10-16 hours was comparable to results obtained by **Rudra et al (57)** ranged between 19±4.2 hours.

These results were also correlated well with the study results obtained by **Abdullatif and EL-Sanabary(45).** That combination of bupivacaine and neostigmine provides superior analgesia than to bupivacaine alone with the mean duration of 22.8±2.9 hours.In their study they had used 1 ml/kg of bupivacaine ,but in our study we used only 0.5ml/kg of bupivacaine,so that might be a reason for difference in the duration of analgesia.

The incidence of nausea and vomiting in Group BN is 6.6%. this was comparable to the results obtained by **Rudra et al(57)** and **Mahajan (5)** coworkers who reported the incidence was less than 20%.

In this study, in spite of using a smaller dose of neostigmine (2µg/kg) the mean duration of analgesia was 14.6 hours, which could due to synergistic effect of bupivacaine and neostigmine.

SUMMARY

In a randomized double blind study, we have examined the analgesic efficacy of caudal bupivacaine alone or a mixture of bupivacaine-neostigmine in sixty children (ASA I, II), aged 2-8 yrs undergoing lower abdominal surgeries. They were randomly allocated into two groups (n -30) to receive a caudal injection of 0.25% bupivacaine alone or a mixture of 0.25% bupivacaine 0.5ml/kg with 2µg/kg neostigmine.Monitoring of scores for pain, post operative nausea and vomiting was performed by an anaesthesiologist blinded to the study allocations. Time to the first analgesic administration(sy.Paracetamol)was longer ($P<0.05$) with mean duration of analgesia of 14.6 hrs in the bupivacaine-neostigmine than in the bupivacaine only group with a mean duration of 4.3hrs.Side effect such as emesis was not significantly different between the two groups. We conclude that a caudal co administration of bupivacaine with neostigmine produces significant prolongation of the duration of post operative analgesia when compared to caudal bupivacaine only.

CONCLUSION

We conclude that caudal epidural analgesia using a combination of 0.25% bupivacaine 0.5ml/kg and neostigmine (2µg/kg) significantly prolong the postoperative analgesia when compared to 0.25% bupivacaine alone in children undergoing lower abdominal general surgical procedures without any significant increase in side effects.

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PROFORMA

NAME AGE SEX WT IPNO.

ASA PHYSICAL STATUS:-

HISTORY

PR BP CVS RS

OTHERS

INVESTIGATIONS

HB% TC DC

BLOOD GP&Rh typing OTHERS

DIAGNOSIS

SURGICAL PROCEDURE:

CAUDAL ADMINISTRATION

TIME

DRUG

VOLUME

SEDATION SCORE

ALDRETES SCORING

DURATION OF ANALGESIA

RESCUE ANALGESIC DRUG USED

COMPLICATIONS

- NAUSEA VOMITING
- HYPOTENSION
- URINARY RETENTION

GROUP B:

GROUP BN

Total	438
Mean	14.6

ANNEXURES

FLACC Behavioural pain scale:

FLACC Behavioral Pain Assessment			
Categories	**Scoring**		
	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, distractable	Difficulty to console or comfort

Each of the five categories is scored from 0-2, resulting in a total score between 0 and 10.
The FLACC scale was developed by Sandra Merkel, MS, RN, Terri Voepel-Lewis, MS, RN, and Shobha Malviya, MD, at C. S. Mott Children's Hospital, University of Michigan Health System, Ann Arbor, MI.
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Children's Hospital Eastern Ontario Pain Scale (CHEOPS)

(Recommended for children 1-7 years old) - A score greater than 4 indicates pain.

Item	Behavioral		Definition	Score
Cry	No cry	1	Child is not crying.	

	Moaning	2	Child is moaning or quietly vocalizing silent cry.	
	Crying	2	Child is crying, but the cry is gentle or whimpering.	
	Scream	3	Child is in a full-lunged cry; sobbing; may be scored with complaint or without complaint.	
Facial	Composed	1	Neutral facial expression.	
	Grimace	2	Score only if definite negative facial expression.	
	Smiling	0	Score only if definite positive facial expression.	
Child Verbal	None	1	Child not talking.	
	Other complaints	1	Child complains, but not about pain, e.g., “I want to see mommy” of “I am thirsty”.	
	Pain complaints	2	Child complains about pain.	
	Both complaints	2	Child complains about pain and about other things, e.g., “It hurts; I want my mommy”.	
	Positive	0	Child makes any positive statement or talks about others things without complaint.	
Torso	Neutral	1	Body (not limbs) is at rest; torso is inactive.	
	Shifting	2	Body is in motion in a shifting or serpentine fashion.	
	Tense	2	Body is arched or rigid.	
	Shivering	2	Body is shuddering or shaking involuntarily.	
	Upright	2	Child is in a vertical or upright position.	
	Restrained	2	Body is restrained.	
Touch	Not touching	1	Child is not touching or grabbing at wound.	
	Reach	2	Child is reaching for but not touching wound.	
	Touch	2	Child is gently touching wound or wound area.	
	Grab	2	Child is grabbing vigorously at wound.	
	Restrained	2	Child's arms are restrained.	
Legs	Neutral	1	Legs may be in any position but are relaxed; includes gentle swimming or separate-like movements.	
	Squirm/kicking	2	Definitive uneasy or restless movements in the legs and/or striking out with foot or feet.	
	Drawn up/tensed	2	Legs tensed and/or pulled up tightly to body and kept there.	
	Standing	2	Standing, crouching or kneeling.	
	Restrained	2	Child's legs are being held down.	