"EFFECT OF INTRANASAL DEXMEDETOMIDINE ON DURATION OF ANAESTHESIA AND POST OPERATIVE ANALGESIA IN PAEDIATRIC PATIENTS UNDERGOING INFRAUMBILICAL SURGERIES UNDER SINGLE SHOT CAUDAL EPIDURAL ANAESTHESIA- A ONE YEAR HOSPITAL BASED DOUBLE BLIND RANDOMISED CONTROL TRIAL"

By

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Dissertation

Submitted to the
KLE Academy of Higher Education and Research,
Belagavi, Karnataka.

In Partial Fulfillment
of the requirements for the degree of

M. D.
in
ANAESTHESIOLOGY

DEPARTMENT OF ANAESTHESIOLOGY,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELAGAVI, KARNATAKA

APRIL– 2019

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH, BELAGAVI, KARNATAKA

Endorsement

This is to certify that the dissertation entitled **"EFFECT OF INTRANASAL DEXMEDETOMIDINE ON DURATION OF ANAESTHESIA AND POST OPERATIVE ANALGESIA IN PAEDIATRIC PATIENTS UNDERGOING INFRAUMBILICAL SURGERIES UNDER SINGLE SHOT CAUDAL EPIDURAL ANAESTHESIA- A ONE YEAR HOSPITAL BASED DOUBLE BLIND RANDOMISED CONTROL TRIAL."** is a bonafide research work done by **REG NO.BA0116002.**

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ABSTRACT

Background and Introduction

Pain is a complex perceptual entity. Pain management is the cornerstone of entire medicine and especially so for anaesthesia. Pain management in Paediatric patients is often overlooked and misunderstood. Caudal Epidural Anaesthesia is a safe and effective mode of anaesthesia in paediatric patients. However, the duration of anaesthesia and the post operative analgesia provided by lone Caudal epidural is short but it can be prolonged using additives. The aim of this study was to overcome this relative shortcoming of caudal epidural with intranasal Dexmedetomidine. The present study titled “Effect of Intranasal Dexmedetomidine on duration of anaesthesia and post operative analgesia in paediatric patients undergoing infraumbilical surgeries under single shot caudal epidural anaesthesia – A one year hospital based Randomised Control Trial” attempted to study the effects of dexmedetomidine on duration of the caudal block and the ensuing post-operative analgesia in paediatric patients.

Methods

After obtaining Institutional Ethical Committee Clearance, we included 60 ASA I and II patients in our study and divided them into two groups randomly. One group received intranasal dexmedetomidine 1µg/kg body weight and the other group received Normal saline immediately after receiving Caudal bupivacaine 0.25% 1ml/kg body weight. Time of induction, intra operative hemodynamics, duration of caudal anaesthesia measured as duration of motor block and time till first rescue analgesic were noted. All the data was collated and tabulated using Microsoft Excel and Students unpaired t test was used for statistical analysis.

Results

The demographic parameters were comparable in both the groups. We found that the duration of motor block which was assessed using Modified Bromage Scale was significantly prolonged in the group receiving Dexmedetomidine (215.83±16.19 minutes) compared to the Group receiving Normal Saline(137±15.52 minutes). This resulted in a highly significant ‘p’ value of <0.0001. Duration of post operative analgesia was measured as the time between the caudal block and the requirement of first rescue analgesic given at a FLACC score of 4. In Group A, mean duration of analgesia was 12.47±2.16 hours and in Group B, it was 3.55±1.18 hours. The ‘p’ value for duration of analgesia was <0.0001, making the inference highly significant. Hemodynamic parameters were comparable.

Conclusion

Our study showed that intranasal administration of Dexmedetomidine significantly increased the duration of motor block in paediatric patients undergoing infra umbilical surgeries under caudal epidural anaesthesia.

Our Study also showed that intranasal dexmedetomidine significantly prolonged the duration of post operative analgesia, thus achieving the primary objectives of the study.

LIST OF ABBREVIATIONS USED

ASA	-	American Society of Anaesthesiologists
PS	-	Physical Status
Mcg	-	Microgram
cc	-	Cubic centimeter
CNS	-	Central nervous system
CSF	-	Cerebrospinal fluid
CVS	-	Cardiovascular system
DBP	-	Diastolic blood pressure
ED	-	Effective dose
FDA	-	Food and Drug Administration
GA	-	General anaesthesia
HR	-	Heart rate
bpm	-	Beats per minute
IV	-	Intravenous
HCL	-	Hydrochloric Acid
KCl	-	Potassium chloride
kg	-	Kilogram
L	-	Lumbar
m	-	Meters
MAP	-	Mean arterial pressure
mg	-	Milligram
v/s	-	Versus
Mins	-	Minutes
ml	-	Millilitre

NIBP	-	Non invasive blood pressure
O_2	-	Oxygen
$PaCO_2$	-	Partial pressure of carbon dioxide
S	-	Sacral
SAB	-	Subarachnoid block
SBP	-	Systolic Blood pressure
DBP	-	Diastolic Blood Pressure
SD	-	Standard deviation
Sec	-	Second
SpO_2	-	Peripheral saturation of oxygen
α	-	Alpha
β	-	Beta
δ	-	Delta
μ	-	Micro
cm	-	centimeter
G	-	Gauge
mEq	-	milliequivalents
Lt	-	litre
Dl	-	decilitre
V_{max}	-	maximum initial velocity or rate of a reaction

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INTRODUCTION

Paediatric patients present a special challenge to the anaesthesiologist with their both subtle and gross deviations from the adult physiology and every child is different in itself due to varying stages of development and growth.

Pain management in paediatric age group is often overlooked with the misconception of decreased pain sensation in the paediatric age group. Pain is one of the most misunderstood, underdiagnosed and undertreated medical problem in this age group.

Various multimodal techniques have been designed for paediatric pain relief. These include both systemic and regional analgesia. The most commonly used regional technique is caudal epidural block. Caudal Epidural block is one of the most popular, reliable and safe techniques in paediatric anaesthesia[(1)]. Although versatile, one of the major limitations of the single shot technique is the relatively short duration of anaesthesia and post-operative analgesia[(2)].

This study aims to provide an acceptable solution for this.

The ideal anaesthetic for perioperative application would be fast in onset and offset, with limited lipid solubility, predictable in response, easy to titrate, reliable in achieving a targeted level of sedation, able to preserve airway tone, and sparing of respiratory effects. This ideal agent would be neuroprotective and exhibit minimal cardiovascular effects.

Dexmedetomidine has become one of the frequently used drugs in anaesthesia practice in recent years due to its hemodynamic stability, sedative, anxiolytic,

analgesic and neuroprotective effects. It also comes with minimal respiratory depression, cardioprotection and renoprotection[3].

High selectivity of dexmedetomidine to α2A receptors has been exploited in various regional anaesthesia practices and yet numerous avenues remain underexplored, intranasal being one of them.

α- 2 agonists interact with local anaesthetics by three possible mechanisms. First, by blocking Aδ and C fibres as a consequence of an increase in potassium conductance in isolated neurons, thus intensifying local anaesthetic conduction block, second by causing local vasoconstriction, thus decreasing local anaesthetic spread, and removal around neural structures. This effect is mediated by drug action on postsynaptic α2 receptors. Thirdly spinal α2 adrenergic agonists may also induce analgesia by activating spinal cholinergic neurons resulting acetylcholine release. Dexmedetomidine has an 8-fold greater affinity for α2a receptors, responsible for the hypnotic and analgesic effects of such drugs. It has no known toxic metabolites[4].

Dexmedetomidine has been studied extensively in various settings and routes in recent times. Various studies have studied its effect as an adjunct to local anaesthetic in caudal epidural anaesthesia. It has been shown that when used as an additive to spinal or epidural anaesthesia, dexmedetomidine prolongs the duration of anaesthesia and post operative analgesia[5].

Various studies have shown that intravenously administered dexmedetomidine also has a significant role in prolonging the duration of anaesthesia and post operative analgesia following neuraxial blocks.

Intranasal route of administration of dexmedetomidine has been shown to have high bio availability on par with intravenous administration with reduced side effects.

Hence we hypothesised that intranasal dexmedetomidine will also prolong the duration of caudal epidural anaesthesia as well as duration of post operative analgesia in paediatric patients undergoing infra umbilical surgeries under caudal epidural block.

OBJECTIVES

Primary objective

To study the effect of intranasal dexmedetomidine on the duration of anaesthesia and post operative analgesia in paediatric patients undergoing infraumbilical surgery under single shot caudal epidural block.

Secondary objective – to study the side effects, if any.

REVIEW OF LITERATURE

Caudal epidural analgesia was first introduced to medicine by Sicard and Cathelin in Paris in 1901[6]. French clinicians Jean. E. Sicard and Fernand Cathelin working independently injected cocaine through the sacral hiatus thus pioneering caudal epidural block . Sicard applied the technique purely for non surgical purpose of pain relief in patients with sciatica and tabes. However, Cathelin used the technique for surgical anaesthesia , considering it to be a safer alternative to spinal anaesthesia for inguinal hernia repair. Stoeckel, a German Obstetrician, is attributed the honour of first introducing this procedure to obstetric practice in 1909. The development of Novocaine by Einhorn in 1905 heralded a new era in the use of local anaesthetics and newer applications became commonplace. Edwards and Hingson, in following the lead given by Lemon and Pascal, developed a method of continuous pain relief in labour. They introduced 'Continuous Caudal Epidural Analgesia,' using an indwelling catheter in the extradural space to facilitate repeated injections as required. A joint programme for the provision of regional analgesia in labour has been in operation in University College Galway since 1972.

Although spinal anesthesia was used in pediatric anesthesia as early as the 1940's, reports of successful paediatric caudal epidural anesthetics initially came from developing countries.

A series from Zimbabwe reported 500 paediatric caudal epidural anaesthesia cases. The reported success rate was high (close to 90%), with little in the way of respiratory or cardiovascular problems. However the children were considerably restless during the procedure which maybe due to the fact that these patients were only sedated, not anesthetized and this could have accounted for some of the technical

difficulties in positioning the caudal epidural needle and the restlessness during the surgery.

In 1967, Fortuna reported a series of 170 patients between the ages of 1-10 years who received caudal epidural anaesthesia for surgical procedures of the lower abdomen and lower extremities. These results showed that caudal anaesthesia either alone or in combination with general anaesthesia was well tolerated with little in the way of respiratory depression or cardiovascular changes.

Caudal epidural anaesthesia with Bupivacaine has been known to provide surgical anaesthesia for a period of 120 to 150 minutes. The use of an additive has been shown to augment the action of caudally administered Bupivacaine.

A study by Rhee K, Kang K, Kim J, Jeon Y, "Intravenous clonidine prolongs bupivacaine spinal anesthesia" was designed to assess the prolongation of spinal anaesthesia by intravenous clonidine. They formulated a double-blind, placebo-controlled, prospective study. Patients scheduled for orthopedic surgery under subarachnoid block, received 12 mg of 0.5% hyperbaric bupivacaine and were randomly divided into three groups (n = 26 in each group). In the clonidine 10-min group, 3 µg / kgof clonidine was administered for 10 min immediately after the spinal block. In the clonidine 60-min group, 3 µg/kgof clonidine was administered for 10 min, 50 min after the spinal block. The control group received normal saline. Sensory block was evaluated by pinprick and the duration was defined as the time for sensory block to regress to L1 dermatome. Duration of motor block was defined as the time required for the patient to flex his or her knee. They found that the duration of sensory block was longer in both the clonidine 10-min and clonidine 60-min groups compared with the control group (196 +/- 42 min, 179 +/- 41 min vs. 125 +/- 25 min, $P < 0.05$). The duration of motor block was longer in the clonidine 10-min group than in the

control group (153 +/- 26 min vs. 131 +/- 29 min, $P < 0.05$). They concluded that the intravenously administered Clonidine significantly prolonged the duration of Spinal block when administered within one hour of administration of the block[7].

Dexmedetomidine is a highly selective α-2 agonist similar to clonidine but with a greater affinity for the α-2 receptor. Clonidine has a specificity of 220 : 1 (α-2 : α-1), whereas dexmedetomidine exhibits a specificity of 1620 : 1. It is a novel α 2 agonist which is making great inroads into clinical anaesthesia. It is one of the highly researched drugs for its sedative, analgesic properties and is favoured by most anaesthesiologists because of the hemodynamic stability it provides.

A Study published in 2016, by Vigya Goyal, Jyotsna Kubre, Krishnaprabha Radhakrishnan at Department of Anaesthesiology and Critical Care, AIIMS, Bhopal, Madhya Pradesh, India Department of Anaesthesiology, GMERS Medical College, Sola Civil Hospital, Ahmedabad, India aimed at studying the effects of dexmedetomidine as an adjuvant to bupivacaine in caudal analgesia in pediatric patients posted for infraumbilical surgeries. This study was conducted in 100 children of American Society of Anesthesiologists physical status I and II, aged 2–10 years, undergoing elective infraumbilical surgeries. They were divided into two groups as follows: Group A: (0.25%) bupivacaine 1 ml/kg + normal saline (NS) 1 ml. Group B: (0.25%) bupivacaine 1 ml/kg + 1 μg/kg dexmedetomidine in 1 ml NS. As this study was double-blind, patients were randomly assigned to receive either (bupivacaine + saline) or (bupivacaine + dexmedetomidine) in each group caudally. The patients were observed for hemodynamic stability, respiratory depression, and postoperative pain using face, legs, activity, cry, consolability (FLACC) pain scale for 24 h postoperatively. Unpaired Student's t test was used for statistical analysis. The study concluded that Dexmedetomidine as adjuvant to Bupivacaine increases duration of

caudal analgesia and improves hemodynamic stability without an increase in adverse effects in children undergoing infraumbilical surgeries[8].

Another study published in 2011 by Anand VG, Kannan M, Thavamani A, Bridgit MJ[9] studied the effects of dexmedetomidine added to caudal ropivacaine in paediatric infraumbilical surgeries. In this randomised, prospective, parallel group, double-blinded study, 60 children were recruited and allocated into two groups: Group RD (n=30) received 0.25% ropivacaine 1 ml/kg with dexmedetomidine 2 μg/kg, making the volume to 0.5 ml and Group R (n=30) received 0.25% ropivacaine 1 ml/kg + 0.5 ml normal saline. Induction of anaesthesia was achieved with 50% N(2)O and 8% sevoflurane in oxygen in spontaneous ventilation. An appropriate-sized LMA was then inserted and a caudal block performed in all patients. Behaviour during emergence was rated with a 4-point scale, sedation with Ramsay's sedation scale, and pain assessed with face, legs, activity, cry, consolability (FLACC) pain score. The study concluded that Caudal dexmedetomidine (2 μg/kg) with 0.25% ropivacaine (1 ml/kg) for paediatric lower abdominal surgeries achieved significant postoperative pain relief that resulted in a better quality of sleep and a prolonged duration of arousable sedation and produced less incidence of emergence agitation following sevoflurane anaesthesia.

In a study titled "The effects of caudal or intravenous dexmedetomidine on postoperative analgesia produced by caudal bupivacaine in children: a randomized controlled double-blinded study", Al-Zaben KR, Qudaisat IY, Alja'bari AN, Ababneh OA, Yousef AM, Al-Shudifat AM[10] compared three groups of patients who received either Caudal epidural with plain bupivacaine, Bupivacaine with Caudal Dexmedetomidine or Caudal Bupivacaine with Intravenous Dexmedetomidine. Patients were randomly allocated to 3 groups. All patients received 1 mL/kg caudal

0.25% bupivacaine. In addition, those in group B (n=25) received 10-mL IV saline, those in group B-Dcau (n=25) received 1 μg/kg caudal dexmedetomidine and 10-mL IV saline, and those in group B-DIV (n=25) received 1 μg/kg IV dexmedetomidine in 10-mL saline. They measured intraoperative mean blood pressure, heart rate, peripheral oxygen saturation, end-tidal sevoflurane, and bispectral index as well as postoperative pain and behavior scores and time to first analgesia were assessed. They concluded that Dexmedetomidine given Caudally or intravenously both prolonged the duration of anaesthesia and post operative analgesia.

A study titled "Effect of supplementation of low dose intravenous dexmedetomidine on characteristics of spinal anaesthesia with hyperbaric bupivacaine" by SS Harsoor, Devika Rani, Bhavana Yalamuru, K Sudheesh, SS Nethra was done to assess the effects of IV dexmedetomidine on sensory, motor, haemodynamic parameters and sedation during subarachnoid block. In this study, they recruited 50 patients scheduled to undergo infra umbilical and lower limb surgeries under Subarachnoid Block and divided them into two groups. Group D received IV dexmedetomidine 0.5 mcg/kg bolus over 10 min prior to SAB, followed by an infusion of 0.5 mcg/kg/h for the duration of the surgery. Group C received similar volume of normal saline infusion. Time for the onset of sensory and motor blockade, cephalad level of analgesia and duration of analgesia were noted. Sedation scores using Ramsay Sedation Score and haemodynamic parameters were assessed. They found that demographic parameters, duration and type of surgery were comparable. Onset of sensory block was 66±44.14 s in Group D compared with 129.6±102.4 s in Group C. The time for two segment regression was 111.52±30.9 min in Group D and 53.6±18.22 min in Group C and duration of analgesia was 222.8±123.4 min in Group D and 138.36±21.62 min in Group C. The duration of motor blockade was prolonged

in Group D compared with Group C. They concluded that intravenous dexmedetomidine successfully prolongs the sensory and motor block in Subarachnoid Block and provides satisfactory arousable sedation.[11]

Another study by Han G , Yu WW , Zhao P published in 2014 in International Journal of Clinical Pharmacology and Therapeutics was a randomized study of intranasal vs. intravenous infusion of dexmedetomidine in gastroscopy. It included 60 patients that were divided into group D1 and D2. Dexmedetomidine (0.5 µg/kg, 1 mL) and normal saline (NS, 1 mL) were given by intranasal route 40 minutes before induction, and then NS (20 mL) and dexmedetomidine (0.5 µg/kg, 20 mL) were given intravenously 10 minutes before induction, respectively. Heart rate (HR), mean arterial pressure (MAP), pulse oxygen saturation(SpO_2), and respiratory rate (RR) were monitored. The latent period of falling asleep, the duration of gastroscopy, the time of awakening, and the total dose of propofol consumption were also recorded. Postoperative sedation scale and adverse reactions were observed. It concluded that Intranasal dexmedetomidine is a new, safe, and effective approach for gastroscopy because it has more stable respiratory and circulatory parameters and less adverse reactions than intravenous dexmedetomidine[12].

Another study published in 2016 by B. L. Li, N. Zhang, J. X. Huang, Q. Q. Qiu, H. Tian, J. Ni, X. R. Song, V. M. Yuen, M. G. Irwin[13] compared intranasal delivery of dexmedetomidine in a dose of 3 µg.kg−1 by either atomiser or drops from a syringe in children < 3 years old undergoing transthoracic echocardiography. Two hundred and seventy-nine children were randomly assigned to one or other group. One hundred and thirty-seven children received dexmedetomidine by atomiser and 142 by drops. The successful sedation rate was 82.5% (95% CI 75.3–87.9%) and 84.5% (95% CI 77.7–89.5%) for atomiser and drops, respectively (p = 0.569).

Sedation tended to be less successful in older children (p = 0.028, OR 0.949, 95% CI 0.916–0.983). There were no significant complications. This study concludes that both modes of dexmedetomidine administration are equally effective. The difference in sedation rate was not found to be statistically significant. (p=0.569)

Dexmedetomidine has repeatedly proven to prolong the duration of caudal epidural anaesthesia and post operative analgesia. It has also been shown that it can be safely used in Paediatric age group, intranasally. Hence this study was undertaken to determine the effect of intranasal dexmedetomidine on duration of caudal epidural anaesthesia and post operative analgesia.

BASIC SCIENCES

An anaesthesiologist requires to have an accurate and in depth knowledge of the anatomy of the caudal space and its contents for a safe and successful administration of caudal epidural anaesthesia.

Anatomy of the Caudal Space

The sacrum is a triangular shaped bone formed by the gradual fusion of lamina of five sacral vertebrae which articulates with 5th lumbar vertebra above and with coccyx caudally.

The caudal epidural space is a triangular space and is continuation of epidural space in the sacrococcygeal region. The anterior surface is smooth and in part supports many important structures such as iliac vessels, rectum. The posterior surface is rough and in midline from above downwards is sacral crest the result of fusion of spinous processes. The fifth is typically unfused.

The anaesthetically important dorsal surface of sacrum is variably convex and irregular with important prominences representing the fused elements of sacral vertebrae. There is a median crest in the midline, with 3 or more but usually 4 variable prominent tubercles representing the sacral spinous processes. Lateral to this crest and medial to the 4 posterior sacral foramina is the intermediate sacral crest with row of 4 tubercles representing the upper 4 sacral articular processes. The posterior foramina are smaller than anterior counter parts and sealed well by multifidus and sacro-spinal muscles.

The remnants of S5 inferior articular processes are free and prominent.

They constitute the sacral cornua and together with the adjacent coccygeal cornua, which they abut, are key landmarks for identification of sacral hiatus and successful caudal blockade. The fused sacral transverse processes give rise to a variably raised lateral sacral crest with transverse tubercles[11].

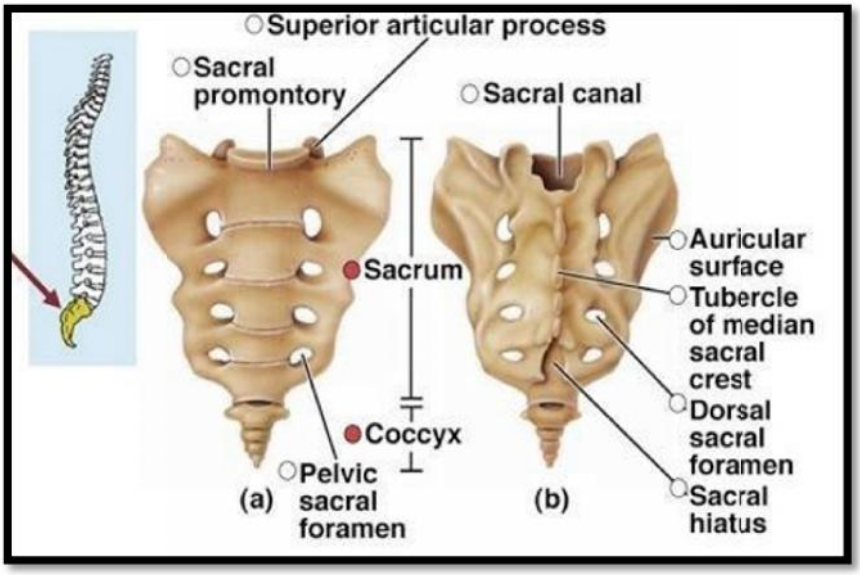

Fig. 1: Sacrum and Coccyx

Sacral hiatus:

The sacral hiatus is a defect in the lower part of the posterior wall of the sacrum, formed by the failure of the lamina of S5 and usually part of S4 to meet and fuse in the median plane. This leaves a space of variable dimension, often described as being like an inverted U or V, which is covered by thick sacrococcygeal ligament which is the continuation of ligamentum flavum. Penetration of this ligament by a needle yields direct access to the caudal limit of epidural space in sacral canal.

The hiatus varies widely in size and shape. The apex of the hiatus lies higher than the lower 1/3 of S4 in about 50% of subjects. The distance between tip of

duralsac and apex of the hiatus is important in order to avoid dural puncture. It is variable but almost exceeds 20mm and is usually closer to 45mm.

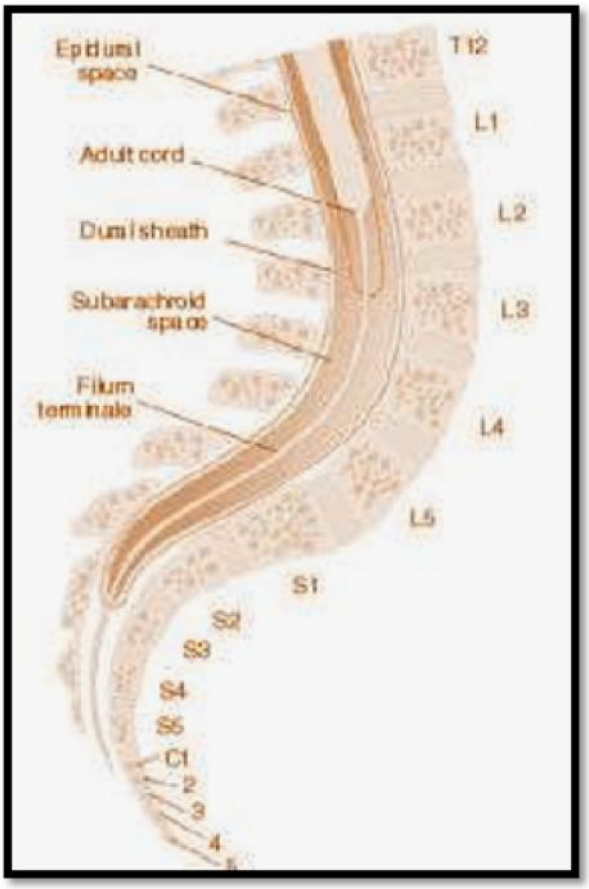

Fig. 2: Sacral canal & its contents

The sacral canal is continuation of lumbar spinal canal which communicates laterally with anterior and posterior sacral foramina. Inferiorly it terminates at sacral hiatus.

Canal capacity: 12 to 65ml with mean capacity of 33ml

Sacral Canal contents:

Terminal part of dural sac, ending between S1 & S3, but generally at S2 on a line joining the posterior iliac spine. Five sacral nerve roots and coccygeal nerve, which constitute the cauda equina.

Filum terminale- the non-nervous terminal filament of spinal cord.

Epidural venous plexus, a part of valveless internal vertebral venous plexus generally end at S4. It tends to lie at the anterior wall of canal and is at risk from needle or catheter puncture.

Sacral and coccygeal nerves:

The anterior and posterior primary rami of S1-S4 exit from the sacral canal by the way of anterior and posterior foramina respectively. Coccygeal nerve exits laterally through the sacral hiatus and winds around the sacrum and the coccyx respectively.

These roots give rise to following nerves:

1. Posterior cutaneous nerve of thigh.
2. Perforating cutaneous nerve.
3. Pudendal nerve
4. Anococcygeal nerves.
5. Pelvic splanchnic nerves.
6. Various muscular branches

These nerves relay total sensory input from vagina, anorectal region, floor of the perineum, anal and bladder sphincters, urethra and scrotal skin.

Technique of caudal block:

Caudal block can be performed as a single shot caudal or continuous caudal by using catheters technique. Single shot caudal blocks are used for ambulatory and minor procedures while continuous catheter techniques are used for undergoing more extensive procedures(14).

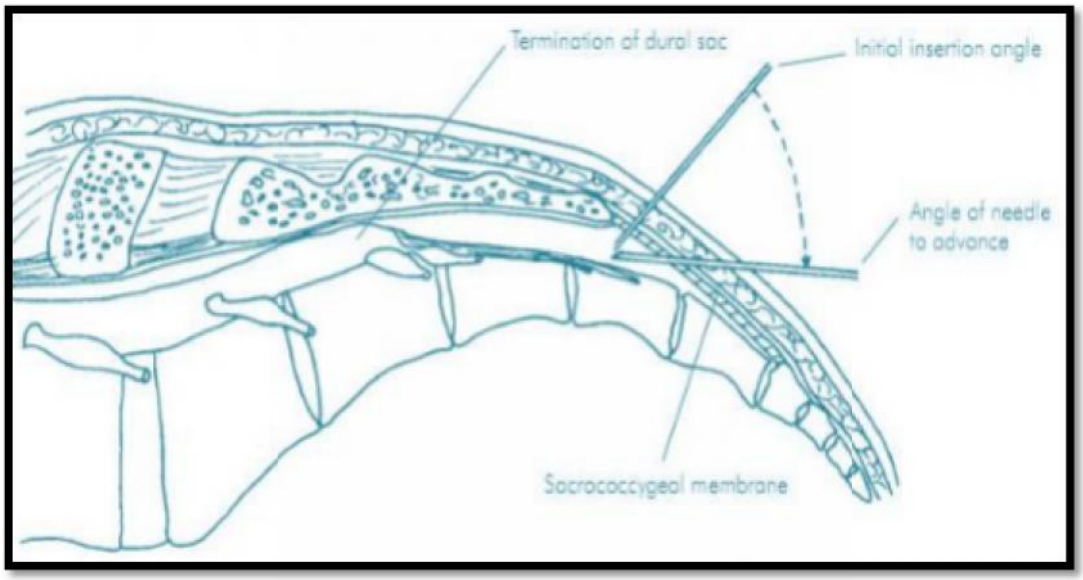

Fig 3: Procedure for caudal epidural

Under all aseptic precautions the following landmarks are palpated:

1. Posterior superior iliac spines
2. Sacral cornua
3. Sacral hiatus between the cornua

The two posterior superior ileac spines were palpated and the line joining the PSIS served as the base of the equilateral triangle, at whose apex, the sacral hiatus was located. The two sacral cornua were identified as two bony prominences and the sacral hiatus identified as the dimple between them. A 23G hypodermic needle can be inserted at this point at an angle of 450 to the sacrum and redirected if the posterior

surface of sacrum came in contact with the needle. A subjective feeling of loss of resistance indicates the piercing of sacro coccygeal ligament. After which the needle will be angulated to 300 to the sacrum and progressed further.

Alternatively, after identifying the midline, a finger is run down the thoracic and lumbar spine towards the sacrum where sacral hiatus may be palpated as a depression between the two sacral cornua. Or, a finger is run upwards towards the sacrum after identifying the tip of the coccyx, which then palpates the hiatus. Once the sacral hiatus is identified, skin over it is punctured with a short bevelled 1.5 inch 23 gauge needle. The bevel of needle should be placed anteriorly to prevent penetration of anterior table of sacrum.

In our study, we palpated the Posterior Superior Iliac Spine to identify the sacral hiatus. The needle is inserted at an angle of approximately 45 degrees to the sacrum, until the characteristic —give in or pop is felt, which indicates that the sacrococcygeal ligament is pierced. On entering the space, the needle is lowered to an angle of 20^0 and advanced 2-3mm to make sure that the entire bevel is inside the space. A Whoosh test has been described for identifying correct needle placement in the caudal canal. This characteristic sound has been noted during auscultation of the thoracolumbar region during the injection of 2 to 3 mL of air into the caudal epidural space.

The volume prescription scheme of Armitage that was published years ago still remains the most reliable.

0.5ml/kg- for sacral dermatomes

1ml/kg - all sacral and lumbar dermatomes.

1.25ml/kg - mid thoracis dermatomes.

DEXMEDETOMIDINE

Dexmedetomidine is a potent and highly selective α-2 adrenoceptor agonist with sympatholytic, sedative, amnestic, and analgesic properties, which has been described as a useful and safe adjunct in many clinical applications(15). It is the most recently developed and commercialized agent in this pharmacological class. It provides a unique "conscious sedation (patients appear to be asleep, but are readily roused), analgesia, without respiratory depression. It decreases central nervous system (CNS) sympathetic outflow in a dose-dependent manner and has analgesic effects best described as opioid-sparing. There is increasing evidence of its organ protective effects against ischemic and hypoxic injury, including cardioprotection, neuroprotection and renoprotection[(3)].

HISTORY

The first α-2 adrenoceptor agonist was synthesized in the early 1960s to be used as a nasal decongestant. Early application of the new substance, now known as clonidine, showed unexpected side effects, with sedation for 24 hours and symptoms of severe cardiovascular depression. Subsequent testing led to the introduction of clonidine as an antihypertensive drug in 1966. Over the years, clonidine gained acceptance as a powerful therapy not only for high blood pressure but also for the management of alcohol and drug withdrawal, for adjunctive medication in myocardial ischemia, and for pain and intrathecal anaesthesia. The use of α2 adrenoceptor agonists as anaesthetics is not new. Veterinarians employed xylazine and detomidine for a long time to induce analgesia and sedation in animals, and much of current knowledge was gained from this application. It has recently become evident that

complete anaesthesia is possible by employing new, more potent α-2 agonists, such as medetomidine and its stereoisomer, dexmedetomidine.

PHYSIOLOGY

α-2 Adrenoceptor agonists - α-2 adrenergic receptors (or adrenoceptors) are transmembrane receptors composed of excitable G-proteins, which cross the cell membrane and link selectively with extracellular ligands: endogenous mediators or exogenous molecules, such as drugs. The α-2 adrenergic receptor consists of three α-2 iso-receptors - α-2a, α-2b and α-2c, which bind α-2 agonists and antagonists with similar affinities and share an amino acid composition homology of approximately 70-75%. Sub-receptor specific agonists or antagonists that enhance advantageous effects while limiting deleterious effects may be forthcoming. α-2 adrenoceptors have been implicated in a variety of physiological functions. The pharmacology of α-2 adrenoceptors is complex, but pharmacological studies, helped by the development of genetic mouse models, have elucidated the physiological effects mediated by the different α-2 adrenoceptor subtypes. Specific α-2 receptor subtypes mediate the varied pharmacodynamic effects of dexmedetomidine. For example, agonism at the α-2a receptor appears to promote sedation, hypnosis, analgesia, sympatholysis, neuroprotection and inhibition of insulin secretion. Agonism at the α-2b receptor suppresses shivering centrally, promotes analgesia at spinal cord sites, and induces vasoconstriction in peripheral arteries. The α-2c receptor is associated with modulation of cognition sensory processing, mood and stimulant-induced locomotor activity, and regulation of epinephrine outflow from the adrenal medulla. Inhibition of norepinephrine release appears to be equally affected by all three α-2 receptor subtypes. These receptors appear to possess presynaptic, postsynaptic and

extrasynaptic sites of action. In fact, α-2 adrenergic receptors have been found in platelets and in a variety of organs, including the liver, pancreas, kidney and eye and in the central and peripheral nervous system, at autonomic ganglia and presynaptic and postsynaptic sites. The presynaptic sites of action are clinically significant because they modulate the release of norepinephrine and adenosine triphosphate through a negative feed-back mechanism. The physiological responses regulated by α-2 receptors vary depending on their location. The stimulation of α-2 receptors in the brain and spinal cord inhibit neuronal firing, which leads to hypotension, bradycardia, sedation and analgesia. The responses from other organs containing α-2 receptors include decreased salivation, secretion, and gastric motility; inhibited renin release; increased glomerular filtration rate; increased secretion of sodium and water in the kidney; decreased intraocular pressure; and decreased insulin secretion from the pancreas. The stimulation of α-2 receptors decreases calcium entry into nerve terminals, which may contribute to its inhibitory effect on neurotransmitter release[16].

MECHANISMS OF ACTION

The hypnotic effect of dexmedetomidine is mediated by the hyperpolarization of noradrenergic neurons in the locus ceruleus of the brain stem (a small bilateral nucleus that contains many adrenergic receptors), which is the primary site in modulating wakefulness. When the α-2 adrenergic receptor is activated, it inhibits adenylyl cyclase. This latter enzyme catalyzes the formation of cyclic AMP (cAMP), a crucial second messenger molecule that acts in many catabolic cell processes. By reducing the amount of cAMP in the cell, dexmedetomidine favours anabolic over catabolic pathways. Simultaneously, there is an efflux of potassium through calcium-activated potassium channels and an inhibition of calcium entry into calcium channels

in nerve terminals. The change in membrane ion conductance leads to a hyperpolarization of the membrane, which suppresses neuronal firing in the locus ceruleus as well as activity in the ascending noradrenergic pathway. The locus ceruleus is also the site of origin for the descending medullospinal adrenergic pathway, which is known to be a key mechanism in regulating nociceptive neurotransmission. The similar mechanisms of α-2 receptors and opioid receptors in this area of the brain have contributed to the thought that there must also be extra-spinal sites of action. When these sites are stimulated, they decrease the firing of nociceptor neurons stimulated by peripheral A and C fibers and also inhibit the release of their neurotransmitters. The analgesic effects are believed to be in the dorsal horn of the spinal cord[(17)].

When a hypnotic dose of dexmedetomidine was administered to laboratory animals, norepinephrine release from the locus ceruleus was inhibited. The absence of inhibitory control over the ventrolateral preoptic nucleus (VLPO) resulted in the release of gammaaminobutyric acid (GABA) and galanin, which further inhibited the locus ceruleus and tuberomamillary nucleus (TMN). This inhibitory response also causes a decrease in the release of histamine, which results in a hypnotic response. This response is similar to that found in normal sleep in that the reduction of norepinephrine release by the locus ceruleus triggers the release of GABA and galanin by the VLPO. The reduced occupancy of the histamine receptors on the cells of the subcortical areas induces a hypnotic state[(18)]

PHARMACOLOGY

Dexmedetomidine is chemically described as (+)-4-(S)-[1(2,3-dimethylphenyl) ethyl]-1 H imidazole monohydrochloride. It has a molecular weight of 236.7. It has a pH in the range of 4.5-7. It is water soluble, has a pKa of 7.1. Its partition coefficient in octanol: water at pH 7.4 is 2.89 Dexmedetomidine is the pharmacologically active dextro enantiomer of medetomidine, the methylated derivative of etomidine. It is considered primarily as α-2 adrenoceptor agonist, but also incorporates an imidazoline structure, thus having an agonist effect on imidazoline receptors. Dexmedetomidine is chemically related to clonidine, but is approximately eight times more specific for α-2 adrenoceptors with α-2:α-1 selectivity ratio of 1620:1, compared with 200:1 for clonidine, especially for the α-2a subtype, which makes it more effective than clonidine for sedation and analgesia. Its effects are dose-dependently reversed by administration of a selective α-2 antagonist, such as atipamezole[19].

PHARMACOKINETICS

Dexmedetomidine follows linear or zero-order kinetics, meaning that a constant amount of the drug is eliminated per hour rather than a constant fraction of the drug eliminated per hour, which is characteristic of first order kinetics. After intravenous administration (IV) in healthy adult volunteers, dexmedetomidine has an onset of action after approximately 15 minutes. Peak concentrations are usually achieved within 1 hour after continuous IV perfusion. Dexmedetomidine is also absorbed systemically through the transdermal, oral, or intramuscular routes, with a mean bioavailability from the latter two routes of 82 and 98%, respectively. Protein binding to serum albumin and α1-glycoprotein is reported to be approximately 94%

and remains constant despite varied concentrations of the drug. The bound fraction is decreased significantly in patients with hepatic dysfunction, compared with healthy patients; therefore, a dose reduction in patients with hepatic dysfunction may be required. It has a rapid distribution phase. Its steady state volume of distribution is 118 L and its distribution half-life (t½α) is 6 min in adults over the manufacturer-suggested dose ranges of 0.2-0.7 µg/kg/h, an elimination half-life (t½β) of between 2.0 and 2.5 hours and a clearance of 39 L/h. Total plasma clearance of dexmedetomidine is age independent; thus, similar rates of infusion can be used in children and adults to effect a steady state plasma concentration. However, in patients aged > 65 years, a greater incidence of hypotension and bradycardia was reported; therefore, a dose reduction in this population may be warranted. In children younger than 2 years of age, the volume of distribution at steady state is increased, suggesting that higher doses are required to achieve steady state; but t½β is prolonged, which may result in increased drug accumulation with time[(20)].

Dexmedetomidine is extensively metabolized in the liver through glucuronide conjugation and biotransformation by the cytochrome P450 enzyme system. There are no known active or toxic metabolites. However, hepatic clearance may be decreased by as much as 50% of normal with severe liver disease. No differences have been seen between healthy patients and those with renal impairment. The metabolites are eliminated to the extent of 95% in the urine and 4% in the feces. Considering that the majority of the metabolites are excreted in the urine, there is a theoretical risk that accumulation may result with prolonged administration.

PHARMACODYNAMICS

1. Hemodynamic effects

A brief biphasic, dose-dependent, cardiovascular response has been reported after the initial administration of dexmedetomidine. The bolus dose of 1 µg/kg results in an initial increase in blood pressure and a reflex drop in heart rate. This response is seen more often with young and healthy patients. The stimulation of the α-2b receptors in vascular smooth muscle is postulated to be the cause of the increase in blood pressure. The rise in blood pressure can be attenuated by a slow infusion and by avoiding bolus administration of the drug. This initial response lasts for 5 to 10 minutes and is followed by a slight decrease in blood pressure due to the inhibition of central sympathetic outflow. The presynaptic α-2 receptors are also stimulated, thereby decreasing norepinephrine release, causing a fall in blood pressure and heart rate. The dose dependent bradycardic effect of dexmedetomidine is primarily mediated by the decrease in sympathetic tone and partly by baroreceptor reflex and enhanced vagal activity[21]. Therefore, the cardiovascular effects of dexmedetomidine are predictable and can be derived from the α2 adrenoceptor pharmacological effects. Slow bolus loading or omitting bolus loading to prevent initial hypertension and reflex bradycardia as well as drug dosing, rate of drug infusion, adequate volume repletion and careful patient selection and monitoring renders dexmedetomidine a substance with predictable side-effects belonging to a pharmacological class with a wide safety margin

2. Central Nervous System effects

Like other α-2 adrenoceptor agonists, dexmedetomidine provides sedation, hypnosis, anxiolysis, amnesia and analgesia. The dose-dependent sedative/hypnotic effects of dexmedetomidine have been well documented in various experimental and clinical trials. With increasing doses of dexmedetomidine, profound anaesthetic actions have been described, leading to the suggestion that dexmedetomidine could be used as a total intravenous anaesthetic. Interestingly, some similarity with natural sleep was observed with dexmedetomidine-induced sedation. This is in accordance with other findings in rats, which proposed that dexmedetomidine converges on a natural sleep pathway, activating pathways that promote endogenous non-rapid eye movement sleep to exert its sedative effect. It also preserves a cerebral blood flow pattern akin to natural sleep. The amnestic effects of dexmedetomidine are far less than the benzodiazepines, which provide profound anterograde amnesia that may contribute to confused states on emergence. In contrast, amnesia is achieved with dexmedetomidine only at high plasma levels (> 1.9 ng/mL), without retrograde amnesia[(22)].

The analgesic properties of dexmedetomidine in humans are more controversial. It has been suggested that the spinal cord is probably the major site of analgesic action of α-2 adrenoceptor agonists. It appears to exert analgesic effects at the spinal cord level and at supraspinal sites[(3)].

Dexmedetomidine may also provide antinociception through non-spinal mechanisms - intraarticular administration during knee surgery improves postoperative analgesia, with less sedation than the IV route. Suggested mechanisms

are activation of α-2a receptors, inhibition of the conduction of nerve signals through C and Aδfibers, and the local release of encephalin.

3. Respiratory System effects

Despite profound sedative properties, dexmedetomidine is associated with only limited respiratory effects, even when dosed to plasma levels up to 15 times of those normally achieved during therapy, leading to a wide safety margin. Hypercapnic arousal is preserved, and the apnea threshold is actually decreased.

In contrast to infusions of opioids, benzodiazepines, or propofol, dexmedetomidine can safely be infused through tracheal extubation and beyond. Despite the lack of respiratory depression, only later dexmedetomidine was originally approved by the FDA for use in "initially intubated, mechanically ventilated patients," that is, it had to be started on ventilated patients but could be continued through and beyond tracheal extubation. In October 2008, dexmedetomidine was approved by the FDA for procedural sedation in non-intubated patients[(23)].

4. Metabolic effects

Dexmedetomidine and other α-2 agonists suppress shivering, possibly by their activity at α-2b receptors in the hypothalamic thermoregulatory center of the brain. Low-dose dexmedetomidine has an additive effect with meperidine on lowering the shivering threshold, when they are combined. It may also be beneficial in decreasing patient discomfort from postoperative shivering and controlling shivering that may delay therapeutic hypothermia for acute stroke or CNS injury. Easley et al., in an open-label prospective paediatric study, found that a single intravenous bolus of

dexmedetomidine, 0.5 µg/kg over 3-5 min, was effective in the treatment of postanesthesia shivering[24].

5. Organ protective effects

i. Myocardial ischemia and cardioprotection

The perioperative period is characterized by increased sympathetic activity, leading to stress induced tachycardia and hypertension. By attenuating sympathetically mediated hyper dynamic responses, α-2 adrenoceptor agonists ameliorate the hemodynamic profile during the perioperative period. Previous studies have shown that hemodynamic stabilization by the application of α-2 adrenoceptor agonists in the perioperative period leads to a reduction in perioperative myocardial ischemia episodes. However, theoretical considerations against the use of α-2 adrenoceptor agonists have been the vasoconstrictive and hypotensive properties, which are potentially proischemic. Laboratory investigations showed that large intravenous doses of dexmedetomidine caused moderate regional coronary vasoconstriction without metabolic signs of myocardial ischemia in young domestic pigs at the same time as a marked vasoconstrictive response in the systemic circulation. At present, a reduction in myocardial ischemia and improved outcomes for patients at risk of cardiac events has only been documented for clonidine as a clinically available α-2 adrenoceptor agonist. The only available data for dexmedetomidine showed that perioperative infusion appeared to benefit the perioperative hemodynamic management of surgical patients undergoing vascular surgery. Future studies will have to be focused on whether dexmedetomidine provides similar properties in reducing the incidence of myocardial ischemia and postoperative mortality compared with clonidine[25].

ii. Neuroprotection

Dexmedetomidine possesses neuroprotective properties in various experimental models of cerebral ischemia, and attenuated hypoxic-ischemic brain injury in developing brains, highly susceptible to neuronal damage. Moreover, a significant improvement in functional neurological outcomes after brain injury was demonstrated. The exact mechanisms of neuroprotection are not clear, but catecholamine pathways play an important role. α-2 adrenoceptors modulate neurotransmitter release in the central and peripheral sympathetic nervous system, thus offering a possible explanation for the neuroprotective properties of dexmedetomidine[(26)].

iii. Renoprotection

The effects of dexmedetomidine on renal function are complex. α-2 agonists exert a diuretic effect by inhibiting the antidiuretic action of vasopressin (AVP) at the collecting duct, most likely through α-2a receptors, resulting in decreased expression of aquaporin-2 receptors and decreased salt and water reabsorption. They also enhance osmolal clearance through non AVP-dependent pathways, possibly mediated by the α-2b receptor. There is experimental evidence that dexmedetomidine attenuates murine radiocontrast nephropathy by preserving cortical blood flow. This mechanism is supported by the observation that dexmedetomidine decreases the renal cortical release of norepinephrine. There is also evidence that it attenuates murine ischemia-reperfusion injury. However, prospective human studies establishing a benefit are not yet available[(27)].

TOXICITY AND ADVERSE EFFECTS

The teratogenic effects of dexmedetomidine have not been adequately studied at this time, but the drug does cross the placenta and should be used during pregnancy only if the benefits justify the risk to the fetus. No studies have been performed in children. As expected from the pharmacological profile, bradycardia and hypotension are the most common side-effects of dexmedetomidine. However, with the use of high concentrations there is also a potential for both pulmonary and systemic hypertension and direct or reflex bradycardia. The incidence of postoperative bradycardia has been reported to be as high as 40% in healthy patients. These temporary effects have been managed with atropine, ephedrine, and volume infusion. Caution should be taken in those clinical situations where the sympatholytic actions of α-2 receptor agonists prove detrimental, such as in patients with left ventricular dysfunction and when administered to patients who are volume depleted, vasoconstricted, or have severe heart block. Recently, severe bradycardia leading to cardiac arrest has been reported with the use of dexmedetomidine. A closer look at these reports reveals several contributing factors that may have interacted, finally resulting in asystole. However, even if dexmedetomidine can probably not be held accountable as the only causative mechanism of these cardiac arrests, such case reports are important. They emphasize potentially deleterious effects that have significant implications for the safe use of these drugs in the critically ill, when multiple factors with negative chronotropic influences convene in a clinical setting, and underline the importance of adequate patient selection for the safe use of dexmedetomidine[(28)].

In summary, the adverse effects of dexmedetomidine include initial hypertension, hypotension, nausea, bradycardia, atrial fibrillation, and hypoxia.

Overdose may cause first-degree or second-degree atrioventricular block. Most of the adverse events associated with dexmedetomidine use occur during or shortly after loading dose.

BUPIVACAINE

Bupivacaine is a synthetic first long acting local anaesthetic of the amide type. It was synthesized by O.F. Ekenstam and his colleagues in 1957 and introduced to clinical practice by Widman in 1963 .

Chemical name:

1-n-butyl-1-DL-piperidine-2-carboxylicacid-2,6-dimethylanilide hydrochloride.

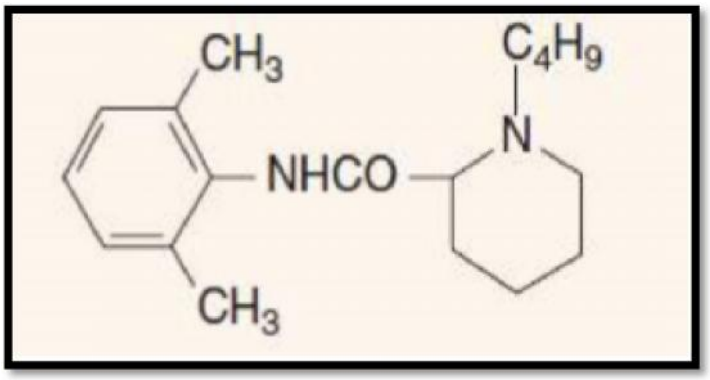

Fig 4: Chemical figure:

Physiochemical properties:

Molecular weight:

Bupivacaine hydrochloride salt is 325 and that of base is 288.

pKa —8.1

pH —5.4

Solubility: The base is sparingly soluble but the hydrochloride is readily soluble in water.

Stability: Bupivacaine is highly stable and can withstand repeated autoclaving.

Protein binding:

It is bound to plasma protein (alpha-1-acid glycoprotein) with a protein binding of 95%. This accounts for the longer duration of action and therefore is good for post-operative analgesia.

Partition coefficient:

Bupivacaine is a highly lipid soluble drug with a partition coefficient of 28. It is 3-4 times more potent than lignocaine because of its high lipid solubility[(29)].

Mechanism of action:

The primary action of local anaesthetic is on cell membrane of axon. Bupivacaine binds to the alpha-subunit of the voltage gated sodium channels from inside the cell. This prevents channel activation and blocks large transient sodium influx associated with membrane depolarisation. This does not alter the resting membrane potential but the impulse conduction is slowed down due to decrease in the rate of rise in action potential. Eventually this leads to failure of propagation of impulse.

Another mechanism is membrane expansion theory. Drugs which do not form cations at physiological pH act by penetrating the axonal membrane.

The membrane swells up and blocks sodium channels. This is non-specific action.

PHARMACOLOGICAL ACTIONS

Central nervous system:

Bupivacaine has a biphasic effect on central nervous system. The initial state involves excitation of CNS due to blockade of inhibitory pathways in cerebral cortex. With higher doses there is depression of both inhibitory as well as facilitatory pathways, resulting in a generalised state of CNS depression.

Cardiovascular system:

Bupivacaine is a cardiotoxic drug. It binds specifically to myocardial proteins. The primary cardiac electrophysiologic effect is the decrease in the rapid phase of depolarisation (V max) in the purkinje fibres and the ventricular muscle due to decrease in availability of fast sodium channels in the cardiac membrane. The rapid phase of depolarisation block by Bupivacaine is by far greater compared to other local anaesthetics like lignocaine and also the recovery rate is slower with Bupivacaine. Thus there is an incomplete restoration of V_{max} between action potential at higher heart rates making it highly arrythmogenic[30].

In higher concentrations Bupivacaine depress myocardial contractility. This is by blocking the calcium transport. A low dose of Bupivacaine produces vasoconstriction while higher doses cause vasodilation in peripheral vascular smooth muscles.

PHARMACOKINETICS

Absorption:

It is related to

1. Site of injection: Rate of systemic absorption is proportional to vascularity of the site of injection (Intercostal > caudal >paracervical> epidural > brachial plexus > subcutaneous)
2. Dose of drug: Linear relationship exists between total dose and peak blood concentration achieved.
3. Presence of vasoconstrictor : Addition of adrenaline to Bupivacaine does not influence the rate of systemic absorption, as the drug is highly lipid soluble and thus uptake into fat is rapid and moreover Bupivacaine has a vasodilatory effect.

Distribution:

The volume of distribution of Bupivacaine in steady state is 72 litres.

Metabolism:

This occurs in liver by N-dealkylation primarily to pipecolyxylidine. N-desbutyl Bupivacaine and 4-hydroxy Bupivacaine is also formed. N desbutyl Bupivacaine has been measured in blood or urine after spinal or epidural anaesthesia.

Excretion:

About 10% of drug is excreted unchanged in urine with in 24hours. About 5% as pipecolyxylidine in urine[31].

Preparations: Solutions of 0.25% and 0.5% concentrations without Epinephrine in 20ml vials.

Toxicity:

Systemic toxic reactions can occur, owing to accidental injection intrathecally or intravascular or due to administration of an excessive dose of Bupivacaine. It mainly involves CNS and CVS. An allergic reaction to amide type local anaesthetics is rare.

The neurotoxic plasma concentration is 1.5-2.5 µg/ml.

Cardiotoxic plasma concentration is 0.5-5 µg/ml.

CNS:Numbness of tongue and circumoral tissues, tingling, tinnitus ,light headedness, confusion, small muscle twitches involving face and distal part of extremities which may progress to generalised tonic clonic seizures. In later stages, it progresses to respiratory arrest.

CVS: Ventricular tachycardia, ventricular fibrillation, myocardial depression, hypotension, bradycardia, bradyarrythmia and syncope.

Dosage: Bupivacaine in caudal epidural is used in a concentration of 0.25% as 1m/kg body weight for infra umbilical surgeries, according to Armitage formula to block lumbar and sacral dermatomes.

PAIN ASSESSMENT

Pain perception is a dynamic process with myriad points of modulation. It is a protective reflex of our body to alert it to potentially injurious and painful stimulus making itself a continuous focus in anaesthesia.

Post-operative pain when poorly controlled evokes harmful physiological, metabolic and behavioural responses and produces adverse long term effects like delayed recovery and chronic pain.

Various scales and measuring modality have been put forth for assessment of pain in paediatric age group. The evaluation of pain in children is a challenge for the anaesthesiologist as children lack the cognitive ability to vocalise their pain and cannot self-report. It therefore becomes imperative that a reliable and objective method be applied to assess pain.

Various pain scales have been propounded to evaluate pain in the young. The notable pain scales being Numerical rating scale over the age of 5years. Faces score for ages above 3 years and FLACC score[32] for children younger than 3 years

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Criteria	Score 0	Score 1	Score 2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, uninterested	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, distractible	Difficult to console or comfort

RAMSAY SEDATION SCALE

The Ramsay Sedation Scale is a six-point scale developed in the 1970s in order to promote adequate sedation in intensive care units.

Ramsay Sedation Scale

1. Anxious and agitated or restless, or both
2. Co-operative, oriented, and calm
3. Responsive to commands only
4. Exhibiting brisk response to light glabellar tap or loud auditory stimulus
5. Exhibiting a sluggish response to light glabellar tap or loud auditory stimulus
6. Unresponsive

Michael Ramsay explained the use of his scale as follows: “The RSS defines the conscious state from a level 1: the patient is anxious, agitated or restless, through the continuum of sedation to a level 6: the patient is completely unresponsive. Therefore, when an assessment is to be made, the first decision to be made is to note if the patient is awake. If the patient is awake: are they anxious, agitated or restless (RSS 1) or are they calm, co-operative and communicative (RSS 2) If the patient is asleep then a test of reusability needs to be made. If the patient responds quickly to a voice command, this is a RSS 3. If the response is slow then the patient is assigned a level 4. If the patient does not respond a stronger stimulus is applied. A louder auditory stimulus or a glabellar (between the eyebrows) tap is enacted. A brisk response to this test of arousability places the patient at a RSS 4. A slow or sluggish response categorizes the patient to a RSS 5. No response at all places the patient at a

level 6. The arousability stimulus was specifically designed not to be a painful test and not to startle the patient. In fact, it was planned that a sleeping patient would not be aroused to a fully awakened state, so that the sleep pattern would not be disturbed.”[33]

METHODOLOGY

The present study titled **"**Effect of intranasal dexmedetomidine on duration of anaesthesia and post operative analgesia in paediatric patients undergoing infraumbilical surgeries under single shot caudal epidural anaesthesia- a one year hospital based double blind randomised control trial.**"** was conducted in the Department of Anaesthesiology , KLE's Dr. Prabhakar Kore Hospital , Belagavi during the period of January 2017 to December 2017 .

Source of data

Paediatric patients between the age group of 6months - 10yrs, belonging to ASA Grade I and II scheduled for elective infraumbilical surgeries at K.L.E`S Dr. Prabhakar Kore Hospital, Nehru Nagar, Belagavi between Jan 2017 to Dec 2017 were included.

Study Design:

A one year randomized controlled trial.

Study Period:

One year from January 2017 to December 2017.

Selection Criteria:

Inclusion Criteria:

- ASA physical status I and II
- Age between 6 months to 10 years.
- Weight less than 25 kg
- Patients undergoing elective infraumbilical surgeries.

Exclusion Criteria:

- ASA Grade III or more
- Patients allergic to Dexmedetomidine or Bupivacaine
- Patients with Contra indications to caudal epidural block.
- Patients with Upper or lower respiratory Infection.

Sample size :

Total sample size-60

Group A – 30

Group B – 30

Sample Size Calculation:

With type I error rate $\alpha = 0.05$ and

type II error rate $\beta = 0.02$

with a power of 80% and using the formula-

$$n=\frac{2\,(Z\alpha+Z\beta)^2\,p(1-p)}{(p_0-p_1)^2}$$

$$n=\frac{2(1.96+0.84)^2(75)(25)}{(5.5-14.5)^2}$$

$$n=19.2$$

n = number of samples

$Z\alpha = 1.96$

$Z\beta = 0.84$

$P_0 = 5.5$

$P_1 = 14.5$

Since the sample size achieved by this formula is inadequate for the study, for the sake of consistent result, sample size has been taken as 60. There are two groups of 30 each.

Methodology

After obtaining the approval of the institutional Ethical committee, a total of 60 ASA I-II children undergoing elective infraumbilical surgeries under caudal epidural anaesthesia were included in the study.

After having met inclusion and exclusion criteria and having obtained informed consent, patients were randomized based on computer generated randomization table into one of the two groups.

- Group A
- Group B

A thorough pre anaesthetic examination was done one day prior to the surgery. Detailed medical history was elicited and diligent physical examination was carried out. The patients were kept nil per orally for 4 hours. Preoperatively routine investigations like Hb, CBC, BT, CT were done.

An intra venous line was secured in the pre-operative holding area and infusion of Ringer Lactate started.

All patients were premedicated with Inj. Glycopyrrolate 0.005mg/kg and Inj. Ketamine 1mg/kg IV in the pre-operative holding area and shifted to Operation Theatre. After arriving in operating room standard monitors were attached (ECG, Spo2, non-invasive blood pressure). A baseline reading of the vitals was recorded. Inj

Ketamine 1mg/kg IV was repeated along with Inj Midazolam 0.05mg/kg IV, Inj Fentanyl 1 mcg/kg IV. Anaesthesia was maintained with O_2+N_2O+Isoflurane 0.4 – 1%.

The child was then shifted to left lateral position and under strict aseptic precautions, the following procedure was carried out. The parts were painted with Povidine Iodine solution from the lower border of the scapula to the gluteal cleft and cleaned with spirit. Sterile drape was then applied.

The two posterior ileac spines were palpated and the line joining the PSIS served as the base of the equilateral triangle, at whose apex, the sacral hiatus was located. The two sacral cornua were identified as two bony prominences and the sacral hiatus identified as the dimple between them. A 23G hypodermic needle was inserted at this point at an angle of 45^0 to the sacrum and redirected if the posterior surface of sacrum came in contact with the needle. A subjective feeling of loss of resistance indicated the piercing of sacro coccygeal ligament. After which the needle was angulated to 30^0 to the sacrum and progressed further. A stethoscope was then placed in the midline and 2ml of air injected. A positive whoosh test confirmed the placement of the needle in the caudal epidural space.

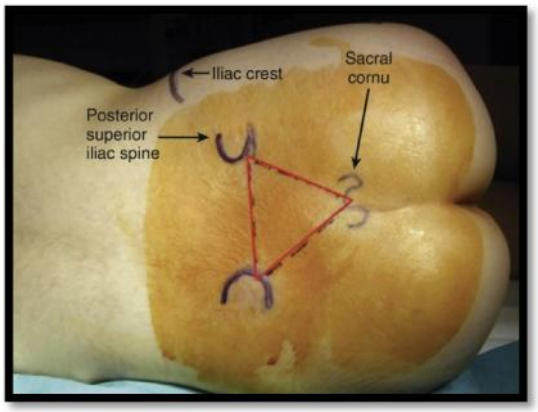


Fig 5: Surface Anatomy for Caudal Epidural Block

Inj Bupivacaine 0.25% 1ml/kg body weight was administered after negative aspiration for blood or CSF.

The patient was then made supine.

The study drugs were prepared by an anaesthesiologist who was not involved in the study and administered by an anaesthesiologist who was blind to the identity of the drug.

In *Group A*,

Patients in this group received Intranasal Inj Dexmedetomidine 1mcg/kg body weight in two divided doses into each nostril using an atomizer connected to a tuberculin syringe.

Group B – patients in this group received 0.01ml/kg Normal Saline intra nasally in both nostrils.

Anaesthesia was maintained with O_2+N_2O+Isoflurane 0.2 %.

The time of administration of block, administration of the intranasal test drug and the time of start of surgery were noted.

Heart rate (HR), BP, respiratory rate (RR), and oxygen saturation were recorded before induction and then immediately after caudal anaesthesia, and every 10 min during surgery thereafter. Adequate analgesia was defined as hemodynamic stability as indicated by the absence of an increase in systolic BP or HR of more than 20% compared with baseline value and from the intraoperative requirement of the inhalational agent. A decrease in mean arterial pressure >20% was defined as

hypotension and was treated with intravenous fluids. A decrease in HR >20% was considered as bradycardia and was treated with Inj Glycopyrrolate 0.005 mg/kg.

Intra operatively, no opioid or sedative was given routinely, and the use of these drugs, if any, was documented.

The following observations were made

- Time of Caudal Block
- Haemodynamics noted every 10 minutes till the end of surgery.
- The time at which patient regains motor function
- Time for 1st rescue analgesia based on the FLACC score

Motor block was assessed using the Modified Bromage Scale by eliciting the response to tickling of the toes or passively flexing the knee joint every half hourly until regression of motor block.

Modified Bromage scale.

Bromage 0:- Free movement of legs and ability to raise extended leg.

Bromage 1:-Inability to raise extended leg and knee flexion is decreased, but full flexion of ankle and feet is present.

Bromage 2:-Inability to raise leg or flex knees, flexion of ankle and feet present.

Bromage 3:-Inability to raise leg, flex knee or ankle or move toes.

Total duration of the motor block was considered to be the duration from the administration of the block to the return of Modified Bromage scale 0.

At the end of the surgery all patients were shifted to recovery room and observed for 2 hours, in recovery room before returning to ward. HR, BP, SpO_2 were monitored continuously. Postoperative pain was assessed at 30 min 1, 2, 4, 6 hours or until the first rescue analgesic was given using the FLACC score.

Criteria	Score 0	Score 1	Score 2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, uninterested	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, distractible	Difficult to console or comfort

The rescue analgesic given was Inj Paracetamol 15mg/kg in 100ml or 50ml NS as slow IV for a FLACC score of 4 and above.

The level of sedation in children was assessed using Ramsay Sedation Score at the end of the surgery, at 2 hours, 6 hours and 12 hours post operatively.

Ramsay Sedation Scale

1. Anxious and agitated or restless, or both
2. Co-operative, oriented, and calm
3. Responsive to commands only
4. Exhibiting brisk response to light glabellar tap or loud auditory stimulus
5. Exhibiting a sluggish response to light glabellar tap or loud auditory stimulus
6. Unresponsive

Side Effects/ Unexpected Intra operative events

Side effects, if any, were duly noted. Any untoward or unexpected intra operative events were treated and documented.

Statistical Analysis

The data was tabulated and master chart was prepared. Microsoft Excel was used to tabulate the data and MedCalc version 17 was used to analyse the data. The categorical data was expressed as ratios and percentages while continuous data was expressed as mean ± standard deviation. Student unpaired 't' test was used to find significance of study parameters on continuous scale between the two groups. A 'p' value of < 0.05 was considered statistically significant. The data was represented in tables and appropriate charts.

RESULTS

This study titled “Effect of intranasal dexmedetomidine on duration of anaesthesia and post operative analgesia in paediatric patients undergoing infra umbilical surgeries under single shot caudal epidural anaesthesia” was conducted in the Department of Anaesthesiology, Jawaharlal Nehru Medical College, KAHER, Belagavi between January 2017 to December 2017. A total of 60 patients were included in the study after having met inclusion and excclusion criteria and written informed consent from the parents. The patients were randomised into two groups of 30 each using a computer generated randomisation table.

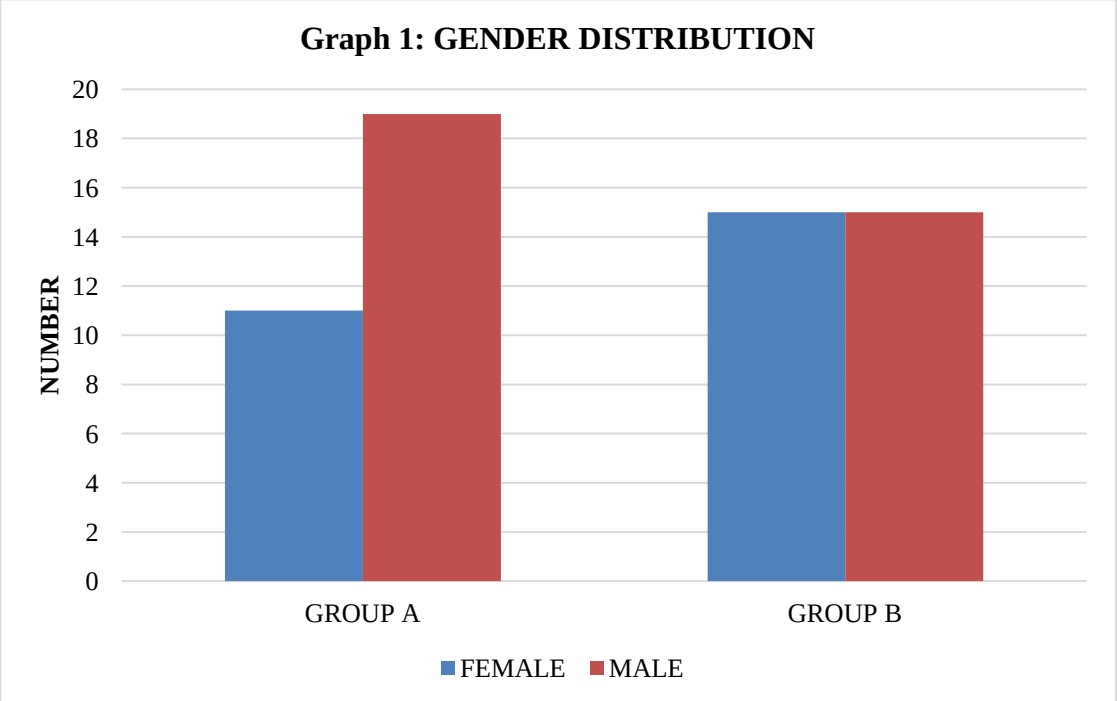
The data was collated using Microsoft Excel and was represented using Mean and Standard Deviation for all sets of data. Quantitative analysis of significance of data was done using Students unpaired ‘t’ test and represented as below.

Gender Distribution

The distribution of gender across both the groups was comparable. There were 11 females in Group A and 19 males. In group B, there were 15 males and 15 females.

	GROUP A	GROUP B	TOTAL
FEMALE	11	15	26
MALE	19	15	34
TOTAL	30	30	60

Table 1 - Gender distribution of the sample

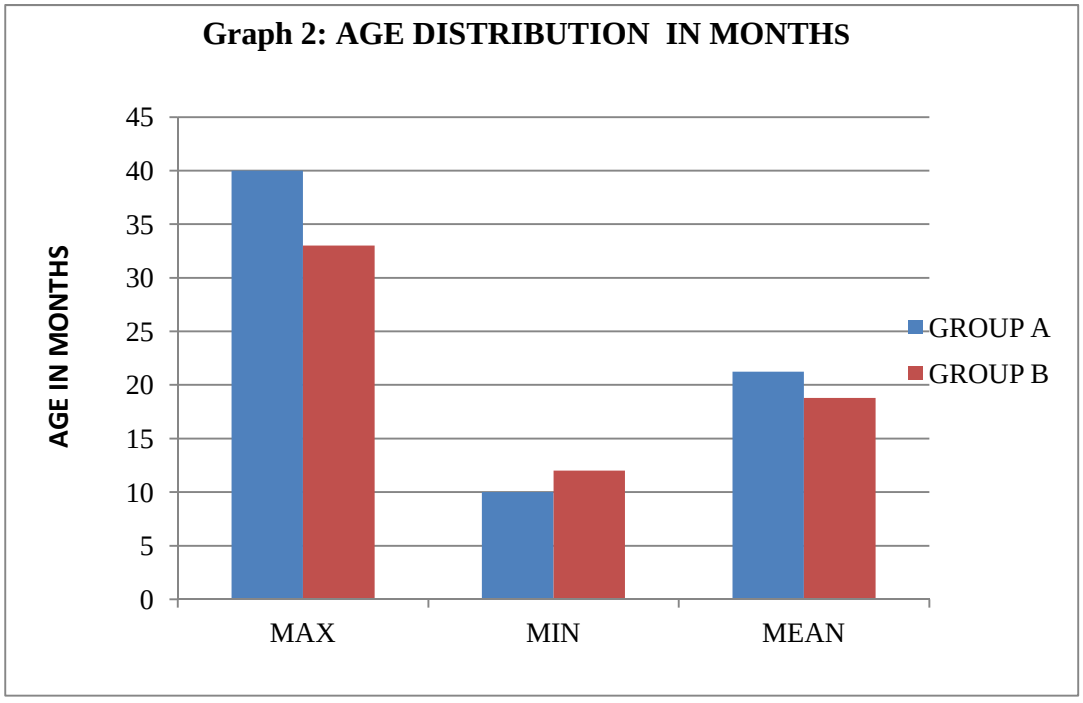


Age Distribution

The minimum age in group A was 10 months and the maximum age was 40 months. The mean age was 21.3 months, which yielded the standard deviation of 8.89. In Group B, the minimum age was 12 months and the maximum age was 33 months with the mean age of 18.80 months and a standard deviation of 6.30. The p value was 0.226 which made the age distribution in two groups comparable.

	Group A				Group B					
	Mean	S.D	Min	Max	Mean	S.D.	Min	Max	P Value	Inference
Age In Months	21.23	8.89	10	40	18.80	6.30	12	33	0.2263	Ns

Table 2 – Age distribution of the sample in months.

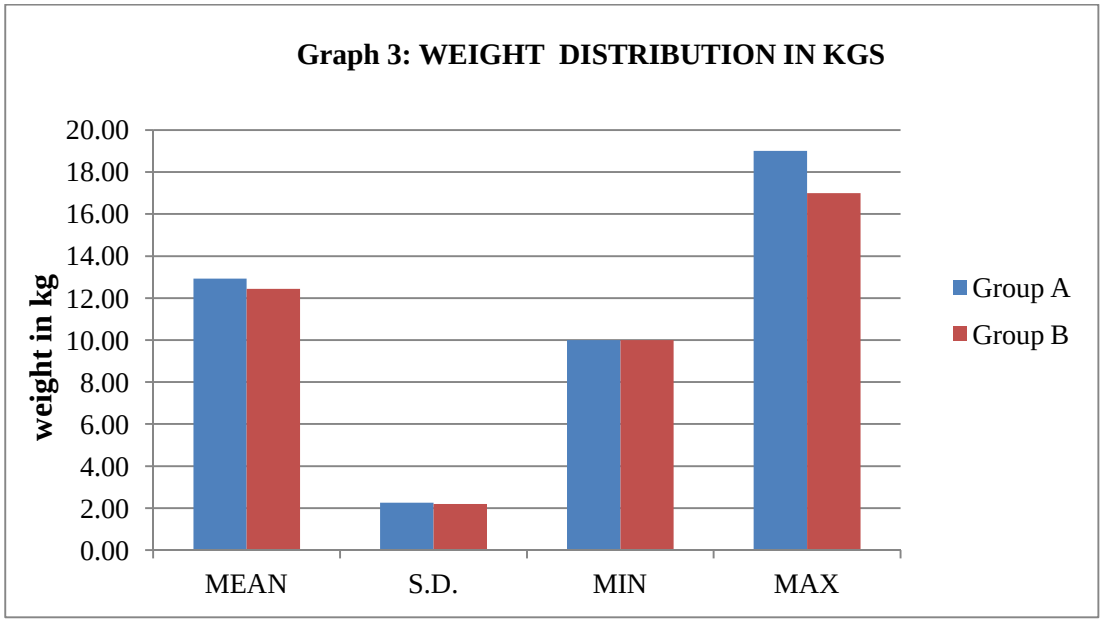


Weight Distribution

In our study, we included children weighing 10 kg or more and the distribution of weight was comparable. In group A, the minimum weight was 10 kg and the maximum was 19kg with a mean weight of 12.93 and a standard deviation of 2.26. In Group B, the minimum weight was 10 kg and the maximum weight was 17kg. The mean weight was 12.43 and the standard deviation was 2.19 with an insignificant p value of 0.3878.

	Group A				**Group B**					
	Mean	**S.D.**	**Min**	**Max**	**Mean**	**S.D.**	**Min**	**Max**	**P Value**	**Inference**
Weight in KG	12.93	2.26	10	19	12.43	2.19	10	17	0.3878	NS

Table 3 – Weight distribution of the sample in kg



Vitals

The preoperative vitals of children were recorded in both the groups and all the baseline readings were comparable.

	GROUP A				GROUP B					
	MEAN	**S.D.**	**MIN**	**MAX**	**MEAN**	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
HR (BPM)	118.53	12.80	99	142	120.20	8.42	109	142	0.4742	NS
SBP	97.27	5.16	90	110	96.27	4.78	90	110	0.4392	NS
DBP	63.67	4.37	56	70	65.00	5.06	60	76	0.2789	NS
SpO2	100.00	0.00	100	100	100.00	0.00	100	100	-	-

Table 4 – Preoperative Vitals

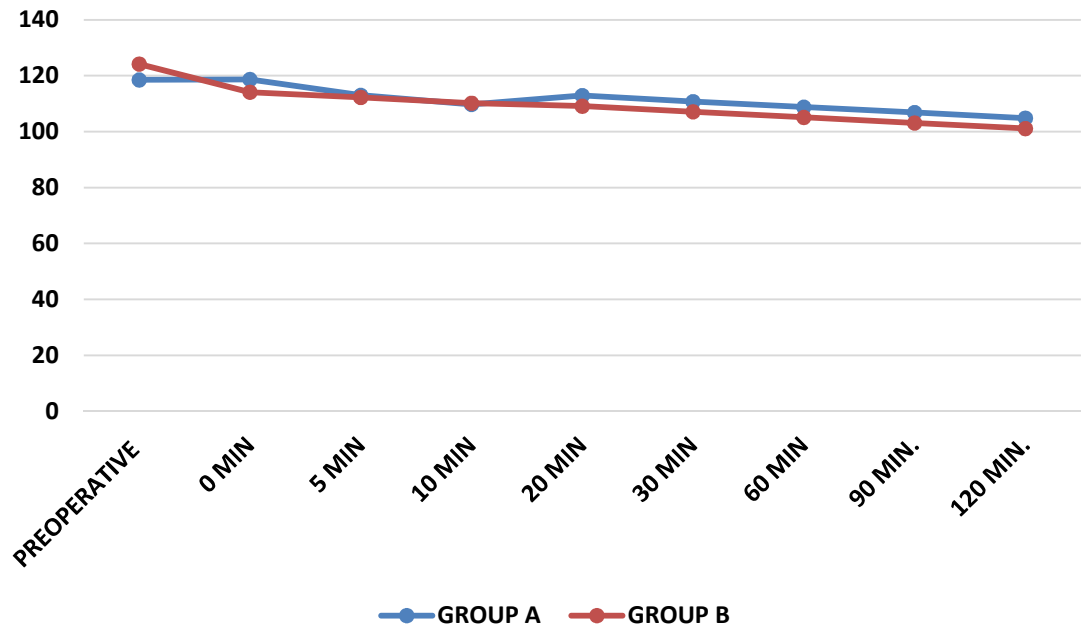
Heart Rate

We found that the mean Pre-operative Heart Rate in Group A was 118.53±12.80. There was no significant change in Heart Rate from the time of caudal epidural block until the first 30 minutes of the surgery. However, we found that the decrease in heart rate at 30 minutes, 60 minutes and 90 minutes was significant. This fall in heart rate however, did not require any therapeutic intervention.In Group B, the mean pre operative heart rate was 120.20±8.42. This was comparable with the pre operative mean heart rate in Group A. Subsequent readings of heart rate in group B were insignificant and comparable with the heart rate at the time of caudal block.

	Group A			Group B		
	HR	SD.	P Value	HR	S.D.	P value
PREOPERATIVE HR	118.53	12.80	0.4775	120.20	8.42	0.212
0 MIN	118.70	11.26	0.449	114.13	11.85	0.476
5 MIN	113.03	10.62	0.432	112.27	10.61	0.448
10 MIN	109.77	10.69	0.417	110.20	10.47	0.378
20 MIN.	112.93	10.90	0.346	119.13	11.85	0.329
30 MIN.	110.77	10.98	< 0.0001	115.13	11.85	0.49
60 MIN	108.80	10.96	< 0.0001	117.13	11.85	0.49
90 MIN	106.87	10.92	< 0.0001	113.13	11.85	0.49
120 MIN	104.87	10.92	<0.0001	110.13	11.85	0.49

Table 5 – Heart Rate

Graph 4: MEAN HR (BPM)

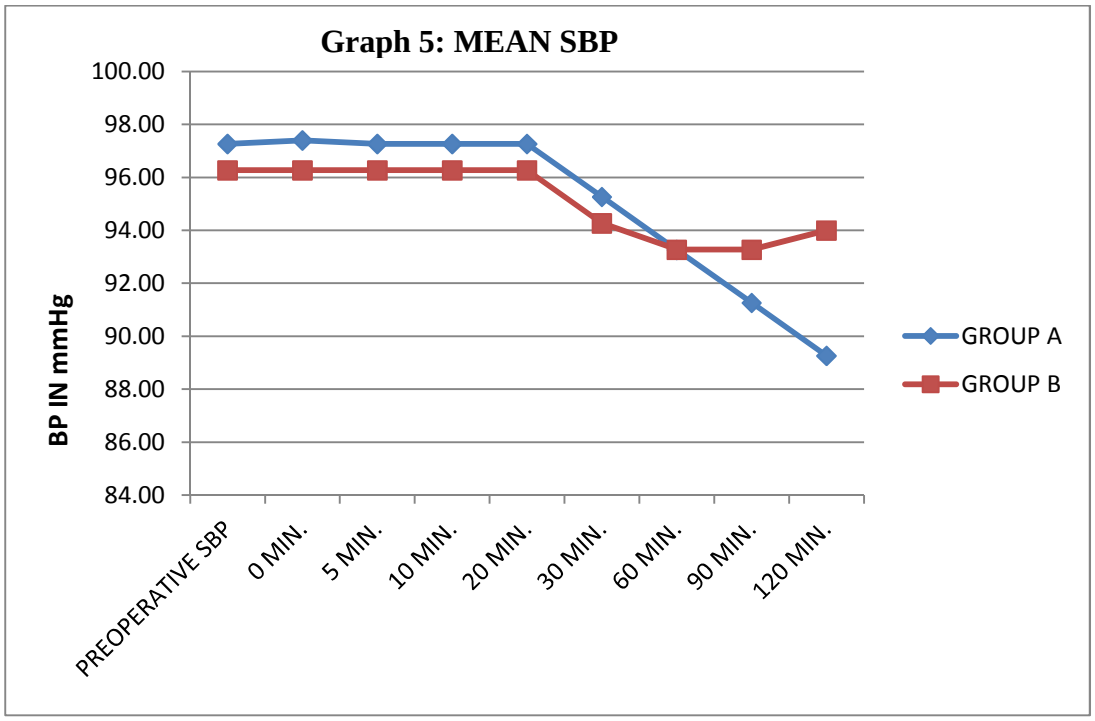


Systolic Blood Pressure

Mean Systolic Blood Pressure at baseline in Group A was 97.27±5.16. There was no significant change in Systolic blood pressure until 30 minutes from the start of the surgery. Then there was a fall in Systolic BP at 30 minutes which when compared was found to be highly significant. Systolic BP at 60 minutes and 90 minutes when compared to pre operative values was also highly significant. However the fall did not warrant any aggressive treatment and was treated with IV fluids. In Group B, mean SBP was 96.27±4.78 and it remained stable until 60 minutes from the start of surgery following which there was a fall till 120 minutes. However this fall in SBP at 90 and 120 minutes when compared to baseline was not significant.

	GROUP A				**GROUP B**			
	MEAN	**S.D.**	**p VALUE**	**INFERENCE**	**MEAN**	**S.D.**	**p VALUE**	**INFERENCE**
PREOPERATIVE SBP	97.27	5.16	0.0804	NS	96.27	4.78	-	-
0 MIN.	97.40	5.12	0.0804	NS	96.27	4.78		
5 MIN.	97.27	5.16	0.0804	NS	96.27	4.78	-	-
10 MIN.	97.27	5.16	0.0804	NS	96.27	4.78	-	-
20 MIN.	97.27	5.16	0.0804	NS	96.27	4.78	-	-
30 MIN.	95.27	5.16	< 0.0001	HS	94.27	4.78	-	-
60 MIN.	93.27	5.16	< 0.0001	HS	92.27	4.78	0.2293	NS
90 MIN.	91.27	5.16	< 0.0001	HS	93.27	4.78	0.2365	NS
120 MIN.	89.27	5.16	< 0.0001	HS	94.00	4.78	0.2241	NS

Table 6 – Systolic Blood Pressure


Graph 5: MEAN SBP
100.00
98.00
96.00
94.00
92.00
90.00
88.00
86.00
84.00
BP IN mmHg
PREOPERATIVE SBP
0 MIN.
5 MIN.
10 MIN.
20 MIN.
30 MIN.
60 MIN.
90 MIN.
120 MIN.
GROUP A
GROUP B

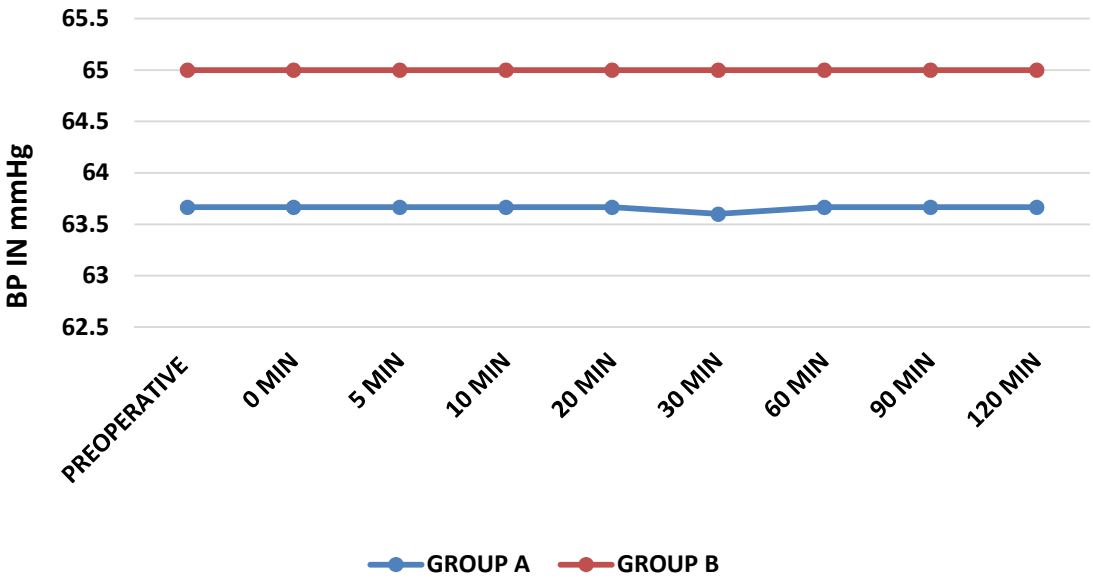
Diastolic Blood Pressure

Mean Diastolic Blood Pressure in Group A was 63.67±4.37 and in Group B was 65.0±5.06. There was no change in DBP as the surgery progressed. When compared, there was no significant difference in mean DBP between the groups.

	GROUP A				GROUP B			
	Mean	S.D	P Value	Inference	Mean	S.D.	P Value	Inference
PREOPERATIVE DBP	63.67	4.37	-	-	65.00	5.06	-	-
DBP AT 0 MIN.	63.67	4.37			65.00	5.06		
DBP AT 5 MIN.	63.67	4.37	-	-	65.00	5.06	-	-
DBP AT 10 MIN.	63.67	4.37	-	-	65.00	5.06	-	-
DBP AT 20 MIN.	63.67	4.37	-	-	65.00	5.06	-	-
DBP AT 30 MIN.	63.60	4.41	0.1628	NS	65.00	5.06	-	-
DBP AT 60 MIN.	63.67	4.37	-	-	65.00	5.06	-	-
DBP AT 90 MIN.	63.67	4.37	-	-	65.00	5.06	-	-
DBP AT 120 MIN.	63.67	4.37	-	-	65.00	5.06	-	-

Table 7 – Diastolic Blood Pressure

Graph 6: MEAN DBP



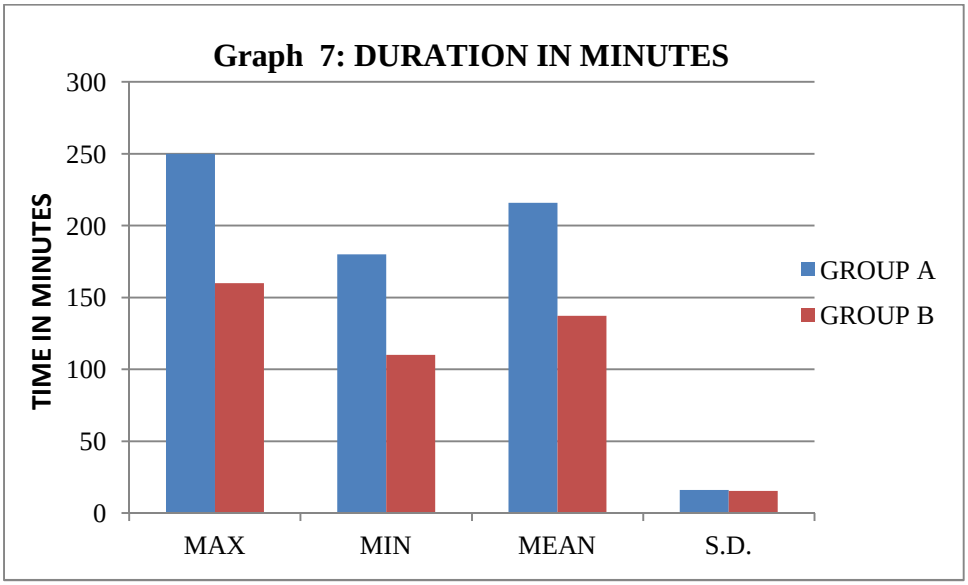
Duration of Motor Block

The maximum duration of motor block in Group A was 250 minutes and the minimum duration was 180 minutes with a mean of 215.83 minutes and a standard deviation of 16.19. In Group B, the minimum duration of motor block was 110 minutes and the maximum duration was 160 minutes with the mean duration of 137 minutes and a standard deviation of 15.52. This yielded a highly significant p value of less than 0.0001.

DURATION OF MOTOR BLOCK IN MINUTES

GROUP A				GROUP B					
MEAN	**S.D.**	**MIN**	**MAX**	**MEAN**	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
215.83	16.19	180	250	137.17	15.52	110	160	< 0.0001	HS

Table 8 - Duration of motor block in minutes



FLACC Score

All the children in Group A had a score of 0 consistently for a period of 6 -8 hours. 24 children had FLACC score of 0 for 10 hours. 13 children had a score of 0 at the end of 12 hours and 11 children had a score of 4. 7 Children had a period of analgesia lasting for 14 to 16 hours. In Group B, all 30 children had a score of 0 immediately at the end of the surgery. 23 children had a score of 0 at 2 hours after the surgery. At 4 hours, 6 children had a score of 2 and 2 children had a score of 3 while 17 children had a score of 4. At the end of 6 hours 8 children had a score of 4.

	FLACC Score											
	No. of Children						No. of Children					
	Group A						Group B					
TIME(hours)	0	1	2	3	4	5	0	1	2	3	4	5
0	30						30					
2	30						23	2			5	
4	30						0		6	2	17	
6	30										8	
8	29				1							
10	24				5							
12	13				11							
14	7				6							
16					7							

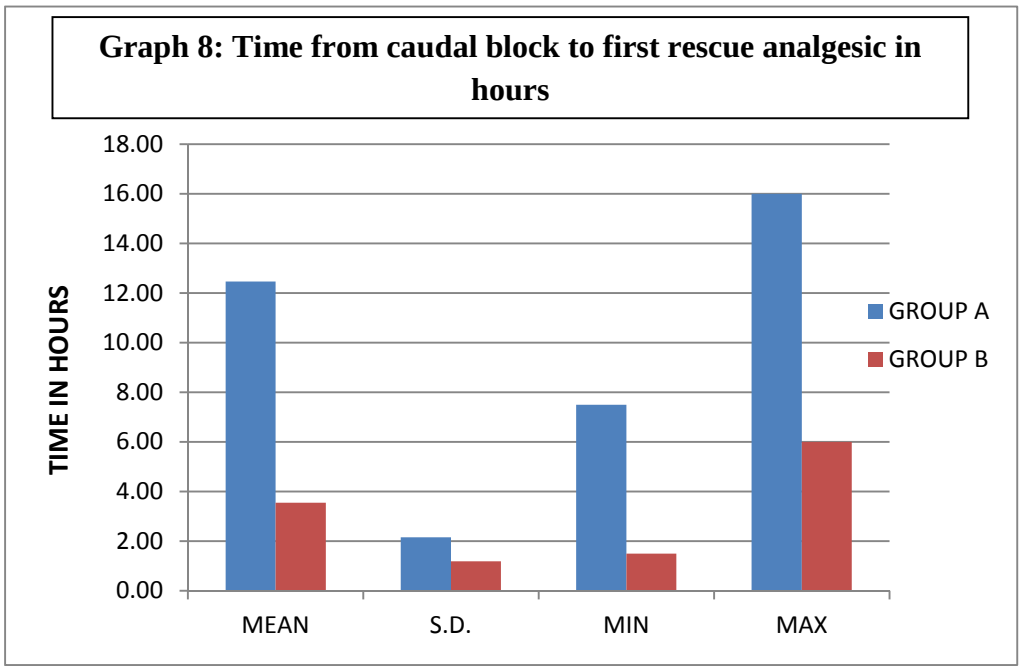
Table 9– Distribution of FLACC Score in the post operative period

Duration of Post Operative analgesia

The duration from the administration of caudal block to the first rescue analgesic was noted. We found that the longest duration of analgesia in Group A was 16 hours and the shortest duration of analgesia was 7.5 hours with a mean duration of analgesia of 12.47 and a standard deviation of 2.16. In Group B, we found the longest duration of analgesia to be 6 hours and the shortest duration of analgesia as 1.5 hours with a mean duration of analgesia of 3.55 hours and a standard deviation of 1.18. The p value was less than 0.0001 making the inference highly significant.

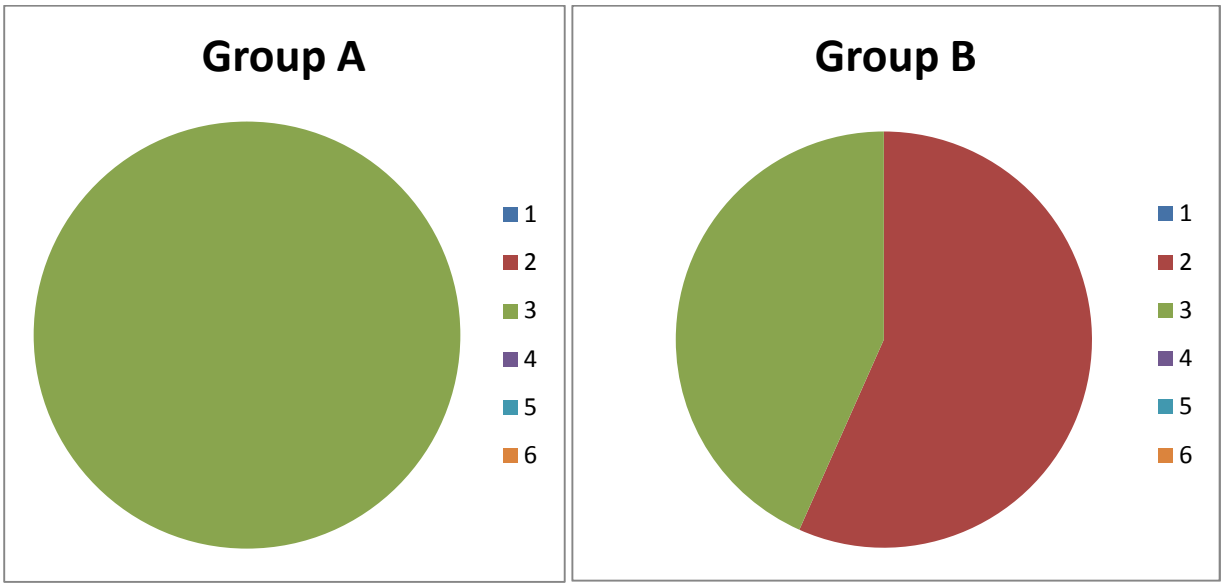
GROUP A				GROUP B					
MEAN	**S.D.**	**MIN**	**MAX**	**MEAN**	**S.D.**	**MIN**	**MAX**	**p VALUE**	**INFERENCE**
12.47	2.16	7.5	16	3.55	1.18	1.5	6	< 0.0001	HS

Table 10 – Time from Caudal Block to first Rescue analgesic in hours



Ramsay Sedation Score

Ramsay Sedation Score was used to assess the level of sedation at 0, 6 and 12 hours after the surgery. A Score of 1 to 6 was assigned. In Group A, at 0 hour i.e immediately at the end of surgery, all 30 children had a score of 3. In Group B, 17 children had score of 2 and 13 children were had a score of 3.



Graph 9: Ramsay Sedation Score at the end of the surgery

Ramsay Sedation Score	Group A (No. of children)	Group B (No. of children)
1	0	0
2	0	17
3	30	13
4	0	0
5	0	0
6	0	0

Table 11 – Ramsay sedation score at the end of surgery

	Group A						Group B					
TIME (hours)	Ramsay Sedation Score						Ramsay Sedation Score					
	1	2	3	4	5	6	1	2	3	4	5	6
0			30					17	13			
6		30					24	6				
12		30					28	2				

Table 12 - Mean Ramsay Sedation Score at 0, 6 hours and 12 hours after surgery.

DISCUSSION

Regional anaesthesia has established itself as the go-to anaesthetic strategy in most cases due to its reliable safety profile. Its advantages over general anaesthesia are well studied and documented. Caudal Epidural anaesthesia is one of the most commonly practised anaesthetic techniques in the paediatric age group and is favoured due to its simplicity, safety and effectiveness.

Dexmedetomidine and clonidine, have been used as adjuvants to local anaesthetics by intrathecal, epidural, caudal, intravenous routes and for peripheral nerve blocks.

Dexmedetomidine is a highly selective α2-adrenoreceptor agonist with α2: α1 binding ratio of 1620:1 compared to 220:1 for clonidine. It has been used intravenously in doses ranging from 0.1 to 10 µg/kg/h, but higher doses have been associated with a significant incidence of bradycardia and hypotension. Aantaa et al.[34], in their study concluded that "The optimal dose of dexmedetomidine for single dose intravenous premedication in minor surgery appears to be in the range of 0.33 to 0.67 µg/kg. Jaakola et al.,[35] demonstrated moderate analgesia with a ceiling effect at a dose of 0.5µg/kg when used intravenously.

The present study titled "Effect of Intranasal Dexmedetomidine on duration of anaesthesia and post operative analgesia in paediatric patients undergoing infraumbilical surgeries under single shot caudal epidural anaesthesia – A one year hospital based Randomised Control Trial" attempted to study the effects of dexmedetomidine on duration of the caudal block and the ensuing post-operative analgesia in paediatric patients. We included 60 ASA I and II patients in our study

and divided them into two groups randomly. One group received intranasal dexmedetomidine 1µg/kg body weight and the other group received Normal saline immediately after receiving Caudal bupivacaine 0.25% 1ml/kg body weight. Time of induction, duration of surgery, intra operative hemodynamics, duration of caudal anaesthesia measured as duration of motor block and time till first rescue analgesic were noted. We found that both duration of anaesthesia and post operative analgesia were significantly prolonged in the dexmedetomidine group. The study also infers that the drug is effective when administered intra nasally and has a wide safety margin in paediatric patients.

All the children included belonged to ASA PS I and the gender distribution across both the groups was comparable. The minimum age in group A was 10 months and maximum age was 40 months. In Group B, the minimum age was 12 months and the maximum was 33 months. The mean age of participants in Group A was 21.23 months and in Group B was 18.80 months. These values are comparable and statistically non significant.

The weight distribution in both the groups was found to be comparable. The minimum weight in Group A was 10 kg and the maximum was 19kg, with the mean weight as 12.93 kg. In Group B, the minimum weight was 10 kg and maximum weight was 17 kg with the mean weight being 12.43. When compared, these values provided a p value of 0.387 which is insignificant.

The participants in the study underwent infra umbilical surgeries like hernia repair, correction of hypospadias, circumcision, ARM repair, Hydrocele repair, Orchidopexy etc. The average duration of surgery was 70 minutes in both the groups.

The duration of motor block which was assessed using Modified Bromage Scale was significantly prolonged in the group receiving Dexmedetomidine (215.83±16.19 minutes) compared to the Group receiving Normal Saline(137±15.52 minutes). The minimum duration of anaesthesia in Group A was 180 minutes and maximum was 250 minutes. In Group B, the minimum period of anaesthesia was 110 minutes and the maximum was 160 minutes. This resulted in a highly significant 'p' value of <0.0001.

The assessment of sensory block was not feasible in children as the procedures were done under general anaesthesia. However we can infer from the intraoperative haemodynamic stability that adequate sensory block was achieved. Lack of motor response and absence of increase in pulse rate and Blood Pressure greater than 20% from baseline on skin incision as well as intra operatively was considered a sign of successful sensory block. Thus, our study showed that intranasal dexmedetomidine prolonged the duration of Caudal epidural anaesthesia. Various theories have been proposed to explain the mechanism by which it does so. Its mechanism of action is related to the activation of the descending medullospinal noradrenergic pathways or to the reduction of spinal sympathetic outflow at presynaptic ganglionic sites. Intravenous administration of Dexmedetomidine has been found to produce analgesic effect by its action at both spinal and supraspinal levels. Analgesic effect primarily results from inhibition of locus coeruleus at the brain stem. Dexmedetomidine infusion also causes increased activation of α2 receptors at spinal cord resulting in inhibition of nociceptive impulse transmission. The effects seem to be mediated through both pre synaptic and post synaptic receptors.

Duration of post operative analgesia was measured as the time between the caudal block and the requirement of first rescue analgesic given at a FLACC score of 4. In Group A, we found that minimum duration of anaesthesia was 7.5 hours and the maximum duration was 16 hours with a mean of 12.47±2.16 hours. In Group B, the minimum duration of analgesia was 1.5 hours and the maximum duration was 6 hours, with a mean of 3.55±1.18 hours. The 'p' value for duration of analgesia was <0.0001, making the inference highly significant.

Dexmedetomidine is known to produce bradycardia, hypotension especially when administered as a bolus dose. In our study however none of the patients showed any significant hypotension or bradycardia.

A study by J-Y.Hong, W. O. Kim, Y. Yoon, Y. Choi, S-H. Kim and H. K. Kil titled "Effects of intravenous dexmedetomidine on low-dose bupivacaine spinal anaesthesia in elderly patients" followed Fifty-one elderly patients undergoing transurethral resection of the prostate and randomized them into two groups receiving either 1.0mg/kg Dexmedetomidine (Dexmedetomidine group, n=26) or normal saline (control group n=25) intravenously prior to spinal anaesthesia with 1.2 ml of bupivacaine, 5 mg/ml. The authors found that administrating intravenous Dexmedetomidine to patients receiving low-dose bupivacaine spinal anaesthesia prolonged the duration of sensory and motor block. Consequently, it delayed the time to first request of analgesia for postoperative pain relief. However, atropine-requiring bradycardia and sedation were more frequent in the patients receiving dexmedetomidine, and the duration of postoperative care unit stay was longer in the dexmedetomidine group than in the control group[(36)].

Our study concurred with their study in terms of post operative analgesia and duration of anaesthesia. We encountered no episodes of bradycardia requiring administration of Glycopyrrolate or atropine and had no patients requiring ICU stay.This advantage can be attributed to the intra nasal administration of the drug rather than the intravenous route used in the above study.

Rapid or bolus administration of intravenous Dexmedetomidine can result in sudden hypertension and bradycardia until the central sympatholytic activity dominates, which results in moderate decreases in heart rate and Blood Pressure, as observed by Mahmoud et al.[(4)], who noticed significant drop in heart rate in patients who received a bolus of IV Dexmedetomidine followed by slow infusion. Our study circumvented this problem faced with intra venous administration. This could be attributed to the slow rise in plasma concentration after an intranasal administration

A study by Katrin Waurick , Cristina Sauerland & Christiane Goeters titled "Dexmedetomidine sedation combined with caudal anesthesia for lower abdominal and extremity surgery in ex-preterm and full-term infants"[(37)] retrospectively analyzed 23 children who underwent lower abdominal or lower extremity surgery with dexmedetomidine sedation and caudal anesthesia from January 2015 to August 2015. Dexmedetomidine was initiated with a total bolus infusion of 0.7–1.1 mcg/kg/hr followed by a continuous infusion of 1 mcg/kg/hr Bupivacaine (2.5 mg/kg) was supplemented with 5–10 mg/kg epinephrine to strengthen and prolong motor block. According to maturity at birth, two groups were defined: ex-preterm and fullterm infants. The study was intended to determine the safety of intravenous dexmedetomidine in infants and the investigators found that the drug could be used without hesitation in that age group. There were no complications encountered. Our

study also showed that Dexmedetomidine can be safely used in paediatric patients without any complication.

Another study by Velayudha Sidda Reddy, Nawaz Ahmed Shaik, Balaji Donthu, Venkata Krishna Reddy Sannala, Venkatsiva Jangam titled "Intravenous dexmedetomidine versus clonidine for prolongation of bupivacaine spinal anesthesia and analgesia: A randomized double-blind study"[38] aimed to compare and evaluate the efficacy of intravenous dexmedetomidine, clonidine and placebo on spinal blockade duration, postoperative analgesia and sedation in patients undergoing surgery under bupivacaine intrathecal block. In this prospective, randomized, double-blind placebo-controlled study, 75 patients of the American Society of Anesthesiologists status I or II, scheduled for orthopedic lower limb surgery under spinal anesthesia, were randomly allocated into three groups of 25 each. Group DE received dexmedetomidine 0.5 µg/kg, group CL received clonidine 1.0 µg/kg and placebo group PL received 10 ml of normal saline intravenously before subarachnoid anesthesia with 15 mg of 0.5% hyperbaric bupivacaine. Onset time and regression times of sensory and motor blockade, the maximum upper level of sensory blockade were recorded. Duration of postoperative analgesia and sedation scores along with side effects were also recorded. They concluded that premedication with intravenous dexmedetomidine is better than intravenous clonidine to provide intraoperative sedation and postoperative analgesia during bupivacaine spinal anaesthesia. They also found that the time for motor regression in the dexmedetomidine group was significantly prolonged when compared to clonidine. This is in direct evidence to the findings of our study which showed that dexmedetomidine significantly prolonged the duration of motor block and post operative analgesia in caudal epidural anaesthesia.

Al-Mustafa MM, Badran IZ, Abu-Ali HM, Al-Barazangi BA, Massad IM, Al-Ghanem SM in the study titled "Intravenous dexmedetomidine prolongs bupivacaine spinal analgesia"[7] demonstrated that a loading dose of 1µg/kg of dexmedetomidine and a following maintenance dose of 0.5µg/kg//h were found to prolong sensory regression (262 min vs. 165 min) and complete motor regression (200 min vs. 138 min) in spinal anaesthesia using 12.5 mg plain bupivacaine, as well as showing good sedation effects and haemodynamic stability. In addition, the intraoperative needs to give ephedrine or atropine were comparable in the two groups. This study concurs with our study in terms of prolonged motor block and haemodynamic stability.

In another study titled "Intravenous dexmedetomidine as an adjunct to subarachnoid block: A simple effective method of better perioperative efficacy" by Rekha Kumari, Anil Kumar, Sushil Kumar, Rakesh Singh[39] at AIIMS Patna India Sixty patients were randomly divided into two groups of thirty each. Group D received dexmedetomidine infusion at 1 mcg/kg over 10 min and then at 0.6 mcg/kg/h for rest of duration during surgery, Group C (control) received a similar volume of normal saline infusion before spinal anaesthesia with 3 ml of bupivacaine 0.5%. Time of onset and regression time for sensory and motor blockade, the maximum upper level of sensory blockade, duration of postoperative analgesia, Ramsay sedation score and hemodynamic parameters were recorded. They found that The duration ofsensorimotor block was significantly longer in D Group (341.7 ± 20.8 min for sensory block and 278.0 ± 11.0 min for motor block) as compared to control group (329.5 ± 22.1 min for sensory block and 250.0 ± 14.8 min for motor block), which was statistically significant ($P < 0.05$). The mean time for two dermatomal regression of sensory blockade was significantly prolonged in dexmedetomidine group(115.5 ± 8.7 min) compared to control group (95.8 ± 11.4) ($P<0.001$).

Intraoperative Ramsay sedation scores were significantly higher in D Group (mean 3.4 ± 0.7, range–2–4) as compared to C Group (mean 2.9 ± 0.3, range – 2–4) ($P < 0.001$). This study is in agreement with the findings of the present study and confirms the role of parenterally administered Dexmedetomidine in prolonging the motor block attained during neuraxial blockade.

The present study was aimed at determining the effect of intranasal dexmedetomidine on the duration of anaesthesia and post operative analgesia in paediatric patients undergoing infraumbilical surgeries under single shot caudal epidural anaesthesia. We have successfully established that dexmedetomidine can safely prolong the duration of motor block and the period of post operative analgesia in children undergoing surgeries under caudal epidural anaesthesia. However, use of intra operative Isoflurane (0.2%) which was required to keep the patient calm produced some amount of sedation which overshadowed the assessment of sedation caused by Dexmedetomidine in the post operative period. A study designed to assess the level of sedation as achieved solely by dexmedetomidine is the need of the hour and it would greatly minimise the use of polypharmacy. Although this may not be practically possible in infants and small children, it can be used in older children. Our study was successful in establishing the advantages of using Dexmedetomidine intranaslly to prolong the duration of anaesthesia and analgesia in Caudal epidural anaesthesia when used in a dose of 1µg/kg body weight. A further study can be conducted using smaller doses of dexmedetomidine to assess whether similar results can be achieved with lesser complications.

CONCLUSION

Our study showed that intranasal administration of Dexmedetomidine significantly increased the duration of caudal epidural anaesthesia in paediatric patients undergoing infra umbilical surgeries under caudal epidural anaesthesia.

This study also showed that intranasal dexmedetomidine significantly prolonged the duration of post operative analgesia. The hemodynamic parameters were found to be stable and satisfactory in both the groups and we did not encounter any untoward complications. Bradycardia seen in the dexmedetomidine group was not significant and did not require intervention.

The children in the post operative period were sedated, calm and were arousable.

We therefore conclude that intranasal dexmedetomidine can be effectively used in paediatric patients to prolong the duration of anaesthesia and post operative analgesia in paediatric patients.

SUMMARY

Caudal Epidural Anaesthesia is an established mode of anaesthesia for paediatric patients undergoing infraumbilical surgeries due to its simplicity and safety.The block can be accomplished by a single-shot injection and the duration can be prolonged using additives. We aimed to study the effect of intranasally administered Dexmedetomidine on duration of anaesthesia and post operative analgesia in paediatric patients undergoing infra umbilical surgeries under single shot caudal epidural anaesthesia.

In our study 60 ASA I and II patients were included and divided into two groups randomly. One group received intranasal dexmedetomidine and the other group received Normal saline immediately after receiving Caudal bupivacaine 0.25% 1ml/kg body weight. Time of induction, intra operative hemodynamics, duration of caudal anaesthesia measured as duration of motor block and time till first rescue analgesic were noted.

We found that the demographic parameters were comparable in both the groups. Hemodynamic parameters pre operatively and intraoperatively were comparable. The duration of motor block was significantly prolonged in the group receiving Dexmedetomidine (Group A)- 215.83±16.19 minutes, compared to the Group receiving Normal Saline (Group B) - 137±15.52 minutes. Duration of post operative analgesia was measured as the time between the caudal block and the requirement of first rescue analgesic given at a FLACC score of 4 or more. In Group A, mean duration of analgesia was 12.47±2.16 hours and in Group B, it was 3.55±1.18 hours. None of the children experienced any significant hypotension, bradycardia or any other side effects underlining its safety in paediatric patients.

We therefore conclude that intra nasal dexmedetomidine can be safely used to prolong the action of caudal epidural anaesthesia as well as for post operative analgesia in paediatric patients undergoing infraumbilical surgeries under Caudal Epidural block.

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ANNEXURE I- CONSENT FORM

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mr/Mrs/Miss. _____ we are requesting you to enrol your child in study titled **"EFFECT OF INTRANASAL DEXMEDETOMIDINE ON DURATION OF ANAESTHESIA AND POST OPERATIVE ANALGESIA IN PAEDIATRIC PATIENTS UNDERGOING INFRAUMBILICAL SURGERIES UNDER SINGLE SHOT CAUDAL EPIDURAL"- A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL.** Conducted by Dr._____ Post Graduate in M.D. Anaesthesiology under the guidance of Dr. _____ M.D. DNB Professor, Department of Anaesthesiology, J.N. Medical College, Belagavi under KLE University, Belagavi.

We request you to enrol your child to participate in our study as your child is eligible for participating in the study. During the study you will be asked some questions regarding your child's present complaint and you are supposed to answer to the best of your knowledge.

Your participation in this research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N.Medical College. If you decide not to participate you are free to withdraw at any time.

Purpose of the study:

The purpose of research is to study the effect of intra nasally administered dexmedetomidine on the duration of anaesthesia and post-operative analgesia in caudal epidural anaesthesia in paediatric patients.

Procedure Involved:

If you agree to enrol your child in our study, we will ask your child's present past and family history. Then your child will be clinically examined in detail and routine investigations like Hb, CBC, BT, CT will be done accordingly. Your child will be allotted into one of the two groups randomly using a computer generated software. One group will receive 1 mcg/kg Dexmedetomidine intranasally and the other group will receive Normal Saline.

Risks:

The risks like sudden tachycardia followed by bradycardia and hypotension maybe seen.

Benefits:

It is found to be safe, easy to administer and is found to provide better sedation.

Voluntary Participation/Withdrawal:

Taking part in the study is voluntary. You may choose not to enrol your child in this study. Your decision will not change present or future health care services offered to you at K.L.E. hospital.

Alternatives:

Even if you decline the participation in the study, you will get the routine line of management.

Privacy and Confidentiality:

The only people to know that your child is a research subject are members of the research team. No information about your child or information provided by you during the research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

Authorization to Publish Results:

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your child's identity. Any information that is obtained in connection with this study and that can be identified with your child's identity remaining confidential.

Financial Incentives for participation:

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

Compensation:

In the event of injury related to the study, treatment will be made available through KLES' Hospital & MRC, Belagavi. There is no compensation or payment for such medical treatment by law.

Questions:

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact Dr._____ Department of Anaesthesiology, KLES Hospital and MRC, Belagavi. Or Dr. _____ M.D. DNB, Professor, Dept. Of Anaesthesiology, KLES Hospital and MRC.

If you have any queries about your child's rights as a study subject, you may call Dr. Ganga Pilli, Professor, Department of Pathology and Chairman, J.N. Medical College Institutional Ethical Committee for Human Subjects Research, Phone number- 9480275601, or extension 4052 at J.N. Medical College, Belagavi.

Consent for participation in research trial. "EFFECT OF INTRANASAL DEXMEDETOMIDINE ON DURATION OF ANAESTHESIA AND POST OPERATIVE ANALGESIA IN PAEDIATRIC PATIENTS UNDERGOING INFRAUMBILICAL SURGERIES UNDER SINGLE SHOT CAUDAL EPIDURAL"- A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL.

I, Mr/Ms/Mrs _____ voluntarily agree for the participation of my child as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left Thumb Print of parent : _____

Date:

Witness Name : _____ Signature:_____

Date:

Investigators Name: _____ Signature:_____

Date:

Place : _____

ANNEXURE II- PROFORMA

"EFFECT OF INTRANASAL DEXMEDETOMIDINE ON DURATION OF ANAESTHESIA AND POST OPERATIVE ANALGESIA IN PAEDIATRIC PATIENTS UNDERGOING INFRAUMBILICAL SURGERIES UNDER SINGLE SHOT CAUDAL EPIDURAL"- A ONE YEAR HOSPITAL BASED RANDOMISED CONTROLLED TRIAL.

Name & Address of the patient:

_____

Age of the Patient: _____ IP. No. _____

Weight of Patient: _____ Sex.

Anaesthesiologist: _____ Surgeon: _____

PREANAESTHETIC EVALUATION:

Chief Complaints:

Past History:

- History of Diabetes Mellitus/ Asthma/Tuberculosis/ Congenital anamolies
- Drug Therapy:
- Previous Anaesthetic procedure/Previous surgeries:
- History of renal disease, hepatic disease and neurological diseases.

Family History:

General Physical Examination:

Weight: Temperature: Pallor: Height

Cyanosis: Pedal Oedema: Clubbing:

Pulse : B.P: RR:

Airway Assessment:

Mouth Opening: Teeth:

Jaw Movements: MP Grading:

SYSTEMIC EXAMINATION:

Cardiovascular System:

Respiratory System:

Per Abdomen:

Central Nervous system:

Spine assessment:

INVESTIGATIONS:

Hb%: CBC: BT: CT:

Any Other:

ASA STATUS: Grade 1 / 2

Diagnosis:

Proposed Surgery:

Pre operative baseline values:

HR:

BP:

Monitors attached:

Pulse oximetry:

NIBP:

ECG:

Observations:

Readings will be recorded in the following manner:

Group: _____.

Time	Heart rate	SBP	DBP

FLACC SCORE

Time	**Score**
30 minutes	
1 hour	
2 hours	
4 hours	
6 hours	

Bromage Scale

Time	**Bromage Scale**

Time of Induction : **Time of Caudal Block:**

Time of administration of test drug: **Time of Rescue Analgesic:**

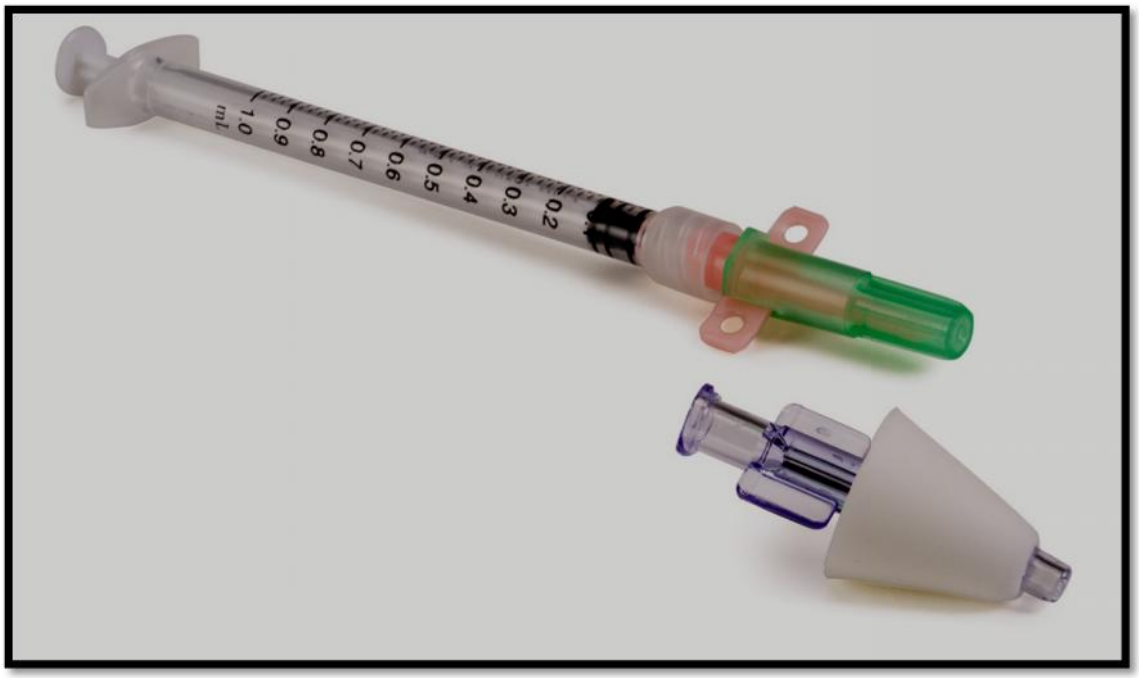
Side Effects/ complications –

Ramsay Sedation Score

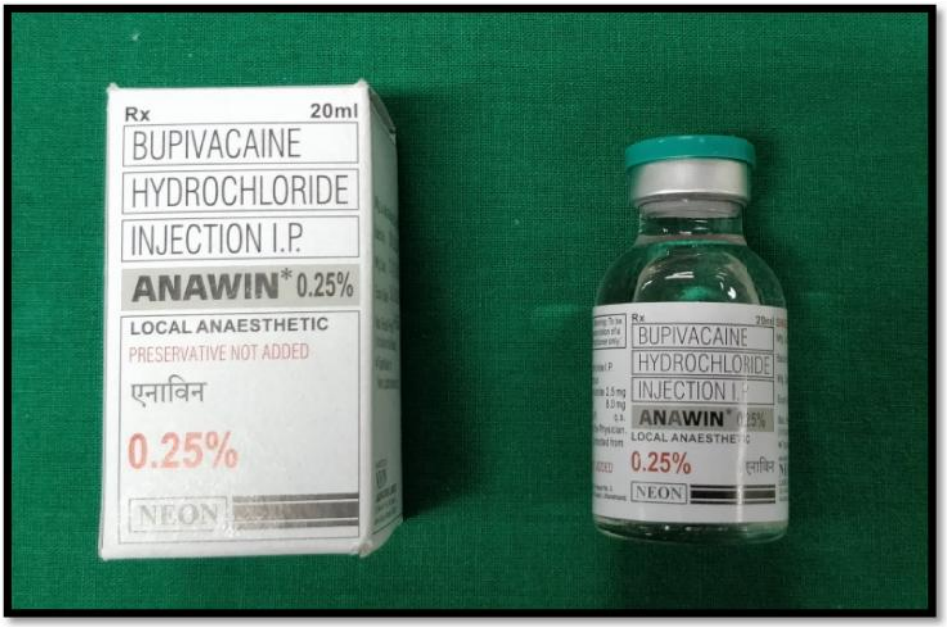
Signature of staff in charge:

ANNEXURE III – PHOTOGRAPHS

Photograph :1. Dexmedetomidine ampoule



Photograph :2 Tuberculin syringe with atomiser



Photograph 3 – Bupivacaine 0.25%

ANNEXURE IV – ETHICAL COMMITTEE CLEARANCE CERTIFICATE

K.L.E.UNIVERSITY'S
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
(Accredited 'A' Grade by NAAC)

Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu

Phone: (+ 91-(0)831 Office : 2471350
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 43 **Date: 17/10/2016**

To,

Dr.
PG student in Anaesthesiology,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"EFFECT OF INTRANASAL DEXMEDETOMIDINE ON DURATION OF ANAESTHESIA AND POST OPERATIVE ANALGESIA IN PAEDIATRIC PATIENTS UNDERGOING INFRAUMILICAL SURGERIES UNDER SINGLE SHOT CAUDAL EPIDURAL ANAESTHESIA – A ONE YEAR HOSPITAL BASED DOUBLE BLIND RANDOMIZED CONTROL TRIAL ",** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Ganga Pilli)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ANNEXURE V – KEY TO MASTER CHART

HR	Heart Rate
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
BPM	Beats Per Minutes

Sl No	IP Number	Group	ASA	Age in months	Sex	Weight IN KG	Diagnosis	Preoperative Vitals				Vitals At 0 min.				Vitals at 5min.				Vitals At 10 Min.				Vitals at 20 min				Vitals at 30 min				Vitals at 60 Min.				Vitals at 90 Min.				Vitals at 120 Min.				FLACC Score at the end of surgery	Mod. Bromage at the end of surgery	Duration of motor block in minutes	Time from induction to rescue analgesic in hours	RSS at the end of surgery
								HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2					
1	761209	A	1	14	F	11	ARM	122	90	60	100	129	92	60	100	122	90	60	100	119	90	60	100	116	90	60	100	114	88	60	100	112	86	60	100	110	84	60	100	108	82	60	100	0	3	210	13.5	3
2	783292	A	1	16	M	11	HYPOSPADIAS	127	100	62	100	130	102	62	100	118	100	62	100	115	100	62	100	110	100	62	100	103	98	60	100	102	96	62	100	102	94	62	100	100	92	62	100	0	3	220	10	3
3	780034	B	1	28	M	15	HYPOSPADIAS	118	96	68	100	120	96	68	100	118	96	68	100	118	96	68	100	115	96	68	100	113	94	68	100	111	92	68	100	109	90	68	100	107	88	68	100	0	3	160	3	2
4	753072	A	1	34	M	14	INGUINAL HERNIA	116	100	70	100	110	100	70	100	100	100	70	100	96	100	70	100	105	100	70	100	103	98	70	100	101	96	70	100	99	94	70	100	97	92	70	100	0	3	180	12	3
5	812867	A	1	14	F	10	VESICULOSTOMY CLOSURE	134	90	64	100	116	90	64	100	106	90	64	100	103	90	64	100	111	90	64	100	109	88	64	100	107	86	64	100	105	84	64	100	103	82	64	100	0	3	200	14	3
6	827536	B	1	26	M	16	HYPOSPADIAS	125	90	60	100	110	90	60	100	108	90	60	100	108	90	60	100	105	90	60	100	103	88	60	100	101	86	60	100	99	84	60	100	97	82	60	100	0	3	150	5.5	3
7	827812	B	1	14	F	12	ARM	126	98	62	100	130	98	62	100	128	98	62	100	128	98	62	100	125	98	62	100	123	96	62	100	121	94	62	100	119	92	62	100	117	90	62	100	0	3	155	4	3
8	827763	B	1	21	M	11	HYDROCELE	122	100	60	100	116	100	60	100	118	100	60	100	118	100	60	100	111	100	60	100	109	98	60	100	107	96	60	100	105	94	60	100	103	92	60	100	0	3	160	5	2
9	828709	A	1	40	F	19	COLOSTOMY CLOSURE	102	90	70	100	118	90	70	100	107	90	70	100	104	90	70	100	113	90	70	100	111	88	70	100	109	86	70	100	107	84	70	100	105	82	70	100	0	3	200	15	3
10	828617	B	1	18	M	10	ARM	122	100	60	100	110	100	60	100	108	100	60	100	109	100	60	100	105	100	60	100	103	98	60	100	101	96	60	100	99	94	60	100	97	92	60	100	0	3	140	3	2
11	826819	A	1	10	M	11	POST URETHRAL VALVE	127	96	62	100	110	96	62	100	108	96	62	100	106	96	62	100	105	96	62	100	103	94	62	100	101	92	62	100	99	90	62	100	97	88	62	100	0	3	240	12.5	3
12	820176	A	1	31	M	15	HYDROCELE	118	100	68	100	122	100	68	100	118	100	68	100	114	100	68	100	117	100	68	100	115	98	68	100	113	96	68	100	111	94	68	100	109	92	68	100	0	3	220	16	3
13	792378	A	1	22	M	12	UNDESCENDED TESTIS	116	90	70	100	106	90	70	100	101	90	70	100	96	90	70	100	101	90	70	100	99	88	70	100	97	86	70	100	95	84	70	100	93	82	70	100	0	3	200	13.5	4
14	797206	B	1	17	M	11	INGUINAL HERNIA	134	90	64	100	108	90	64	100	105	90	64	100	105	90	64	100	103	90	64	100	101	88	64	100	99	86	64	100	97	84	64	100	95	82	64	100	0	3	130	5	2
15	828132	B	1	15	F	12	COLOSTOMY CLOSURE	125	98	60	100	100	98	60	100	99	98	60	100	98	98	60	100	95	98	60	100	93	96	60	100	91	94	60	100	89	92	60	100	87	90	60	100	0	3	130	2	2
16	817649	B	1	16	M	10	INGUINAL HERNIA	126	100	62	100	108	100	62	100	109	100	62	100	108	100	62	100	103	100	62	100	101	98	62	100	99	96	62	100	97	94	62	100	95	92	62	100	0	3	110	4	2
17	759308	B	1	27	F	17	ARM	122	96	60	100	104	96	60	100	102	96	60	100	100	96	60	100	99	96	60	100	97	94	60	100	95	92	60	100	93	90	60	100	91	88	60	100	0	3	140	3	2
18	824597	A	1	35	M	18	HYDROCELE	102	102	70	100	110	102	70	100	102	102	70	100	98	102	70	100	105	102	70	100	103	100	70	100	101	98	70	100	99	96	70	100	97	94	70	100	0	3	190	7.5	3
19	768367	B	1	12	F	11	ARM	119	110	76	100	100	110	76	100	98	110	76	100	99	110	76	100	95	110	76	100	93	108	76	100	91	106	76	100	89	104	76	100	87	102	76	100	0	3	140	3	2
20	793720	A	1	13	F	11	ARM	142	94	56	100	110	94	56	100	106	94	56	100	102	94	56	100	105	94	56	100	103	92	56	100	101	90	56	100	99	88	56	100	97	86	56	100	0	3	210	10	3
21	822983	A	1	24	M	15	HYDROCELE	134	90	68	100	143	90	68	100	134	90	68	100	129	90	68	100	138	90	68	100	136	88	68	100	134	86	68	100	132	84	68	100	130	82	68	100	0	3	220	12	3
22	801738	A	1	21	M	13	UNDESCENDED TESTIS	125	100	64	100	108	100	64	100	101	100	64	100	97	100	64	100	103	100	64	100	101	98	64	100	99	96	64	100	97	94	64	100	95	92	64	100	0	3	210	15	3
23	783002	B	1	16	F	14	RECTAL POLYP	126	96	70	100	138	96	70	100	136	96	70	100	133	96	70	100	133	96	70	100	131	94	70	100	129	92	70	100	127	90	70	100	125	88	70	100	0	3	160	5	3
24	773928	B	1	19	M	11	HYPOSPADIAS	122	100	60	100	132	100	60	100	126	100	60	100	123	100	60	100	127	100	60	100	125	98	60	100	123	96	60	100	121	94	60	100	119	92	60	100	0	3	120	1.5	2
25	783990	A	1	23	M	12	POST URETHRAL VALVE	102	90	62	100	108	90	62	100	102	90	62	100	99	90	62	100	103	90	62	100	101	88	62	100	99	86	62	100	97	84	62	100	95	82	62	100	0	3	250	10	3
26	828606	B	1	14	F	11	ARM	119	90	60	100	138	90	60	100	128	90	60	100	125	90	60	100	133	90	60	100	131	88	60	100	129	86	60	100	127	84	60	100	125	82	60	100	0	3	130	4	2
27	765839	B	1	15	M	12	INGUINAL HERNIA	142	98	70	100	100	98	70	100	100	98	70	100	97	98	70	100	95	98	70	100	93	96	70	100	91	94	70	100	89	92	70	100	87	90	70	100	0	3	120	6	3
28	750289	A	1	21	F	12	RECTAL POLYP	112	100	60	100	124	100	60	100	120	100	60	100	117	100	60	100	119	100	60	100	117	98	60	100	115	96	60	100	113	94	60	100	111	92	60	100	0	3	200	12	3
29	773482	A	1	27	F	13	COLOSTOMY CLOSURE	133	110	62	100	120	110	62	100	117	110	62	100	114	110	62	100	115	110	62	100	113	108	62	100	111	106	62	100	109	104	62	100	107	102	62	100	0	3	230	15	3
30	754937	B	1	31	M	16	POST URETHRAL VALVE	124	94	68	100	108	94	68	100	107	94	68	100	104	94	68	100	103	94	68	100	101	92	68	100	99	90	68	100	97	88	68	100	95	86	68	100	0	3	160	3	2

Sl No	IP Number	Group	ASA	Age in months	Sex	Weight IN KG	Diagnosis	Preoperative Vitals				Vitals At 0 min.				Vitals at 5min.				Vitals At 10 Min.				Vitals at 20 min				Vitals at 30 min				Vitals at 60 Min.				Vitals at 90 Min.				Vitals at 120 Min.				FLACC Score at the end of surgery	Mod. Bromage at the end of surgery	Duration of motor block in minutes	Time from induction to rescue analgesic in hours	RSS at the end of surgery
								HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR. (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2	HR (BPM)	SBP	DBP	SpO2					
31	810082	B	1	33	M	17	INGUINAL HERNIA	119	90	70	100	120	90	70	100	118	90	70	100	115	90	70	100	115	90	70	100	113	88	70	100	111	86	70	100	109	84	70	100	107	82	70	100	0	3	120	3	2
32	820342	B	1	25	F	14	ARM	132	100	64	100	120	100	64	100	121	100	64	100	118	100	64	100	115	100	64	100	113	98	64	100	111	96	64	100	109	94	64	100	107	92	64	100	0	3	140	2	2
33	830245	A	1	19	M	13	POST URETHRAL VALVE	121	96	60	100	120	96	60	100	112	96	60	100	109	96	60	100	115	96	60	100	113	94	60	100	111	92	60	100	109	90	60	100	107	88	60	100	0	3	225	11.5	3
34	830122	A	1	12	F	11	ARM	130	100	62	100	124	100	62	100	120	100	62	100	117	100	62	100	119	100	62	100	117	98	62	100	115	96	62	100	113	94	62	100	111	92	62	100	0	3	210	12	3
35	830101	B	1	12	F	11	ARM	121	90	60	100	114	90	60	100	110	90	60	100	107	90	60	100	109	90	60	100	107	88	60	100	105	86	60	100	103	84	60	100	101	82	60	100	0	3	140	4	3
36	763920	A	1	22	M	14	HYDROCELE	100	90	70	100	104	90	70	100	100	90	70	100	97	90	70	100	99	90	70	100	97	88	70	100	95	86	70	100	93	84	70	100	91	82	70	100	0	3	210	9	3
37	829378	B	1	14	F	11	ARM	109	98	68	100	108	98	68	100	106	98	68	100	103	98	68	100	103	98	68	100	101	96	68	100	99	94	68	100	97	92	68	100	95	90	68	100	0	3	130	3	3
38	798231	A	1	15	M	11	HYDROCELE	114	100	70	100	104	100	70	100	102	100	70	100	99	100	70	100	99	100	70	100	97	98	70	100	95	96	70	100	93	94	70	100	91	92	70	100	0	3	210	9.5	3
39	770384	B	1	17	F	13	ARM	117	96	64	100	110	96	64	100	110	96	64	100	107	96	64	100	105	96	64	100	103	94	64	100	101	92	64	100	99	90	64	100	97	88	64	100	0	3	140	2	2
40	774879	B	1	16	M	11	INGUINAL HERNIA	142	102	60	100	100	102	60	100	99	102	60	100	96	102	60	100	95	102	60	100	93	100	60	100	91	98	60	100	89	96	60	100	87	94	60	100	0	3	120	3	3
41	816695	A	1	15	F	12	ARM	102	90	62	100	110	90	62	100	102	90	62	100	99	90	62	100	105	90	62	100	103	88	62	100	101	86	62	100	99	84	62	100	97	82	62	100	0	3	220	14	3
42	817240	A	1	18	F	15	ARM	111	98	60	100	143	98	60	100	132	98	60	100	129	98	60	100	138	98	60	100	136	96	60	100	134	94	60	100	132	92	60	100	130	90	60	100	0	3	230	12	3
43	830132	B	1	26	M	16	HYDROCELE	134	90	70	100	108	90	70	100	104	90	70	100	101	90	70	100	103	90	70	100	101	88	70	100	99	86	70	100	97	84	70	100	95	82	70	100	0	3	140	4	3
44	801435	B	1	20	F	14	COLOSTOMY CLOSURE	127	98	76	100	138	98	76	100	132	98	76	100	129	98	76	100	133	98	76	100	131	96	76	100	129	94	76	100	127	92	76	100	125	90	76	100	0	3	130	3.5	2
45	816034	A	1	18	M	11	POST URETHRAL VALVE	118	100	56	100	132	100	56	100	128	100	56	100	125	100	56	100	127	100	56	100	125	98	56	100	123	96	56	100	121	94	56	100	119	92	56	100	0	3	200	11	3
46	742743	B	1	18	F	12	ARM	116	96	68	100	108	96	68	100	110	96	68	100	107	96	68	100	103	96	68	100	101	94	68	100	99	92	68	100	97	90	68	100	95	88	68	100	0	3	120	4	2
47	794066	A	1	12	M	11	HYDROCELE	104	102	64	100	138	102	64	100	130	102	64	100	127	102	64	100	133	102	64	100	131	100	64	100	129	98	64	100	127	96	64	100	125	94	64	100	0	3	230	16	4
48	768042	B	1	12	M	11	UNDESCENDED TESTIS	126	90	60	100	100	90	60	100	100	90	60	100	97	90	60	100	95	90	60	100	93	88	60	100	91	86	60	100	89	84	60	100	87	82	60	100	0	3	110	2	2
49	785031	A	1	24	M	14	HYDROCELE	121	98	62	100	124	98	62	100	120	98	62	100	117	98	62	100	119	98	62	100	117	96	62	100	115	94	62	100	113	92	62	100	111	90	62	100	0	3	210	12	3
50	829389	A	1	38	F	15	RECTAL POLYP	129	100	60	100	120	100	60	100	116	100	60	100	113	100	60	100	115	100	60	100	113	98	60	100	111	96	60	100	109	94	60	100	107	92	60	100	0	3	240	13	3
51	828606	B	1	12	F	11	INGUINAL HERNIA	110	96	70	100	108	96	70	100	107	96	70	100	104	96	70	100	103	96	70	100	101	94	70	100	99	92	70	100	97	90	70	100	95	88	70	100	0	3	160	5	2
52	829319	A	1	13	M	11	UNDESCENDED TESTIS	132	102	60	100	120	102	60	100	118	102	60	100	115	102	60	100	115	102	60	100	113	100	60	100	111	98	60	100	109	96	60	100	107	94	60	100	0	3	240	15	3
53	824597	A	1	39	M	17	INGUINAL HERNIA	99	102	62	100	120	102	62	100	120	102	62	100	117	102	62	100	115	102	62	100	113	100	62	100	111	98	62	100	109	96	62	100	107	94	62	100	0	3	230	13	3
54	739727	B	1	29	M	11	POST URETHRAL VALVE	125	90	68	100	120	90	68	100	117	90	68	100	114	90	68	100	115	90	68	100	113	88	68	100	111	86	68	100	109	84	68	100	107	82	68	100	0	3	150	3	2
55	738867	A	1	23	F	12	INGUINAL HERNIA	106	98	70	100	124	98	70	100	120	98	70	100	117	98	70	100	119	98	70	100	117	96	70	100	115	94	70	100	113	92	70	100	111	90	70	100	0	3	220	15	3
56	817382	A	1	12	M	12	HYDROCELE	142	100	64	100	114	100	64	100	112	100	64	100	109	100	64	100	109	100	64	100	107	98	64	100	105	96	64	100	103	94	64	100	101	92	64	100	0	3	220	12	3
57	793620	B	1	12	F	10	COLOSTOMY CLOSURE	129	96	60	100	104	96	60	100	104	96	60	100	101	96	60	100	99	96	60	100	97	94	60	100	95	92	60	100	93	90	60	100	91	88	60	100	0	3	150	4	3
58	774387	B	1	14	M	11	RECTAL POLYP	138	102	62	100	124	102	62	100	120	102	62	100	117	102	62	100	119	102	62	100	117	100	62	100	115	98	62	100	113	96	62	100	111	94	62	100	0	3	140	2	2
59	826493	A	1	12	M	12	INGUINAL HERNIA	115	100	60	100	100	100	60	100	97	100	60	100	94	100	60	100	95	100	60	100	93	98	60	100	91	96	60	100	89	94	60	100	87	92	60	100	0	3	200	11	3
60	810628	B	1	15	F	11	COLOSTOMY CLOSURE	109	98	70	100	120	98	70	100	120	98	70	100	117	98	70	100	115	98	70	100	113	96	70	100	111	94	70	100	109	92	70	100	107	90	70	100	0	3	120	5	3