"COMPARISON OF TWO DIFFERENT DOSES OF DEXMEDETOMIDINE WITH BUPIVACAINE IN PAEDIATRIC CAUDAL ANAESTHESIA FOR INFRAUMBILICAL SURGERIES: A RANDOMISED DOUBLE BLINDED CLINICAL STUDY"

By

DR. SINDHURA N. M.B.B.S.

Dissertation

Submitted to the

Rajiv Gandhi University of Health Sciences, Karnataka, Bengaluru

In partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE

IN

ANESTHESIOLOGY

Under the guidance of

DR. VINOD HOSALLI M.D

Associate Professor

DEPARTMENT OF ANESTHESIOLOGY

B.V.V.SANGHA'S S.NIJALINGAPPA MEDICAL COLLEGE AND HANAGAL SRI KUMARESHWAR HOSPITAL AND RESEARCH CENTRE BAGALKOT (KARNATAKA)

2015

RAJIV GANDHI UNIVERSITY OF HEALTH SCIENCES,

KARNATAKA

Declaration by the Candidate

I hereby declare that this dissertation/thesis entitled **"COMPARISON OF TWO DIFFERENT DOSES OF DEXMEDETOMIDINE WITH BUPIVACAINE IN PAEDIATRIC CAUDAL ANAESTHESIA FOR INFRAUMBILICAL SURGERIES: A RANDOMISED DOUBLE BLINDED CLINICAL STUDY"** is a bonafide and genuine research work carried out by me under the guidance of **DR. VINOD HOSALLI. M.D. ASSOCIATE PROFESSOR, Department Of Anaesthesiology, B.V.V.Sangha's S.Nijalingappa Medical College And Hanagal Sri Kumareshwar Hospital And Research Centre, Bagalkot.**

Date: 20/11/2014

Place: BAGALKOT

Signature of the Candidate

DR.SINDHURA N M.B.B.S
Post graduate student,
Department of Anesthesiology,
S. Nijalingappa Medical College.
Bagalkot - 587101

RAJIV GANDHI UNIVERSITY OF HEALTH SCIENCES,

KARNATAKA

Certificate by the Guide

This is to certify that the dissertation entitled **"COMPARISON OF TWO DIFFERENT DOSES OF DEXMEDETOMIDINE WITH BUPIVACAINE IN PAEDIATRIC CAUDAL ANAESTHESIA FOR INFRAUMBILICAL SURGERIES: A RANDOMISED DOUBLE BLINDED CLINICAL STUDY"** is a bonafide research work done by **DR. SINDHURA N** in partial fulfillment of the requirement for the degree of **MD (ANAESTHESIOLOGY).**

Date: 20/11/2014

Place: BAGALKOT

Signature of the Guide

DR.VINOD HOSALLI. M.D
Associate Professor,
Department of Anesthesiology,
S. Nijalingappa Medical College,
Bagalkot – 587101.

RAJIV GANDHI UNIVERSITY OF HEALTH SCIENCES,

KARNATAKA

Endorsement by The HOD,Principal/Head Of The Institution

This is to certify that the dissertation entitled **"COMPARISON OF TWO DIFFERENT DOSES OF DEXMEDETOMIDINE WITH BUPIVACAINE IN PAEDIATRIC CAUDAL ANAESTHESIA FOR INFRAUMBILICAL SURGERIES: A RANDOMISED DOUBLE BLINDED CLINICAL STUDY"** is a bonafide research work done by **DR. SINDHURA N** under the guidance of **DR. VINOD HOSALLI .MD.** Associate Professor, Department of Anaesthesiology, S. Nijalingappa Medical College, Bagalkot.

Seal & Signature of the HOD

DR. PRAKASHAPPA D. S.
Prof. & HOD of Anesthesia,
S.N.Medical College &
H.S.K. Hospital & RC.
BAGALKOT.

Date: 20/11/2014

Place: BAGALKOT

Seal & Signature of the Principal

DR. ASHOK. S. MALLAPUR
Principal.
S. Nijalingappa Medical College &
H.S.K. Hospital & Research Centre
Navanagar, BAGALKOT

Date: 20/11/2014

Place: BAGALKOT

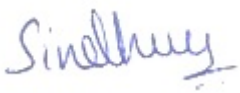
RAJIV GANDHI UNIVERSITY OF HEALTH SCIENCES,

KARNATAKA

Copyright

Declaration by the Candidate

I hereby declare that the Rajiv Gandhi University of Health Sciences, Karnataka shall have the rights to preserve, use and disseminate this dissertation / thesis in print or electronic format for academic / research purpose.



Date: 20/11/2014

Place: BAGALKOT

Signature of the Candidate

DR. SINDHURA N

ACKNOWLEDGEMENT

I realize that dissertation being a work of co-operation and assistance, it would be far from complete without due acknowledgement of the help gratefully received.

It is my distinct honor and privilege to have under the able supervision of my teacher and guide Dr. Vinod Hosalli, M.D, Associate Professor , Department of Anesthesiology, S. Nijalingappa Medical College and Hanagal Sri Kumareshwar Hospital and Research Centre, Bagalkot for his valuable guidance and constant encouragement in task of completion of this dissertation.

My sincere thanks to Dr.Prakashappa D S, Professor and Head of Department of Anaesthesiology, S.Nijalingappa Medical College, Bagalkot for his valuable guidance and help in preparing this dissertation.

I thank Dr. S.Y.Hulakund, Dr. Ramesh Koppal, Dr. D.A.Hiremath Professor, Department of Anaesthesiology for their help and concern.

I thank Dr.Chhaya Joshi Associate Professor, Department of Anaesthesiology for her help and concern.

I take this opportunity to thank Dr. Uday Ambi, Dr. Adarsh E S, Dr.Anilkumar G, Dr. Shilpa Masur, Dr. Sangamesh N, Dr Archana E, Dr. Vishwas U Assitant professors for their help and guidance during various stages of study.

I am thankful to Dr.Manjula R, Assistant Professor, Department of Community Medicine, for their constant support and guidance in preparing this dissertation.

I take this opportunity to thank Dr. Ramesh Hatti M.S., Mch., and Dr.Vijay Mahantesh M.S., Mch., paediatric surgeons for cooperating for the study.

I express my sincere thanks to my friends Dr. Niharika, Dr. Arati and post graduate colleagues Dr. Rudresh IP, Dr. Bhanupriya, Dr. Arjun, Dr. Preetham, Dr. Suvir, Dr.Neeraj and especially Dr Riyas who has helped me in preparing this dissertation.

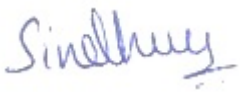
I would also like to thank all OT technicians and all other theatre staff for their help and assistance.

I would like to express my gratitude to my Father Malakondaiah, my mother Amrutha and sisters Dr. Madhu, Dr Sravanthi for their constant support in completion of this thesis.

I express my special thanks to all my patients and their parents and without whom this study would not have been possible.

I would like to acknowledge the tireless work of Mr. Arun & Mr. Anand of Shri Vighneshwara Associates Computers of J.N.M.C for excellent data processing and completion of this dissertation.

I also thank the library staff for their kind assistance and help in providing me the required reference materials and books for my study.



Date: 20/11/2014 **Signature of the Candidate**

Place: BAGALKOT **DR. Sindhura N**

LIST OF ABBREVIATIONS

ASA	-	American Society of Anaesthesiologists
cAMP	-	Cyclic Adenosine Mono Phosphate
CNS	-	Central Nervous System
CSF	-	Cerebro Spinal Fluid
CVS	-	Cardio Vascular System
G	-	Gauge
GABA	-	Gamma Amino Butyric Acid
hrs	-	Hours
HR	-	Heart Rate
Iv	-	Intravenous
MAP	-	Mean Arterial Pressure
min	-	minute
NS	-	Not Significant
PCA	-	Patient Controlled Analgesia
RS	-	Respiratory System
S	-	Significant
SL No	-	Serial Number

SD	-	Standard Deviation
Temp	-	Temperature
Yr	-	Year
µgm	-	Micro gram
Kg	-	kilogram
%	-	Percentage
Ml	-	Millilitre
A	-	alpha
B	-	Beta
mm of Hg	-	Millimetre of Mercury

ABSTRACT

Background: Caudal epidural analgesia is one of the most commonly performed regional techniques in paediatric anaesthesia for intra and post-operative analgesia. However, the duration of analgesia is limited by the duration of action of local anaesthetics. Various adjuvants like α-2 agonists, ketamine, opioids etc have been used to prolong the caudal analgesia. α-2 agonists such as clonidine and dexmedetomidine have been used . With favorable results dexmedetomidine, has been popularly used. Both drugs have been compared in various routes with same doses. Here we intend to study two different doses, 1µg/kg which has been proved to increase analgesia duration in comparison with 0.5µg/kg dexmedetomidine as an adjuvant.

Methods: 60 children (aged 6months- 6years) posted for infraumbilical surgeries were randomly assigned in two groups. Group A (30) received caudal block 1ml/kg of 0.25% bupivacaine with 1 µ/kg dexmedetomidine and Group B (30) received caudal block 1ml/kg of 0.25% bupivacaine with 0.5µ/ kg dexmedetomidine. After giving premedication with 0.8 mg / kg of oral midazolam 30 minutes prior to surgery, patients were induced with propofol 2mg/kg and infusion 100µ/kg/hr started. Caudal block was performed and appropriate dosage of drug given depending on group. Patients were maintained on spontaneous respiration. Patient's heart rate, oxygen saturation and blood pressure were recorded every 5 minutes intraoperatively and postoperatively every 15 minutes for next 2 hours and then every 30 minutes until the requirement of first rescue analgesia.

Results:

The groups were comparable with respect to in age, sex and weight. The hemodynamic parameters like heart rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), were also similar between the two groups before and after administering caudal block.

Duration of 1st rescue analgesia of Group A was 1111.33 ± 74.9 minutes in compared Group B was 896.5 ± 40.8 minutes which was statistically significant (P value- 0.001). Incidence of postoperative vomiting was higher in group A in compared to group B which was statistically significant. Other side effects were comparable in both the groups.

Conclusion: Caudal dexmedetomidine (1µg/kg) with 0.25% bupivacaine for pediatric infraumbilical surgeries achieved significant post-operative pain relief compared to caudal dexmedetomidine (0.5µg/kg) with 0.25% bupivacaine. However, 0.5µg/kg dexmedetomidine had lesser side effects in comparison to 1µg/kg dexmedetomidine.

Key words: *caudal block , bupivacaine , dexmedetomidine , children.*

TABLE OF CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

INTRODUCTION

Pain is perhaps the most feared symptom of disease, which a man is always trying to alleviate and conquer since ages. It is defined by the international association for study of pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage''.[1]

Popular dogma had suggested that the human child does not feel pain, and that it is dangerous to give him powerful analgesia because of the risk of addiction.[2] Under treatment of post-operative pain even in the children and newborns may trigger biochemical and physiologic stress response and cause impairments in pulmonary, cardiovascular, neuro endocrinal, gastrointestinal, immunological, and metabolic functions.[3]

The society of Pediatric Anesthesia, at its 15th annual meeting at New Orleans, Louisiana (2001) clearly defined the alleviation of pain as a "basic human right", irrespective of age, medical condition, treatment, primary service response for the patient care or medical institution.[4]

Langlade et al suggested that the postoperative pain treatment must be included in the anaesthetic planning even before induction of anesthesia, adopting the idea of 'managing pain before it occurs'. Now, postoperative pain management is an integral part of practice of paediatric anaesthesia in all major hospitals.[5]

Several methods have been employed in pediatric pain relief with different degree of success.

Caudal epidural block is one of the most common regional techniques in paediatric anesthesia.[6]

Caudal block is safe and reliable technique, easy to perform and has been found to be very effective in children, especially in infra-umbilical surgeries when combined with general anaesthesia . It allows rapid recovery from anaesthesia with good post-operative analgesia.[5]

The main disadvantage of caudal analgesia is duration of action after a single injection which is limited by duration of action of local anesthetics. Placement of a catheter has an inherent risk of infection. Prolongation of caudal analgesia using a single-shot technique has been achieved by the addition of various adjuvants such as opioids, ketamine, neostigmine, midazolam and α2 agonists. Many of these adjuvants have side effects like respiratory depression, vomiting, pruritus etc.[7,8]

Both Clonidine and dexmedetomidine have been used to prolong analgesia through various routes viz intravenous, intrathecal, epidural, caudal and peripheral nerve blocks.

Dexmedetomidine is more selective alpha-2 agonist especially for the 2A subtype receptor, it is 8 times more selective than clonidine and its lipophilic ratio is 3.5 times greater than clonidine which makes it much more effective sedative and analgesic agent, without undesirable cardiovascular effects from alpha-1 receptor activation.[9,10]

So we conducted this study to compare two different doses, 1µg/kg dexmedetomidine which has been proved to increase analgesia duration in comparison with 0.5µg/kg dexmedetomidine as an adjuvant for duration of postoperative analgesia, hemodynamic changes and adverse effects.

OBJECTIVES

This study has been undertaken to compare caudal bupivacaine 0.25% (1ml/kg) with dexmedetomidine 1µg/kg and caudal bupivacaine 0.25% (1 ml/kg) with dexmedetomidine 0.5µg/kg in a single shot caudal block for infraumbilical surgeries in children aged between 6months to 6 years with the Primary objective of finding out,

- Duration of analgesia (Defined as the time interval between the administration of caudal block and the first requirement of rescue analgesia postoperatively)

And Secondary objectives were,

- Hemodynamic changes like heart rate, blood pressure.
- Adverse effects- vomiting, bradycardia, hypotension etc.

REVIEW OF LITERATURE

In the review of caudal analgesia of children, it was suggested that caudal route is one of the simplest and safest techniques in pediatric surgery, with high success rate. Caudal block has been used for both intraoperative and postoperative analgesia in children undergoing infraumbilical surgeries. Caudal analgesia could reduce the amount of inhaled and intravenous anesthetic administration, attenuate the stress response to surgery, facilitate a rapid, smooth recovery and provide good immediate postoperative analgesia.[11]

Saadawy et al conducted a randomized double blind study involving 60 children aged 1-6 year undergoing unilateral inguinal hernia repair or orchidopexy, a comparison was done between 1ml/kg of 2.5mg/ml bupivacaine and same dose of bupivacaine with dexmedetomidine1µgm/kg during sevoflurane anaesthesia. They concluded that addition of dexmedetomidine to bupivacaine prolongs duration of postoperative analgesia (18.5 ± 2.8hrs) versus bupivacaine alone (6.2±2.8hrs), end-tidal sevoflurane concentration and the incidence of agitation were lower in dexmedetomidine group and there was no statistically difference in hemodynamics between two groups .[12]

Bharti N et al conducted study on 80 children of ASA grade 1 and 2, aged 1-8 yrs posted for lower abdominal and perineal surgeries were randomly allocated into 4 groups. Group 1 received 0.2% plain ropivacaine 0.75 ml/kg , while group 2, 3, and 4 received dexmedetomidine 0.5, 1.0, and 1.5 µg/kg , respectively, along with 0.2% ropivacaine 0.75 ml/kg under sevoflurane and Nitrous oxide anesthesia. They showed that postoperative analgesia was significantly prolonged in all dexmedetomidine groups compared to plain ropivacaine and patients receiving dexmedetomidine 1.5

μg/kg were more sedated as compared to the other groups (P < 0.01), but it did not delay discharge of the patients.[13]

Bhaskar et al conducted study on 60 ASA grade 1 and 2 patients ,aged 1-12 yrs undergoing lower abdominal and lower limb surgeries were randomly allocated in to either group RD (receiving 1ml of 0.2% ropivacaine with dexmedetomidine 2 μg/kg) or group RF (receiving 1ml/kg of 0.2% ropivicaine with fentanyl 2 μg/kg) under general anesthesia. The results showed that mean duration of analgesia in group RD was significantly longer compared to group RF (714±149 min vs 384±71.80 min). They concluded that dexmedetomidine offers longer postoperative analgesia, along with more arousable sedation and lower incidence of emergence reactions with comparable hemodynamic and side effect profile.[14]

El Shamaa H A et al has done study on 50 patients aged 1-5 yrs with ASA grade 1 and 2 scheduled for lower abdominal and perineal surgeries. Patients enrolled into 2 groups, group A received dexmedetomidine 2μg/kg with 1 ml /kg of 0.25% bupivacaine and group B received morphine 30μg/kg with 1 ml /kg of 0.25% bupivacaine after LMA insertion. They concluded that dexmedetomidine group patients had longer duration of analgesia and lesser side effects than morphine group.[15]

El-Hennawy et al randomly assigned 60 subjects (6 months to 6 yrs) into three groups in a double-blinded manner. After sevoflurane and oxygen inhalation, each subject was given single caudal dose of bupivacaine 0.25% (1ml/kg) combined with either dexmedetomidine 2μg/kg in normal saline 1ml, clonidine 2μg/kg in normal saline 1ml or corresponding volume of normal saline. They concluded that adding dexmedetomidine or clonidine to caudal bupivacaine significantly promoted

analgesia time [16(14-18) hrs and 12(3-21) hrs respectively) than the use of bupivacaine alone (5 (4-6)hrs)] without an increase in side effects.[16]

Study was done by Neogi M et al on 75 children aged 1 -6yrs who underwent elective inguinal herniotomy were divided into three groups. After induction with 50% Nitrous oxide and 8% sevoflurane and LMA insertion with spontaneous ventilation, Group R received 1ml/kg of 0.25% ropivacaine. Second group (Group C) received 1ml/kg of 0.25% ropivacaine and 1µgm/kg clonidine and third group (Group D) were given 1ml/kg of 0.25% ropivacaine and 1µgm/kg dexmedetomidine. The mean duration of analgesia was prolonged in group C (13.17±0.68 hrs) and group D (15.26±0.86 hrs) in compared to group R (6.32±0.46 hrs) with no significant difference in adverse effects.[17]

Anand VG et al conducted a study using, 0.25% ropivacaine 1ml/kg with dexmedetomidine 2µg/kg and the same dose of ropivacaine with 0.5 ml normal saline in children (6months to 6 yrs) undergoing lower abdominal surgeries. They concluded that addition of dexmedetomidine to ropivacaine prolongs duration of postoperative analgesia (14.5hrs versus 5.5hrs) and the difference between means of mean sedation score, emergence behavior score, mean emergence time was statistically significant but perioperative hemodynamics were stable in both groups.[11]

Jamali et al randomly divided 45 paediatric patients, aged 1-7 years, presenting for sub-umbilical surgery into three groups of 15 each. Caudal anaesthesia was performed with 1ml/kg of 0.25% bupivacaine. Epinephrine was added in one group (EG), 1µg/kg of clonidine in another group (CG) and no additional medication in another group (BG). The mean duration of analgesia was longer in CG (987±573 min) than in the EG (377±341 min) and BG (460±439); $p< 0.01$.[18]

Upadhyay KK et al randomly divided 50 children, aged 6 months to 6 years, undergoing elective lower abdominal and lower limb surgeries, into 2 groups. Group B, which received 0.75ml/kg of 0.25% plain bupivacaine by caudal route, achieved 5.59 hours of mean duration of analgesia. Group BC, that received additional 1 µg/kg of caudal clonidine, achieved 10.33 hours of analgesia. Hence it was concluded that clonidine significantly prolongs the duration of postoperative analgesia when added to bupivacaine without any fall in heart rate, blood pressure, respiratory rate and oxygen saturation.[19]

Cook B et al randomly allocated 60 boys, aged 1 – 10 year, undergoing orchidopexy, to receive one of the following three solutions. Group A received 0.25% bupivacaine 1ml/kg with adrenaline 5µg/ml (1/2,00,000), group C received 0.25% bupivacaine 1ml/kg with clonidine 2µg/kg and group K received 0.25% bupivacaine 1ml/kg with ketamine 0.5mg/kg. The mean duration of analgesia was 12.5 hours in group K, 5.8 hours in group C ($p < 0.05$) and 3.2 hours in group A ($p < 0.01$) with no difference between the groups regarding incidence of motor block, urinary retention or post-operative sedation.[20]

Constant I et al conducted a study among 64 children, aged 6 months to 9 years, scheduled to undergo bilateral correction of vesicoureteric reflux, which was expected to last more than 30 minutes. Addition of clonidine and fentanyl to bupivacaine, separately and together, was compared. Single shot caudal block was sufficient in only 57% of children in bupivacaine only group, 93% of children who received clonidine or fentanyl and 86% of children who received both. It was concluded that though both prolonged the duration of surgical analgesia, clonidine

had some advantages over fentanyl as it did not produce clinically significant side effects.[21]

Hansen et al compared the effects of caudal and iv clonidine on postoperative analgesia produced by caudal bupivacaine after hypospadias repair. 46 children (ASA I or II) aged 24-104 months, a caudal block with bupivacaine 0.25%, 0.5 ml/kg was randomised in a double blind fashion to two groups: the iv group received clonidine 2 µg /kg iv. The caudal group received clonidine 2 µg /kg caudally. The median time to first activation of PCA/NCA pump was similar in two groups. Morphine consumption during 0-24 h and 24-48 h was similar between groups.[22]

Klimscha W et al studied the analgesic efficacy, hemodynamic and respiratory safety of clonidine when added to bupivacaine for caudal blocks in 58 children, mean age of 3 years, scheduled for hernia repair. They were randomly given a caudal injection (0.75ml/kg) of either saline placebo (group P), bupivacaine 0.25% (group B), bupivacaine with epinephrine 1:200,000 (group BE), bupivacaine with clonidine 1 µg/kg (group BC1) or bupivacaine with clonidine 2 µg/kg (group BC2). The duration of analgesia was significantly longer ($p<0.05$) in BC1 (360 [270-360] min) and BC2 (360 [335-360] min) compared to P (77 min), B (346 min) and BE (300 min). It was concluded that clonidine 1 and 2 mcg/kg can be safely added to bupivacaine caudal blockade to achieve an increased duration of analgesia compared with bupivacaine alone or bupivacaine with epinephrine.[23]

Kundra et al has evaluated pre-emptive caudal bupivacaine and morphine for post-operative analgesia in children. 30 patients of ASA 1 and 2, undergoing elective hernia repair under general anaesthesia were randomly allocated to two groups; Group 1 (preemptive group) received 0.6 ml/kg 0.25% bupivacaine with morphine

0.02mg/kg caudally 15 min before surgery. Group 2 (post incision group) received the same drug mixture after surgery. Pain was assessed using and objective pain scale (OPS). In this study, they demonstrated that the preemptive caudal bupivacaine and small dose of morphine administration is superior to the same mixture given at the conclusion of surgery for pain relief.[24]

Lee JJ et al studied 46 children, aged 1-10 years, undergoing elective orthopedic surgery. They were randomly allocated to two equal groups to receive 0.25% bupivacaine 1ml/kg with either normal saline 1ml (group A) or clonidine 2µg/kg in 1 ml normal saline (group B). It was found that addition of clonidine improved the efficacy of caudal analgesia significantly compared to that provided by bupivacaine alone (9.2 hours vs 5.2 hours, $p < 0.0001$). Requirement of supplementary post-operative analgesics at 12 and 24 hours were also significantly reduced in the clonidine group ($p<0.01$).[25]

Koul A et al divided 40 children undergoing inguinal hernia repair into 2 groups. One group was given caudal injection of 0.75ml/kg of 0.25% bupivacaine alone and the other group was given clonidine 2µg/kg along with 0.75ml/kg of 0.25% bupivacaine. Duration of post-operative analgesia was 4.55 hours in the group receiving only bupivacaine and 10.25 hours in the group receiving bupivacaine with clonidine ($p<0.001$). Bradycardia, hypotension and sedation were not observed in clonidine group.[26]

Luz G et al conducted another study in children, aged 0.5- 6 years, undergoing inguinal hernia repair, orchidopexy and circumcision. It was found that the mean duration of analgesia in children receiving 0.18% bupivacaine 1.5ml/kg with clonidine 1 µg/kg or morphine 30 µg/kg was 6.3 hours and 7.1 hours respectively.[27]

ANATOMICAL REVIEW IN CAUDAL EPIDURAL BLOCK [28,29]

Vertebral column consists of 7 Cervical, 12 Thoracic, 5 Lumbar, 5 Sacral and 4-5 coccygeal vertebrae.

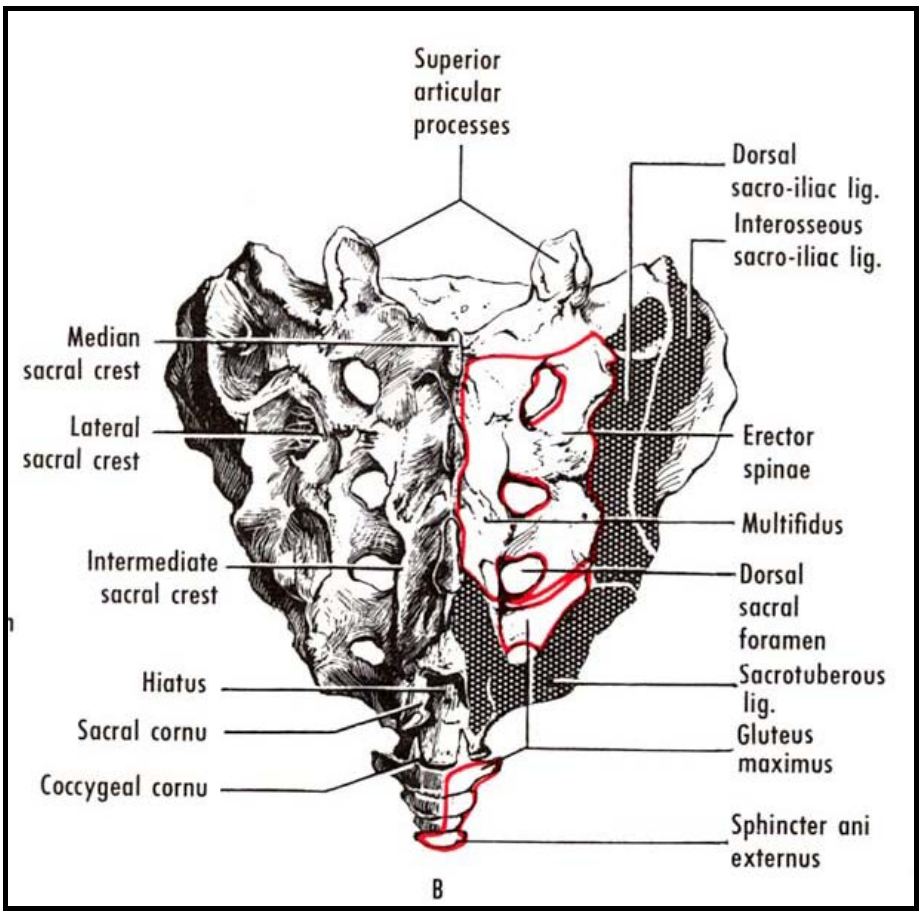
SACRUM :

It is a triangle shaped bone formed by the gradual fusion of the lamina of five sacral vertebrae, which is completed by 20 years of life. It articulates cephalad with the fifth lumbar vertebrae and caudally with the coccyx.

The concave anterior surface features four pairs of large anterior sacral foramina that provide passage from the midline sacral canal for the anterior rami of the upper four sacral nerves. In contrast with their posterior counterparts, the anterior foramina are unsealed and provide a ready passage for escape of local anaesthetic solution injected into the sacral canal.

The dorsal surface of the sacrum is variably convex and irregular, with important prominences representing the fused elements of the sacral vertebrae. In the midline, there is a median crest with three or more, but commonly four, variably prominent tubercles, representing the sacral spinous processes.

Figure 1: Anatomy of sacrum dorsal aspect

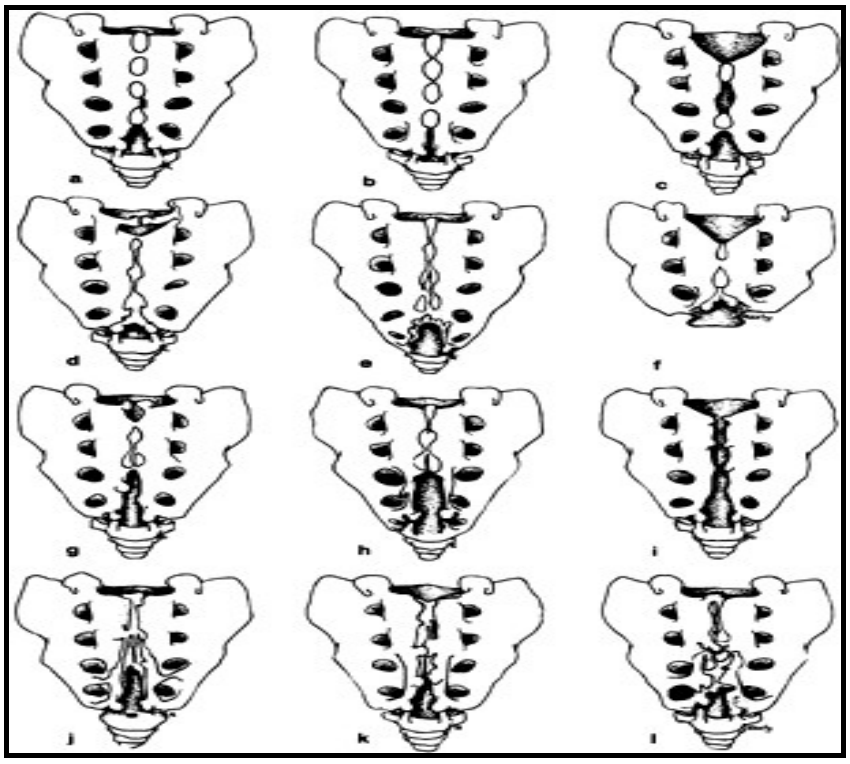


The remnants of the S5 inferior articular processes are free and prominent, and flank the sacral hiatus. They constitute the sacral cornua, and together with the adjacent coccygeal cornua, which they abut, are key landmarks for identification of the sacral hiatus and successful caudal blockade. The fused sacral transverse processes give rise to a variably raised lateral sacral crest with transverse tubercles, the most caudad of which occurs where the lateral border of the sacrum deviates more medially at the inferior lateral sacral angle. This is clinically important because it may be confused with one of the cornua. The shape of the sacrum varies somewhat between sexes and between different races.

SACRAL HIATUS :

It is a defect in the lower part of the posterior wall of the sacrum, formed by the failure of the laminae of S5, and usually part of S4, to meet and fuse in the median plane. This leaves a space of median dimension, often described as being like an inverted U or V, which is covered by the thick fibrous posterior sacrococcygeal ligament, part of a network of fibrous ligaments covering the sacroiliac and sacrococcygeal areas. Penetration of this ligament by a needle yields direct access to the caudal limit of the epidural space in the sacral canal. It is in this area that there is considerable variation in "normal" anatomy. Anatomic studies of sacrum of mixed sex and race have confirmed this variability.

Figure 2 : Anatomical variants of dorsal wall of sacrum and sacral hiatus.



a) Normal; b) Longitudinal slit-like hiatus; c) Second midline hiatus; d) Transverse hiatus; e) Large hiatus with absent cornua; f) Transverse hiatus with absent coccyx and two prominent cornua, with two proximal "decoy" hiatus lateral to the cornua; g ,h, i) Large midline defects in posterior sacral wall continuous with sacral hiatus; j.k.l) Enlarged longitudinal hiatus, each with an overlying "decoy hiatus".

SACRAL CANAL AND ITS CONTENTS :

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

The canal contains the terminal part of the dural sac, ending between S1 and S3, but generally at S2, on a line joining the posterior superior iliac spines. The five sacral nerve roots and the coccygeal nerve, which constitute the cauda equina, all transit the canal. The sacral epidural venous plexus, a part of valveless internal vertebral venous plexus, generally ends at S4, but may extend throughout the canal. It tends to lie against the anterior wall of the canal, but this is an inconsistent feature and is very much at risk from needle or catheter puncture. Also found in the canal is the filum terminale, the non-nervous terminal filament of the spinal cord, which exits through the sacral hiatus to attach to the back of coccyx. The remainder of the canal is filled with epidural fat, the character of which changes from the loose texture in children to a more fibrous, closed mesh structure in adults. It is this difference that gives rise to the predictability of caudal local anaesthetic spread in children and its unpredictability in adults.

TECHNIQUE OF CAUDAL BLOCK [28, 30, 31]

Caudal block can be performed as a single shot caudal or a continuous caudal using catheter techniques. Single shot caudal blocks are used for ambulatory and minor procedures while continuous catheter techniques are used for in-patients undergoing more extensive procedures.

Figure 3 : Method of palpation of sacral hiatus – with spine of S4 above, sacral cornua on either side and coccyx below.

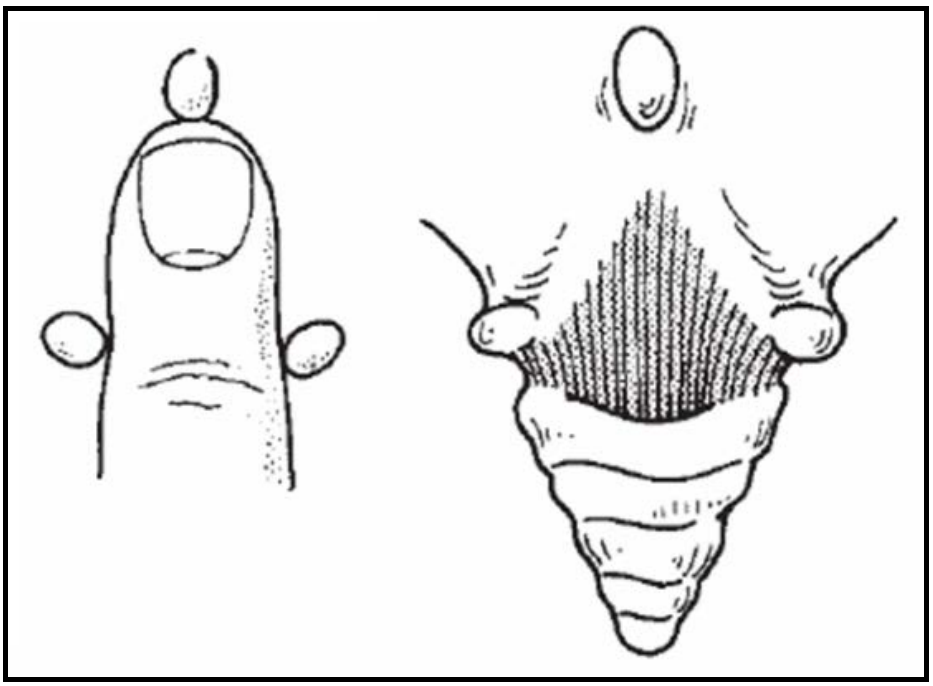
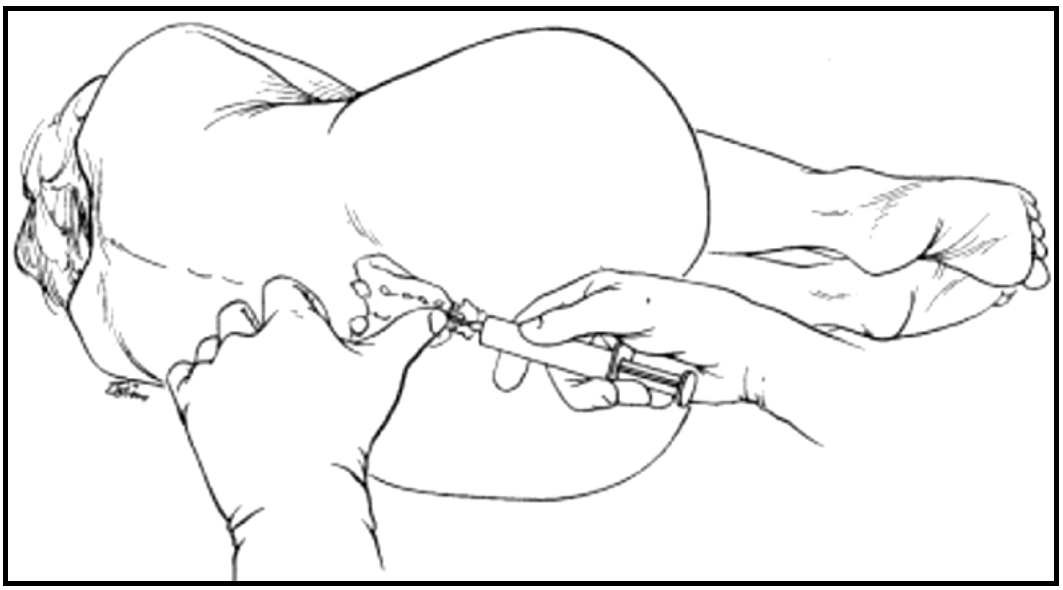


Figure 4: Positioning for caudal block and method of needle insertion.



SINGLE-SHOT CAUDAL BLOCK :

Most children will not accept this procedure while awake, and so they are sedated or anaesthetised prior to receiving caudal block. Once the child is anaesthetised and all the vitals are stable, the child is placed in the left lateral or prone position. Under strict aseptic precautions the following landmarks are palpated: Posterior superior iliac spines, sacral cornua and sacral hiatus between the cornua.

After identifying the midline, a finger is run down the tips of thoracic and lumbar spine towards the sacrum where the sacral hiatus may be palpated as a depression between the two sacral cornua. Alternatively, a finger is run upwards towards the sacrum after identifying the tip of the coccyx, which then palpates the hiatus. The sacral hiatus is also found at the apex of the equilateral triangle based on a line drawn between the two posterior superior iliac spines.

Once the sacral hiatus is identified, the hiatus is punctured with a short beveled 1.5 inch 23 gauge needle. The bevel of the needle should be placed anteriorly to prevent the penetration of anterior table of sacrum. The needle is inserted at an angle of 60-70° to the skin, until the characteristic “give” is felt, which indicates that the sacrococcygeal ligament is pierced. On entering the space, the needle is lowered to an angle of 20° and advanced 2-3 mm to make sure that the entire bevel is inside the space.

Figure 5: Bony landmarks for caudal block

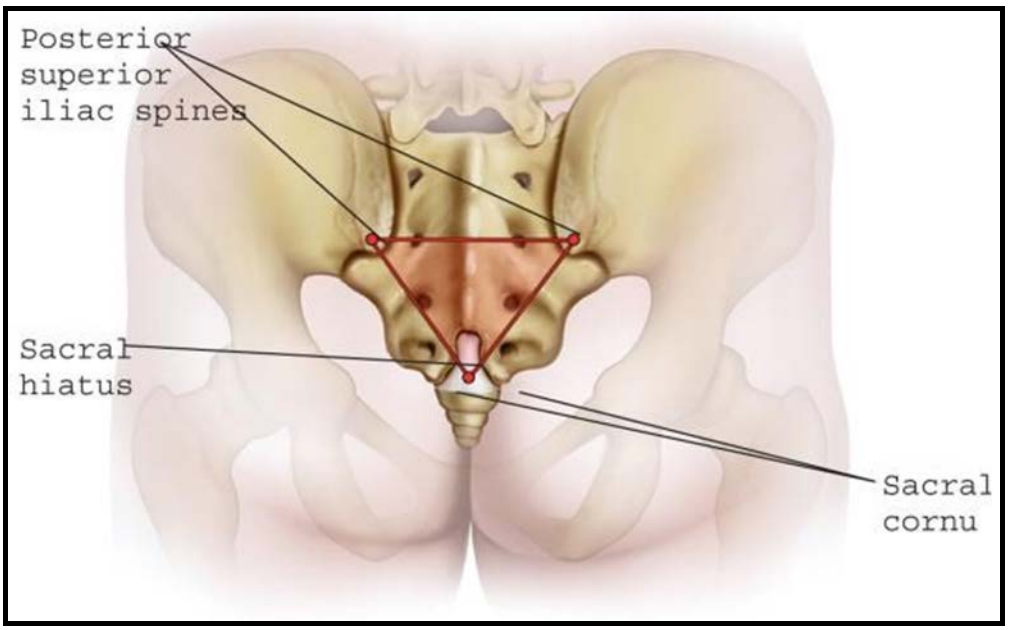
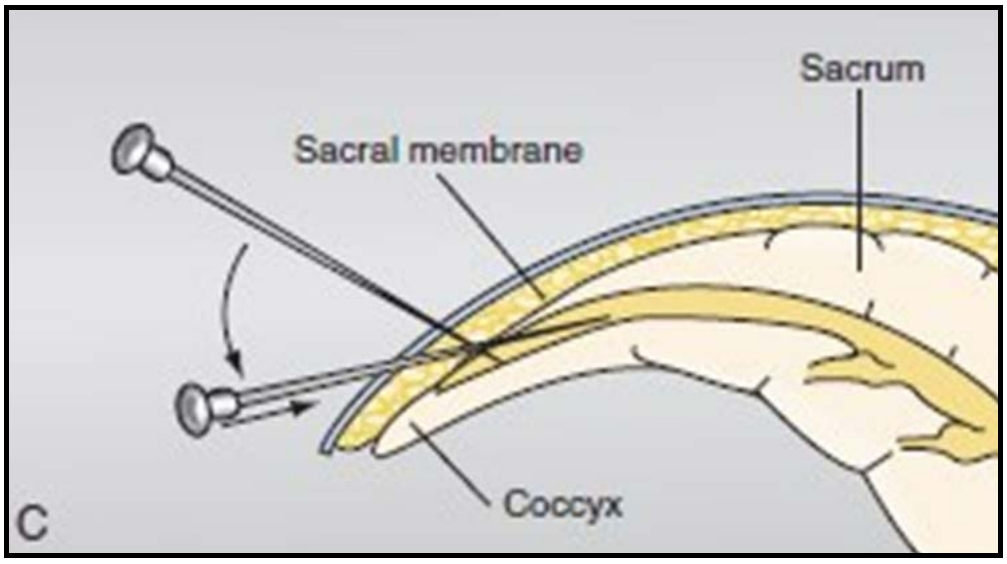


Figure 6: Method of needle insertion through Sacrococcygeal membrane



The angle of the needle with the skin is reduced parallel to the sacrum, and the needle is advanced into the caudal canal.

Signs of correct needle placement :

1. Definite “pop” is felt on piercing the sacrococcygeal ligament.

2. Absence of cerebrospinal fluid or blood on aspiration.

3. ‘Whoosh test’ – this involves listening with a stethoscope over the lumbar spine in the midline for a characteristic “whoosh” sound on injection of 2 to 3 ml of air via the caudal needle.

4. Absence of superficial bulge or crepitus on injection of drug or air.

5. There should be no tissue resistance to injection; the force required to inject should not exceed that necessary to overcome syringe or needle resistance.

6. There should be no local pain on injection of the solution.

CONTINUOUS CAUDAL :

It is mainly used for major surgeries which require patient to stay in the hospital. An 18 or 19 gauge needle (Crawford type) with a 20 or 21 gauge catheter is placed into the caudal space. Epidural catheters introduced through this route can be advanced in the epidural space to levels as high as thoracic spine in young children because of loose epidural fat. However, because of the proximity of the anus, the risk of infection precludes the use of these catheters for more than 3 days.

COMPLICATIONS :

1. ABSENT OR PATCHY BLOCK : This may be due to the failure of anatomical identification of landmarks or due to low dosage of the drug.

2. ACCIDENTAL INTRAVENOUS INJECTION : Occurs in 0.5% of patients. This is due to puncture of venous plexus in the caudal canal.

3. DURAL PUNCTURE: Inadvertent dural puncture is usually a rare complication.

4. INTRAOSSEOUS INJECTION : It is produced by penetrating of the thin layer of the cortical bone of the anterior wall of the sacral canal.

5. MOTOR WEAKNESS : This is related to the concentration of the local anaesthetic used. More weakness is observed with greater concentration.

6. URINARY RETENTION: It might be due to interference with bladder control, which depends on S2-S4 sacral roots.

7. INFECTION : Occurs due to close proximity of the sacral hiatus to the rectum and anal canal.

8. MISCELLANEOUS: Other complications include bleeding with hematoma formation, neurological damage, injury to pelvic viscera, pruritis, broken needles and catheters inside the sacral canal.

PAIN IN CHILDREN

Pain experienced by infants and children often goes unrecognized, even neglected because they cannot express it.[2]

Surgical pain not only causes immediate nociceptive response but also results in changes in nociceptive activation pathways leading to hypersensitivity, hyperalgesia and allodynia.[32]

Various studies have shown that pain pathways, as well as cortical and sub-cortical centres necessary for pain perception, are well developed late in gestation. Newborn infants, even preterm, can appreciate pain and react to it with tachycardia, hypertension, increased neuro-endocrine response and intracranial pressure.[33]

In paediatric patients, optimum pain relief is a big challenge because it is difficult to differentiate restlessness or crying due to pain from that of hunger or fear. An effective therapy to block or modify the physiological responses to painful stimulus is an essential component of paediatric anaesthesia practice.[5]

NEUROPHYSIOLOGY OF PAIN [34, 35, 36]

The basic mechanism of pain perception in infants and children are similar to those of adults and include (a) transduction and transmission (b) perception (c) modulation.

Noxious mechanical, thermal and chemical stimuli excite primary afferent fibres that transmit information from the periphery to dorsal horns of the st conducting) and C (small, unmyelinated and slow conducting) nerve fibres are primarily responsible for pain impulse transmission. These signals can be amplified by the inflammatory mediators caused by tissue injury like bradykinin, prostaglandins, cytokines, substance P, catecholamines and potassium.

Neurotransmitters in the spinal cord attenuate or amplify the pain signals from the periphery.Substance P, calcitonin and gene related peptides amplify while endogenous opioids, norepinephrine, serotonin, GABA and glycine attenuate the pain signal. Nociceptive impulse reaches the thalamus by second order neurons in the spinothalamic, spinoreticular and spinomesencephalic tracts and is often distributed in

the brain. Central sensitization occurs when excitatory amino acids act on N-methyl D-aspartate receptors to induce prolonged depolarization.

Descending modulation occurs when efferent projections from supra-spinal areas, such as peri-aqueductal gray, raphe nucleus and locus ceruleus release inhibitory neurotransmitters. The major neurotransmitters mediating descending inhibition are nor-epinephrine, serotonin, endogenous opioids, GABA and acetylcholine.

CLINICAL ASSESSMENT OF PAIN IN CHILDREN [34, 35, 37]

Assessment of pain has proved difficult in the paediatric age group because of limited cognitive and language skills, limited behavioral expression and few previous experiences of pain. Assessment of pain and management are interdependent, so without adequate assessment of childs pain, treatment is ineffective.

Presently, no easily administered, widely accepted, uniform techniques exist for assessing pain in children. An ideal pain assessment scale should be sensitive to changes in pain intensity, reliable and generalized, simple to use for patients and staff and used to assess the efficacy of analgesic interventions. Different scales vary in their ability to fulfill these criteria and an appropriate tool should be chosen based on the developmental stage of the child and the required application.

VARIOUS METHODS OF ASSESSING PAIN IN CHILDREN :

Pain assessment may be based on recording the child's self- report of pain, behavioral measures and biological methods.

1. **Self- report measures :**

Self- report measures rely on children reporting their own subjective pain experience. Since the child must have adequate cognitive and communication skills, the lower limit of age for the application of these measures is approximately four. It includes:

a) **Direct questioning :** Interviews, Children Comprehensive Pain questionnaire, Varni Thompson's Paediatric Pain questionnaire.

b) **Pain adjective descriptors :**

1) Visual Analogue scale

2) Category rating scale

- Pokers chip scale
- Faces scale
- Oncher's scale

3) Numerical scales

Pain thermometers,Pain diaries.

c) **Non- verbal scales :** Projective Method – Colours, Shapes, Drawings and Cartoons.

2. **Behavioral measures:**

Pain assessment tools that measure pain-related behaviors should be used when child self-reports cannot be obtained or to supplement self-report or physiologic measures. A number of behavioral scales have been developed which include:

a) Children Hospital of Eastern Ontario Pain Scale (CHEOPS)

b) Objective Pain Scale (OPS)

c) Procedural Behavioral Rating scale

d) Observational scale of behavioral distress

e) COMFORT scale

3. **Biological methods:**

Pain is a stressor that activates the compensatory mechanisms of the autonomic nervous system.

It includes measurement of heart rate, blood pressure, respiratory rates, body movements, facial expression, increased secretion of catecholamines, cortisol and endorphin levels. Changes in heart rate, blood pressure and respiratory rate are useful when child is constantly monitored, but measurement of hormone levels is only applicable in research settings.

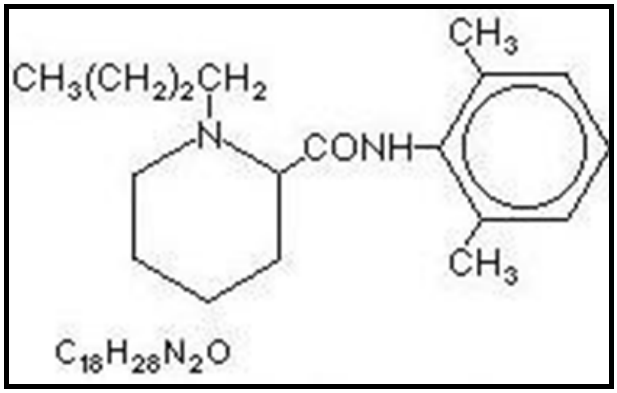
PHARMACOLOGICAL REVIEW

BUPIVACAINE:[38, 39]

- It was first synthesized by Swedish investigator A F Ekenstam et al
- It is an amino amide local anaesthetic.
- It is chemically known as 1-n-butyl-lDL-piperidine-2-carboxylic acid-2, 6 dimethyl anilide

CHEMICAL STRUCTURE:

Figure 7: Bupivacaine chemical structure



PHYSICAL AND CHEMICAL PROPERTIES:

- Molecular weight – 325.
- pH of saturated solution – 5.
- Specific gravity-1.025 at 37o C.
- Stability and sterilization - highly stable, can withstand repeated autoclaving at 247 to 258 degree Celsius.
- Melting point - 247 to 258 degree Celsius.
- pKa – 8.1. bupivacaine has an intermediate onset of action because it is more ionized at physiological pH and only 19% unionized drug is available.
- Protein binding: It is highly bound to plasma proteins (α1-acid glycoprotein), with a protein binding of 95%. This accounts for the longer duration of action.
- Lipid solubility: bupivacaine is a highly lipid soluble drug with a partition coefficient of 28. Hence it is 3 to 4 times more potent than lignocaine

MECHANISM OF ACTION:

Mechanism of action of bupivacaine is similar to that of any other local anaesthetics. The primary action of local anaesthetic is on the cell membrane of the axon. Bupivacaine binds to the α sub-unit of the voltage gated sodium channel from the inner surface of the cell membrane.

This subsequently prevents channel activation and blocks large, transient sodium influx necessary for membrane depolarization. Thus the resting membrane potential is maintained.

Initially the threshold for electrical excitation is raised, the rate of rise of action potential reduced and conduction slowed, eventually propagation of impulse fails.

Another mechanism of action is the “membrane expansion theory”. Drugs that do not form cations at physiological pH act by penetrating the axonal membrane. The membrane swells up and blocks sodium channels. This is a non-specific action compared to the more specific drug-receptor interaction.

PHARMACODYNAMICS:

CENTRAL NERVOUS SYSTEM:

Bupivacaine has a biphasic effect on the central nervous system. The initial state of CNS excitation involves the selective blockade of inhibitory pathways in the cerebral cortex. With increasing doses there is inhibition of both inhibitory and excitatory pathways, resulting in a generalised state of CNS depression.

CARDIOVASCULAR SYSTEM:

Bupivacaine is markedly cardiotoxic. It binds specifically to myocardial proteins. The primary cardiac electrophysiological effect is the decrease in the rapid phase of depolarization (Vmax) in the purkinje fibers and ventricular muscle due to decrease in the availability of fast sodium channels in the cardiac membrane. Action potential duration and effective refractory period is also decreased. The depression of rapid phase of depolarization by bupivacaine is far greater when compared to lignocaine; also the rate of recovery of block is slower with bupivacaine.

Therefore, there is incomplete restoration of Vmax between action potentials at higher rates,which make it highly arrhythmogenic. In higher concentration, bupivacaine depresses myocardial contractility which is by blocking the calcium transport. Low doses of bupivacaine produce vasoconstriction while higher doses cause vasodilatation.

RESPIRATORY SYSTEM:

Respiratory depression may be caused by depression of medullary respiratory centre if excessive plasma level is reached. It may also be caused by paralysis of respiratory muscles as may occur in high spinal blocks.

PHARMACOKINETICS:

Absorption of local anaesthetics is determined by site of injection, dosage and addition of a vasoconstrictor. Absorption is faster in regions of higher vascularity (intercostals > caudal > epidural > brachial plexus > subcutaneous). Addition of vasoconstrictor does not prolong the duration of action of bupivacaine significantly but decrease its absorption.

DISTRIBUTION:

The volume of distribution of bupivacaine in steady state is 72 liters. t1/2 α is 2.7 minutes (uptake by rapidly equilibrating tissues). t ½ β is 28 minutes (redistribution to moderately perfused tissues). t1/2 γ is 3-5 hrs. The clearance rate of bupivacaine is 0.47litre/min.

The blood concentration of the drug decreases markedly as it passes through the pulmonary vasculature. Because of the mass of skeletal tissue, it makes it the largest reservoir of bupivacaine.

METABOLISM:

Metabolism occurs in the liver by N- dealkylation primarily to pipecolyloxylidine and hydroxylation and then conjugation to form a water soluble compound.

EXCRETION:

About 10 % of the drug is excreted unchanged in urine within 24 hours. About 5 % is excreted in urine as pipecolyloxylidine.

AVAILABILITY:

Bupivacaine hydrochloride is available in solutions of 0.125%, 0.25% and 0.5% concentrations in 20 ml vials. It is also available as 0.5% (heavy) solution containing 80 mg/ml of dextrose in 4 ml ampoule.

TOXICITY:

Allergic reactions to amide type of local anaesthetics are rare. Systemic toxic reactions can occur, usually due to accidental intrathecal or intravascular injections or

administration of excessive dose of bupivacaine. It involves mainly the central nervous system. The toxic plasma concentration of bupivacaine is 4-5 µg/ml.

The earliest signs of central nervous system toxicity are circumoral or tongue numbness, tinnitus, restlessness, light headedness and dizziness, confusion, small muscle twitches involving face and distal part of the extremities, which may progress to generalized tonic-clonic seizures. In later stages, it progresses to respiratory arrest.

The ratio of dose required for irreversible cardiovascular collapse and the dose needed to produce central nervous system toxicity (CC/CNS ratio) is lower for bupivacaine which is 3.7 ± 0.5. The cardiovascular manifestations of bupivacaine toxicity include arrhythmias, myocardial depression, hypotension, bradycardia and cardiac arrest. Cardiac resuscitation is more difficult following bupivacaine induced cardiovascular collapse. Acidosis and hypoxia potentiates the cardiotoxicity.

TREATMENT:

Treatment is mainly supportive. Administering 100% oxygen and treating the complications such as seizures with anticonvulsants like thiopentone 2-3 mg/kg or diazepam 0.1-0.2 mg/kg IV. Maintaining cardiovascular stability with intravenous fluids and inotropic support. Treating ventricular tachycardia and fibrillation with Defibrillation (2 J/kg up to 6 J/kg) , using drugs like Inj. amiodarone (5 mg/kg IV) or Inj. bretylium (5 mg/kg IV, maximum of 300mg).

PREVENTION:

1. Lowest dose that gives adequate anaesthesia should be used.

2. Calculated dose be given as fractionated dose.

3. Debilitated, elderly and patients with severe liver disease dose should be reduced because hypoprotenemia increases free drug concentration.

DEXMEDETOMIDINE:[40, 41]

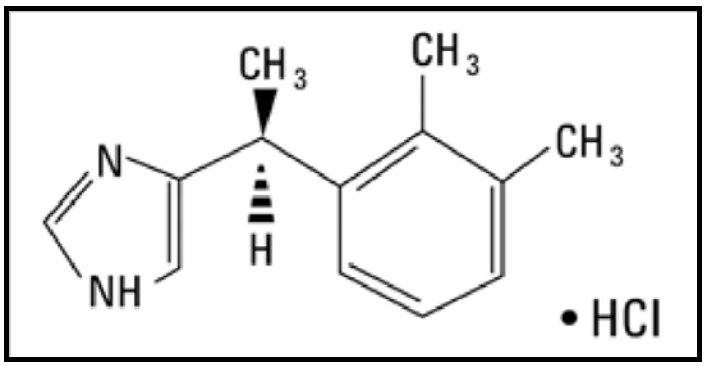
- It is highly selective α2 agonist.
- It is an imidazole compound, pharmacologically active dextroisomer of medetomidine.

PHYSICAL AND CHEMICAL STRUCTURE :

Chemical name: (+) -4 -(S) - [1 - (2, 3 -dimethylphenyl) ethyl] -1H- imidazole monohydrochloride.

- Molecular formula: C13H16N2 • HCl
- Molecular mass: 236.7
- Structural formula:

Figure 8: Dexmedetomidine chemical structure



- pKa 7.1.
- pH 4.5 to 7.0.

PREPARATION:

Available as a clear, colourless, preservative free, isotonic solution, 100 µg/ml in 0.5ml, 1ml and 2ml glass ampoules.

MECHANISM OF ACTION [42, 43]

α-2 adrenoceptors (α2AR) are part of the large guanine nucleotide binding regulatory protein (G protein) coupled family of cell surface receptors.

There are 3 subtypes of alpha-2 receptors:

- α2A: mediate sedation, analgesia and sympatholysis.
- α2B: mediate vasoconstriction and possibly anti-shivering mechanisms.
- α2C: mediate startle response.

On stimulation of α2 adrenoceptor, the inwardly rectifying G1-protein-gated potassium channels are activated resulting in membrane hyperpolarization, decreasing the firing rate of excitable cells.

Another mechanism is the reduction of calcium conductance into cells, thus inhibiting neurotransmitter release. α2 receptors are located in the locus ceruleus, the predominant noradrenergic nucleus and site of origin for the descending medullospinal noradrenergic pathways in the brain. The hypnotic, sedative and analgesic effects of α2-adrenoceptor activation have been attributed to this site in the CNS.

α2 receptors are also found in the substantia gelatinosa of the dorsal horn of the spinal cord, when stimulated, inhibit the firing of nociceptive neurons stimulated by

peripheral Aδ and C fibres and also inhibit the release of the nociceptive neurotransmitter substance P.

Dexmedetomidine is a highly selective α2 agonist with a α2 / α1 selectivity ratio of 1600:1, which is eight times more potent than clonidine (200:1). It is more specific for α2 A subtype which mediates sedation, analgesia and sympatholysis.

PHARMACOKINETICS

When administered intravenously it has a,

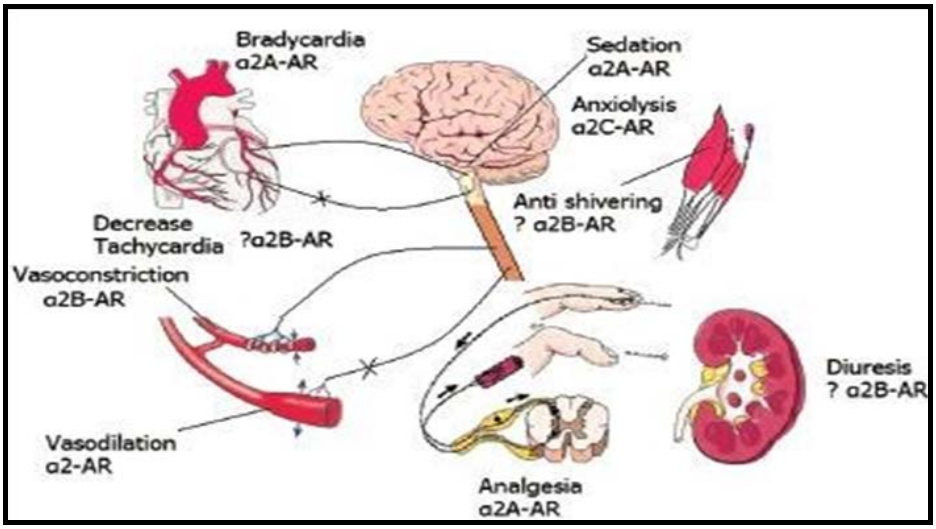
- Distribution half-life (t1/2) of 6 min
- Terminal elimination half-life (t1/2) of 2 hrs
- Steady-state volume of distribution (Vss) of 118 litres
- Clearance of 15mL/kg/min
- Protein binding of 94%

METABOLISM

Dexmedetomidine is biotransformed in the liver to inactive metabolites, with 85% undergoing glucuronidation by UDP-glucuronyl transferase (UGT) and 15% by cytochrome P450 2A6. A very small fraction of dexmedetomidine is excreted unchanged in urine and feces.

PHARMACODYNAMICS

Figure 9: Physiology of various α2 receptors



CARDIOVASCULAR:

The cardiovascular effects of dexmedetomidine are mediated via adrenoreceptors in both the central and peripheral nervous systems result in sympatholysis. It has a biphasic blood pressure response, a short hypertensive and subsequent hypotensive response. The initial reaction can be explained by the peripheral α2B-adrenoceptor stimulation of vascular smooth muscle and can be attenuated by a slow infusion over 10 or more minutes. The initial response lasts for 5 to 10 minutes and is followed by a decrease in blood pressure of approximately 10 to 20% below baseline and a stabilization of the heart rate, also below baseline values; both of these effects are caused by the inhibition of the central sympathetic outflow overriding the direct stimulating effects. Bradycardia and sinus arrest can occur which will respond to anticholinergics.

CENTRAL NERVOUS SYSTEM:

Dexmedetomidine reduces cerebral blood flow and cerebral metabolic rate of oxygen. Activation of the receptors in the brain and spinal cord inhibits neuronal firing causing analgesia, sedation and anxiolysis. Sedation mediated through the locus ceruleus closely mimics endogenous sleep.

It produces good degree of sedation, still patients are easily arousable. Dexmedetomidine does not affect intracranial or lumbar cerebrospinal fluid pressure or cerebral perfusion pressure.

When administered via the neuraxial route, it confers some analgesic and anti-nociceptive actions. Being highly lipophilic, dexmedetomidine is rapidly absorbed into CSF and binds to α2A adrenoreceptors of dorsal horn of spinal cord. It prolongs the duration of both sensory and motor blockade caused by local anaesthetics.

RESPIRATORY SYSTEM:

Dexmedetomidine does not cause respiratory depression. Upper airway patency is maintained despite good sedation.

THERMOREGULATION:

Dexmedetomidine interferes with thermoregulation by diminishing shivering, vasoconstriction, and non-shivering thermogenesis. Dexmedetomidine attenuates shivering mediated via a dose dependent decrease in thermoregulatory vasoconstriction and shivering thresholds.

MISCELLANEOUS:

Activation of the α2 receptors in other areas causes decreased salivation, decreased secretion, and bowel motility in the gastrointestinal tract; contraction of vascular and other smooth muscle; inhibition of renin release, increased glomerular filtration, and increased secretion of sodium and water in the kidney; decreased intraocular pressure; and decreased insulin release from the pancreas.

SIDE EFFECTS:

Side effects are due to its central α2 adrenoreceptor agonist action. They include bradycardia hypotension sedation, nausea and vomiting.

ANTAGONIST:

All effects of dexmedetomidine could be antagonized easily by administering the α2-adrenoceptor antagonist atipamezole. It reverses sedation and sympatholysis and has a half-life of 1.5 - 2 h.

Supportive care may include atropine sulfate for bradycardia, intravenous fluids and/or vasopressors for hypotension and vasodilators for hypertension.

CLINICAL USES

1. **Premedication:**

Because of its anxiolytic, sedative, analgesic, sympatholytic and stable hemodynamic profile, it is a useful adjunct for premedication.

Dose: Oral- 3-4 µg/kg 20 - 30 min prior.

Transmucosal /nasal -1µg/kg 45 min preoperatively.

Intravenous - 0.5µg/kg 15 min prior.

2. **Intraoperative uses:**

Dexmedetomidine attenuates hemodynamic stress response to laryngoscopy, intubation and extubation. It can be continued at extubation as it does not cause respiratory depression. It maintains upper airway patency despite good degree of sedation. This property makes it suitable for the management of the difficult airway. Fibre optic intubation can be done under an infusion of dexmedetomidine 2.5 µg/kg/h. Dexmedetomidine reduces the requirements of other anaesthetic agents and opioids.

In regional Anaesthesia:

Dexmedetomidine prolongs duration of both sensory and motor blockade of local anaesthetics irrespective of route of administration. Dexmedetomidine 1-2µg/kg when combined with bupivacaine 2.5% 1ml/kg for caudal analgesia, decreases the anaesthetic requirements, incidence of emergence agitation and the need for analgesics postoperatively in comparison with bupivacaine alone.

3. **Procedural sedation:**

Dexmedetomidine can be safely used for procedures like endoscopy, awake craniotomy and MRI. The dose is 1 µg/kg IV over 10 minutes followed by infusion 0.2µg/kg/hr.

4. **ICU sedation:**

Dexmedetomidine is suitable in ICU because it produces cooperative sedation; patients remain calm, arousable and can communicate.

METHODOLOGY

This study was conducted in S Nijalingappa Medical College and Hanagal Shri Kumareshwar Hospital and Research Centre, Navanagar, Bagalkot, from : 1st January 2013 to 31st December 2013.

This study included 60 children, of both genders, coming for various elective infra-umbilical surgical procedures such as herniotomy, orchidopexy, circumcision etc.Ethical clearance from institutional ethical committee was obtained. Informed consent was obtained from the parent before including the children in the study.

INCLUSION CRITERIA

- Age group of 6months-6 years.
- ASA grade 1and 2.
- Children posted for infraumbilical surgeries.

EXCLUSION CRITERIA

- Parents not willing to participate in the study
- ASA grade 3, 4 and 5.
- Contraindications of epidural anesthesia-

1. Spine abnormalities.
2. Hematological disease.
3. Bleeding or coagulation test abnormalities.
4. Local skin infection.
5. Drug allergy.

PRE- ANAESTHETIC ASSESSMENT

All patients were visited on the pre-operative day and a detailed general physical examination, systemic examination including airway and spine examination was done. Baseline parameters like heart rate, blood pressure were noted. Relevant laboratory investigations were done .Informed consent was obtained from the parent. All children were secured appropriate size iv cannula, a day prior to surgery.

PRE-OPERATIVE FASTING:

Solid foods were restricted for 6 hours, breast milk for 4 hours and clear fluids for 2 hours prior to surgery.

SAMPLING PROCEDURE

Sample size was calculated using open Epi 2.3.1 version with 95% confidence interval,

α-=0.05(level of significance) and Power (1-β) of 80 %.

Sample size calculated in each group is 26 which was approximated to 30 in each group.

Patients fulfilling the inclusion criteria were selected for the study and randomly allocated to either Group A (n= 30, received caudal 1ml/kg of 0.25% bupivacaine with 1 µ/kg dexmedetomidine constituted to 1 ml) or Group B (n=30, received caudal 1ml/kg of 0.25% bupivacaine with 0.5µ/ kg dexmedetomidine constituted to 1ml) by computer generated random table.

All patients and their parents were blinded to the caudal medications administered. All medications were prepared by anesthesiologists not participating in the study except for preparing the drugs. The anesthesiologist who administered anaesthesia also monitored the patient peri-operatively and was unaware of the study drug.

EQUIPMENT

- A tray containing sterile towel, bowl, betadine solution, spirit, swabs, sponge holding forceps.
- 23 G hypodermic needle.
- Drugs: bupivacaine 0.25% vial, dexmedetomidine 100µg/ml ampule, propofol for infusion.
- 10 ml, 2ml (for whoosh test) and 1ml (for dexmedetomidine dilution) syringes, normal saline for dilution.
- 20ml syringe and 100cm extension for propofol infusion
- Infusion pump
- Appropriate size airways and masks.
- Working laryngoscope, appropriate size blades.
- Jackson Rees circuit.
- Suction apparatus.
- Drugs necessary for resuscitation were kept ready.

PRE-MEDICATION:

All patients were pre-medicated with syrup midazolam 0.8mg/kg, 30 min prior to induction.

PROCEDURE

After adequate sedation child will be separated from parents. Inside operation theatre SPO2, NIBP, ECG monitors were attached. After starting O2 by simple mask all patients were induced with Inj propofol 2mg/kg and then intravenous infusion of 100µ/kg/min was started and maintained on spontaneous respiration. An infusion of Ringer Lactate was started and was administered according to the calculated requirements. Patient heart rate, oxygen saturation and blood pressure were recorded every 5 minutes from starting to the end of procedure.

CAUDAL BLOCK

Patient was placed in the left lateral position, vitals and adequacy of respiration were checked. Under strict aseptic conditions, sacral hiatus was identified by running the thumb up from coccyx towards the sacrum. After identifying the sacral hiatus, a 23 G hypodermic needle with its bevel facing anteriorly was inserted at an angle of 60-70° to the skin till the sacro-coccygeal membrane was pierced, when a distinct “pop” was felt. The needle was now lowered to an angle of 20° and advanced 2-3 mm to make sure that the entire bevel was inside the space. Confirmation of the needle point being in the epidural space was done with the “whoosh” test . After negative aspiration for blood and CSF, to rule out intravascular or subarachnoid placement of needle the study drug was injected according to the group allocated.

After injection was complete, the needle was removed and the child was placed in supine position.

Figure 10: Technique of caudal block

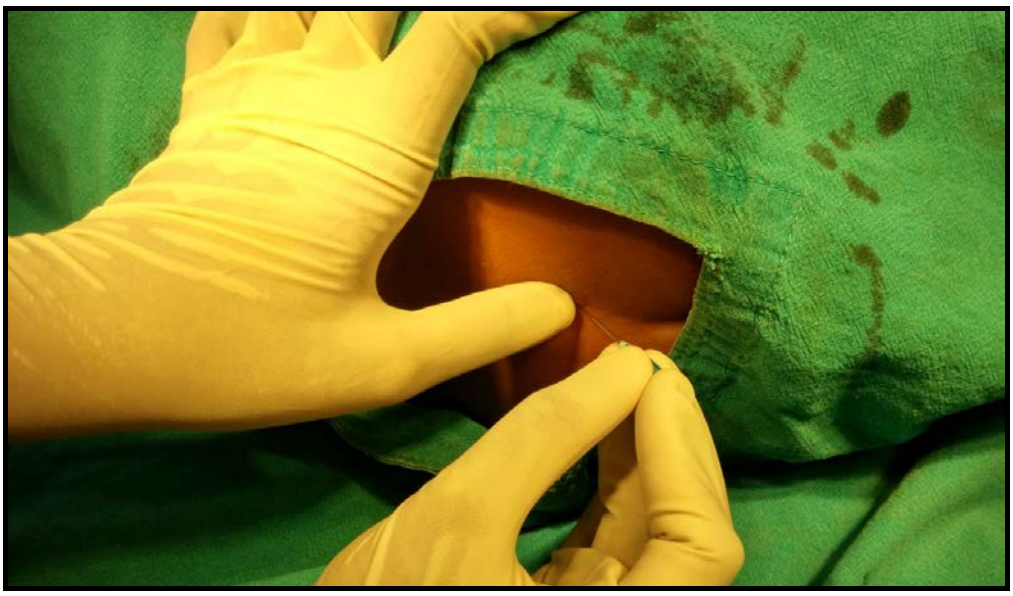
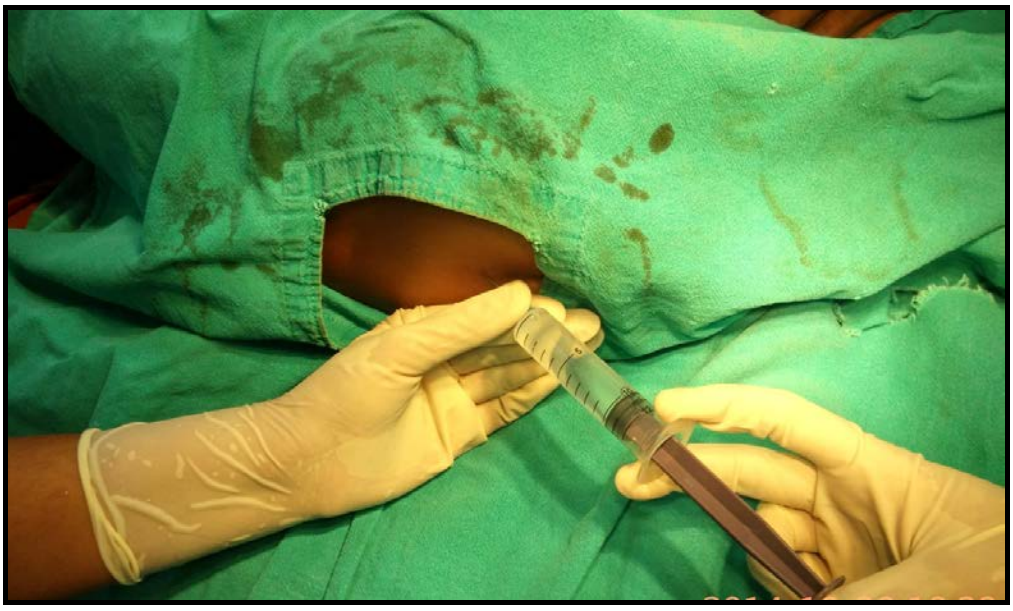


Figure 11: Caudal injection of drug



The block was deemed as successful if there is absence of gross movement of limbs to painful stimulus and when increase in heart rate or systolic arterial pressure in response to skin incision was ≤20%. [44]

No analgesia was given by any route intraoperatively. Failed caudal block cases were excluded from the study.

Towards the end of surgery propofol infusion was stopped and the duration of surgery and time of recovery from propofol was noted. Bolus intravenous propofol 1mg/kg is given as and when required during intraoperative period to maintain Ramsay sedation score 4 or 5. Number of boluses required intraoperatively were noted.

Ramsay's sedation score[11]

1. Anxious and agitated or restless, or both.
2. Co-operative, oriented, and calm.
3. Responsive to commands only.
4. Exhibiting a 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.

Intraoperatively any adverse effects such as bradycardia(Heart rate <80bpm for age < 1yr and <60bpm for ages > 1yr) were noted and treated with 20µ/kg of Inj Atropine and hypotension (defined as systolic arterial pressure 70 plus twice the age in years and associated with altered peripheral perfusion) were noted and treated with fluid boluses.[16]

Once the vitals were stable and the child was awake, the child was shifted to post operative recovery room and was monitored for heart rate , non- invasive blood pressure, oxygen saturation and pain score using modification of the objective pain scale by Hannallah and colleagues every 15 minutes for first 2 hours and there after every 30 minutes until the requirement of first rescue analgesia, time of which was noted.

Duration of first rescue analgesia is defined as the time interval between the administration of caudal block and the first requirement of rescue analgesia postoperatively.

Pain scoring (modification of the objective pain scale by Hannallah and colleagues),[45]

OBSERVATION	CRITERIA	POINTS
Crying	No crying	0
	Crying but responds to TLC	1
	Crying not responding to TLC	2
Movement	None	0
	Restlessness	1
	Thrashing	2
Agitation	Asleep/ calm	0
	Mild	1
	Hysterical	2

TLC- Tender Loving Care

Pain defined by pain score >3 points

When the pain score was >3 rescue analgesia was given with fentanyl 1µg/kg, and duration was noted. Any episodes of hypotension or bradycardia and adverse effects like postoperative vomiting etc.. in the postoperative period were noted.

STATISTICAL ANALYSIS

Statistical analysis was done using SPSS software version 11.0. All the values are expressed as mean±SD .Unpaired t test was applied to know the difference between 2 groups in quantitative data. Chi- square test was applied for proportions and qualitative data. $P<0.05$ was considered as statistically significant

RESULTS

A total of 60 subjects of ASA grade 1 and 2 , aged 6 months to 6 yrs were enrolled in this study . They were divided into 2 groups randomly ,

Group A, n= 30 received caudal 1ml/kg of 0.25% bupivacaine with 1 µ/kg dexmedetomidine.

Group B, n=30 received caudal 1ml/kg of 0.25% bupivacaine with 0.5µ/ kg dexmedetomidine.

DEMOGRAPHIC DATA

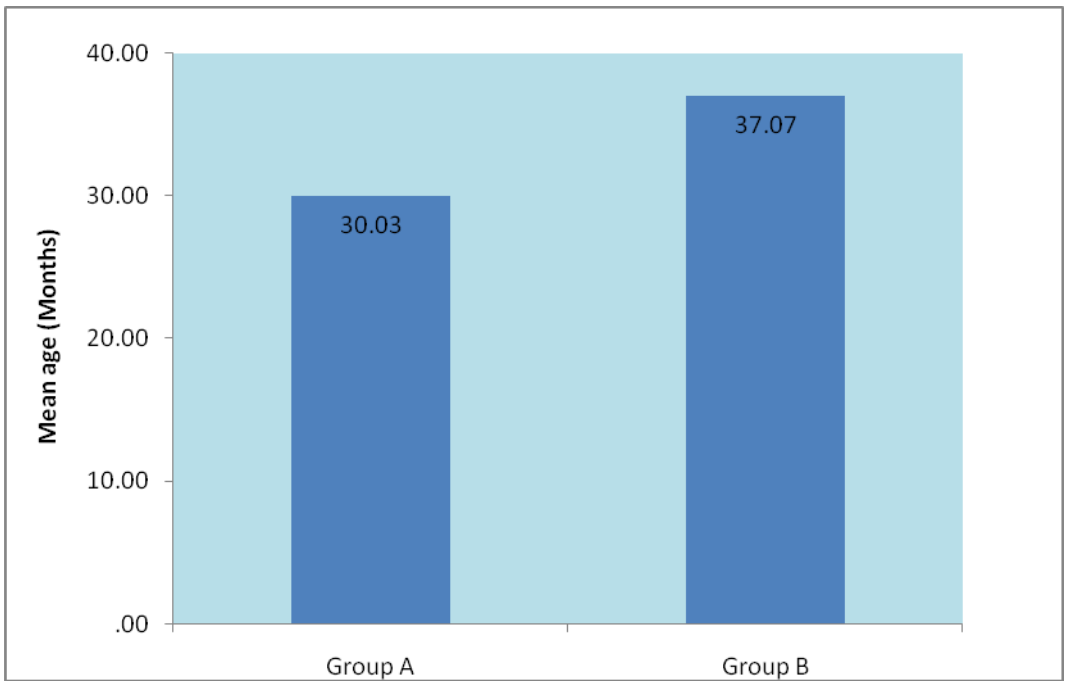
AGE

Mean age in months of group A was 30.03±15.38 and group B was 37.07±16.17 months . The two groups did not differ significantly with respect to their age.

Table 1: Mean age of patients

GROUP	MEAN AGE (IN MONTHS)	STANDARD DEVIATION	p- VALUE	STATISTICAL SIGNIFICANCE
A	30.03	15.38	0.090	NS
B	37.07	16.17		

Graph 1 : Mean age of patients



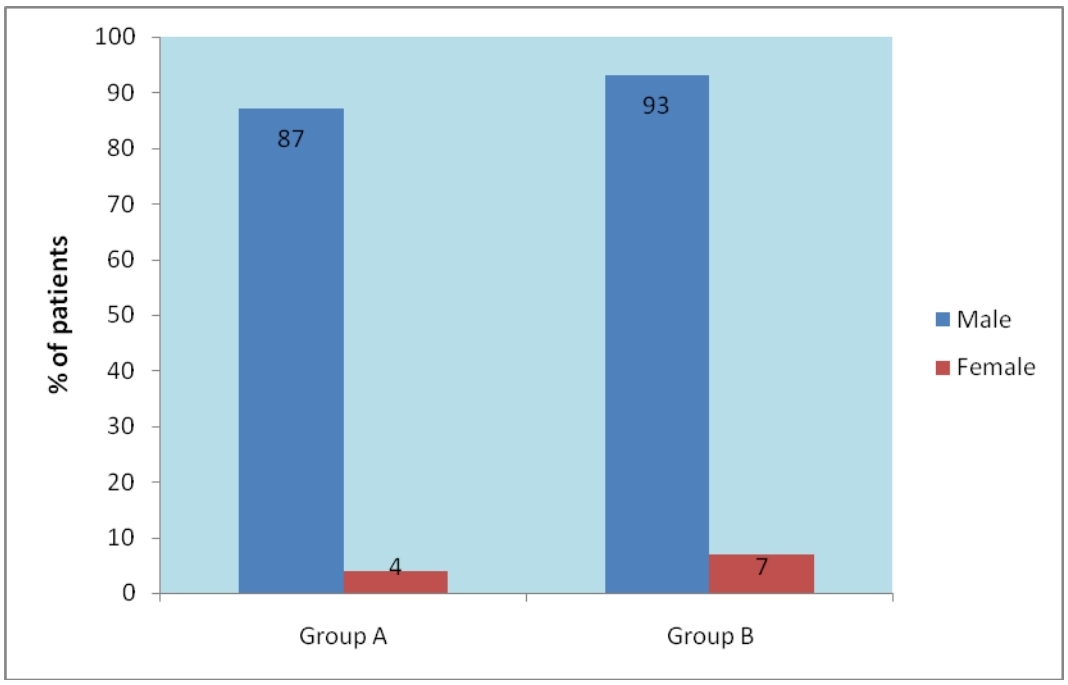
SEX DISTRIBUTION

Table 2: Sex distribution

Gender	Group A (n%)	Group B (n%)	p- Value	Statistical significance
Male	26 (87)	28 (93)	0.39	NS
Female	4 (13)	2 (7)		
Total	30 (100)	30 (100)		

In group A there were 26 (87%) males and 4 (13%) females. Group B had 28 (93%) males and 2 (7%) females. The groups were comparable with respect to sex distribution.

Graph 2: Sex distribution



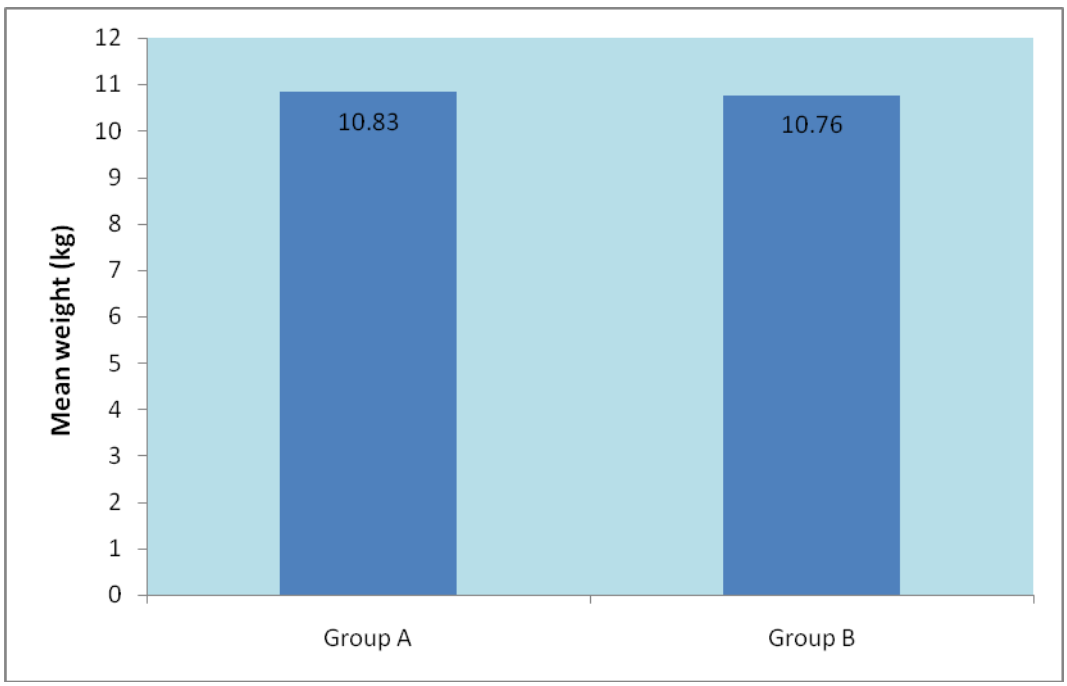
Mean Weight

Table 3: Mean weight of patients

Group	Mean Weight(kg)	Standard deviation	p- value	Statistical significance
A	10.83	3.03	0.92	NS
B	10.76	2.86		

The mean weight of the children in group A was 10.83 ± 3.03 kg. In group B the mean weight of the children was 10.76 ± 2.86 kg. The two groups did not differ significantly with respect to weight.

Graph 3: Mean weight of patients



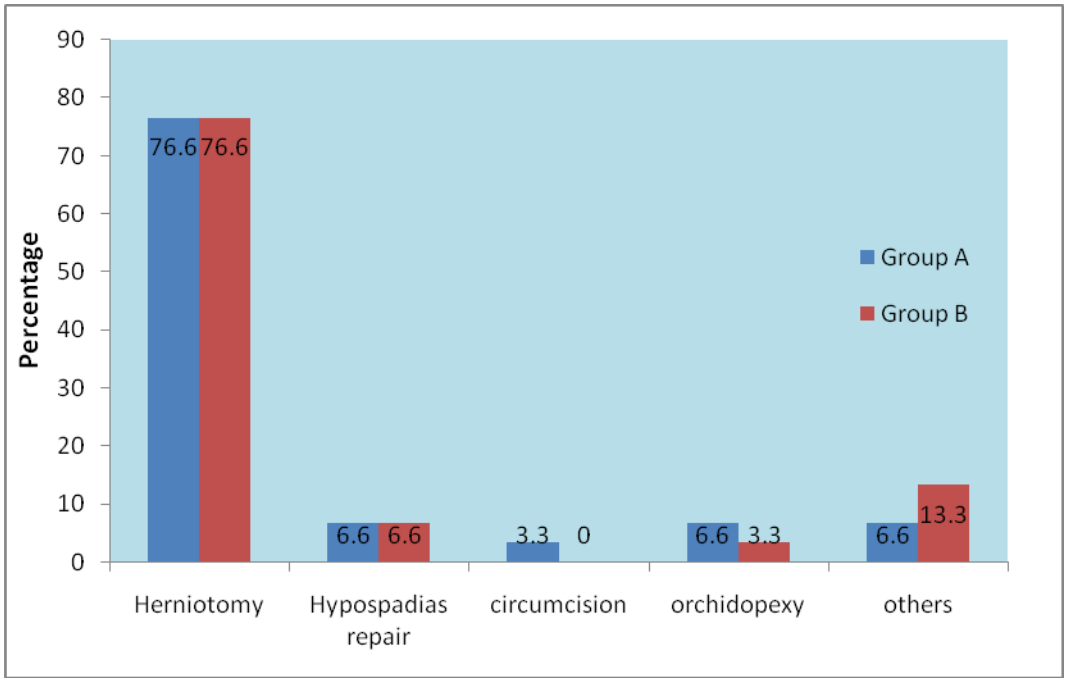
SURGICAL PROCEDURES

Table 4: Types of surgical procedures

Surgery	Group A (n%)	Group B (n%)
Herniotomy	23 (76.6)	23 (76.6)
Hypospadias repair	2 (6.6)	2 (6.6)
Circumcision	1 (3.3)	0
Orchidopexy	2 (6.6)	1 (3.3)
Others	2 (6.6)	4 (13.3)
Total	30 (100)	30 (100)

The different surgical procedures performed during the study in the two groups are shown in table and graph. In our study, herniotomy accounted for around 75 % of cases, 23 (76.66%) in both the groups. Hypospadias repair done for 2cases (6.6%) in both groups. Circumcision was done in 2(6.6%) cases in group A only, while orchidopexy accounted for 2(6.6%) cases and 1(3.3%) group A and group B respectively. Other cases like anorectal cases, cement bead removal from femur and cystoscopy constituted 2 (6.6%) and 4 (13.3%) in group A and B respectively.

Graph 4: Types of surgical procedures



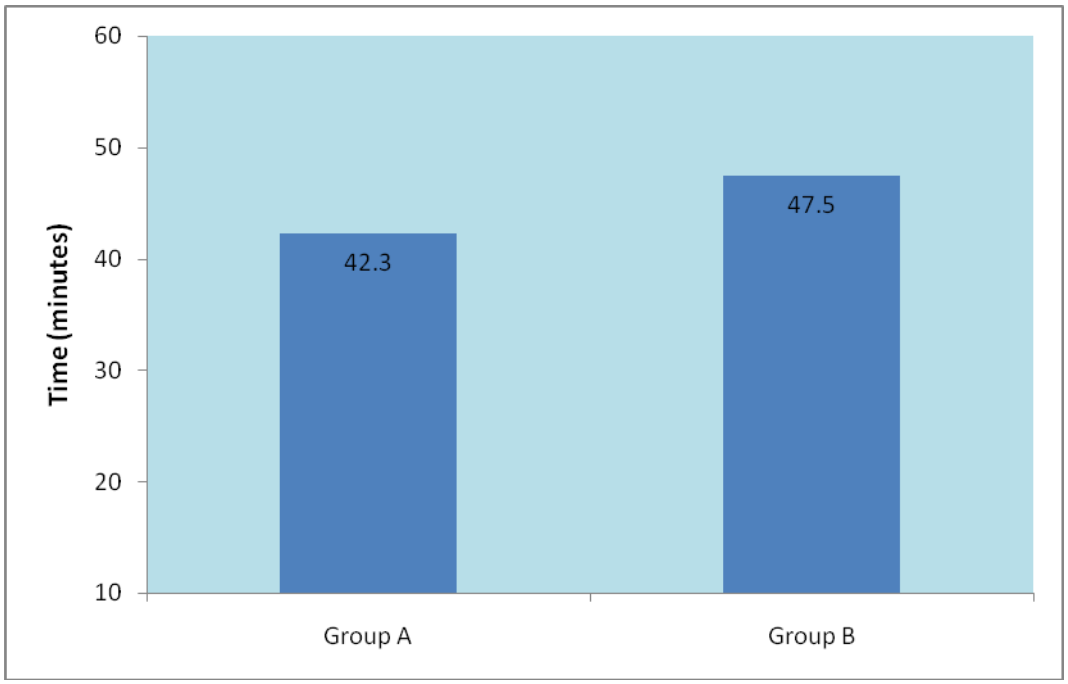
DURATION OF SURGERY

The mean duration of surgery was 42.3± 31.6 minutes and 47.5± 34.31 minutes in Group A and Group B respectively which was statistically not significant.

Table 5: Mean duration of surgery

Group	Mean Duration (minutes)	Standard deviation	p- value	Statistical significance
A	42.3	31.6	0.54	NS
B	47.5	34.3		

Graph 5: Mean duration of surgery



INTRAOPERATIVE HEMODYNAMIC VARIATIONS

CHANGES IN HEART RATE

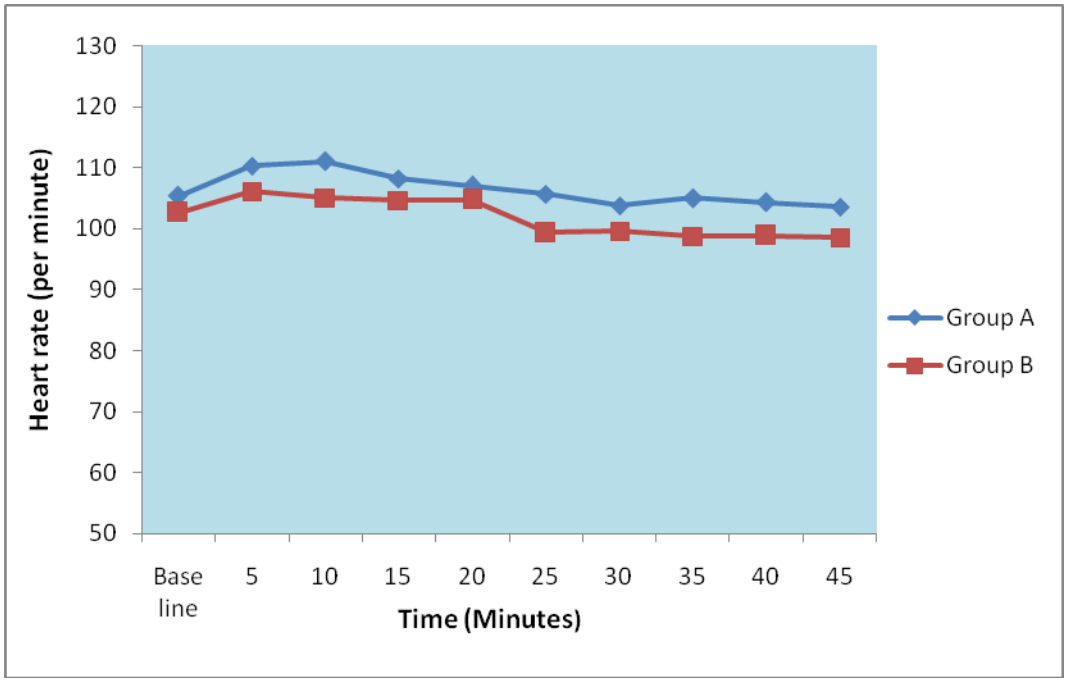
Table 6 : Changes in intraoperative Heart rate

Time interval (minutes)	Group A Mean ±SD	Group B Mean ±SD	p- value	Statistical significance
Base line	105.4±9.4	102.6±13.3	0.35	NS
5	110.3±11.1	106.1±15.5	0.23	NS
10	111±14.2	105±14.9	0.11	NS
15	108.2±14.2	104.7±0.3	0.36	NS
20	107±13.2	104.7±23.1	0.64	NS
25	105.7±14	99.3±14.3	0.08	NS
30	103.8±12.7	99.6±14.2	0.23	NS
35	105±12.9	98.7±14.6	0.87	NS
40	104.2±12.4	98.8±14.6	0.13	NS
45	103.6±11.4	98.5±15.3	0.15	NS

In group A, the mean baseline heart rate was 105.4±9.4 per minute which increased to 110.3±11.1 at 5min. The heart rate gradually decreased to 103.8±12.7 per minute at 30 minutes. The mean baseline heart rate in group B was 102.6±13 per minute which increased to 106.1±15.5 at 5 minutes and gradually decreased to 99.3±14.3 at 25 minutes and remained so till 45 minutes.

However, there was no significant difference in the heart rate between the two groups at any time interval.

Graph 6: Changes in intraoperative Heart rate



CHANGES IN SYSTOLIC BLOOD PRESSURE

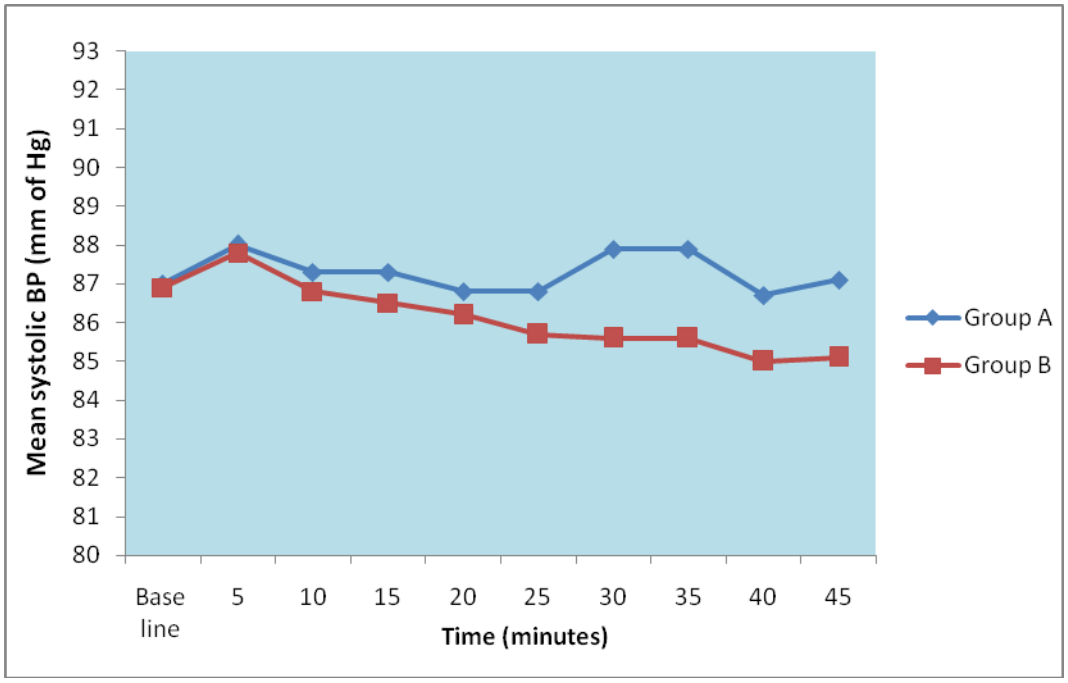
Table 7: Changes in intraoperative Systolic blood pressure

Time interval (minutes)	Group A Mean ±SD	Group B Mean ±SD	p- value	Statistical significance
Base line	87±8.8	86.9±10.3	0.98	NS
5	88.1±9.2	87.8±11	0.9	NS
10	87.3±9.7	86.8±8.3	0.84	NS
15	87.3±8.9	86.5±7.8	0.72	NS
20	86.8±9.1	86.2±7.6	0.77	NS
25	86.8±9.4	85.7±8.3	0.64	NS
30	87.9±9	85.6±8.2	0.32	NS
35	87.9±8.5	85.6±8.4	0.29	NS
40	86.7±8.2	85±7.3	0.4	NS
45	87.1±7.3	85.1±7.6	0.3	NS

The mean baseline systolic blood pressure was 87±8.8 mm Hg in group A and was maintained around 87.1±7.3mm of Hg till 45 minutes.

In group B, the mean baseline systolic blood pressure was 86.9±10.3 mm Hg, which was also maintained around 85.1±7.6 mm of Hg till 45 minutes. There was no significant difference in Mean Systolic BP between the two groups at any time interval.

Graph 7: Changes in intraoperative Systolic blood pressure



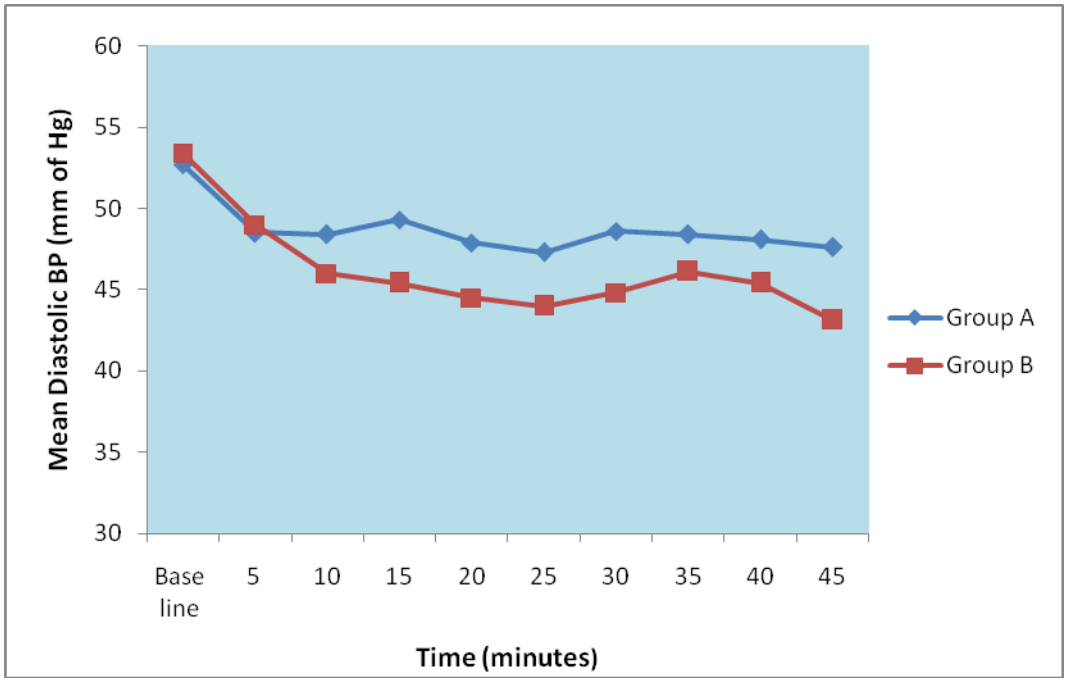
CHANGES IN DIASTOLIC BLOOD PRESSURE

Table 8: Changes in intraoperative Diastolic blood pressure

Time interval (minutes)	Group A Mean ±SD	Group B Mean ±SD	p- value	Statistical significance
Base line	52.7±7.4	53.4±6.6	0.73	NS
5	48.5±8.7	49±7.7	0.81	NS
10	48.4±9.2	46.7±8	0.45	NS
15	49.3±11.1	45.4±5.8	0.09	NS
20	47.9±9.1	44.5±7.3	0.11	NS
25	47.3±10.8	44±8.7	0.19	NS
30	48.6±9.7	44.8±8.8	0.11	NS
35	48.4±8.6	46.1±8.4	0.32	NS
40	48.1±8.0	45.4±9	0.23	NS
45	47.6±8.3	43.1±11.6	0.09	NS

The baseline diastolic blood pressure in group A was 52.7±7.4 mm Hg where as in group B, it was 53.4±6.6 mm Hg, which is statistically not significant. It gradually decreased to 47.9±9.1 mm Hg in group A and 44.5±7.3 mm of Hg in group B at 20 minutes , then it was maintained in the same range in both the groups without significant increase or decrease in pressure and there was no significant difference in between the two groups at any time interval.

Graph 8: Changes in intraoperative Diastolic blood pressure



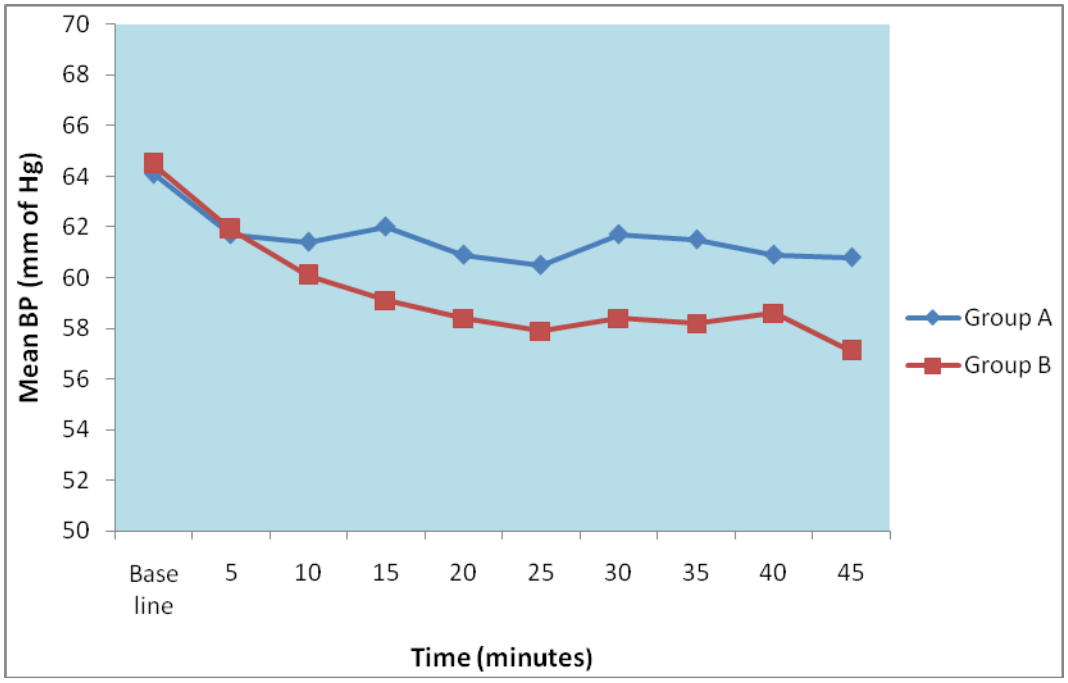
CHANGES IN MEAN ARTERIAL PRESSURE

Table 9: Changes in intraoperative Mean arterial pressure

Time interval (minutes)	Group A Mean ±SD	Group B Mean ±SD	p- value	Statistical significance
Base line	64.1±8.1	64.5±8.4	0.84	NS
5	61.7±8.3	61.9±8.1	0.91	NS
10	61.4±9	60.1±6.7	0.53	NS
15	62±10.1	59.1±5.6	0.17	NS
20	60.9±8.9	58.4±6.1	0.21	NS
25	60.5±10	57.9±7.7	0.27	NS
30	61.7±9.1	58.4±7.7	0.13	NS
35	61.5±8.1	58.2±8.8	0.14	NS
40	60.9±7.5	58.6±7.5	0.23	NS
45	60.8±7.4	57.1±8.7	0.08	NS

The base line mean arterial blood pressure was 64.1±8.1mm of Hg in Group A and 64.5±8.4mm of Hg in Group B was gradually decreased to 60.5±10mm of Hg and 57.9±7.7 in Group A and Group B respectively at 25minutes and then it was maintained around the same till 45 minutes. There was no statistically significant difference of values between both the groups at any point of time.

Graph 9: Changes in intraoperative Mean arterial pressure



INTRAOPERATIVE COMPLICATIONS

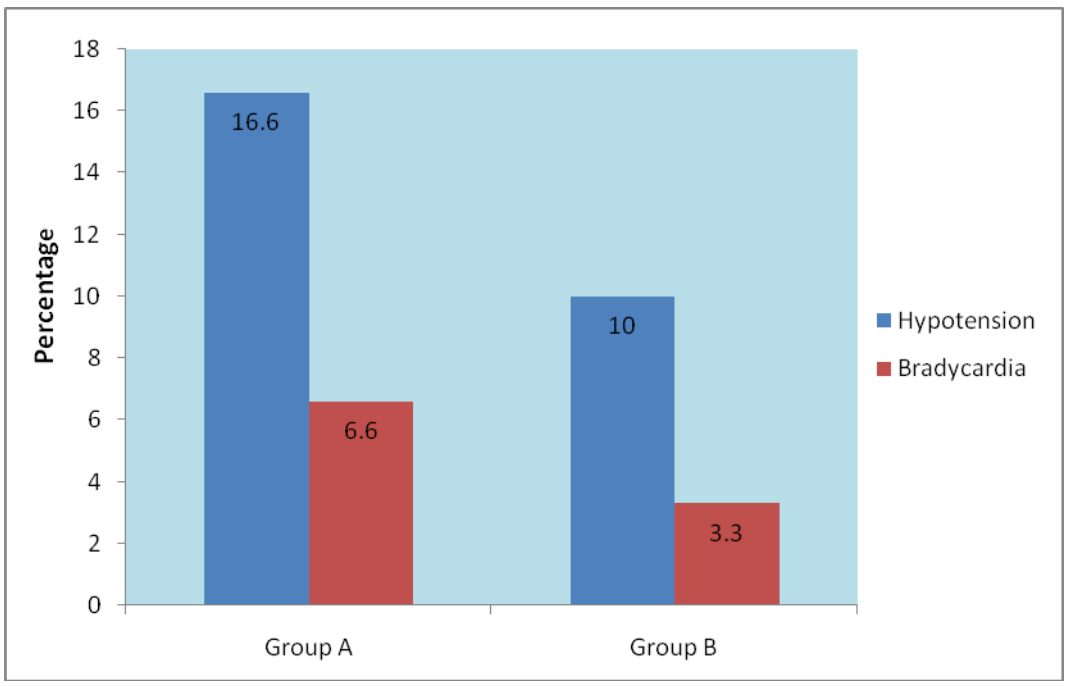
The incidence of intraoperative hypotension requiring fluid bolus was seen in 5(16.6%) and 3(10%) children in group A and group B respectively. This was not statistically significant.

Bradycardia requiring administration of atropine was seen in 2 (6.6%) and 1 (3.3%) of cases in group A and B respectively which was not statistically significant.

Table 10: Incidence of intraoperative complications

Complication	Group A (n%)	Group B (n%)	Chi square value	p- value	Statistically significance
Hypotension	5 (16.6%)	3 (10%)	0.57	0.44	NS
Bradycardia	2 (6.6%)	1 (3.3%)	0.35	0.55	NS

Graph 10: Incidence of intraoperative complications



REQUIREMENT OF BOLUS PROPOFOL

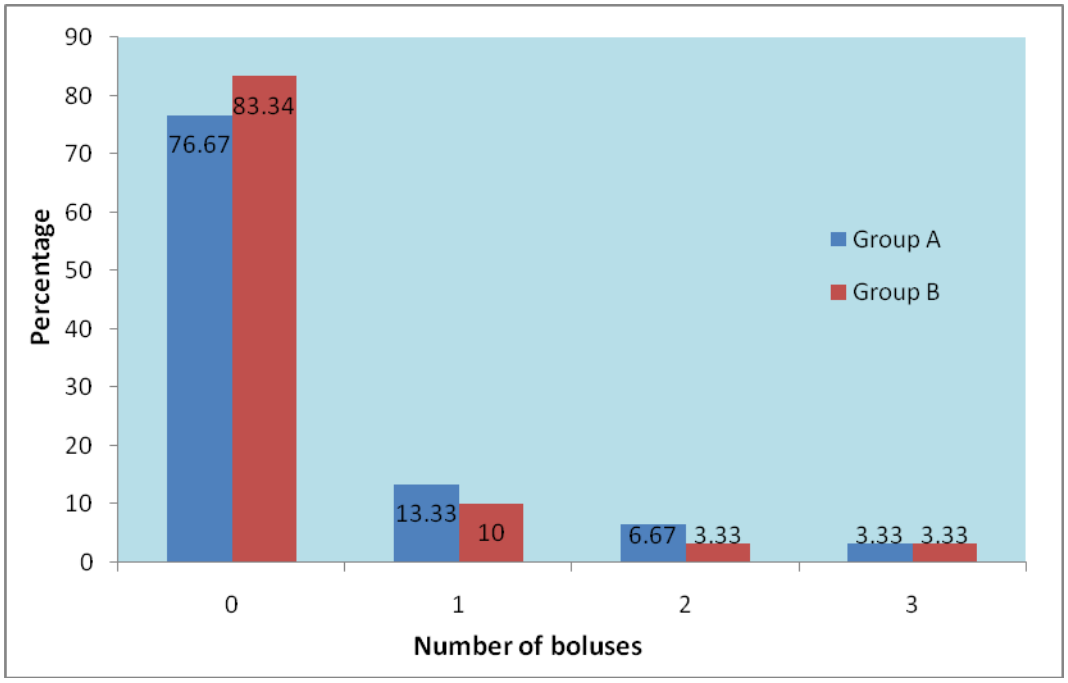
Table 11: Requirement of bolus propofol

Bolus propofol (number of boluses)	Group A (number of patients) (n %)	Group B (number of patients) (n %)
0	23 (76.67)	25 (83.34)
1	4 (13.33)	3 (10)
2	2 (6.66)	1 (3.33)
3	1 (3.33)	1 (3.33)
Total	30 (100%)	30 (100%)

Chi square- 0.20, p- value- 0.97

During surgery, 23 (76.67%) patients in group A and 25 (83.34 %) patients did not require any propofol boluses. But 4 (13.33%) patients and 3(10%) patients in group A and group B respectively required 1 bolus whereas 2 (6.66%)patients in group A and 1(3.33%) patients required 2 boluses and 1 (3.33%) patient in both group A and group B required 3 boluses to maintain a Ramsey sedation score of 4 or 5 . There was no statistically significant difference in the requirement of boluses among both groups.

Graph 11: Requirement of bolus propofol



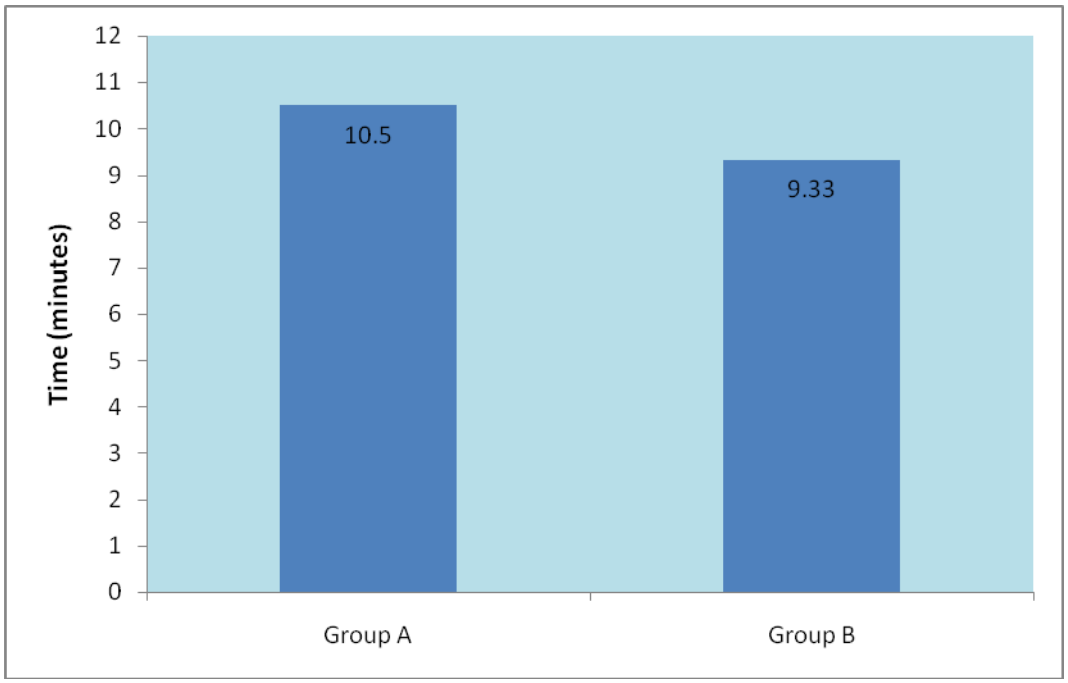
MEAN DURATION OF RECOVERY

Duration of recovery from anaesthesia following discontinuing propofol infusion was 10.50± 3.83 minutes in group A and 9.33±3.99 minutes in group B, which was statistically not significant.

Table 12: Mean duration of recovery

Group	Mean duration (minutes)	Standard deviation	p- value	Statistical significance
A	10.5	3.83		
B	9.33	3.99	0.25	NS

Graph 12: Mean duration of recovery



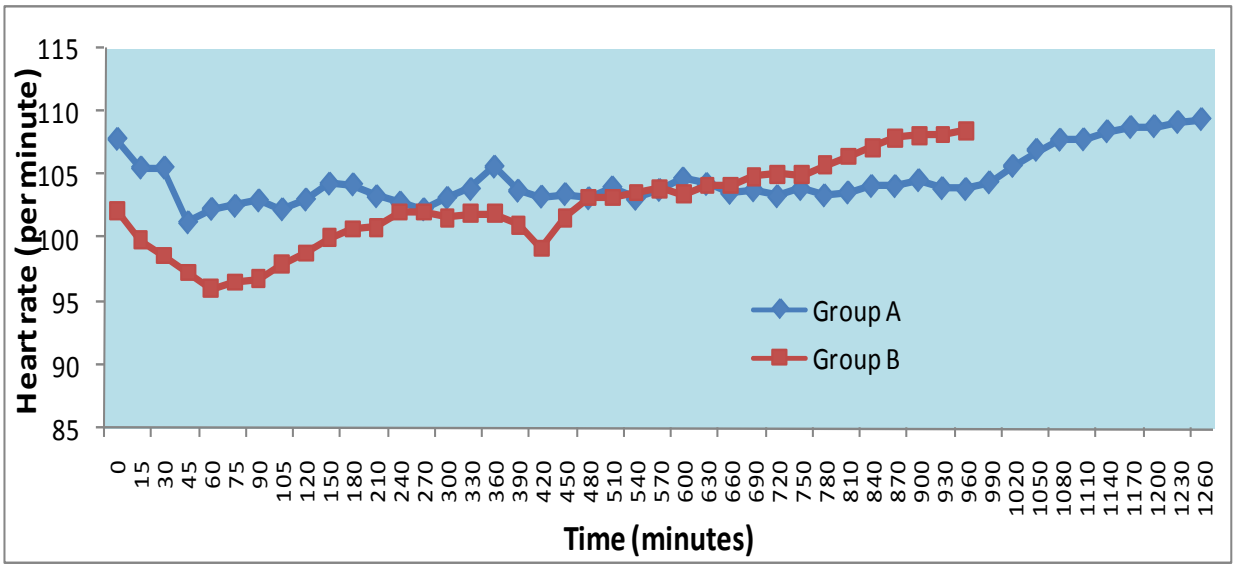
POST-OPERATIVE HEMODYNAMIC VARIATIONS

POST-OPERATIVE CHANGES IN HEART RATE

Post-operatively patient was monitored for every 15 minutes in the first 2hrs and thereafter every 30 minute till the requirement of rescue analgesia. Results were compared among both the groups.

Postoperatively when both the groups mean heart rate were compared, though there was increase in heart rate in group B due to pain it was not statistically significant difference at any point of time.

Graph 13: Changes in postoperative Heart rate

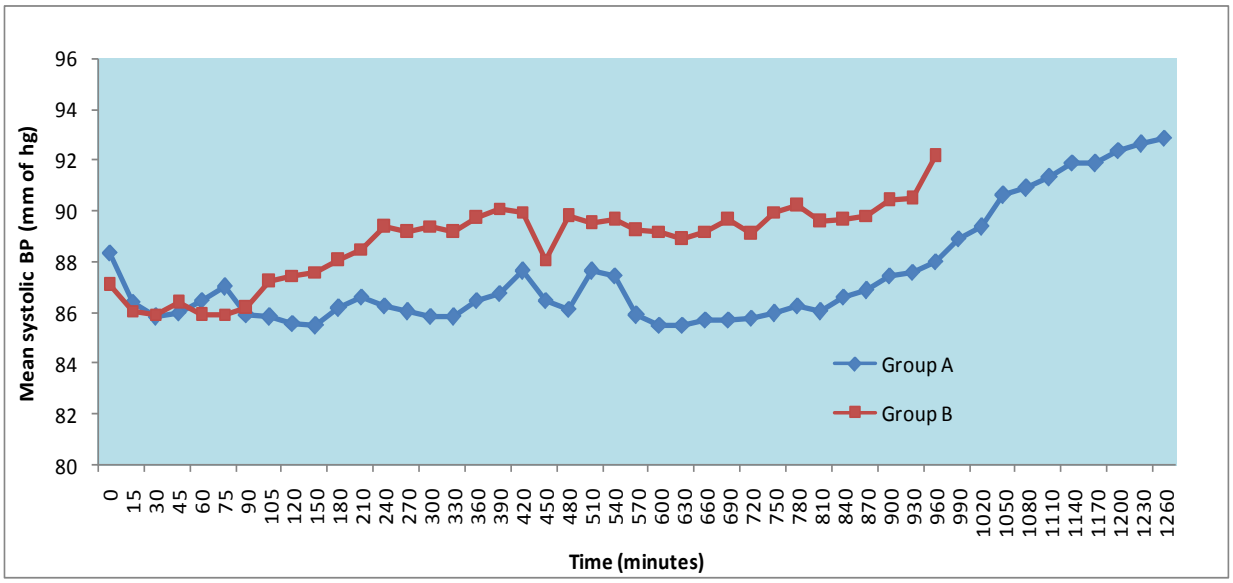


POST-OPERATIVE CHANGES OF BLOOD PRESSURE

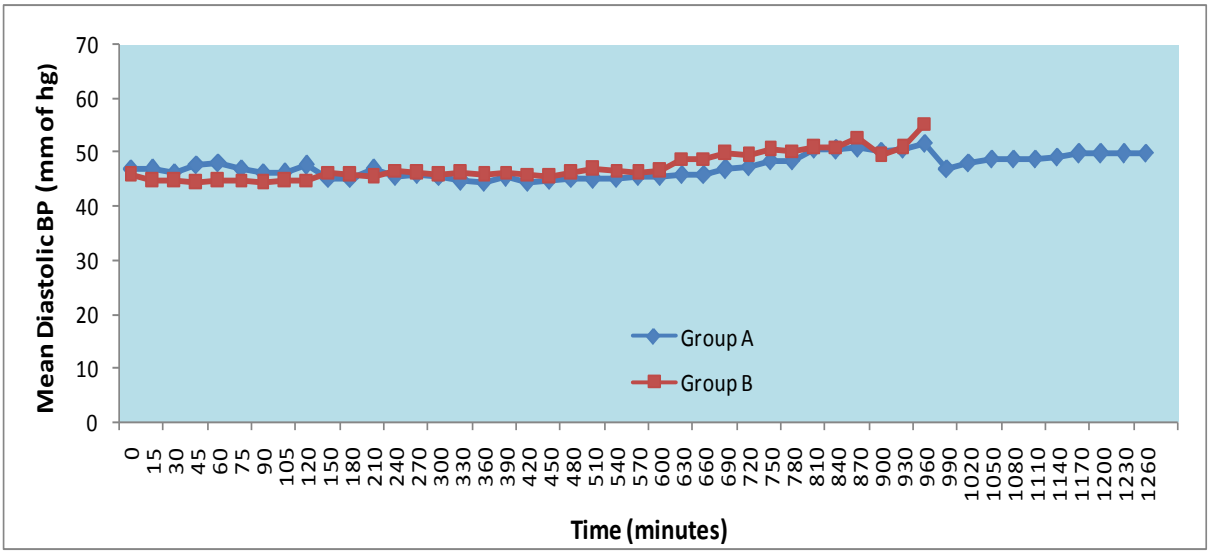
When the mean systolic, diastolic and mean arterial blood pressure was compared in group A and group B there was no statistically significant changes of blood pressure was seen at any point of time except at the time of requirement of rescue analgesia in group B when compared to group A.

Mean changes in systolic, diastolic and mean arterial blood pressure are shown in the graphs below.

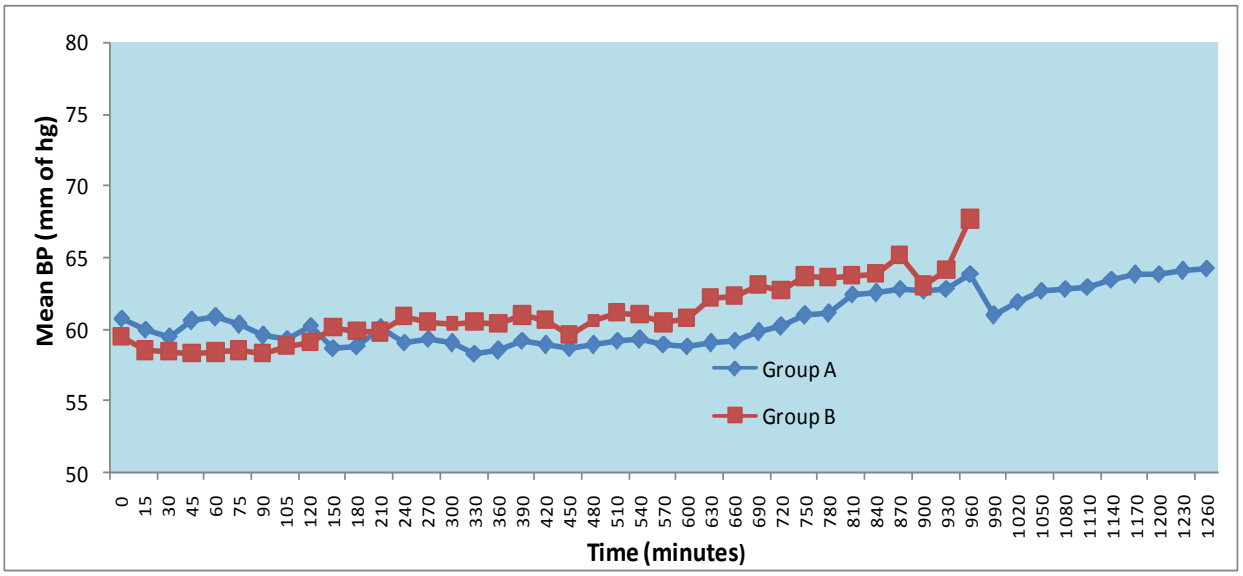
Graph 14: Changes in postoperative Systolic blood pressure



Graph 15: Changes in postoperative Diastolic blood pressure



Graph 16: Changes in postoperative Mean arterial pressure



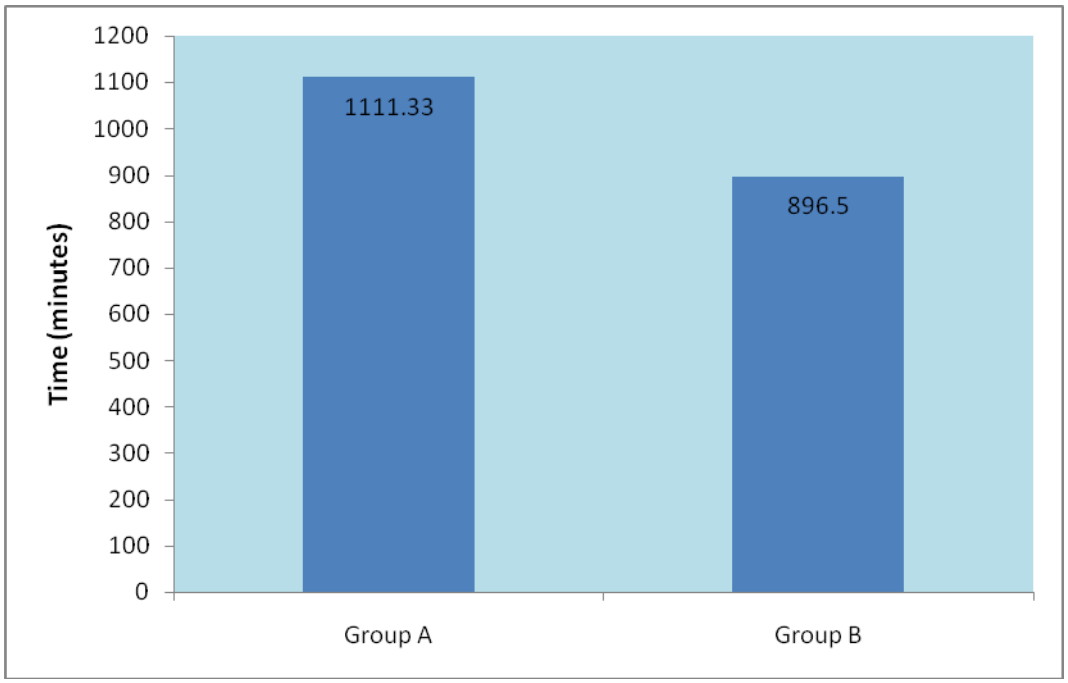
DURATION OF ANALGESIA

The total mean duration of analgesia in group A was 1111.33 ± 74.9 minutes with a range of 990 – 1260 minutes, while in group B, it was 896.5 ± 40.8 minutes with a range of 830 –995 minutes. This difference between the two groups is highly significant .

Table 13: Mean duration of analgesia

Group	Mean duration of analgesia	Standard deviation	p- value	Statistical significance
A	1111.33	74.9	0.0001	Significant
B	896.5	40.8		

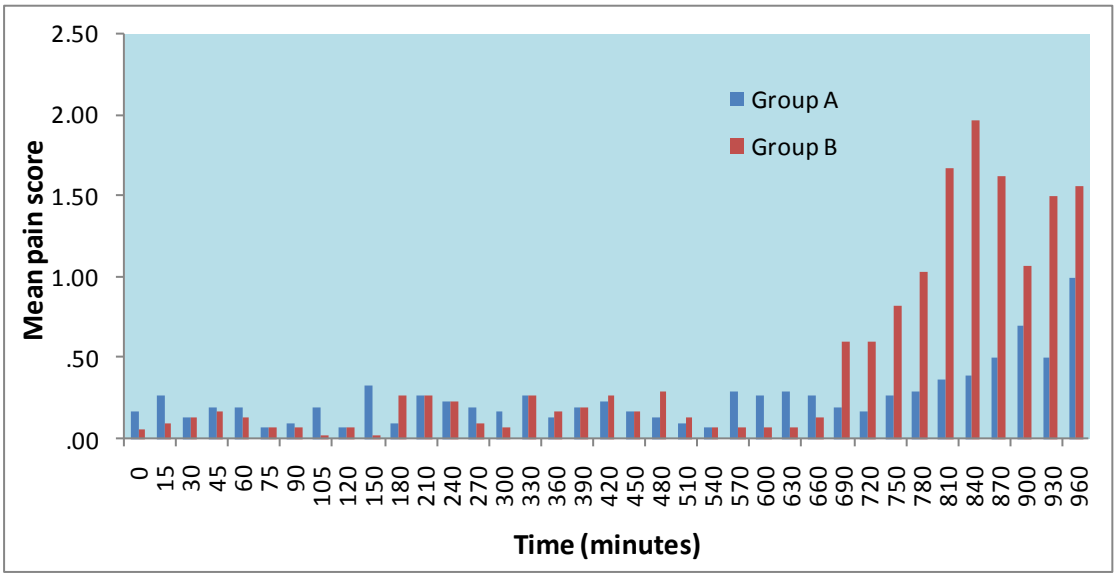
Graph 17 : Mean duration of analgesia



MEAN PAIN SCORE

When mean pain scores (assessed by objective pain scale modified Hanallah pain scale) between the 2 groups were compared in postoperative period scores were comparable in groups till 660 min but later the mean pain scores were higher in group B in compared to group A from 660 min to the time of rescue analgesia (when score >3) , which was statistically significant.

Graph 18: Mean pain scores



POST-OPERATIVE COMPLICATIONS

Table 14: Incidence of postoperative complications

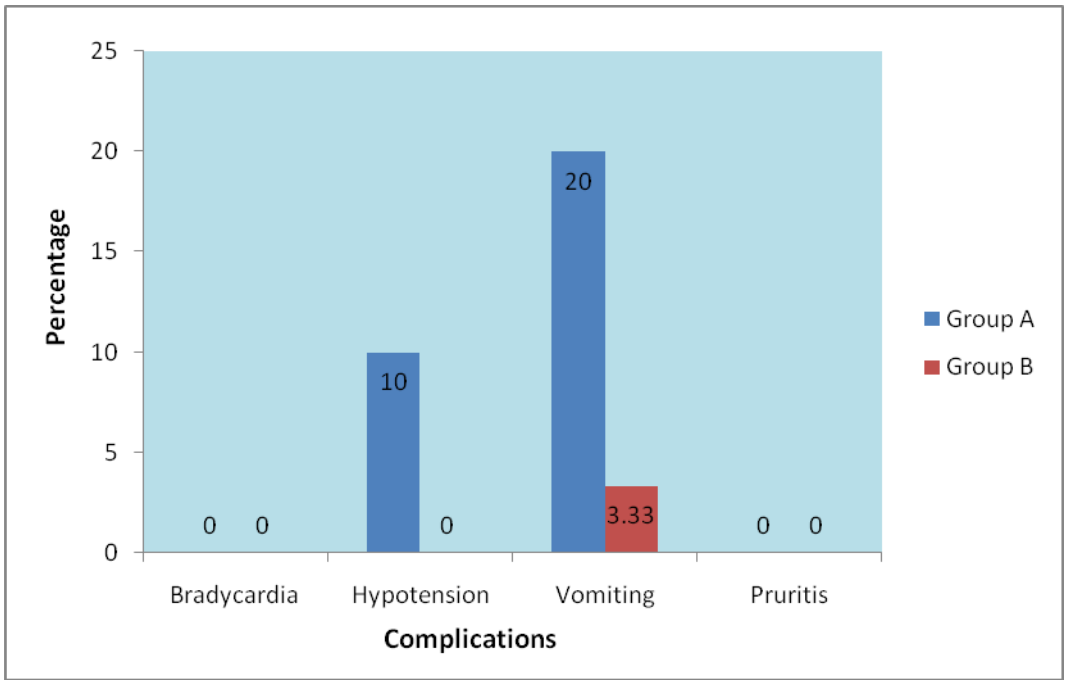
Complication	Group A (n%)	Group B (n%)	Chi square value	p- value	Statistical significance
Bradycardia	0	0	-	-	-
Hypotension	3 (10%)	0	3.05	0.08	NS
Vomiting	6 (20%)	1 (3.33)	4.04	0.04	Statistical significant
Pruritis	0	0	-	-	-

In the postoperative period 3(10%) patients in group A had hypotension but no case had hypotension in group B and it was statistically not significant.

Postoperative vomiting was seen among 6 (20%) patients in group A and 1 (3.33%) patient in group B which was statistically significant as p value was <0.05.

None of the patients had bradycardia, pruritis or any other complications in both the groups.

Graph 19: Incidence of postoperative complications



DISCUSSION

Historically it was believed that children do not feel pain and it was dangerous to give them powerful analgesics due to the risk of addiction.[2] So under treatment of pain was common pediatric age group.

But now alleviation of pain is felt as basic human right and in present day postoperative pain management has become an integral part of pediatric anesthesia.[4,5]

Caudal epidural analgesia is most common regional anesthesia technique for providing anesthesia and analgesia in children undergoing infra umbilical surgeries which is safe, reliable, effective and easy to perform.[5,6]

The duration of action after single injection is limited by duration of action of local anesthetic used and to prolong its effect wide range of additives have been used in combination with local anesthetics to promote analgesia.[46]

The use of additives during caudal anesthesia have increased in the last decade by 58%,[47] specially with ketamine 38% and clonidine 42%, whereas the use of opioids as additives has decreased from 36% to 18% due to the higher incidence of side-effects as nausea and vomiting, itching and respiratory depression specially in children.[48, 49]

Dexmedetomidine potentiates the action of local anesthetics without increasing the incidence of side-effects and compared to clonidine. It is a highly selective α2 adrenergic receptor agonist, and this facilitates its use in larger doses for analgesia and sedation without the fear of inadvertent effects on the hemodynamics.[50]

Epidural dexmedetomidine has been used in the range of 1.5–2 μg/kg without any incidence of neurological deficits.[51, 52] Saadawy et al[12] has mentioned in his study that in the absence data for caudal dexmedetomidine in children they have adopted a cautious study design by using a low dose of dexmedetomidine of 1 μg/kg which was based on previous reports in adults. So we have conducted this study to compare the duration of analgesia by decreasing the dose i.e with 0.5 μg/kg of dexmedetomidine and 1 μg/kg of dexmedetomidine with 0.25% bupivacaine caudally in patients coming for infraumbilical surgeries.

DEMOGRAPHIC DATA

In the present study, both the groups were similar with respect to demographic data like age, weight and sex of the children. In our study, age of the children were in the range from 6 months to 60 months , which was similar to studies conducted by El Hennewy et al[16] and Anand VG[11] et al both studies included patients age ranging from 6 months to 72 months. In the present study mean age in group A was 30.03±15.38 months and group B was 37.07±16.17 months which was statistically not significant.

The mean weight was 10.83 ± 3.03 kg in group A and 10.76 ± 2.86 kg in group B.It was statistically not significant.

There were 4 females in group A and 2 in group B which was comparable in both the groups . Cook et al [8] studied the effect of caudal analgesia in paediatric patients in the age group of 1-10 years, undergoing only orchidopexy, hence all the cases were male (100%).

METHOD OF INDUCTION

Xiang D et al [53] done a study with caudal dexmedetomidine with bupivacaine to inhibit the response to hernial sac traction in children undergoing inguinal hernia repair. All patients were premedicated with oral midazolam and penehyclidine hydrochloride , then induced with ketamine 2mg/kg with spontaneous respiration, caudal block was given with either bupivacaine 0.25% 1ml/kg or 0.25% bupivacaine 1ml/kg along with 1 µg/kg dexmedetomidine. Ketamine 2 mg/kg was given for the movement of patients during surgery as rescue. They concluded that dexmedetomidine group had significant duration of analgesia (860minutes) in compared to bupivacaine group (320minute) and also requirement of total fentanyl in postoperative period was less in compared to bupivacaine only group.

Brenner et al[54] carried out a study of caudal anaesthesia under sedation (with i.v. nalbuphine 0.1 mg/ kg i.v. and propofol 1 mg /kg i.v., and maintained with propofol 5 mg /kg/ hr i.v. infusion) with ropivacaine (0.2% and 0.35%) in 512 patients and concluded that caudal anaesthesia under sedation is associated with high success rates and a low incidence of adverse events with careful perioperative management.

Locatelli B et al[44] included 99 patients divided into 3 groups, premedicated all patients with rectal atropine 0.01mg/kg and midazolam 0.5mg/kg 30 minutes prior to surgery later induced with propofol 2 mg/ kg and fentanyl 0.002 mg/kg by i.v. route. Anaesthesia was maintained with a propofol infusion of 0.125–0.130 mg/ kg /min and the airway was controlled with a facial mask or laryngeal mask airway . Each group received levobupivacaine 0.25% or ropivacaine 0.25% or bupivacaine 0.25% by the caudal route. Total dose of 1ml/kg for orchidopexy and inguinal hernia

repair, 0.5ml/kg for phimosis or incision level below L3 level. They concluded that all three groups had comparable analgesic efficacy but bupivacaine group had higher incidence of residual motor blockade and longer analgesia block than other 2 groups.

Similarly in our study all the patients were given premedication with oral midazolam (0.8mg/kg) and induced with inj propofol 2 mg/kg and then 100µgm/kg/min[55] of infusion started and maintained under spontaneous respiration , then later caudal block was performed.

CONCENTRATION AND DOSE OF DRUG

In our study we have used a single dose of 0.25% bupivacaine 1ml/kg. Armitage[56] has recommended 0.25% bupivacaine in a dose of 0.5 ml/kg for lumbosacral, 1 ml/kg for thoraco-lumbar 1.25 ml/kg for mid-thoracic level of block and the plasma bupivacaine levels were always below 1.2µg/ml, which was below the toxic levels. Gunter et al[39] have reported that 0.175% bupivacaine offered the best combination of effectiveness and rapid recovery and discharge for paediatric surgical outpatients.

However, Jamali et al[18] and Cook et al[20] used 0.25% bupivacaine 1ml/kg for paediatric herniotomy and orchidopexy respectively, as a single shot caudal block. Higher concentration can produce motor blockade in the immediate post-operative period and delay discharge. Since all our patients were monitored for 24 hours postoperatively in the hospital, 0.25% bupivacaine was used which gives a better quality of analgesia.

El-Hennawy et al[16] compared bupivacaine 0.25% 1ml/kg alone and dexmedetomidine 2µg/kg or clonidine 2 µg/kg with bupivacaine 0.25%, 1ml/kg

caudally. They concluded that the addition of dexmedetomidine or clonidine to caudal bupivacaine significantly promoted analgesia time [16 (14–18) and 12 (3–21) h respectively] than the use of bupivacaine alone [5 (4–6) h] with a $p< 0.001$.

Saadawy et al[12] showed that the duration of analgesia was significantly longer with dexmedetomidine administration 1µg/kg with bupivacaine 0.25% 1ml/kg (18.5 h) than plain bupivacaine 0.25% 1ml/kg (6.2 h) ($p<0.001$) and the incidence of agitation following sevoflurane anaesthesia was significantly lower with dexmedetomidine ($p<0.05$).

Bharti N et al[13] compared patients of one group receiving 0.2% plain ropivacaine 0.75 ml/kg and group 2, 3, and 4 receiving dexmedetomidine 0.5, 1.0, and 1.5 µg/kg, respectively, along with 0.2% ropivacaine 0.75 ml/kg under sevoflurane and Nitrous oxide anesthesia. They concluded that postoperative analgesia was significantly prolonged in all dexmedetomidine groups compared to plain ropivacaine .

Bhaskar et al[14] conducted study on patients receiving 1ml of 0.2% ropivacaine with dexmedetomidine 2 µg/kg and patients receiving 1ml/kg of 0.2% ropivacaine with fentanyl 2 µg/kg under general anesthesia. They showed mean duration of analgesia in dexmedetomidine group was significantly longer compared to fentanyl group (714±149 min vs 384±71.80 min). they concluded that dexmedetomidine offers longer postoperative analgesia.

In our study, we chose 0.25% bupivacaine which provides better quality of analgesia when compared to lower concentrations and dexmedetomidine 1µ/kg, with observed prolonged duration of analgesia significantly with 0.5 µ/kg dexmedetomidine group.

CHANGES IN HEMODYNAMIC PARAMETERS:

In the present study, heart rate and blood pressure of all the patients were monitored at regular intervals.

The mean baseline heart rate was similar in both groups. The mean baseline rate was 105.4±9.4 per minute in group A and 102.6±13.3 per min in group B. Initially there was a rise in heart rates to 110.3±11.1 and 106.1±15.5 per minute respectively in both the groups at 5 minutes. On commencement of action of caudal block, there was a decrease in heart rate in both the groups which gradually reached 103.8±12.7 per minute in group A and 99.3±14.3 in group B at 25 minutes. Later there were no statistically significant changes in heart seen in both the groups at any time interval intraoperative and postoperative period till the requirement of rescue analgesia.

Similarly, there was no significant difference in the blood pressure (systolic, diastolic and mean) between the two groups at any time interval till rescue analgesia requirement. The mean baseline systolic blood pressure was 87±8.8 mm H g in group A and 86.9±10.3 mm Hg mm Hg in group B. the mean systolic BP was maintained around 87.1±7.3mm of Hg in group A and 85.1±7.6 mm of Hg in group B at 45 minutes and thereafter there were no statistically significant differences between the groups.

The mean baseline diastolic blood pressure was 52.7 ± 7.4 mm Hg in group A and 53.4 ± 6.6 mm Hg in group B. It gradually decreased to 47.9 ± 9.1 in group A and 44.5± 7.3 mm Hg in group B at 20 min which was statistically not significant . Thereafter no significant difference between the both groups seen at any time interval.

The base line mean arterial blood pressure was 64.1±8.1mm of Hg in Group A and 64.5±8.4mm of Hg in Group B which was statistically not significant. It was gradually decreased to 60.5±10mm of Hg and 57.9±7.7 in Group A and Group B respectively at 25minutes and then it was maintained around the same till the requirement of rescue analgesia. There was no statistically significant difference of values between both the groups at any point of time.

There was no drop in arterial saturation in both the groups during intraoperative and postoperative period.

Similar hemodynamic stability with respect to heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure was seen in previous studies conducted by El-Hennawy et al[16], Saadawy et al[12] and El shamaa HA et al. [15]

INTRAOPERATIVE COMPLICATIONS

In our study intraoperative hypotension requiring fluid bolus was seen in 5 and 3 patients in group A and group B respectively which was statistically not significant. Bradycardia requiring administration of atropine was seen in 2 cases in group A and 1 case in group B which was also not statistically significant. Similar results were seen in study conducted by Anand VG et al[11], Neogi et al[17], Jamali et al[18] and Lee JJ et al.[25]

INTRAOPERATIVE SEDATION SCORE

In our study we used Ramsay sedation score in assessment of sedation intraoperatively. Bolus propofol was given to maintain the score of 4 or 5 in all subjects if required. Anand et al[11] used Ramsay sedation score was used in 6 months

to 6yrs of age patients. Similarly Thakker et al[57] used this score in their study for patients aged between 1 month to 12 yrs.

MEAN DURATION OF ANALGESIA

Mean duration of analgesia in group A was 1111.33 ± 74.9 minutes and in group B was 896.5 ± 40.8 minutes , it showed high statistical significance.

In a study conducted by Saadwy et al[12] compared 1 ml/kg of 2.5 mg/ml bupivacaine alone and along with dexmedetomidine 1µg/kg showed that there was significant prolongation of duration of analgesia in dexmedetomidine group 18.5±2.8hrs in compared to 6.2±2.8hrs in bupivacaine alone group.

Similarly Bhaskar et al [14] showed that when ropivacaine with dexmedetomidine 2 µg/kg compared with ropivacaine with fentanyl 2µg/kg, the duration of analgesia was 714±149 minutes vs 384±71.8 minutes in dexmedetomidine and fentanyl group respectively which was highly significant .

El Shamaa H A et al[15] has done study dexmedetomidine 2µg/kg with 1 ml /kg of 0.25% bupivacaine in one group and other group received morphine 30µg/kg with 1 ml /kg of 0.25% bupivacaine. They concluded that dexmedetomidine group patients had longer duration of analgesia than morphine group.

Neogi et al[17] compared ropivacaine 0.25% 1ml/kg alone and dexmedetomidine 1µg/kg or clonidine 1µg/kg with ropivacaine 0.25% 1ml/kg caudally. The mean duration of analgesia was 6.32±0.46 hours in the ropivacaine group, 13.17±0.68 hours in the clonidine group and 15.26±0.86 hours in the dexmedetomidine group. They concluded that addition of both clonidine and dexmedetomidine to ropivacaine administered caudally significantly increases the duration of analgesia.

Anand et al[11] also studied ropivacaine 0.25% 1ml/kg and ropivacaine 0.25% 1ml/kg with dexmedetomidine 2 µg/kg caudally. The mean duration of postoperative analgesia in the ropivacaine group was 5.5 hours and in the ropivacaine - dexmedetomidine group 14.5 hours with a p value of < 0.001.

MEAN PAIN SCORES

Manjunath et al[58] conducted study on 90 children age 3-6yrs, ASA 1 and 2 , to study the adjuvant effect of fentanyl 1µg/kg or clonidine 2µg/kg to ropivacaine 0.2 % 1ml/kg for pediatric caudal analgesia for lower abdominal surgeries for assessment of postoperative duration of rescue analgesia. They used Hanallah pain scale scores to assess pain. They concluded that fentanyl or clonidine when added to ropivacaine prolongs the duration and quality of analgesia when compared to ropivacaine alone group and clonidine is better adjuvant due to more prolonged analgesia and lesser side effects.

In our study when mean pain scores (assessed by objective pain scale modified Hanallah pain scale) between the 2 groups were compared in postoperative period, scores were comparable in groups till 660 min but later the mean pain scores were higher in group B in compared to group A from 660 min to the time of rescue analgesia (when score >3) , which was statistically significant .

POSTOPERATIVE COMPLICATIONS

In our study 3(10%) patients in group A had hypotension but no case had hypotension in group B and it was statistically not significant. Anand et al[11] showed similar results.

Postoperative vomiting was seen among 6 (20%) patients in group A and 1 (3.33%) patient in group B which was statistically significant as p value was <0.05.

In studies conducted by Saadawy et al[12] , Bhaskar et al[14], El shamma et al[15] and Xiang et al[55] had incidence of postoperative vomiting but it was statistically not significant .

CONCLUSION

In our study we conclude that, Caudal dexmedetomidine (1µg/kg) with 0.25% bupivacaine for pediatric infraumbilical surgeries achieved significant post-operative pain relief compared to caudal dexmedetomidine (0.5µg/kg) with 0.25% bupivacaine without any significant difference in hemodynamic parameters. However incidence of side effects was less in 0.5µg/kg dexmedetomidine group when compared to1µg/kg dexmedetomidine group which was statistically significant.

SUMMARY

This clinical study entitled "Comparison of two different doses of dexmedetomidine with bupivacaine in paediatric caudal anaesthesia for infraumbilical surgeries: a randomised double blinded clinical study" was conducted at S Nijalingappa Medical College and Hanagal Shri Kumareshwar Hospital and Research Centre, from : 1st January 2013 to 31st December 2013.

After obtaining ethical committee clearance and written informed consent, Sixty children of ASA grade I and II in the age group of 6 months to 6 yrs, coming for various elective infra-umbilical surgeries were included in the study. They were divided into two groups of 30 each.

All patients received 0.8 mg/kg midazolam syrup orally as premedication and inside operation theatre after attachment of saturation probe , NIBP and ECG monitors they were induced with 2mg/kg propofol and followed by 100µ/kg/min infusion and then received caudal injection where,

Group A received caudal bupivacaine 0.25% (1ml/kg) with 1 µg/kg dexmedetomidine and

Group B received caudal bupivacaine 0.25% (1ml/kg) with dexmedetomidine 0.5µg/kg.

The parameters studied were duration of 1st rescue analgesia, hemodynamic changes both intraoperative and postoperatively and incidence of side-effects.

Both the groups were comparable with respect to age, sex and weight distribution. There was no significant difference between the two groups with respect

to haemodynamic parameters like heart rate, systolic blood pressures, diastolic blood pressures, mean arterial pressure and oxygen saturation .

Post-operative analgesia was assessed by using objective pain scale modified Hanallah pain score and when score >4, rescue analgesia with inj fentanyl 1 µg/kg was given.

The mean duration of 1st rescue analgesia in group A was 1111.33 ± 74.9 minutes and in group B was 896.5 ± 40.8 minutes which showed high statistical significance, thereby reducing the requirement of analgesics in group A in the post-operative period.

The mean pain scores were comparable in both the groups till 660 min postoperatively but later the mean pain scores were higher in group B in compared to group A from 660 min to the time of rescue analgesia (when score >3) , which was statistically significant .

BIBLIOGRAPHY

1. International association for study of pain, Subcommittee on Taxonomy. Pain terms: a list with definitions and notes on usage. Pain 1979;6:249-52.

2. Green AA. Pain and stress in infancy and childhood where to now? Paediatr Anaesth 1996;6:167-72.

3. Rawal N, Sjostrand U, Christofferson E, Dahlstrom B,Arvill A,Rydman H. Comparison of intramuscular and epidural morphine for postoperative analgesia in the grossly obese: influence on postoperative ambulation and pulmonary function. Anaesth Analg 1984;63:583-92.

4. Frank HK. The society of Pediatric anesthesia :15th annual meeting, New Orleans, Louisiana. Anesth analag 2002;94:1661-8.

5. Gehdoo RP. Postoperative pain management in pediatric patients. Indian J Anaesth 2004;8(5):406-14

6. Hansen TG, Henneberg SW, Larsen SW, Lund J, Hansen M. Caudal bupivacaine supplemented with caudal or intravenous clonidine in children undergoing hypospadias repair: A double blinded study. Br J Anaesth 2004;92:223-7.

7. De-Beer DAH, Thomas ML. Caudal additives in children – solutions or problems? Br J Anaesth 2003; 90(4):487-98.

8. Cook B, Doyle E. The use of additives to local anaesthetic solutions for caudal epidural blockade. Paediatric Anaesth 1996;6:353-9.

9. Hideaki I,Kohno T,Yamakura T, Ikoma M, Baba H. Action of dexmedetomidine on the substansia gelatinosa neurons of the rat spinal cord. Eur j neurosci 2008;27:3182-90.
10. Grosu I, Lavand'homme P. Use of dexmedetomidine for pain control. F1000 Med Rep2010;2:90.
11. Anand VG, Kannan M, Thavamani A, Bridgit MJ. Effects of dexmedetomidine added to caudal ropivicaine in paediatric lower abdominal surgeries. Indian J Anaesth 2011;55:340-6.
12. Saadawy I, Boker A, Elshahawy MA, Almazrooa A, Melibary S, Abdellatif AA, et al. Effect of dexmedetomidine on the characteristics of bupivacaine in a caudal block in pediatrics. Acta Anaesthesiol Scand 2009;53:251-6.
13. Bharti N, Praveen K, Bala I. A dose-response study of caudal dexmedetomidine with ropivacaine in pediatric day care patients undergoing lower abdominal and perineal surgeries: A randomized controlled trial. Pediatr anesth 2014;24(11):1158-63.
14. Bhaskar D, Kumar P N, Mridul S, Vipin D, Tyagi V, Mohamed A. Comparison of caudal dexmedetomidine and fentanyl for postoperative analgesia: A randomiseed double blinded study. JARBS 2014;6:51-7.
15. El Shamaa HA, Ibrahim MA. Comparative study of effect of caudal dexmedetomidine versus morphine added to bupivacaine in pediatric infraumbilical surgery. Saudi J Anaesth 2014;8(2):155-60.
16. El-Hennawy AM, Abd-Elwahab AM, Abd-Elmaksoud AM, El-Ozairy HS, Boulis SR. Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. Br J Anaesth 2009;103:268-74.

17. Neogi M, Bhattacharjee DP, Dawn S, Chatterjee N. A Comparative Study Between clonidine and dexmedetomidine used as adjuncts to ropivacaine for Caudal Analgesia in Paediatric Patients. J Anaesthesiol Clin Pharmacol 2010; 26:149-53.
18. Jamali S, Monin S, Begon C, Dubousset A, Ecoffey C. Clonidine in paediatric caudal anaesthesia. Anaesth Analg 1994;78:663-76.
19. Upadhyay KK, Handa R, Prabhakar T, Haridas B. Study of efficacy and safety of clonidine as an adjunct to bupivacaine for caudal analgesia in children. Indian J Anaesth 2005;49(3):199-201.
20. Cook B, Grubb DJ, Aldridge LA, Doyle E. Comparison of the effects of epinephrine, clonidine and ketamine on the duration of caudal analgesia produced by bupivacaine in children. Br J Anaesth 1995;75:698-701.
21. Constant I, Gall O, Gouyet L, Chauvin M, Murat I. Addition of clonidine or fentanyl to local anaesthetics prolongs the duration of surgical analgesia after single shot caudal block in children. Br J Anaesth 1998;80:294-8.
22. Hansen TG, Henneberg SG, Walther-Larsen, Lund J, Hansen M. Caudal bupivacaine supplemented with caudal or intravenous clonidine in children undergoing hypospadias repair: a double-blind study. Br J Anaesth 2004; 92:223-7.
23. Klimscha W, Chiari A, Michalek-Saubere A, Wilding E, Lerche A, Lorber C et al. The efficacy and safety of caudal clonidine/bupivacaine combination in caudal blockade for pediatric hernia repair. Anesth Analg 1998;86(1):54-61.
24. Kundra P, Deepalakshmi K, Ravishanker M. Preemptive caudal bupivacaine and morphine for post-operative analgesia in children. Anaesth Analg 1998;87:52-6.

25. Lee JJ, Rubin AP. Comparison of a bupivacaine-clonidine mixture with plain bupivacaine for caudal analgesia in children. Br J Anaesth 1994;72:258-62.
26. Koul A, Pant D, Sood J. Caudal clonidine in day-care paediatric surgery. Indian J Anaesth 2009;53(4):450-4.
27. Luz G, Innerhofer P, Oswald E, Salner E, Hager J, Sparr H. Comparison of clonidine 1µg/kg with morphine 30µg/kg for post-operative caudal analgesia in children. Eur J Anaesthesiol 1999:16:42-6.
28. Willis RJ. Caudal epidural blockade, In: Cousins MJ, Bridenbaugh PO,editors. Neuraxial blockade in clinical anaesthesia and management of pain. 3rd ed. Philadelphia:Lippincott-Raven;1998.p.323-42.
29. Collins VJ,editor. Caudal analgesia. In : Principles of anaesthesiology- general and regional anaesthesia. 3rd ed. Pennsylvania: Lea and Febiger;1993.p.1611-21.
30. Suresh S, Wheeler M. Practical pediatric regional anaesthesia. Anaesthesiol Clin North America 2002;20(1):83-90.
31. Sethna NF, Berde CB. Paediatric regional anaesthesia. In : Gregory GA,editor. Paediatric anaesthesia. 4th ed. New York: Churchill Livingstone;2002.p.279-86.
32. Anand KJ, Hickey PR. Pain and its effects in the human neonate and fetus. N Engl J Med 1987; 317:1321-9.
33. Steward DJ, editor. Anatomy and physiology relevant to pediatric anaesthesia. In: Manual of pediatric anaesthesia. 4th ed. New York: Churchill Livingstone; 1995:9-39

34. Weisman SJ, Rusy LM. Pain management in infants and children. In : Motoyama EK, Davis PJ,editors. Smith's anaesthesia for infants and children.7th ed. Philadelphia:Mosby Elsevier;2006.p.436-58.
35. Costigan M, Woolf CJ. Pain: Molecular mechanisms.J Pain 2000;1(3):35-44.
36. Woolf CJ, Max MB. Mechanism based pain diagnosis: issues for analgesic drug development. Anesthesiology 2001;95:241-9.
37. Peutrell JM, Prys-Roberts C. Regional analgesia and acute pain management in children. In: Prys-Roberts C, Brown BR,editors. International practice of anesthesia. Oxford: Butterworth-Heinemann;1996.vol 2.p.105
38. Strichartz GR, Berde CB. Local anaesthetics. In: Miller RD, editor. Miller's Anaesthesia. 6th ed. Philadelphia: Elsevier Churchill Livingstone; 2005.p.573-603.
39. Gunter JB, Dunn CM, Bennie JB, Pentecost DL, Bower RJ, Ternberg JL Optimum concentration of bupivacaine for combined caudal-general anaesthesia in children. Anaesthesiology 1991;75(1):57-61.
40. Gertler R, Brown HC, Mitchell DH, Slivius EN. BUMC proceedings 2001;14:13-21
41. Grewal A. Dexmedetomidine:New avenues. J Anaesthesiol Clin Pharmacol 2011; 27: 297-2.
42. Mason KP. Dexmedetomidine in Children: Current Knowledge and Future Applications. Anesth Analg 2011;113(5):1129-42
43. Kaur MPM. Current role of dexmedetomidine in clinical anaesthesia and intensive care. Anaesth Essays Res 2011;5(2):128-33.
44. Locatelli B, Ingelmo P, Sonzogni V, Zanella A, Gatti V, Spotti A et al. Randomized, double blinded, phase III, controlled trial comparing

levobupivacaine 0.25%, ropivacaine 0.25% and bupivacaine 0.25% by the caudal route in children. Br J Anaesth 2005;94(3):366-71.

45. Adarsh ES, Mane R, Sanikop CS, Sagar SM. Effect of pre-operative rectal diclofenac suppository on post-operative analgesic requirement in cleft palate repair: A randomised clinical trial. Indian J anaesth 2012;56:265-9.
46. Peutrell JM, Mather SJ. Regional anesthesia for babies and children. Oxford: oxford university press 1997; 187-233.
47. Menzies R, Congreve K, Herodes V, Berg S, Mason DG. A survey of pediatric caudal extradural anesthesia practice. Paediatr Anaesth 2009;19:829-36.
48. Lönnqvist PA, Ivani G, Moriarty T. Use of caudal-epidural opioids in children: Still state of the art or the beginning of the end? Paediatr Anaesth 2002;12:747-9.
49. Lönnqvist PA. Adjuncts to caudal block in children — Quo vadis? Br J Anaesth 2005;95:431-3.
50. Yoshitomi T, Kohjitani A, Maeda S, Higuchi H, Shimada M, Miyawaki T. Dexmedetomidine enhances the local anesthetic action of lidocaine via an alpha-2A adrenoceptor. Anesth Analg 2008;107:96-101
51. Schnaider TB, Vieira AM, Brandao ACA, Lobo MVT. Intraoperative analgesic effect of epidural ketamine, clonidine or dexmedetomidine for upper abdominal surgery. Rev Bras Anestesiol 2005;55:525–31 .
52. Bajwa SJ, Bajwa KB, Kaur J, Singh G, Arora V, Gupta S et al. dexmedetomidine and clonidine in epidural anaesthesia: a comprehensive evaluation. Indian J Anaesth 2011;55:116-21.
53. Xiang Q, Huang DY, Zhao YL, Wang GH, Liu YX, Zhong L et al. Caudal dexmedetomidine combined with bupivacaine inhibit the response to hernial

sac traction in children undergoing inguinal hernia repair. Br J Anesth 2012;109(5):890-5.

54. Brenner L, Kettner SC, Marhofer P, Latzke D, Willschke H, Kimberger O et al. Caudal anesthesia under sedation. Br J Anesth 2010;104(6):751-5
55. Miller RD, editor. Anesthesia. 7th ed. Philadlphia: Elsevier Churchill Livingstone.2005.p.2519-2859.
56. Armitage EN. Caudal block in children. Anaesthesia 1979; 34:396.
57. Thakker A, Shanbag P. A randomized controlled trial of intranasal-midazolam versus intravenous-diazepam for acute childhood seizures. J Neurol 2013;260(2):470-4.
58. Manjunath HG, Sumalatha A. A prospective randomized, double blinded, controlled clinical study of adjuvant effect of fentanyl (1µg/kg) or clonidine (2µg/kg) to ropivacaine 0.2% 1ml/kg for caudal analgesia in children undergoing lower abdominal surgeries. J of Evolution of Med and Dent Sci 2014;3(52):12063-72.

ANNEXURES

B. V. V. Sangha's
S. NIJALINGAPPA MEDICAL COLLEGE
& HANAGAL SHRI KUMARESHWAR HOSPITAL & RESEARCH CENTRE,
NAVANAGAR-BAGALKOT - 587 102.
KARNATAKA, INDIA

Recognised by Medical Council of India New Delhi No.U.12012/72/1999-ME (P-II) And
Affiliated to Rajiv Gandhi University of Health Sciences, Bangalore. Karnataka.

Dr. Ashok S. Mallapur M.S. (Gen. Surgery) FAIS
Principal,
Chairman, BOS for U.G. Studies (Clinical),
Member of Academic Council,
Rajiv Gandhi University of Health Sciences, Bangalore.

Phone : Office - 08354 - 235360, 235340
08354 - 235400 Extn. 1160
Tel. Fax : 08354 - 235360
Cell : 9482539899, 9342149099
Email : snmcmedbgk@yahoo.co.in (Office)
Website : www.snmcbgk.in

Ref: PG/2012-13/3030

Date: 28-11-2012

CERTIFICATE OF ETHICAL CLEARANCE

This is to certify that Dr. Sindhura N., is a Post Graduate student in the Department of MD Anaesthesiology. She was admitted to this course during the academic year 2012-13. The Institutional Ethical Committee has issued **ETHICAL CLEARANCE** for the synopsis titled as "COMPARISON OF TWO DIFFERENT DOSES OF DEXMEDETOMIDINE WITH BUPIVICAINE IN PAEDIATRIC CAUDAL ANAESTHESIA FOR INFRAUMBULICAL SURGERIES: A RANDOMISED DOUBLE BLINDED CLINICAL STUDY". She is permitted to carry out the work.

Principal 29/11
Ethical Committee Chairman,
S. Nijalingappa Medical College &
HSK Hospital & Research Centre
Bagalkot.

G:\PG Dept\PG Student\Ethical Certificate.doc

Res : Dr. Ashok S. Mallapur, Principal's Quarters, No. A-3, S.N.M.C.Campus Navanagar,Bagalkot - 587 102 (R) ☎:08354-200219
email : drmallapur@gmail.com

CONSENT FORM

Department of Anesthesiology

RESEARCH INFORMED CONSENT FORM

Study Title: COMPARISON OF TWO DIFFERENT DOSES OF DEXMEDETOMIDINE WITH BUPIVACAINE IN PAEDIATRIC CAUDAL ANAESTHESIA FOR INFRAUMBILICAL SURGERIES: A RANDOMISED DOUBLE BLINDED CLINICAL STUDY

Principal investigator: Dr. Sindhura N Guide's Name: Dr. Vinod Hosalli

Name of the subject:

Age:

Sex:

1. **I have been informed that this study requires comparison of two doses of drug for determination of duration of analgesia and will not cause any harm to me.**

2. **I understand that my participation in the study may not have a direct benefit to me.**

3. **I understand that medical information produced by this study will become part of institutional record & will be kept confidential by the said institute.**

4. **I understand that my participation is voluntary & I may refuse to participate or may withdraw my consent & discontinue participation at any time without prejudice to my present or future care at this institution.**

5. **I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose (s)**

I confirm that Dr. Sindhura N has explained to me the purpose of research & the study procedure that I will undergo and the possible risks & discomforts as well as benefits that I may experience, in my own language. Therefore, I agree to give consent to participate as a subject in this research project.

Participant's signature **Date:**

I have explained to _____(Subject) the purpose of the research, the possible risks and benefits to the best of my ability.

Investigator/ P.G (Guide) signature **Date**

PROFORMA

"COMPARISON OF TWO DIFFERENT DOSES OF DEXMEDETOMIDINE WITH BUPIVICAINE IN PAEDIATRIC CAUDAL ANAESTHESIA FOR INFRAUMBILICAL SURGERIES: A RANDOMISED DOUBLE BLINDED CLINICAL STUDY"

Principal investigator: Dr Sindhura N **Guide:Dr Vinod Hosalli**

Name: IP/OP no:

Age: DOA:

Sex: Diagnosis:

Address: Proposed surgery:

Date of surgery:

Preanaesthetic evaluation:

H/O previous anaesthesia:

H/O co existing diseases:

H/O medication:

H/O allergy:

Developmental history:

General physical examination;

Body weight: kg Height: cm

PR: /min RR: /min

BP: mmHg Temp:

Neck :

Spine:

Venous access:

Systemic examination

CVS:

RS:

PA:

CNS:

ASA class: I II III IV V VI E

Consent:

NPO status:

Premedication:

Fluids:

IV cannulation;

Caudal epidural procedure:

Drug:

Prepared by:

Given and monitored by:

Time of caudal anaesthesia:

Sedation maintained :

Sugery started at:

Surgery ended at:

Bolus propofol:

Time :

Dosage :

RAMSAY SEDATION SCORE:

TIME(min)	0	15	30	45	60	75
SCORE						

TIME(min)	90	105	120	135	150	165
SCORE						

PARAMETERS RECORDED:

TIME(min)	0	5	10	15	20	25	30	35	40
Heart rate									
Spo2									
NIBP									

TIME(min)	45	50	55	60	65	70	75	80	85
Heart rate									
Spo2									
NIBP									

TIME(min)	90	95	100	105	110	115	120	125	130
Heart rate									
Spo2									
NIBP									

*ATROPINE REQUIRED AT AND DOSAGE:

PROPOFOL INFUSION STOPPED AT:

RECOVERY:

No of episodes of hypotension:

No of episodes of bradycardia:

Time of recovery from propofol sedation:

POSTOPERATIVE MONITERING:

TIME(min)	0	15	30	45	60	75	90	105	120	150	180	210	240
HR													
SPO2													
NIBP													

TIME(min)	270	300	330	360	390	420	450	480	510	540	570	600	630
HR													
SPO2													
NIBP													

TIME(min)	660	690	720	750	780	810	840	870	900	930
HR										
SPO2										
NIBP										

TIME(min)	960	990	1020	1050	1080	1110	1140	1170	1200	1230	1260
HR											
SPO2											
NIBP											

POSTOPERATIVE PAIN SCALE (MODIFIED HANNALLAH AND COLLEGUES)

TIME (min)	0	15	30	45	60	75	90	105	120	150	180	210	240
Cry													
Movement													
Agitation													
Total													

TIME(min)	270	300	330	360	390	420	450	480	510	540	570	600
Cry												
Movement												
Agitation												
Total												

TIME(min)	630	660	690	720	750	780	810	840	870	900	930
Cry											
Movement											
Agitation											
Total											

TIME(min)	960	990	1020	1050	1080	1110	1140	1170	1200	1230	1260
HR											
SPO2											
NIBP											
TIME(min)											

Time of rescue analgesia-

CONCERNED ANAESTHESIA

STAFF SIGNATURE

DEXMEDETOMIDINE 0.5µg/ Kg GROUP B MASTER CHART

Sl no	Ip / OP no	Name	Age (Months)	Sex	Diagnosis	Surgery	weight (kgs)	Duration of surgery(min)	Baseline			Intraoperative heart																													
									HR	SBP	DBP	5 min	10 min	15 min	20 min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min	65 min	70 min	75 min	80 min	85 min	90 min	95 min	100 min	105 min	110 min	115 min	120 min	125 min	130 min	135 min
1	28545	Danamma	36	F	ARM with colostomy	colostomy closure	9	100	80	100	60	82	83	80	85	80	79	74	76	78	74	75	76	80	78	78	79	80	88	90	100							
2	294364	Balram	60	M	llt hydrocoele and Rt UDT	Lt herniotomy and rt orchidopexy	17	110	88	90	50	106	86	102	78	75	77	75	78	75	73	70	70	69	65	78	80	79	78	79	77	79	74					
3	294567	Prajwal	24	M	Rt inguinal hernia	rt herniotomy	9	25	120	90	50	130	127	124	120	114																						
4	277111	Muttu	48	M	Lt hydrocoele	lt herniotomy with circumscion	13	30	90	80	50	90	90	90	88	92	89																						
5	1276	Manjunath	36	M	Rt hydrocole	rt herniotomy	10	35	80	76	45	82	78	66	58	73	77	80																				
6	29937	Vikas	12	M	Lt hernia	Lt herniotomy	8	30	100	94	54	102	104	110	102	100	102																					
7	640	Ramesh	25	M	Lt hernia	lt herniotomy	9	45	110	86	50	114	114	106	114	106	106	104	102	101																		
8	17807	Buvan	12	M	Rt hernia	rt herniotomy	7	60	130	80	50	126	124	119	113	110	110	110	110	109	110	107	106															
9	30980	Yallappa	48	M	Rt hydrocoele	rt herniotomy	10	30	100	80	40	92	93	88	92	95	95																					
10	4272	Praveen	48	M	Lt hydrocoele	lt herniotomy	15	35	86	80	50	80	85	84	85	81	81	82																				
11	5360	Basavaraj	37	M	Mid penile hypospadiasis	repair	9	160	112	70	60	105	113	110	104	105	104	104	104	101	98	97	92	92	92	92	91	90	90	88	88	87	90	88	92	83	82	85
12	7325	Subhramanya	16	M	B/l UDT	B/l orchidopexy	9	60	100	80	50	104	108	109	107	108	108	106	108	108	107	110	108															
13	7512	Ragavendra	24	M	Distal penile hypospadiasis	repair	10	130	90	90	60	97	94	92	90	87	84	84	81	83	84	87	88	90	88	94	86	85	90	90	94	95	87	85	76	78	80	
14	7600	Nishant	60	M	Rt hernia	rt herniotomy	14	35	100	90	60	97	94	92	90	87	88	85																				
15	5755	Maruti	36	M	Rt hernia	rt herniotomy	9	40	90	84	60	100	110	112	114	108	107	108	110																			
16	115437	Shreyas	36	M	Rt hernia	rt herniotomy	8	25	100	84	50	102	92	95	92	92																						
17	19885	Prajwal	48	M	Rt hernia	rt herniotomy	12	30	110	70	40	108	110	112	106	106	105																					
18	6770	Mahantesh	60	M	Post op hypospadiasis fistula	fistula repair	10	80	100	84	40	100	104	105	102	100	100	100	101	104	110	102	110	112	108	103	103										
19	12087	sangeeta	5	F	Low ARM	Anoplasty	5	30	130	70	60	128	128	130	132	132	134																				
20	23585	Sangappa	24	M	Lt hydrocoele	lt herniotomy	7.5	30	106	80	50	106	102	112	114	108	105																					
21	2160	Kumaresh	18	M	Rt hernia	rt herniotomy	10	20	110	86	50	128	126	126	124																						
22	32518	Mohan	36	M	Lt tibia varus with ext fixator	lt osteotomy	9	45	110	90	60	140	140	138	120	120	120	120	126	136																		
23	8020	Manjunath	60	M	Rt hernia	Rt herniotomy	16	25	127	108	60	130	109	100	94	92																						
24	14207	Virupakshappa	48	M	Lt hydrocoele	lt herniotomy	13	30	110	100	60	116	113	111	98	89	90																					
25	8676	Mahantesh	53	M	Rt hernia	rt herniotomy	14	30	90	100	60	86	90	89	87	88	88																					
26	8878	sashi	60	M	Rt hernia	rt herniotomy	13	30	100	110	55	99	99	100	100	100	99																					
27	9042	shiva kumar	24	M	Lt hydrocoele	lt herniotomy	9	35	103	82	50	106	102	108	114	108	105	100																				
28	10134	uday kumar	30	M	Lt hernia	lt herniotomy	10	30	90	85	62	100	110	112	114	110	108																					
29	10689	shekar	48	M	Rt hydrocoele	rt herniotomy	14	30	108	100	56	116	113	111	195	90	93																					
30	10284	venkatesh	40	M	Rt hernia	rt herniotomy	14	30	108	90	60	112	110	107	111	96	100																					

					Intraoperative systolic blood pressure																																Intraoperative Diast															
140 min	145 min	150 min	155 min	160 min	5 min	10 min	15 min	20 min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min	65 min	70 min	75 min	80 min	85 min	90 min	95 min	100 min	105 min	110 min	115 min	120 min	125 min	130 min	135 min	140 min	145 min	150 min	155 min	160 min	5 min	10 min	15 min	20 min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min	65 min	70 min	75 min	80 min
					90	90	100	100	100	100	98	90	99	99	99	99	98	98	99	99	98	98	100	100													60	68	60	66	70	70	70	70	74	70	78	60	60	60	60	67
					112	100	105	93	104	90	84	87	83	81	81	84	88	91	85	91	85	87	97	91	86	84											70	60	63	56	55	55	54	50	49	46	48	52	53	56	57	56
					97	92	89	83	78																												53	49	45	42	32											
					80	88	80	80	88	86																											40	40	46	40	48	50										
					70	83	91	88	85	86	88																										40	37	44	41	40	39	55									
					90	88	90	90	86	86																											45	40	50	50	54	54										
					89	84	83	83	80	80	84	83	80																								49	44	41	42	42	40	44	45	43							
					80	78	78	82	76	76	78	82	82	80	76	78																					50	40	45	40	36	38	38	40	42	40	38	40				
					87	84	86	88	91	96																											43	41	46	44	46	56										
					91	93	86	81	83	80	74																										56	60	45	40	51	45	43									
87	88	89	84	83	80	82	78	77	76	72	69	70	78	73	73	75	75	74	78	77	77	78	79	86	82	81	81	78	76	76	74	75	81	77	75	82	40	44	43	44	44	38	37	34	37	34	38	39	40	44	43	42
					82	88	82	84	88	80	84	80	76	78	80	88																					45	40	45	40	40	53	54	40	38	34	40	38				
					83	85	85	86	84	83	82	84	81	87	85	86	84	90	94	90	92	90	95	88	90	94	95	90	88	90							41	45	38	39	42	39	38	38	39	45	54	40	40	40	44	38
					85	86	84	84	81	88	92																										43	39	40	38	39	38	53									
					76	70	74	77	77	78	80	78																									50	40	40	38	34	45	40	36								
					85	83	81	82	84																												54	48	42	48	52											
					73	78	81	85	80	80																											47	54	40	54	40	40										
					86	84	84	80	82	86	83	80	81	82	89	84	87	90	92	92	93	89															42	43	42	45	45	50	45	43	42	47	55	38	46	45	46	40
					78	70	72	70	72	72																											60	60	55	55	50	50										
					80	80	88	90	84	80																											42	45	43	50	35	40										
					80	88	90	87																													45	38	52	50												
					100	100	90	88	88	88	90	88	90																								60	60	50	30	35	30	40	43	40							
					101	100	101	102	102																												48	45	45	48	49											
					106	97	95	98	93	92																											58	52	46	44	43	42										
					88	90	86	81	80	92																											46	45	38	33	35	43										
					110	102	95	96	98	94																											55	46	42	42	46	42										
					76	78	80	83	83	80	82																										42	40	43	50	35	40	46									
					80	80	78	77	77	78																											40	42	43	38	34	45										
					106	97	94	98	93	92																											58	52	46	44	43	42										
					94	88	90	94	98	102																											48	46	45	45	61	55										

tolic blood pressure																Intraoperative SPO2																															
85 min	90 min	95 min	100 min	105 min	110 min	115 min	120 min	125 min	130 min	135 min	140 min	145 min	150 min	155 min	160 min	5 min	10 min	15 min	20 min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min	65 min	70 min	75 min	80 min	85 min	90 min	95 min	100 min	105 min	110 min	115 min	120 min	125 min	130 min	135 min	140 min	145 min	150 min	155 min	160 min
66	60	60	60													100	100	100	100	100	100	100	100	99	100	100	100	100	100	100	100	100	100	100	100												
59	59	54	54	52	53											100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100										
																100	100	99	100	100																											
																100	100	100	100	100	100																										
																100	100	100	100	100	100	100																									
																100	100	100	100	100	100																										
																100	100	100	100	100	100	100	100	100																							
																100	100	100	100	100	100	100	100	100	100	100	100																				
																100	100	99	100	100	100																										
																100	100	100	100	100	100	100																									
39	41	44	51	57	46	43	48	41	40	34	40	43	41	44	43	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
																100	100	100	100	100	100	100	100	100	100	100	100																				
40	47	50	40	38	45	44	38	45	44							100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100						
																100	100	100	100	100	100	100																									
																100	100	100	99	100	100	100	100																								
																100	100	100	100	100																											
																100	100	100	100	100	100																										
42	50															100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100																
																100	100	100	98	100	100																										
																100	100	100	100	100	100																										
																100	100	100	100																												
																100	100	100	100	100	100	100	100	100																							
																100	100	100	100	100																											
																100	100	100	100	100	100																										
																100	100	100	100	100	100																										
																100	100	100	100	100	100																										
																100	100	100	100	100	100	100																									
																100	100	100	100	100	100																										
																100	100	100	100	100	100																										
																100	100	100	100	100	100																										

DEXMEDETOMIDINE 1µg/ Kg GROUP A MASTER CHART

Sl no	Ip / OP no	Name	Age (Months)	Sex	Diagnosis	Surgery	weight (kgs)	Duration of surgery(min)	Baseline			Intraoperative heart rate																														
									HR	SBP	DBP	5 min	10 min	15 min	20 min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min	65 min	70 min	75 min	80 min	85 min	90 min	95 min	100 min	105 min	110 min	115 min	120 min	125 min	130 min	135 min	140 min	145 min
1	260036	Prajwal	36	M	Mid penile hypospadiasis	repair	11	150	94	100	54	90	84	80	81	76	77	78	72	72	72	70	71	72	68	58	75	80	84	86	88	82	88	87	86	84	82	86	84	85
2	155914	Arun	42	M	Mid penile hypospadiasis	repair	19	150	80	100	60	82	84	89	92	90	87	76	84	96	98	101	102	100	94	90	90	92	94	96	98	98	96	99	100	98	97	94	92	88
3	27522	Salman	60	M	Rt hydrocoele with Lt hernia	Rt and Lt herniotomy	15	45	100	100	50	120	135	141	130	135	129	125	121	114																				
4	29077	Bhimesh	12	M	Rt hernia	Rt herniotomy	8.3	30	100	100	60	120	128	117	110	105	100																							
5	4707	Varun	24	M	Rt hydrocoele	Rt herniotomy	12	40	110	100	70	112	112	108	104	100	99	100	104																					
6	596	Jivan	48	M	Rt hydrocoele and hernia	Rt herniotomy	11	35	105	100	60	110	114	94	98	99	99	104																						
7	1617	Prakash	36	M	Osteomyelitis of Rt femur	cement bead removal	11	30	100	90	60	102	110	105	101	100	97																							
8	34971	shaiestabhanu	48	F	Rt hernia	Rt herniotomy	15	30	100	80	50	87	85	77	73	71	86																							
9	4856	Bagyashree	36	F	Rt hernia	Rt herniotomy	12	30	108	93	55	108	110	100	107	107	103																							
10	5775	Gurunath	36	M	Rt hernia	Rt herniotomy	11	35	90	90	60	104	100	98	102	104	102	103																						
11	4883	sanjay	9	M	B/L hernia	B/L herniotomy	6.6	40	110	78	50	117	126	123	123	121	119	126	127																					
12	5155	Bhageerati	36	F	Lt hernia	Lt herniotomy	12	35	110	90	60	112	110	107	111	96	97	103																						
13	53008	Moulasab	24	M	Rt hernia	Rt herniotomy	11	40	110	80	40	117	128	118	105	109	94	93	91																					
14	5540	Uday	18	M	Lt VUR	Diagnostic cystoscopy	7.8	20	110	80	46	120	118	115	119																									
15	5678	Karthik	10	M	Lt hernia	Lt herniotomy	7	35	120	70	40	123	121	118	120	125	117	112																						
16	120298	Siddaramesh	8	M	Lt hernia	Lt herniotomy	8.5	35	100	90	50	120	130	128	124	121	119	117																						
17	6780	Rajappa	16	M	Rt UDT	Rt orchidopexy	8	25	120	78	40	125	128	130	132	133																								
18	14075	Mastana	7	M	Rt hernia	Rt herniotomy	8	30	110	70	50	120	110	108	110	112	117																							
19	7004	Mallikarjun	24	M	Phimosis	Circumcision	10	25	110	90	60	114	110	114	110	114																								
20	243762	Harshith	18	M	Rt hernia	Rt herniotomy	6	30	100	80	50	108	110	108	103	100	99																							
21	24914	Maush	48	M	Rt hernia	Rt herniotomy	13	35	122	86	56	120	118	119	120	110	111	107																						
22	29058	Santosh	48	M	Rt hernia	Rt herniotomy	14	25	120	90	60	118	116	110	109	108																								
23	7873	Ravi	19	M	Lt hernia	Lt herniotomy	6	40	110	80	50	118	112	112	110	108	108	110	108																					
24	19547	Sunil	60	M	Rt hernia	Rt herniotomy	14	30	110	90	50	114	105	101	100	102	102																							
25	12891	Shrishail	18	M	B/L UDT	B/l orchidopexy	9	80	110	90	60	108	106	105	106	101	99	100	98	98	97	105	104	110	102	103	103	114										
26	13118	Veerabhadra	48	M	Lt hydrocoele	Lt herniotomy	10	30	100	80	54	103	109	106	110	105	98																							
27	8432	varsha	30	F	Rt hydrocoele	Rt herniotomy	13	30	90	80	53	92	91	90	90	92	92																							
28	10060	sanju	24	M	Rt hernia	Rt herniotomy	11	40	104	90	40	117	128	118	105	109	93	93	91																					
29	11422	naseer	24	M	Rt hydrocoele	Rt herniotomy	11	35	106	80	50	106	102	112	114	108	102	100																						
30	11691	karthik	34	M	Lt hydrocoele	Lt herniotomy	14	35	103	85	45	102	92	95	92	92	96	93																						

			Intraoperative systolic blood pressure																														Intraoperative Diastolic bl															
150 min	155 min	160 min	5 min	10 min	15 min	20 min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min	65 min	70 min	75 min	80 min	85 min	90 min	95 min	100 min	105 min	110 min	115 min	120 min	125 min	130 min	135 min	140 min	145 min	150 min	155 min	160 min	5 min	10 min	15 min	20 min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min	65 min	70 min	75 min	80 min	85 min
86			100	92	91	97	100	97	89	93	93	92	92	89	88	92	94	88	93	88	91	95	95	96	94	86	94	86	82	80	82	83				53	50	57	52	64	52	52	57	55	59	54	52	57	55	57	57	57
94			100	102	90	90	88	90	102	84	91	100	106	93	89	87	84	90	99	94	92	90	88	92	92	90	96	98	93	98	98	99				70	65	55	60	50	53	65	45	63	54	50	44	40	40	40	54	56
			106	104	108	107	102	98	94	95	93																									48	67	65	66	61	58	55	54	55								
			110	113	101	90	90	86																													60	62	64	60	60	48											
			90	92	90	93	92	92	88	93																											60	60	50	48	43	53	40	48									
			99	96	101	107	106	99	99																												64	63	68	72	71	63	61										
			90	88	92	94	94	98																													56	56	56	50	55	60											
			88	80	73	75	75	84																													44	36	40	40	38	40											
			92	88	84	92	91	91																													51	56	55	50	44	54											
			78	80	80	73	71	70	73																												40	40	45	38	36	40	45										
			83	87	88	80	78	83	83	83																											57	39	43	40	47	40	45	45									
			94	82	87	90	98	104	107																												48	46	47	51	61	66	70										
			90	89	91	84	85	84	82	83																											52	54	53	50	51	49	46	45									
			86	94	85	77																															46	51	40	38													
			77	71	74	75	70	72	74																												34	35	40	36	33	33	34										
			81	85	84	90	85	83	90																												39	46	49	50	48	46	46										
			78	83	92	85	87																														42	43	49	46	47												
			78	72	78	72	78	76																													40	43	45	40	40	42											
			74	81	78	78	80																														34	39	37	37	37												
			80	82	86	87	90	87																													45	43	45	45	40	43											
			80	74	78	85	90	88	80																												46	43	42	42	42	44	44										
			80	80	81	83	81																														40	40	40	45	31												
			82	78	78	80	82	90	92	88																											40	42	37	40	34	50	52	44									
			92	84	80	80	79	84																													51	38	40	38	40	47											
			92	100	108	99	103	104	97	92	92	94	93	98	101	100	101	100	100																	53	60	88	61	69	69	63	60	60	58	59	65	76	73	66	60	60
			100	100	93	98	98	95																													54	50	53	57	56	48											
			90	88	88	88	88	87																													40	45	40	40	42	43											
			90	89	91	84	85	84	82	83																											52	54	53	50	51	49	46	49									
			80	83	88	90	80	80	88																												42	40	43	50	40	40	46										
			85	83	81	83	84	99	85																												54	48	42	46	52	67	50										

lood pressure															Intraoperative SPO2																															
90 min	95 min	100 min	105 min	110 min	115 min	120 min	125 min	130 min	135 min	140 min	145 min	150 min	155 min	160 min	5 min	10 min	15 min	20 min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min	65 min	70 min	75 min	80 min	85 min	90 min	95 min	100 min	105 min	110 min	115 min	120 min	125 min	130 min	135 min	140 min	145 min	150 min	155 min	160 min
60	57	57	57	58	58	52	58	52	52	51	49	53			100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100		
56	60	60	45	60	60	56	67	56	54	40	54	60			100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100		
															100	100	100	100	100	100	100	100	100																							
															100	100	100	100	100	100																										
															100	100	100	100	100	98	100	100																								
															100	100	100	100	100	100	100																									
															100	100	100	100	100	100																										
															100	100	100	100	100	100																										
															100	100	100	100	100	100																										
															100	100	100	100	100	100	100																									
															100	100	100	100	100	100	100	100																								
															100	100	100	100	100	100	100																									
															100	100	100	99	100	100	100	100																								
															100	100	100	100																												
															100	100	100	100	100	100	100																									
															100	100	100	100	100	100	100																									
															100	100	100	100	100																											
															100	100	100	100	100	100																										
															100	100	100	100	100																											
															100	100	100	100	100	100																										
															100	100	100	100	100	100	100																									
															100	100	99	100	100																											
															100	100	100	100	100	100	100	100																								
															100	100	100	100	100	100																										
															100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100																
															100	100	100	100	99	100																										
															100	100	100	100	100	100																										
															100	100	100	100	100	100	100	100																								
															100	100	100	100	100	100	100																									
															100	100	100	100	100	100	100																									

Intraoperative complications		Number of doses of Bolus propofol	Duration of recovery (min)	Postoperative HR (min)																																									
Episodes of hypotension	Episodes of bradycardia			0 min	15 min	30 min	45 min	60 min	75 min	90 min	105 min	120 min	150 min	180 min	210 min	240 min	270 min	300 min	330 min	360 min	390 min	420 min	450 min	480 min	510 min	540 min	570 min	600 min	630 min	660 min	690 min	720 min	750 min	780 min	810 min	840 min	870 min	900 min	930 min	960 min	990 min	1020 min	1050 min	1080 min	1110 min
_	1	2	15	81	80	78	70	76	87	87	90	90	92	83	85	85	87	83	88	89	90	90	92	87	90	92	94	94	88	86	82	82	82	83	83	95	99	104	100	106	106	106			
_	1	3	10	89	88	90	92	92	92	90	90	96	99	100	90	90	90	94	96	96	99	99	100	100	90	90	92	92	92	94	96	99	90	99	101	100	100	100	100	100					
_	_	0	20	88	97	98	98	98	96	94	102	110	110	115	115	120	130	130	135	143	143	150	140	140	140	143	139	130	128	128	128	128	126	120	130	124	128	130	130	138	140	128	120	122	136
1	_	0	15	96	97	95	80	79	80	78	79	79	79	78	76	80	82	86	90	90	90	90	90	95	99	95	96	96	96	96	96	96	100	102	102	102	103	104	110	104	108	108	108	110	110
_	_	0	15	108	108	110	108	108	108	108	108	110	110	110	105	105	108	108	108	110	110	105	100	100	100	100	98	104	105	102	109	110	109	109	109	109	110	105	105	105	107	107	107	107	107
_	_	0	10	108	108	11	94	98	98	99	110	112	120	110	113	120	120	121	121	121	120	120	112	121	112	112	112	112	113	112	101	101	102	102	102	102	102	102	100	100	100	100	108	108	
_	_	0	15	118	108	102	103	100	94	98	110	110	98	98	98	98	98	100	100	98	94	94	94	94	90	90	90	90	98	98	98	98	98	95	98	98	98	94	94	93	90	91	98	90	90
1	_	0	10	96	95	100	100	102	94	88	84	100	100	98	98	85	78	85	98	85	85	85	90	90	90	90	90	90	90	92	89	85	84	88	89	94	91	90	88	87	82	85	85		
_	_	0	5	96	94	92	92	90	99	87	92	90	90	90	90	88	88	89	92	87	87	85	93	88	88	89	90	95	94	95	90	95	99	98	97	98	98	92	88	84	85	84	92	100	98
1	_	0	15	90	89	87	89	107	110	108	108	100	100	100	98	98	98	96	99	94	94	90	95	89	89	89	88	88	88	87	87	87	84	85	89	88	88	88	90	89	88	87	88	90	90
_	_	0	10	118	118	119	119	120	123	120	120	118	123	124	124	122	122	121	121	122	121	120	120	120	118	118	110	110	110	112	118	118	118	110	110	110	110	109	109	109	109	110	120	122	122
_	_	0	10	110	108	107	111	110	96	98	96	103	102	96	89	91	90	90	87	88	88	88	87	90	93	88	88	85	89	88	88	85	90	88	93	89	94	93	90	90	87	95	88	87	87
_	_	1	10	80	77	73	74	78	82	78	81	80	80	82	78	84	88	88	90	94	96	102	100	110	107	105	103	100	100	102	106	106	107	108	110	112	114	115	108	105	109	104	110	110	110
1	_	0	5	98	107	108	98	110	116	118	110	106	104	104	105	106	110	110	110	105	108	106	105	110	110	116	116	118	114	114	110	110	110	111	116	111	114	109	108	108	108	117			
_	_	0	10	128	126	126	130	131	134	138	132	140	130	128	128	120	120	118	120	120	128	119	120	120	121	124	123	122	121	121	120	120	122	122	129	120	118	115	121	121	124				
_	_	0	5	128	128	128	124	124	121	120	128	128	129	121	125	126	120	124	129	118	116	120	121	124	125	128	128	120	117	117	118	118	119	120	128	122	122	120	128	126	122	129			
_	_	0	10	118	120	119	110	110	110	110	112	112	120	124	120	120	121	123	120	121	121	120	118	110	120	121	120	123	120	121	118	116	118	114	114	110	110	110	108	108	108	110	110	114	115
_	_	1	5	118	120	121	122	120	121	118	118	115	115	114	114	120	120	123	123	122	121	122	130	134	128	120	125	118	124	127	127	124	112	118	118	120	115	113	110	118	116	116	114	115	117
_	_	0	10	110	108	114	110	114	112	110	110	110	111	112	112	110	119	109	119	110	110	115	110	110	103	103	110	116	116	117	113	120	115	118	110	111	112	112	112	112	112				
_	_	0	10	108	108	117	120	120	114	118	120	120	121	118	116	119	112	108	107	110	110	118	120	121	122	121	120	126	121	120	116	123	123	120	120	112	116	114	114	112	121	120			
1	_	0	10	118	116	103	98	95	90	88	106	88	90	94	99	100	100	100	95	88	88	87	86	84	80	89	94	94	94	88	88	85	84	88	88	88	90	90	89	90	100	105			
_	_	0	15	128	126	126	120	119	118	125	120	120	120	116	116	100	108	100	100	98	98	90	90	90	89	90	95	88	85	88	89	90	90	92	93	93	96	94	90	94	95	98	94	96	104
_	_	0	8	130	126	120	129	120	121	124	124	125	126	121	129	120	119	120	117	118	120	122	120	125	120	115	122	126	127	118	118	116	119	120	116	118	119	120	120	123					
_	_	0	10	128	112	105	101	100	103	108	98	90	90	93	92	88	90	98	98	88	87	88	86	89	90	92	94	88	85	87	88	86	89	89	88	88	87	78	87	88	90	100			
_	_	1	12	122	95	86	92	90	96	92	94	104	100	100	101	105	108	110	107	110	101	98	101	104	103	109	110	102	100	110	114	113	110	113	111	110	109	110	110	117	118				
_	_	2	15	104	100	98	90	90	96	88	78	87	88	89	86	85	89	90	92	92	92	90	90	90	88	90	96	96	96	95	95	99	96	90	90	90	89	90	97	105					
_	_	0	10	98	100	98	95	95	98	102	90	104	102	108	102	102	105	111	113	110	103	108	106	106	109	110	113	112	113	114	104	104	108	108	104	106	106	106	106	104	110	110	115	110	
_	_	0	10	115	112	110	108	105	100	98	97	97	100	100	104	105	103	100	110	103	100	102	101	101	100	103	103	105	106	109	110	114	110	110	115	109	105	118	110	100	111	116	117	114	110
_	_	1	5	93	89	90	88	87	87	85	89	89	89	84	87	84	80	89	90	93	88	88	84	85	87	90	93	98	90	92	94	93	93	93	97	99	94	94	95	91	90	94	93	88	
_	_	0	5	114	108	107	105	89	94	94	96	97	90	90	90	93	93	93	95	90	91	94	94	94	93	93	90	91	88	84	90	96	95	96	100	96	101	100	100	106	108				

					Postoperative systolic BP (mm of Hg)																																													
1140 min	**1170 min**	**1200 min**	**1230 min**	**1260 min**	**0 min**	**15 min**	**30 min**	**45 min**	**60 min**	**75 min**	**90 min**	**105 min**	**120 min**	**150 min**	**180 min**	**210 min**	**240 min**	**270 min**	**300 min**	**330 min**	**360 min**	**390 min**	**420 min**	**450 min**	**480 min**	**510 min**	**540 min**	**570 min**	**600 min**	**630 min**	**660 min**	**690 min**	**720 min**	**750 min**	**780 min**	**810 min**	**840 min**	**870 min**	**900 min**	**930 min**	**960 min**	**990 min**	**1020 min**	**1050 min**	**1080 min**	**1110 min**	**1140 min**	**1170 min**	**1200 min**	**1230 min**
					90	98	100	100	106	98	90	90	90	90	90	92	92	100	100	98	100	101	101	99	105	105	103	103	101	102	102	103	104	101	100	100	100	100	100	100	102	105	105							
					80	80	85	90	90	90	90	100	100	100	90	90	90	94	94	94	95	99	99	95	100	99	101	102	104	100	100	99	100	99	99	99	95	93	93	93	93									
134	130	140			110	106	100	100	100	110	106	107	110	110	107	106	107	110	100	98	95	93	93	92	95	92	92	100	100	106	105	103	100	100	100	100	102	103	103	103	102	107	106	106	107	108	108	108	106	
110					75	68	68	70	72	70	70	70	70	70	70	70	78	78	69	79	79	70	70	72	75	74	74	73	75	75	76	74	76	73	73	73	74	72	72	75	76	76	75	75	75	74	76			
110					80	80	80	78	78	75	75	75	75	78	78	78	80	80	80	80	81	80	82	83	86	85	85	84	85	90	93	92	92	92	92	90	93	93	93	92	93	92	90	93	94	94	99			
					80	82	80	81	80	78	84	84	82	83	85	85	80	80	80	82	83	79	80	82	80	80	80	78	80	82	83	82	79	78	77	77	76	76	75	75	78	78	80	85	85					
90	93	93	100		98	94	89	84	91	88	94	94	94	88	88	87	85	85	87	80	81	81	80	77	80	78	79	86	80	80	81	83	86	88	87	85	85	85	86	84	88	88	80	83	82	85	80	80	90	90
					100	101	98	90	98	98	90	90	94	98	98	100	99	99	97	90	93	91	88	87	89	88	87	86	86	84	83	88	88	88	88	87	88	90	88	90	90	88	88	96						
					90	88	90	90	90	88	88	85	90	89	90	90	89	89	90	88	89	86	88	87	88	88	88	89	88	83	86	85	85	84	84	83	84	84	85	85	84	84	85	87	87	88				
90					90	98	94	100	105	108	108	104	100	100	100	100	98	90	90	92	91	89	90	89	94	96	98	98	98	98	101	100	98	98	98	98	100	100	100	100	100	102	103	105	106	107	108			
121					80	80	82	82	80	80	80	82	82	80	80	80	80	80	80	80	86	84	81	89	81	80	80	80	78	78	78	78	78	78	78	80	80	82	82	78	78	80	78	78	78	80	84			
89	92				103	93	98	94	100	96	94	94	94	90	90	98	98	98	97	95	96	93	93	96	98	95	88	88	88	80	79	78	78	78	78	80	80	83	83	84	84	80	80	80	84	84	85	85		
112					82	82	75	74	74	73	83	80	80	78	70	74	78	78	80	84	85	93	92	93	92	92	88	88	88	87	89	88	88	86	87	82	88	87	80	78	78	78	78	78	80	81	85			
					107	95	91	91	99	98	90	92	90	88	88	86	80	78	78	78	79	76	78	82	80	76	77	78	78	82	81	78	79	80	77	78	73	73	77	77	77	78	80							
					76	76	84	85	85	105	106	100	90	88	100	104	100	100	96	95	91	87	80	77	78	80	79	78	76	77	77	78	80	78	80	83	82	80	80	82	82	82								
					81	85	84	90	85	83	83	83	80	82	82	83	83	80	85	88	81	82	80	79	74	82	83	83	78	80	83	80	80	79	79	78	77	77	78	77	78	82	86							
					80	80	78	78	78	78	73	74	72	74	74	72	74	74	75	74	75	77	74	75	74	73	75	74	71	74	74	77	78	77	77	74	74	74	73	73	73	75	76	76	73	73				
					78	73	70	72	72	70	72	72	72	72	74	74	74	74	75	74	76	74	73	75	80	74	75	74	77	75	73	72	73	74	74	74	74	74	74	76	76	76	80	78	80	82				
					73	72	74	78	78	77	77	76	78	80	80	80	78	81	72	74	75	75	81	80	84	80	79	78	79	83	83	83	85	78	80	80	88	88	84	86	88	88								
					78	73	75	74	80	80	80	82	84	80	83	80	80	78	80	80	82	80	80	80	83	78	77	76	79	78	79	80	83	81	80	80	78	78	80	84	84	84	90							
					80	85	85	85	80	85	81	80	80	85	86	80	80	80	85	86	85	81	80	80	80	80	80	80	80	80	83	84	88	88	88	90	84	88	90	90	90	98	98							
					80	82	80	80	78	79	80	80	76	76	78	82	82	80	80	82	81	79	79	80	83	81	90	88	87	84	85	87	88	90	94	88	93	90	94	94	90	90	96	98	98	102				
					74	78	72	74	70	75	74	75	73	70	72	74	74	75	75	74	76	73	75	74	74	72	75	78	78	77	77	78	75	76	78	78	80	80	87	88	88									
					88	85	96	90	90	102	94	92	100	100	103	106	106	100	100	100	108	102	100	98	102	98	97	96	95	95	87	88	85	99	99	98	100	101	100	98	100	102	104							
					94	95	90	85	89	89	80	76	74	74	78	78	75	75	80	80	81	80	80	80	84	85	80	80	82	80	81	79	78	78	80	80	80	80	86	87	87	88								
					100	90	94	98	98	95	92	90	93	90	90	90	92	94	94	94	96	96	95	96	98	90	90	96	98	104	101	98	94	100	105	103	104	102	104	104	108									
					100	100	96	96	90	90	90	91	88	92	94	90	90	88	88	88	81	79	81	79	80	80	80	80	81	79	79	80	77	78	80	82	82	87	89	88	87	88	88	90	90					
116					94	84	80	85	80	80	80	82	80	80	84	90	85	83	84	80	81	78	79	79	80	78	88	87	81	81	79	80	80	79	77	78	82	80	83	83	80	83	80	88	87	88	88			
					100	96	94	93	88	84	86	88	87	89	90	90	90	88	90	93	93	88	91	91	91	93	98	99	98	96	97	98	98	100	99	103	100	104	104	100	102	101	100	103	106					
					110	94	93	93	90	88	88	87	90	90	93	90	91	92	95	95	99	97	96	89	96	92	98	97	96	95	97	98	100	101	100	100	103	102	101	104	104	106								

	ve Diastolic BP																																																	
1260 min	0 min	15 min	30 min	45 min	60 min	75 min	90 min	105 min	120 min	150 min	180 min	210 min	240 min	270 min	300 min	330 min	360 min	390 min	420 min	450 min	480 min	510 min	540 min	570 min	600 min	630 min	660 min	690 min	720 min	750 min	780 min	810 min	840 min	870 min	900 min	930 min	960 min	990 min	1020 min	1050 min	1080 min	1110 min	1140 min	1170 min	1200 min	1230 min	1260 min	0 min	15 min	30 min
	60	60	60	62	65	60	60	50	50	40	40	40	60	60	62	60	62	55	55	50	55	55	60	60	60	55	60	60	62	61	56	57	54	60	60	58	62	54	54									100	100	100
	40	40	40	50	55	54	52	60	60	60	50	50	60	60	60	60	60	60	50	50	56	50	60	60	60	60	58	59	60	57	56	53	56	60	60	60	62											100	100	100
	60	60	50	50	52	50	50	55	60	56	58	60	60	58	56	56	56	58	60	60	60	58	56	57	56	56	56	59	60	63	62	63	60	66	58	60	62	56	60	60	50	50	50	60	60			100	100	100
	31	44	35	45	44	40	45	45	40	40	40	43	45	45	40	40	40	40	40	40	40	43	40	40	40	38	40	41	40	48	47	48	48	49	50	46	48	44	45	43	45	45	45					100	100	100
	50	50	50	50	46	45	45	45	50	50	50	50	40	40	40	40	40	43	43	45	45	45	40	40	45	54	54	54	54	57	56	56	54	56	55	56	52	50	50	48	46	46	46					100	100	100
	50	50	52	50	50	50	50	60	60	60	60	60	60	60	38	53	56	56	56	50	50	49	50	50	50	52	52	56	50	58	57	58	60	50	46	56	54	52	52	54	54							100	100	100
	55	61	53	53	50	52	71	73	70	50	50	48	40	43	45	40	40	45	45	54	54	54	54	54	45	45	44	48	47	48	45	50	45	48	46	47	46	43	43	54	56	45	40	39	40	40		100	100	100
	50	60	45	45	44	44	50	53	54	48	48	60	45	40	43	40	45	44	44	50	55	54	53	53	45	50	54	41	49	51	50	51	50	46	42	45	48	40	50	50								100	100	100
	45	45	50	50	48	43	43	45	50	45	50	50	45	44	56	45	50	44	40	45	40	45	43	44	46	45	48	49	49	55	52	53	48	53	46	47	46	40	50	44	42	48						100	100	100
	45	45	56	60	63	60	60	56	60	60	60	60	56	50	66	45	40	45	43	45	54	50	60	60	60	66	60	61	60	69	72	73	64	69	67	64	66	60	60	55	55	58	58					100	100	100
	45	48	43	36	36	36	38	34	45	42	42	42	45	45	43	44	38	39	38	40	40	40	39	40	45	40	45	41	40	43	42	48	46	48	45	45	46	40	40	40	40	35	43					100	100	100
	61	57	62	61	60	59	60	56	62	45	54	54	55	55	56	45	45	45	40	56	50	56	45	45	40	45	46	44	47	43	42	49	47	48	40	46	46	45	40	43	43	45	45	50				100	100	100
	50	50	48	44	44	42	51	45	46	45	40	45	45	50	45	40	40	60	60	60	45	40	40	40	40	40	40	41	47	48	47	57	55	53	50	50	50	44	30	45	45	40	50					100	100	100
	66	54	62	62	57	65	56	45	46	40	40	45	45	40	40	40	50	40	38	40	43	40	43	43	40	40	40	41	42	48	44	48	45	43	47	47	44	45	50									100	100	100
	30	35	38	50	50	42	40	40	40	40	45	46	45	40	39	45	40	45	39	39	40	45	40	40	40	40	45	46	42	46	47	48	44	46	40	45	54	43										100	100	100
	39	45	49	50	48	46	43	44	40	40	45	43	45	45	45	40	45	43	44	45	45	45	40	40	45	43	40	43	42	45	42	43	44	43	42	44	48	44	52									100	100	100
	40	48	40	40	40	40	43	40	40	40	40	40	38	45	44	44	40	43	40	40	40	40	43	43	45	43	42	46	40	43	42	48	45	48	46	47	44	40	38	38	40	44						100	100	100
	40	40	40	40	40	40	43	42	42	42	44	40	42	43	40	42	43	40	43	38	40	40	40	40	44	45	45	40	40	43	42	43	44	43	44	45	45	41	40	40	40	40						100	100	100
	45	37	34	39	38	45	40	45	45	40	36	36	37	39	40	40	40	40	38	40	45	40	40	40	45	48	44	47	46	42	42	43	44	42	44	44	44	40										100	100	100
	40	39	45	44	40	40	40	40	40	38	43	48	38	40	40	40	40	41	39	38	40	38	38	40	40	43	38	43	43	45	44	47	45	47	42	44	45	40	46									100	100	100
	40	40	40	43	43	43	41	38	40	45	40	40	40	42	41	43	39	42	42	39	45	43	40	40	34	40	40	44	47	46	45	43	46	48	44	44	44	40	45									100	100	100
	43	44	40	43	45	40	42	41	34	38	31	45	45	40	40	38	38	40	40	48	45	31	30	38	42	42	43	43	50	43	46	46	43	43	44	44	42	40	40	43	40	40						100	100	100
	40	40	42	39	35	38	35	35	43	40	38	37	38	35	35	36	45	43	42	34	31	38	40	40	45	43	40	44	44	43	42	46	40	43	35	42	42											100	100	100
	57	54	45	70	70	62	45	40	61	60	50	56	50	60	60	60	48	49	50	40	40	45	53	50	54	45	46	41	39	43	47	47	54	59	47	47	58	55	56									100	100	100
	45	45	43	43	54	52	40	39	31	36	45	43	38	38	40	42	42	41	42	43	43	43	50	50	44	44	43	43	43	46	43	43	44	43	45	47	45	50										100	100	100
	50	54	54	57	54	48	42	40	43	43	44	45	39	45	46	45	43	45	44	45	43	50	50	50	45	45	50	55	55	46	68	63	56	63	54	55	60											100	100	100
	40	46	45	40	40	40	40	40	43	43	43	40	42	45	39	45	40	43	42	40	43	45	34	35	41	38	40	40	46	42	42	43	44	43	42	44	46	36	35	46	46							100	100	100
	52	31	34	35	40	40	43	45	45	40	43	43	45	43	38	40	42	42	45	45	45	40	38	38	40	43	40	44	42	40	41	48	44	47	42	42	46	43	40	45	50	54	54					100	100	100
	40	35	45	37	44	54	44	45	45	45	40	44	38	43	45	43	42	39	38	39	40	40	39	40	43	40	40	40	44	43	42	56	53	57	48	44	46	45	52	50	60							100	100	100
	60	45	45	46	44	39	38	45	40	46	45	50	45	45	45	46	45	50	54	45	45	46	56	55	45	45	46	50	50	48	50	48	60	60	54	48	56	60										100	100	100

Postoperative SPO2																																												Pain scores						
45 min	60 min	75 min	90 min	105 min	120 min	150 min	180 min	210 min	240 min	270 min	300 min	330 min	360 min	390 min	420 min	450 min	480 min	510 min	540 min	570 min	600 min	630 min	660 min	690 min	720 min	750 min	780 min	810 min	840 min	870 min	900 min	930 min	960 min	990 min	1020 min	1050 min	1080 min	1110 min	1140 min	1170 min	1200 min	1230 min	1260 min	0 min	15 min	30 min	45 min	60 min	75 min	90 min
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100									0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100											0	1	1	1	2	0	1
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100			0	2	2	3	2	1	0
99	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	0	0	0	0
100	100	100	99	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100							0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	99	100	100	100	100	100	100	100		0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100								0	0	0	0	0	0	0
100	100	100	100	100	100	100	98	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100						0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	99	100	100	100	100	100	100	100	100	100				0	0	0	0	1	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100									0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100										0	0	0	1	0	0	0
100	100	100	100	100	100	100	99	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100									0	1	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100						0	0	0	0	0	0	0
99	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100						0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100										0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100									0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100									2	2	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100						0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100											0	0	0	0	0	0	0
100	100	100	100	99	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100									1	0	1	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100										1	1	0	0	0	0	0
100	100	100	100	100	100	100	100	99	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100											0	0	0	0	0	0	1
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100							0	1	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	99	100	100	100	100					1	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100							0	0	0	1	1	1	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100										0	0	0	0	0	0	1

105 min	120 min	150 min	180 min	210 min	240 min	270 min	300 min	330 min	360 min	390 min	420 min	450 min	480 min	510 min	540 min	570 min	600 min	630 min	660 min	690 min	720 min	750 min	780 min	810 min	840 min	870 min	900 min	930 min	960 min	990 min	1020 min	1050 min	1080 min	1110 min	1140 min	1170 min	1200 min	1230 min	1260 min	Duration of analgesia (min)	Adverse effects
0	0	1	0	1	1	1	1	0	1	1	1	1	1	0	0	1	1	1	0	1	1	1	1	1	2	1	1	2	2	2	4									1170	_
1	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1	0	1	1	0	0	0	0	0	1	4											1110	_
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	0	0	1	1	1	1	1	0	0	0	0	1	1	2	2	2	4			1245	_
0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	2	0	0	0	0	0	0	0	1	1	0	1	0	1	1	2	2	4					1170	Hypotension
2	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	3	3	4					1210	_
0	0	2	0	3	2	0	0	0	0	0	1	1	2	2	0	0	0	0	1	1	0	0	0	1	1	1	2	0	2	2	3	4								1085	_
2	0	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	4			1260	_
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	3	4									1050	vomiting
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	2	2	2	2	3	4						1140	vomiting
0	0	1	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	2	2	4					1175	vomiting
0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	1	1	1	2	3	4					1180	_
0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	1	2	2	4				1200	_
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	2	0	0	1	0	2	2	4					1180	_
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	1	1	1	1	2	2	3	4									1040	_
0	0	3	0	0	0	0	0	2	0	1	0	0		0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	2	3	4									1025	vomiting
0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	1	2	4									1055	_
0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	2	2	0	0	0	0	0	0	0	0	0	1	1	1	0	1	2	3	4						1140	vomiting
1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0	1	1	1	2	3	3	4						1140	_
0	0	0	0	0	0	0	0	1	0	1	0	2	0	0	0	0	0	0	0	0	0	0	1	2	1	1	1	1	2	2	3	4								1015	Hypotension
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	1	1	1	1	2	2	3	4									1050	_
0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	2	4								1055	_
0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2	0	0	0	0	0	0	0	0	1	1	1	2	2	3	4						1135	vomiting
0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	2	4										1000	Hypotension
0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	4								1050	_
0	0	0	0	0	0	2	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	4										1070	_
0	1	1	0	0	0	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	1	2	4											990	_
0	0	0	0	0	0	1	0	1	1	0	0	0	0	0	0	2	0	0	1	1	0	0	0	0	0	0	0	1	0	1	1	2	4							1110	_
0	0	0	0	0	1	0	0	0	0	2	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	1	2	2	3	4					1180	_
0	0	0	0	0	0	0	0	0	0	1	2	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	3	4							1085	_
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	1	2	2	3	4									1025	_

Intraoperative complications		Number of doses of Bolus propofol	Duration of recovery (min)	Postoperative HR (min)																																				
Episodes of hypotension	Episodes of bradycardia			0 min	15 min	30 min	45 min	60 min	75 min	90 min	105 min	120 min	150 min	180 min	210 min	240 min	270 min	300 min	330 min	360 min	390 min	420 min	450 min	480 min	510 min	540 min	570 min	600 min	630 min	660 min	690 min	720 min	750 min	780 min	810 min	840 min	870 min	900 min	930 min
_	_	3	10	84	84	78	79	80	98	98	98	98	114	120	122	149	117	120	120	120	110	114	115	120	120	122	123	120	122	123	120	120	124	120	121				
_	_	1	15	74	72	88	86	86	86	80	86	88	90	90	92	92	94	90	94	94	95	94	92	90	95	96	99	100	101	104	105	100							
_	_	0	5	108	107	108	100	98	98	96	99	96	96	90	98	100	104	104	100	96	98	98	99	103	104	106	105	110	112	112	112	112	112	114	116	115	115	118	119
_	_	0	15	84	83	82	82	83	85	85	85	90	88	85	88	87	90	92	88	84	84	89	89	89	89	87	90	90	92	92	92	92	94	94	94	94	92	95	
_	1	0	10	88	92	85	90	90	96	110	120	118	119	120	122	122	121	121	121	120	118	121	121	120	120	125	124	123	125	120	120	118	116	120	120				
_	_	0	10	105	105	110	100	98	100	104	104	106	98	105	110	110	110	110	108	108	105	106	106	106	106	106	110	110	110	111	112	110	112	112	113	112	113		
_	_	0	15	130	131	127	110	100	98	95	99	100	110	115	115	116	116	120	120	121	116	120	121	121	121	121	120	118	118	118	123	123	124	125	122	122			
_	_	0	10	110	111	112	110	112	110	110	108	108	108	106	105	110	115	118	112	111	112	112	112	121	120	120	120	120	114	118	120	123	123	121	121	121	123		
_	_	2	10	84	84	81	81	82	81	82	103	98	102	102	100	100	110	106	110	108	108	108	108	110	110	113	112	110	102	102	111	110	110	108	111	114	116		
1	_	0	15	83	80	76	80	83	83	82	84	90	92	88	88	87	87	87	87	87	90	90	93	93	92	91	90	93	95	90	88	90	90	94	94	93	94	94	96
1	_	0	15	114	112	110	96	81	77	79	84	84	86	86	86	88	89	90	88	84	84	84	85	88	89	90	93	88	90	90	90								
_	_	0	10	112	110	108	104	100	98	99	89	100	100	101	104	104	104	104	106	106	106	105	100	101	102	103	101	100	107	107	108	108	106	106	109	110	110		
1	_	0	15	83	80	76	80	83	83	82	84	90	92	88	88	87	87	87	87	87	90	90	93	93	92	91	90	93	95	90	88	90	90	94	94	93	94	94	96
_	_	0	10	112	110	108	104	100	98	99	89	100	100	101	104	104	104	104	106	106	106	105	100	101	102	103	101	100	107	107	108	108	106	106	109	110	110		
_	_	0	5	94	98	106	110	103	104	109	110	110	110	108	106	108	108	108	107	106	110	110	111	110	110	105	114	108	109	110	114	114							
_	_	0	5	85	85	84	86	98	108	110	100	100	100	100	98	101	101	105	107	103	100	100	102	102	101	101	101	101	104	105	103	104	104	100	102	104	105	108	
1	_	0	5	103	101	88	94	93	95	89	100	98	98	94	93	93	90	88	94	90	90	90	90	93	93	95	93	95	94	94	94	93	93	94	96	96			
_	_	0	18	85	83	80	80	78	76	72	80	82	90	96	88	90	93	93	93	91	94	94	96	96	99	99	100	98	98	101	101	105	105	104	104	102	101		
_	_	0	12	94	92	88	88	84	89	90	85	86	90	91	91	91	94	92	93	95	92	90	90	93	93	93	95	95	93	90	90	88	87	90	93	93	95	95	
_	_	0	5	102	101	98	103	100	98	95	99	100	101	98	98	93	90	88	93	93	94	96	96	99	90	90	88	90	93	94	94	95	96						
_	_	0	10	134	131	131	131	132	131	134	132	129	128	140	142	140	138	134	132	140	132	133	131	132	135	136	133	134	132	131	131	132	133	135	136	137			
_	_	1	5	106	103	98	100	102	100	100	98	101	98	105	105	107	110	110	110	110	110	107	108	108	108	109	108	110	111	110	110	106	103	108	110	112	112		
_	_	0	5	122	122	123	124	120	120	120	118	120	120	121	120	120	122	122	122	121	121	123	122	120	120	119	117	120	121	123	120	121	119	121	120	122			
_	_	0	5	132	122	128	133	130	125	124	123	120	120	118	115	118	118	120	120	120	117	115	117	120	110	110	111	111	113	115	115	118	120	124	126	126			
_	_	0	8	134	110	100	97	96	96	97	98	99	100	101	98	94	98	94	94	95	94	94	96	100	100	101	103	101	100	100	98	99	98	100	100	103	106		
_	_	0	5	92	89	86	82	84	83	82	83	84	85	88	88	89	88	87	84	88	84	88	90	90	94	94	94	90	95	90	93	93	93	90	94	94	98	97	96
_	_	0	10	97	95	94	93	93	90	91	91	92	93	90	88	84	84	83	89	90	92	90	88	93	95	95	95	95	97	97	100	100	101	102	102	106			
_	_	1	12	93	93	94	93	93	92	93	90	92	92	92	95	95	98	94	92	94	94	96	91	93	91	91	90	88	90	93	93	96	90	92	90	92	94		
_	_	0	5	95	95	103	99	95	94	94	90	94	90	88	85	88	85	82	84	89	83	8	85	89	90	94	94	94	95	93	92	95	95	95	95	100			
_	_	0	5	111	105	98	94	93	95	94	94	94	94	92	93	92	93	90	93	95	100	98	94	94	96	95	97	97	96	95	97	98	98	99	100	98	100		
_	_	0	10	96	92	85	88	88	85	85	84	83	84	85	85	89	90	90	91	89	89	93	92	92	92	92	92	90	92	90	92	93	92	93	95	95			
_	_	0	10	115	108	110	105	105	105	105	103	105	106	106	108	105	105	107	107	110	110	110	109	110	111	110	105	105	105	108	108	106	108	112	110	112	118		

		Postoperative systolic BP (mm of Hg)																																				tive Diastolic BP (		
960 min	990 min	0 min	15 min	30 min	45 min	60 min	75 min	90 min	105 min	120 min	150 min	180 min	210 min	240 min	270 min	300 min	330 min	360 min	390 min	420 min	450 min	480 min	510 min	540 min	570 min	600 min	630 min	660 min	690 min	720 min	750 min	780 min	810 min	840 min	870 min	900 min	930 min	960 min	990 min	0 min	15 min	30 min
		98	98	99	99	98	98	100	100	100	100	112	114	110	100	100	98	92	92	95	93	95	97	91	88	87	87	96	95	100	94	93	95							60	60	60
		90	88	90	94	90	90	90	92	92	94	94	94	92	92	94	92	90	92	91	99	94	95	96	95	93	94	93	95	94										50	50	50
		70	68	76	75	75	82	84	85	85	85	85	86	90	90	90	90	92	92	91	92	90	90	91	91	91	92	91	87	90	90	91	90	91	90	91	93			46	39	46
		80	80	82	80	82	80	86	86	88	88	88	88	90	90	90	92	90	92	91	91	96	94	95	94	94	90	94	95	94	93	93	92	90	90	91				45	46	45
		81	81	82	88	88	99	98	96	98	106	100	102	104	105	100	100	100	102	101	99	100	99	101	100	100	100	101	98	97	98	101	100							40	30	40
		80	80	82	82	82	80	80	84	80	80	82	82	90	90	88	80	78	79	81	83	82	81	81	78	76	78	80	80	79	80	79	80	80	80					40	43	40
		95	95	93	95	95	88	80	84	82	84	87	87	86	88	88	84	87	90	91	93	90	88	90	90	92	90	87	90	92	94	93	92	92						41	41	41
		80	82	80	80	80	80	80	80	82	84	84	84	88	88	85	85	84	87	89	81	84	85	87	91	94	91	88	87	87	87	86	85	84	85					40	40	43
		96	90	88	88	88	87	89	88	87	88	82	80	80	81	82	82	82	90	83	83	80	79	80	80	79	79	78	80	82	76	83	85	84	85					44	40	45
100		80	84	88	90	93	90	90	90	100	100	100	100	100	101	100	100	103	105	101	101	101	100	98	98	96	97	99	101	94	93	87	86	97	100	101	91	93		30	37	40
		92	90	80	80	80	81	77	76	76	74	78	80	83	84	84	84	86	90	89	90	88	87	87	84	88	88	89	91											52	50	40
		88	90	90	90	92	90	90	91	92	95	90	88	88	85	84	83	82	84	83	82	80	80	80	80	81	80	80	81	84	85	85	82	81	82					45	45	46
		91	91	91	90	90	90	92	88	88	87	88	88	88	88	88	90	90	94	91	90	88	87	87	86	86	85	77	85	86										46	49	49
		90	85	80	81	84	84	83	85	82	80	80	88	90	90	90	90	92	95	93	92	93	93	91	91	91	90	90	90	88	87	88	90	91	90	91				45	47	40
		88	89	80	80	80	83	84	89	89	90	90	90	92	92	92	94	96	98	95	95	93	92	92	89	89	89	91	91	89	90	95	96	102						45	45	45
		82	81	83	82	80	83	83	84	89	84	86	86	88	88	88	87	90	92	91	91	90	90	91	90	91	90	93	91	92	91	88	88	87	86					47	46	45
		80	80	80	82	85	80	80	80	82	83	82	83	84	82	82	83	85	90	91	91	88	89	88	88	88	86	87	85	89	92	90	90	90	90	91				40	43	44
		88	90	93	102	95	90	90	93	93	90	94	90	90	90	90	92	92	94	95	95	93	93	95	96	98	87	87	87	98	99									45	40	45
		70	70	72	72	70	78	76	78	78	74	74	76	76	76	78	78	78	80	78	78	77	75	73	74	74	75	75	78	76	74	75	70	73						50	40	46
		90	88	85	85	84	84	82	82	80	80	80	79	80	82	82	80	82	84	81	83	81	81	83	82	85	83	83	83	82	84	93	90	81	84					60	45	40
		80	82	80	78	78	79	78	80	80	80	80	82	82	82	82	84	80	79	75	78	77	74	75	74	74	74	75	76	80	76	78	77	81						40	42	42
		84	84	80	80	82	82	80	85	84	84	86	85	85	85	88	88	88	92	93	96	93	90	93	95	94	95	95	95	95	96	97	98	102						46	45	45
		85	80	82	80	80	80	83	84	80	80	80	82	86	85	88	88	90	92	91	93	90	89	93	91	86	88	88	90	90	91	90	90	90	90					54	50	48
101		90	90	88	88	90	92	90	92	92	94	93	90	90	90	92	95	98	100	99	96	98	97	95	96	96	95	96	97	94	95	96	97	90	90	93	91	93		40	45	54
		90	90	94	95	88	85	90	94	95	92	90	94	92	92	96	92	100	102	96	95	90	92	91	92	92	95	95	96	95	95	96	92	91						50	54	44
		102	100	100	105	100	98	100	100	100	101	100	100	100	101	100	100	100	102	101	97	96	99	100	98	98	98	99	95	97	96	97	94	96	98					45	44	40
		90	90	95	92	90	88	92	90	90	92	96	96	96	96	96	101	102	103	101	101	98	100	97	100	98	98	98	95	96	100	97	98	99						50	54	55
		95	88	87	87	88	88	89	90	90	90	92	92	92	92	95	94	95	96	95	96	93	93	93	92	91	94	93	95	94	95	96	98	93	95					50	45	40
		90	88	88	87	86	85	86	86	86	84	83	84	84	84	85	85	85	90	91	91	90	89	89	88	88	90	91	93	90	91	90	88	91						40	45	42
		98	90	90	84	84	84	84	84	84	85	85	85	85	86	85	84	83	87	86	87	86	87	87	86	86	88	87	88	87	88	83	84	81	85					45	40	40

45 min	**60 min**	**75 min**	**90 min**	**105 min**	**120 min**	**150 min**	**180 min**	**210 min**	**240 min**	**270 min**	**300 min**	**330 min**	**360 min**	**390 min**	**420 min**	**450 min**	**480 min**	**510 min**	**540 min**	**570 min**	**600 min**	**630 min**	**660 min**	**690 min**	**720 min**	**750 min**	**780 min**	**810 min**	**840 min**	**870 min**	**900 min**	**930 min**	**960 min**	**990 min**	**0 min**	**15 min**	**30 min**	**45 min**	**60 min**	**75 min**	**90 min**	**105 min**
60	68	60	60	60	60	60	60	60	70	70	60	60	60	60	52	50	60	60	60	60	60	60	50	59	50	51	50	52							100	100	100	100	100	100	100	100
56	52	50	60	50	60	60	60	60	60	56	50	55	55	56	55	60	60	60	60	60	58	56	58	61	61										100	100	100	100	100	100	100	100
38	42	44	47	44	44	45	45	45	40	41	41	41	40	38	40	40	45	45	40	40	40	42	42	43	55	56	48	48	55	50	50	56			100	100	100	100	100	100	100	100
46	46	40	40	38	40	38	38	38	50	48	45	40	40	40	40	43	50	45	45	45	40	40	46	45	42	44	58	58	56	58	55				100	100	100	100	98	100	100	100
37	38	34	34	66	56	68	60	50	60	60	56	56	60	60	60	45	45	48	56	55	50	50	50	45	50	53	52	54							100	100	100	100	100	100	100	100
39	40	40	40	45	46	45	42	42	40	45	45	45	40	45	46	45	38	45	38	38	45	45	45	42	42	49	46	46	46	44					100	100	100	100	100	100	100	100
41	42	47	47	47	45	45	50	56	54	54	56	56	45	56	54	55	54	50	50	54	50	56	52	49	55	55	58	60	60						100	100	100	100	100	100	100	100
43	43	43	45	38	34	40	38	38	38	38	45	40	43	42	45	45	40	40	40	41	41	45	44	44	40	41	38	43	44	44					100	100	100	100	100	100	100	100
40	43	40	45	40	40	40	45	40	40	41	42	42	40	40	40	40	38	43	42	45	44	44	43	43	43	47	40	38	40	40					100	100	100	100	100	100	100	100
40	43	44	44	44	40	45	44	45	46	56	56	55	54	53	50	53	45	60	60	60	56	56	58	59	56	58	60	60	54	53	50	53	58		100	100	100	100	100	100	100	100
40	44	43	41	45	41	42	45	46	45	45	40	40	45	45	40	40	45	46	47	40	45	47	46	55											100	100	100	100	98	100	100	100
46	47	47	47	41	42	45	42	45	40	40	38	42	45	45	44	44	44	42	42	43	44	56	50	55	45	52	58	60	58	58					100	100	100	100	100	100	100	100
40	44	43	41	45	41	42	45	46	45	45	40	40	45	45	40	40	45	46	47	40	45	47	46	55											100	100	100	100	98	100	100	100
46	47	47	47	41	42	45	42	45	40	40	38	42	45	45	44	44	44	42	42	43	44	56	50	55	45	52	58	60	58	58					100	100	100	100	100	100	100	100
40	42	40	42	42	38	43	42	40	40	42	40	40	40	43	56	55	53	53	45	45	50	50	50	55	54										100	100	100	100	100	100	100	100
39	42	44	38	45	45	44	40	45	40	40	40	38	42	43	40	40	45	39	43	40	38	40	45	44	43	44	45	46	48	58	60				100	100	100	100	100	100	100	100
44	44	46	45	45	45	56	57	55	56	46	45	56	45	40	53	50	40	40	40	43	44	44	45	44	48	50	54	54	56						100	100	100	100	100	100	100	100
47	43	44	44	38	45	45	50	50	56	50	50	47	40	40	40	42	42	43	44	40	40	46	50	53	53	52	43	48	50	52					100	100	100	100	100	100	100	100
44	45	45	45	44	45	42	42	50	54	45	50	43	45	43	40	40	40	42	41	43	56	56	40	44	44	57	54	54	56	58	55				100	100	100	100	100	100	100	100
45	45	45	40	43	42	45	54	44	42	42	40	40	43	43	40	42	40	48	54	50	60	60	56	60	55	57									100	100	100	100	100	100	100	100
45	47	45	40	40	45	45	45	45	40	40	46	42	40	40	40	40	42	44	44	40	40	42	42	40	41	40	42	40	42						100	100	100	100	100	100	100	100
43	43	44	42	42	38	36	38	34	38	36	38	38	38	40	42	42	40	40	45	45	40	38	40	45	44	44	45	43	48	48					100	100	100	100	100	100	100	100
38	40	39	36	40	39	38	38	38	38	38	38	36	36	44	40	40	40	40	43	42	40	40	40	38	37	42	40	40	45						100	100	100	100	100	100	100	100
40	40	42	43	43	44	45	40	40	40	45	40	44	45	40	40	34	43	43	44	40	45	54	56	54	55	57	50	46	47						100	100	100	100	100	100	100	100
40	40	43	43	40	42	42	42	42	50	45	54	56	44	45	45	42	44	42	42	45	45	45	48	48	49	46	47	48	55	58					100	100	100	100	100	100	100	100
40	40	52	42	42	53	54	43	40	42	39	37	45	40	40	40	45	60	60	45	56	56	55	54	52	58	56	54	53	56	60	55	54	56		100	100	100	100	100	100	100	100
45	40	45	40	43	45	42	40	43	42	42	44	43	60	60	45	44	44	45	44	38	40	54	54	55	56	52	50	54	54						100	100	100	100	99	100	100	100
70	60	60	56	55	54	51	50	54	55	56	60	60	60	60	60	60	60	56	60	56	50	50	60	60	55	53	52	58	62	63					100	100	100	100	100	100	100	100
52	54	48	52	50	48	54	45	45	54	54	60	56	57	60	60	60	60	56	56	50	55	55	59	60	55	57	60	63	55						100	100	100	100	100	100	100	100
40	40	43	45	40	43	44	42	42	42	40	38	40	40	40	40	40	42	50	50	46	45	50	50	52	53	50	55	54	56	52					100	100	100	100	100	100	100	100
43	45	45	45	45	45	45	50	44	45	45	40	43	45	45	46	42	42	42	40	40	40	42	46	44	44	42	43	40	56						100	100	100	100	100	100	100	100
45	40	42	43	45	43	45	45	46	43	46	40	44	43	44	45	43	40	40	40	40	40	45	45	44	45	44	44	40	43	45					100	100	100	100	100	100	100	100

Postoperative SPO2																													Pain scores												
120 min	150 min	180 min	210 min	240 min	270 min	300 min	330 min	360 min	390 min	420 min	450 min	480 min	510 min	540 min	570 min	600 min	630 min	660 min	690 min	720 min	750 min	780 min	810 min	840 min	870 min	900 min	930 min	960 min	990 min	0 min	15 min	30 min	45 min	60 min	75 min	90 min	105 min	120 min	150 min	180 min	210 min	240 min
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100							0	0	0	0	0	0	0	0	1	2	2	3	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100										0	0	0	0	0	0	0	0	0	1	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100			0	0	0	0	0	0	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100				0	0	0	0	0	0	0	0	0	0	0	0	1
100	100	100	100	100	100	100	99	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100							0	0	0	0	0	0	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100				0	0	0	0	0	0	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	1	0	0	0	0	0	1	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	0	0	0	1	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	0	0	0	0	0	0	0	2	2	
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100		0	1	0	0	0	0	0	0	0	0	0	0	
100	100	100	100	100	100	100	99	100	100	100	100	100	100	100	100	100	100	100	100											0	0	0	0	0	0	0	0	0	0	0	0	0
100	99	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	1	0	0	0	0	0	0	0	0	0
100	100	100	100	100	100	100	99	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	0	0	0	0	0	0	0	0	0	0	0	0	0
100	99	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	0	0	0	1	0	0	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	1	0	2	0	0	0	1	1	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	0	0	0	0	2	0	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	1	1	0	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	99	100	100	100	100	100					0	0	0	0	0	1	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100				0	0	0	0	0	0	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	2	0	0	0	0	1	1	0	0	0
100	99	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	2	2	0	0	0	0	0	0	3	3	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	0	1	1	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100							1	0	0	0	0	0	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100							0	0	0	0	0	0	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	0	0	0	0	0	0	1	0	2	2
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100		0	0	0	0	0	0	0	0	0	0	0	0	1
100	99	100	100	100	100	100	100	100	100	100	99	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	0	0	0	0	0	0	1	0	0	
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100				0	0	0	0	0	0	0	0	0	1	1	1	
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	0	0	0	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100				0	0	0	0	0	0	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	0	0	0	0	0	0	0	0	0	0
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100					0	0	0	0	0	0	0	0	0	1	0	0	0

270 min	300 min	330 min	360 min	390 min	420 min	450 min	480 min	510 min	540 min	570 min	600 min	630 min	660 min	690 min	720 min	750 min	780 min	810 min	840 min	870 min	900 min	930 min	960 min	990 min	Duration of analgesia (min)	Adverse effects
0	0	1	0	0	1	0	0	0	0	0	0	0	0	2	0	0	2	4							910	_
0	1	1	0	0	0	0	0	0	0	0	0	0	0	2	4										830	_
0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	1	1	1	1	1	4			955	_
0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	2	2	3	4				930	_
0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	1	1	3	4							845	_
0	0	0	0	0	1	1	0	0	0	0	0	0	0	1	1	1	1	2	2	4					900	_
0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	2	2	3	4						885	_
2	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	2	2	4					930	_
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	2	4					900	_
0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	2	4		995	_
0	0	0	0	0	1	1	0	0	0	0	0	1	3	4											850	_
0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	1	1	1	2	4					930	vomiting
0	0	0	0	0	0	0	2	0	1	0	1	0	0	2	4										850	_
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	1	1	1	4				935	_
0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	2	3	4						880	_
0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	1	1	1	2	4					895	_
0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	2	4				930	_
0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	4									830	_
0	0	2	2	0	0	0	0	2	0	0	0	0	0	1	1	2	2	2	4						870	_
0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	1	2	2	4					900	_
0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	1	2	2	3	4						860	_
1	1	0	0	0	0	0	2	0	0	0	0	0	0	1	1	1	1	3	4						885	_
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	2	4					895	_
0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	1	1	2	3	4		990	_
0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	4						870	_
0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	1	1	1	2	4					900	_
0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	2	2	3	4						875	_
0	0	0	1	1	0	0	0	0	0	0	0	0	0	1	1	1	1	2	2	4					900	_
0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	3	4						870	_
0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	4					900	_