"A COMPARATIVE STUDY OF EQUIPOTENT DOSES OF INTRATHECAL CLONIDINE AND DEXMEDETOMIDINE ON CHARACTERISTICS OF BUPIVACAINE SUBARACHNOID BLOCK"

Submitted by

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M. D.

in

ANAESTHESIOLOGY

Under the guidance of

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LIST OF ABBREVIATIONS

ANOVA	:	Analysis of Variance
ASA	:	American Society of Anaesthesiologists
ATP	:	Adenosine triphosphate
CBF	:	Cerebral blood flow
CGRP	:	Calcitonin Gene-Related Peptide
$CMRO_2$	:	Cerebral metabolic rate for oxygen
CNS	:	Central nervous system
CSF	:	Cerebrospinal fluid
DEX	:	Dexmedetomedine
ECG	:	Electrocardiogram
EEG	:	Electroencephalogram
GABA	:	Gamma butyric acid
ICP	:	Intracranial pressure
IV	:	Intravenous
NIBP	:	Non-Invasive Blood Pressure
NMDAR	:	N-Methyl D-Aspartate Receptors
NSAIDs	:	Non-steroidal anti-inflammatory drugs
PDPH	:	Post dural puncture headache
PONV	:	Postoperative nausea and vomiting
$SP0_2$	:	Oxygen saturation by pulseoximetry
SAB	:	Sub arachnoid block
α	:	Alpha
β	:	Beta
δ	:	Delta

C	:	Cervical
T	:	Thoracic
L	:	Sacral
GROUP B	:	Bupivacaine
GROUP C	:	Clonidine
GROUP D	:	Dexmedetomidine
Hr	:	HOUR
Mins	:	Minutes
Secs	:	Seconds
HR	:	Heart rate
RR	:	Respiratory rate
P	:	Page number
DEX	:	Dexmedetomidine
µg	:	Micrograms
mg	:	Milligram
ml	:	Milliliter
mmHg	:	Millimeter of mercury
MAP	:	Mean arterial pressure
SBP	:	Systolic blood pressure
DBP	:	Diastolic blood pressure
pKa	:	Dissociation constant
VDSS	:	Volume of distribution at steady state
VAS	:	Visual analogue scale
ICP	:	Intracranial pressure
TENS	:	Transcutaneous electrical nerve stimulator

Sl. No	:	Serial number
Vs	:	Versus
CRIF	:	closed reduction internal fixation
ORIF		Open reduction internal fixation
EF	:	External Fixation
TBW	:	Tension Band Wiring
IL	:	Interlocking
IMIL	:	Intramedullary interlocking
NOF	:	Neck of femur
ITF	:	Inter trochanteric fracture of femur
AMP	:	Austin moore prosthesis
SOF	:	Shaft of Femur
PFN	:	Proximal Femur Nailing
TFN	:	Teflon femur nailing
THR	:	Total Hip Replacement
LT	:	Left
RT	:	Right
ns	:	Not Significant
vhs	:	Very Highly Significant
sig	:	Significant

ABSTRACT

To increase the duration of analgesia produced by local anaesthetics a number of adjuvants have been added to centrineuraxial block. Administration of intrathecal Clonidine or Dexmedetomidine has shown to improve the quality of spinal anaesthesia. It abolishes pain of somatic origin without any neurotoxicity. In view of the above considerations, this clinical study was undertaken to assess the behaviour and feasibility of administration of intrathecal Clonidine or Dexmedetomidine as an adjuvant for bupivacaine intrathecally in patients posted for elective lower abdominal or lower limb surgeries.

Method

This clinical study was conducted on 156 adult patients of ASA physical status I, II and III in the age group of 18-60years of either sex posted for elective lower abdominal or lower limb surgeries under spinal anaesthesia after taking informed consent.

Patients were randomly divided on an alternative basis into 3 groups of 52 each

Group-B: 0.5% Bupivacaine 15mg + 0.5 ml Normal saline

Group-C: 0.5% Bupivacaine 15mg + 50 µg Clonidine (Test solution was diluted with Normal saline to a total volume of 3.5ml)

Group-D : 0.5% Bupivacaine 15mg + 5 µg Dexmedetomidine(Test solution was diluted with Normal saline to a total volume of 3.5ml)

Parameters

Onset and duration of sensory block and motor block, highest level of sensory blockade, duration of analgesia, vitals and side effects were assessed.

Results

The onset of motor block was faster in group C and group D as compared to group B, fastest in group C followed by group D. The duration of sensory and motor blockade and duration of analgesia was longer in group C and D as compared to group B, longest in group D followed by C and B. There was no significant haemodynamic changes in all the three groups.

Conclusion

Supplementation of bupivacaine spinal block with a low dose of intrathecal Dexmedetomidine (5 µg) or Clonidine (50 µg) produces a significantly shorter onset of motor and sensory block and a significantly longer sensory, motor block and longer analgesia than bupivacaine alone. These doses have an effect on sedation level, heart rate and mean arterial pressure which does not however require any therapeutic intervention.

Key words:

Spinal anaesthesia, Dexmedetomidine, Bupivacaine, Clonidine,

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INTRODUCTION

As stated by Hippocrates - **"Divine is the task to relieve pain"**

Relief of pain during surgery is one of the components of balanced anaesthesia but this pain relief should be extended to the postoperative period also. According to **Perkins** and co-workers poorly managed acute pain like postoperative pain can lead to the occurrence of chronic pain.[1] Postoperative pain relief is a growing concern for an anaesthesiologist as an uneventful postoperative period makes surgery a comfortable experience for surgical patients.[2]

Spinal anaesthesia was introduced into clinical practice by Karl August Bier in 1898.[3.]More than a century has passed and even today it is one of the most popular techniques for both elective and emergency surgical procedures particularly caesarean sections, lower abdominal surgeries, orthopaedic and urological surgeries just to name a few. [4]

Spinal anaesthesia is popular and commonly used worldwide. The advantages of an awake patient, minimal drug cost and rapid patient turnover has made this a method of choice for many surgical procedures. These advantages are sometimes offset by relatively short duration of action and complain of post operative pain.

Spinal anaesthesia with hyperbaric Bupivacaine hydrochloride is popular for longer procedure due to its prolonged duration. But there is still a need to intensify and increase the duration of sensory block without increasing the intensity and duration of motor blockade and thus prolong the duration of post operative analgesia.

Central neuraxial opioids, intrathecal as well as epidural offer the perceived benefit of selective analgesia without sensory or motor blockade. However side effects such as potentially catastrophic delayed respiratory depression have prompted further research to develop non opioid analgesics with lesser side effects.[5] Intrathecal

Clonidine is being extensively evaluated in last 25 years as an alternative to neuraxial opioids for control of pain and has proven to be a potent analgesic, free of at least some of the opioids related side effects.[6] Unlike spinal opioids, Clonidine does not produce pruritis or respiratory depression. It also prolongs the necessary blockade[7,8] and reduces the amount or concentration of local anaesthetic required to produce postoperative analgesia. [9,10]

Dexmedetomidine is a new highly selective, an alpha 2 adrenergic receptor agonist. It has an alpha2/alpha1 selectivity ratio which is eight times higher than that of Clonidine. Dexmedetomidine has been approved by Food and Drug Administration (FDA) in 1999 as a short term sedative and analgesic for mechanically ventilated intensive care unit (ICU) patients. Its use is often associated with a decrease in heart rate and blood pressure.[11]

This drug is under evaluation as a neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and postoperative analgesia with minimal side effects.

The present study is aimed at evaluating the efficacy of the use of intrathecal Clonidine and Dexmedetomidine as an adjuvant to hyperbaric Bupivacaine in providing better intraoperative and post operative analgesia and hemodynamic stability.

AIMS AND OBJECTIVES

To compare the following factors in 3 groups of 52 each

Group-B: 0.5% Bupivacaine 15mg + 0.5 ml Normal saline (Total volume 3.5ml)

Group-C: 0.5% Bupivacaine 15mg + 50 µg Clonidine (Test solution was diluted with Normal saline to a total volume of 3.5ml)

Group-D: 0.5% Bupivacaine 15mg + 5 µg Dexmedetomidine (Test solution was diluted with Normal saline to a total volume of 3.5ml)

With respect to

1. Sensory blockade- time to reach T10, time to peak sensory blockade, highest level of sensory block,
2. Motor blockade-time to reach Bromage scale 3.
3. Recovery parameter-Time to two segment regression, time to complete sensory and motor recovery (Bromage scale 0).
4. Analgesia – Duration of analgesia (the time of first rescue dose requested).
5. Intraoperative hemodynamic variations
6. Side effects

REVIEW OF LITERATURE

HISTORICAL REVIEW

The introduction of the hollow needle and a conveniently sized glass syringe by Alexander Wood in 1853 and the clinical demonstration of the local analgesic properties of Cocaine by Koller in 1884 were direct steps leading to spinal analgesia. The first person to perform spinal anaesthesia was Leonard Corning, a New York neurologist in 1885 who accidentally pierced the duramater while experimenting with cocaine on the spinal nerves of a dog.[12] Heinrich Irenaeus Quincke of Kiel Germany in 1891 demonstrated the usefulness and practicality of spinal puncture as a diagnostic procedure and outlined the proper technique of introducing a needle through the duramater to obtain spinal fluid. A German surgeon, August Bier performed the first planned spinal analgesia for surgery in man on 16th August 1898, at Royal Surgical Hospital of the University of Kiel , Germany , for a labourer undergoing resection of tuberculous ulceration of the ankle, wherein he injected 3 ml of 0.5% Cocaine solution.

Einhorn introduced Procaine (Novocaine) for spinal anaesthesia in l905.[13]

Arthur E Barker (1850-1916) a surgeon at University college hospital introduced hyperbaric heavy Stovaine 5% (Stovaine in 5% dextrose) in 1907 in the UK. He was the first to use solutions made hyper baric by the addition of glucose.[13] Lofgren and Lundquist introduced the most commonly used drug Lignocaine in 1943 in Sweden. It was first used clinically by Gordh at Korlinska hospital, Stockholm in 1948.[12]

During the period 1950 to 1960, the most commonly used drugs were Amethocaine and Lignocaine. The disadvantages of both these local anaesthetics were short duration of action (Lignocaine) and instability (Amethocaine). Attempts

were made to increase the duration of block by the addition of vasoconstrictors to the local anaesthetic solution.

But many workers attributed the ischemia of spinal cord and neurological damage to the addition of vasoconstrictors due to anterior spinal artery syndrome.

Bupivacaine was introduced by Ekenstam in 1957 and used clinically by Telivuo in 1963. The introduction of bupivacaine is the most important exciting contribution to spinal anaesthesia. Tuominen in 1991 has reviewed Bupivacaine in spinal anaesthesia. He showed that hyperbaric, hypobaric and isobaric solutions are available for use. When long acting anaesthesia and postoperative analgesia is required 0.5% Bupivacaine is a good choice. A dose of at least 15mg will generally produce sufficient anaesthesia. Hyperbaric Bupivacaine would allow improved prediction of block and variation of cephalad spread.

In 1973, Opioid receptors were localized in mammalian brain and in 1976, they were found to exist in primate spinal cord. Yaksh and Reddy in 1976 first demonstrated the effectiveness of intrathecal Opioids in abolishing experimental pain in animal model.

In 1984, Tamsen and Gordh, after testing for neurotoxicity in animals, injected a parenteral preparation of the alpha 2 adrenergic agonists, Clonidine, epidurally in two patients with chronic pain. Since then a complete toxicological assessment (effects on spinal cord blood flow, behaviour after lumbar and cervical intrathecal injection in sheep and monkeys, and histopathology in rats and dogs) has suggested that Clonidine is safe for intraspinal use.

CLINICAL REVIEW

D.J. Fogarty *et al,*[17] conducted a comparative study on anaesthetic and analgesic properties of intrathecal Clonidine and intrathecal Morphine in patients

undergoing total hip replacement under spinal anaesthesia in the year 1993 on 90 patients. After routine spinal anaesthesia with 0.5% plain Bupivacaine 2.75ml, patients were allocated randomly to receive intrathecal Clonidine, Morphine or saline (control) as adjuvant to the Bupivacaine. Postoperative analgesic effects were measured by consumption of Morphine via patient controlled analgesia and visual analogue pain scores. Both intrathecal Clonidine and intrathecal Morphine prolonged the time to first analgesia compared with saline [mean 278 (S.D. 93.2) min, 498 (282.4) min and 54 (61.9) min, respectively] {P<0.001}. Intrathecal Clonidine prolonged the duration of spinal analgesia, but was markedly inferior to the intrathecal Morphine in providing subsequent postoperative analgesia.

I. Dobrydnjov *et al,*[18] in the year 2003 conducted a study on 45 patients , to see whether the addition of small dose Clonidine to small dose Bupivacaine for spinal anaesthesia prolonged duration of postoperative analgesia and also provided a sufficient block duration that would be adequate for inguinal herniorrhaphy. The patients were randomized into 3 groups receiving intrathecal hyperbaric Bupivacaine 6mg combined with saline (group B), Clonidine 15µg (group BC15), or Clonidine 30µg (group BC 30); all solutions were diluted with saline to 3ml. Patients in groups BC15 and BC30 had a significantly higher spread of analgesia (two to four dermatomes) than those in group B. Two segment regression, return of S1 sensation and regression of motor block were significantly longer in group BC30 than in group B. The addition of Clonidine 15 and 30µg to Bupivacaine prolonged time to first analgesic request and decreased postoperative pain with minimal risk of hypotension.

In 2004 Stephen strebel, [19] examined the dose response relationship of intrathecal Clonidine at small doses (<150µg)with respect to prolonging Bupivacaine

spinal anaesthesia in 80 orthopaedic patients. The patients were randomly assigned to intrathecally receive isobaric 0.5% Bupivacaine 18mg, plus saline (group I), Clonidine 37.5µg (group II), Clonidine 75µg (group III) and Clonidine 150µg (group IV).Duration of sensory block (regression below L1) was increased in patients receiving intrathecal Clonidine; 288+62 min (group I), 311 + 101 (group II), 325 + 169 (group III) and 337 + 78 (group IV). Duration of pain relief from intrathecal Clonidine administration until the first request for supplemental analgesia was significantly prolonged.

Relative hemodynamic stability was maintained and there were no differences between groups in the sedation score. They concluded that small doses of intrathecal Clonidine (< 150µg) significantly prolonged the anaesthetic and analgesic effects of Bupivacaine in a dose dependent manner and that 150µg of Clonidine seems to be the preferred dose, in terms of effect versus unwarranted side effects, when prolongation of spinal anaesthesia is desired.

I.Van Tuijl *et al,*[20] investigated the effects of the addition of Clonidine (75 µg) to hyperbaric Bupivacaine on post operative Morphine consumption after caesarean section in a randomized controlled double blind trial. A group of106 women received spinal anaesthesia using either Bupivacaine 0.5% (2.2 ml) heavy with 0.5 ml normal saline 0.9% (B) or Bupivacaine 0.5% (2.2ml) heavy with Clonidine (75 µg) in 0.5 ml normal saline 0.9% (BC). Total Morphine consumption was similar in both study groups. The mean time to the first analgesic request in the BC group was 129 (SD 13.8) min, compared with55 (14.2)mins. In the B group, in the BC group 22 (42%) patients had a complete motor block 1 hour after surgery compared with 4(8%) patients in the B group. The addition of Clonidine (75 µg) to hyperbaric Bupivacaine prolongs spinal anaesthesia after caesarean section and

improves early analgesia, but does not reduce the postoperative Morphine consumption during the first 24 hours.

In 2006, a prospective, double blind study conducted by **G E Kanazi** *et al,*[14] 60 patients undergo transurethral resection of prostate or bladder tumor under spinal anaesthesia were randomly allocated to one of three groups. Group B received 12 mg of hyperbaric Bupivacaine, group D received 12 mg of Bupivacaine supplemented with 3 μg of Dexmedetomidine and group C received 12 mg of Bupivacaine supplemented with 30 μg of Clonidine . The mean time of sensory regression to the S1 segment was 303+75 min in group D, 272 ± 38 min in group C and 190±48 min in group B (B Vs.D and B Vs.C, P<0.001). The regression of motor block to Bromage 0 was 250 + 76 min in group D, 216+35 min in group C and 163 + 47 min in group B. The mean arterial pressure, heart rate and level of sedation were similar in the three groups intraoperatively and post operatively.

B.S.Sethi *et al,* (2007) [21] studied the efficacy of analgesic effects of low dose intrathecal Clonidine as adjuvant to bupivacaine on sixty adult patients belonging to ASA grade I & II, scheduled for gynaecological surgery .They were randomly divided into two groups. Clonidine group received Clonidine 1 μg/kg with 12.5 mg 0.5% Bupivacaine and the control group received an identical volume of saline mixed with 12.5mg of 0.5% Bupivacaine. The mean time from injection to regression of the level of sensory analgesia by two segments was longer in the Clonidine group than in control group (P <0.001) . The duration of motor blockade was longer in Clonidine group than in control group (P<0.05). The rescue analgesia was required earlier in the control group (mean 223 min) compared to the Clonidine group (mean 614 min). The patients in the Clonidine group had a significant fall in mean arterial pressure and heart rate and were more sedated than those in control group. However,

no therapeutic interventions needed.

Al-Mustafa MM (2009), [22] Investigated intrathecal Dexmedetomidine added to Bupivacaine for neuraxial anaesthesia in urological procedures. Sixty six patients randomly were assigned into 3 groups. Each received spinal Bupivacaine 12.5mg combined with normal saline (group N) or Dexmedetomidine 5 µg (group D5) or Dexmedetomidine 10 µg (group D 10). The mean time of sensory block to reach the T10 dermatome was 4.7 ±2.0 minutes in D 10 group, 6.3 ±207 minutes in D5 and 9.5 ±3.0 minutes in group N. The mean time to reach Bromage 3 scale was 10.4 ±8.4 minute in group D 10, 13.0±3.45 minutes in D 5 and 18.0 ±3.3 minutes in group N. The regression time to reach S_1 dermatome was 338.9 ±44.8 minutes in group D 10, 277.1 ±23.2 minutes in D5 and 165.5 ±32.9 minutes in group N, The regression to bromage 0 was 302.9 ±36.7 minute in D 10, 246.4 ±25.7 minute in D5 and 140.1 ±32.3 minutes in N. It was concluded the Dexmedetomidine prolonged the duration of effect early onset of effect.

In 2010 **Hema Saxena** *et al*,[23] conducted a study on eighty adult patients belonging to ASA grade I and II, whether low dose intrathecal Clonidine with Bupivacaine improves onset and duration of block with hemodynamic stability , scheduled for below umbilical surgeries dividing them into four groups. Control group received 13.5mg 0.5% hyperbaric Bupivacaine (Group I), study groups received Clonidine 15µg (Group II), 30µg (Group III) and 37.5µg (Group IV) made to 3 ml volume with 13.5 mg 0.5% hyperbaric Bupivacaine. The mean time from injection to onset of block was longer in all the Clonidine groups (most significant) in Group IV. The changes were less significant or not significant in Group III and Group IV.30% of patients in Group IV as compared to Group III had a significant fall in mean arterial pressure and heart rate.90% patients were sedated in Group IV. They

concluded that addition of Clonidine to Bupivacaine significantly reduces the onset time with increase in the duration of spinal block as compared to bupivacaine alone with 30µg as optimum dose.

In 2011**Hala E A Eid** *et al,*[24] conducted a study with aim to investigate the effect of intrathecal administration of Dexmedetomidine on the duration of sensory and motor block and postoperative analgesic requirements produced by spinal Bupivacaine. Forty eight adult patients scheduled for anterior cruciate ligament reconstruction were randomized to one of three groups. Each patient was given 3.5 ml spinal injectate that consisted of 3 ml 0.5% hyperbaric Bupivacaine and 0.5 ml containing either 10µg Dexmedetomidine (Group D1), 15µg Dexmedetomidine (D2) or normal saline (Group B). Heart rate, arterial blood pressure, sensory level, motor block, pain and level of sedation were assessed intraoperatively and up to 24 hours after spinal anaesthesia. The incidence of adverse effects was recorded. Dexmedetomidine significantly prolonged time to two segment regression, sensory regression to S1, regression of motor block to modified Bromage 0 and time to first rescue analgesic. In addition, it significantly decreased postoperative pain scores. The effects were greater in group D2 than in group D1. In addition, group D2 patients had higher sedation scores and lower postoperative analgesic requirements than Group D1 or B. Hemodynamic stability was maintained in the three groups. Thus, Intrathecal Dexmedetomidine in doses of 10 µg and 15 µg significantly prolong the anesthetic and analgesic effects of spinal hyperbaric bupivacaine in a dose-dependent manner. A fifteen µg dose may be of benefit for prolonged complex lower limb surgical procedures.

Rajni Gupta, Jaishri Bogra, Monica Kohli, Rajesh Reetu, verma Raman[25] in Nov. 2011 conducted a study the purpose of the study was to evaluate the onset and duration of sensory and motor block as well as post operative analgesia and adverse effects of Dexmedetomidine or Fentanyl given intrathecally with plain 0.5% Bupivacaine of patients classified in Anesthesiologists classes 1 and 11 scheduled for lower abdomen surgeries. Patients were randomly allocated to receive either 12.5 mg hyperbaric Bupivacaine plus 5µg Dexmedetomidine (group D, *n*=30) or 12.5 mg hyperbaric bupivacaine plus 25µg Fentanyl (group F, *n*=30) given intrathecally. The mean time of sensory regression to S1 was 476±23 min in group D and 187±12 min in group F ($P<0.001$). The regression time of motor block to reach modified Bromage 0 was 421±21 min in group D and 149±18 min in group F ($P<0.001$). There was no difference in onset of modified Bromage score 3 [11.6+1.8 min in group D and 11.2 +1.3min in group F] but the regression time of motor block to reach modified Bromage 0 was significantly slower with the addition Dexmedetomidine.

Solanki SL1, Bharti N, Batra YK, Jain A, Kumar P, Nikhar SA[26] in Jan 2013 conducted a study to compare the duration of analgesia and adverse effects following intrathecal administration of Dexmedetomidine or Clonidine, both with Bupivacaine, in trauma patients Ninety adult trauma patients of American Society of Anesthesiologists physical status I-II, scheduled for lower limb surgery under subarachnoid block, were randomly allocated to one of three groups. All groups received hyperbaric Bupivacaine 0.5% 3 ml, to which was added saline 0.5 ml (Group B): Clonidine 50 µg (Group C) or Dexmedetomidine 5 µg (Group D) There was no significant difference in the onset time of the block but the duration of sensory and motor blockade was prolonged in Groups C and D, compared with Group B. The time to analgesia was significantly prolonged in Group D (824±244 minutes) compared

with Group C (678±178 minutes; P=0.01), the latter being longer than Group B (406±119 minutes; P=0.0001). Postoperative pain scores were lower in Groups C and D compared with group B. The requirement for rescue analgesia during the first 24 postoperative hours was significantly less in Groups C and D as compared to Group B (P=0.0001), but comparable between Groups C and D (P=0.203) Dexmedetomidine 5 µg added to intrathecal Bupivacaine 15 mg produces longer postoperative analgesia than Clonidine 50 µg among trauma patients undergoing lower limb surgery

Hem Anand Nayagam, N Ratan Singh, H Shanti Singh[27] in Jul-Aug 2014 conducted a study aimed to find out whether quality of anaesthesia is better with low dose Bupivacaine and Fentanyl or with low dose Bupivacaine and Dexmedetomidine prospective randomized double-blinded study was carried out on 150 patients by randomly allocating them into two groups using a computer generated randomization table. Group F (n = 75) received Bupivacaine 0.5% heavy (0.8 ml)+Fentanyl 25 µg (0.5 ml) + normal saline 0.3 ml and Group D (n = 75) received Bupivacaine 0.5% heavy (0.8 ml) + Dexmedetomidine 5 µg (0.05 ml) + normal saline 0.75 ml, aiming for a final concentration of 0.25% of Bupivacaine (1.6 ml), administered intrathecally. There were no significant differences between the groups in the time to reach T10 segment block (P > 0.05) and TTSR[time to two segment regression] (P > 0.05);time to reach PSBL (P < 0.05) and modified Bromage scales (P < 0.05) were significant. PSBL[peak sensory block level] (P = 0.000) and time to first analgesic request (P = 0.000) were highly significant. All patients were haemodynamically stable and no significant difference in adverse effects was observed. They concluded that Dexmedetomidine is superior to Fentanyl since it facilitates the spread of the block and offers longer post-operative analgesic duration.

ANATOMY OF THE SPINE

"I advise those who contemplate practicing spinal anaesthesia to take a look at the skeleton, especially the relations of the lumbar vertebrae. An intelligent glance of this sort is worth many words" - Corning (1990)

Knowledge of the anatomy of the vertebral column and of the lumbar vertebrae in particular is essential for the anaesthesiologist. The vertebral column forms a canal and protects the spinal cord.

The vertebral column, which is made up of vertebrae affords protection to the spinal cord. It is composed of 33 vertebrae (7 cervical, 12 thoracic, 5 lumbar, 5 fused sacral and 4 coccygeal) and has 4 curves. The cervical and lumbar (primary) curves are convex anteriorly while the thoracic and sacral (secondary) curves are convex posteriorly. The curves of the vertebral column have a significant influence on the spread of local anaesthetics in the subarachnoid space. In the supine position, the high points of the cervical and lumbar curves are at C_5 and L_4; the low points of the thoracic and sacral curves are at T_5 and S_2, respectively.[15]

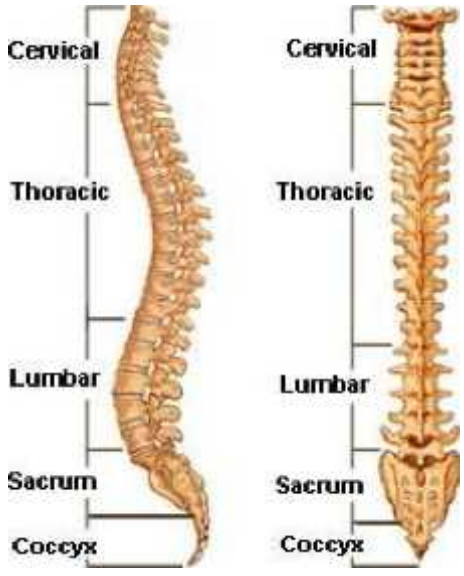


FIG 1: VERTEBRAL COLUMN

A typical vertebra is made up of

- ❖ A body which bears and transmits weight, and forms the base.
- ❖ An arch composed of pedicles and laminae, which surround and protect the cord laterally and posteriorly.

There are seven projections from these vertebral or neural arches. They are:

a. Three muscular processes - two transverse and one spinous, for the attachment of muscles and ligaments and

b. Four articular processes - two upper and two lower, which in the lumbar region prevent rotation but allow limited flexion and extension between contiguous vertebrae.

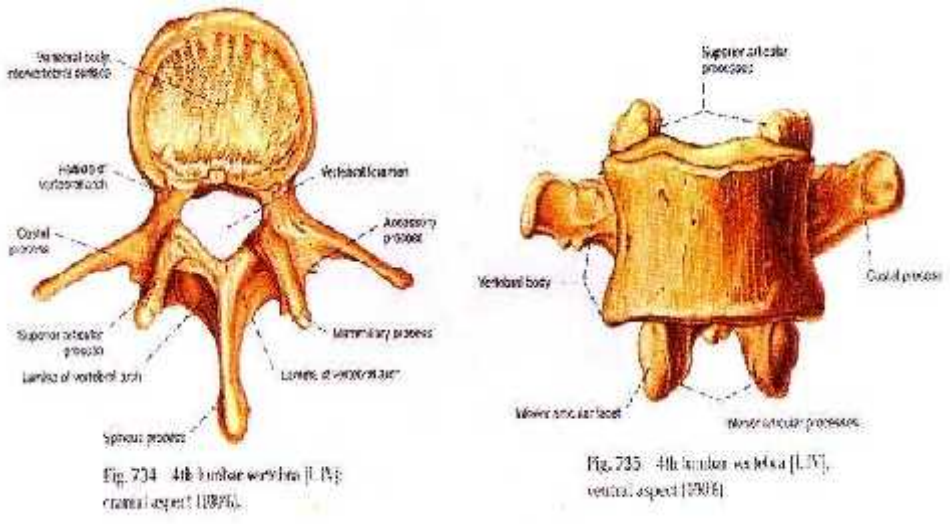


FIG 2:.TYPICAL LUMBAR VERTEBRA

The Lumbar Vertebrae [13]

The bodies of the lumbar vertebrae are large and kidney shaped. The vertebral foramina are triangular and intermediate in size between those in the thoracic and cervical region. The pedicles are thick. The transverse processes are slender increasing in length from L1 to L5 and then becoming shorter again. The laminae are short and do not overlap each other and the lumbar spines are horizontal and oblong.

The 5th lumbar vertebra produces the lumbosacral angle. Its transverse processes although short and thick are strong and arise not only from the arch but also from the side of the vertebral body. It can be distinguished from any of the other thoracic vertebrae by the absence of articular facets for the ribs.

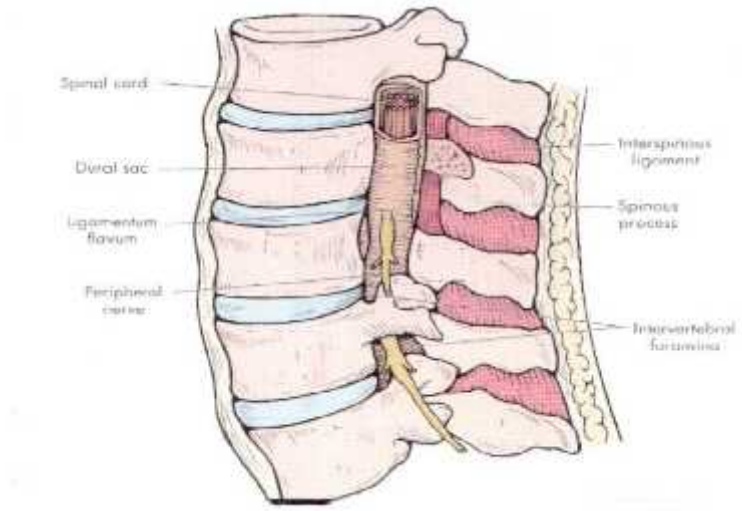


FIG 3: LUMBAR VERTEBRA

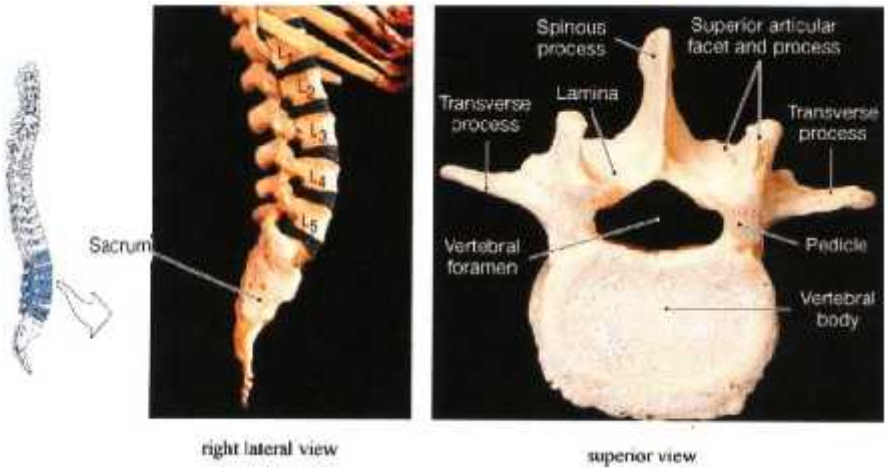


FIG 4: LONGITUDINAL SECTION OF VERTEBRA

The vertebral column is bound together by several ligaments, which give it stability and elasticity. They are:

i. Supraspinous ligament

ii. Interspinous ligament

iii. Ligamentum Flavum

iv. Longitudinal ligament

The posterior surface of the vertebral bodies together with the vertebral arches , intervertebral discs and connecting ligaments collectively form the vertebral canal containing the spinal cord and the investing membranes.

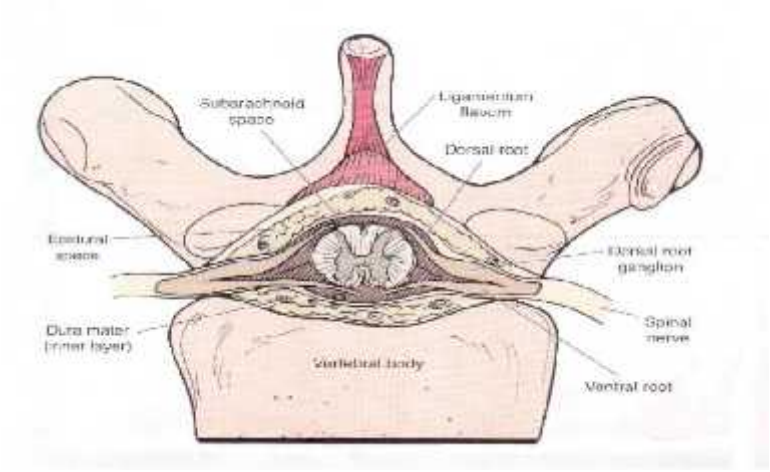


FIG 5: CROSS SECTION OF VERTEBRA

Epidural space

The epidural space surrounds spinal meninges and extends from the foramen magnum where the duramater is fused to the base of the skull, to the sacral hiatus which is covered by the sacrococcygeal ligament. In addition to nerve roots that traverse the epidural space, the contents of the epidural space are fat, areolar tissue, lymphatics, arteries, and the extensive internal vertebral venous plexus of Batson.

Spinal meninges

The spinal cord is protected by the bony vertebral column and three connective tissue coverings, the meninges. The names of the enveloping meninges of the central nervous system are self-descriptive. The duramater is tough, the arachnoid cobweb-like and the piamater tender and clinging.

a) **Duramater :** It is the outermost membrane and is a tough, fibro elastic tube whose fibers run longitudinally. At the spinal level, superiorly, it is firmly attached to the circumference of the foramen magnum of the occipital bone. Inferiorly or caudally, the dural sac ends at the lower border of S_2, where it is pierced by the filum terminale. The spinal duramater also provides a thin cover for the spinal nerve roots, becoming progressively thinner near the inter-vertebral foramina.

b) **Arachnoid mater :** Arachnoidmater is the middle of the three coverings of the brain and the spinal cord. It is delicate nonvascular membrane closely attached to the duramater, and with it ends at the lower border of S_2. It contains a minute quantity of serous fluid, but it has no connection with the subarachnoid space that contains the CSF.

c) **Piamater :** Piamater is a delicate, highly vascular membrane closely investing the spinal cord and brain. The space between arachnoid and piamater is called the subarachnoid space, which contains the spinal nerves and CSF. Many blood vessels that supply the spinal cord are also found in this space.

d) **Spinal cord:** The spinal cord is continuous above with the medulla oblongata, beginning at the level of foramen magnum and ending below as the conus medullaris. At birth, the cord ends at the level of L_3, but rises to the lower border of L_1 in adult life.

Spinal nerves

There are 31 pairs of symmetrically arranged spinal nerves, which are attached to the spinal cord by anterior and posterior nerve roots.

Subarachnoid space[13]

Subarachnoid space is bounded internally by the piamater and externally by the arachnoid trabeculae, which form a delicate, sponge like mass .The subarachnoid space extends separately along both the dorsal and ventral roots to the level of the dorsal root ganglion. It is traversed by the cranial and spinal nerves. It houses the main blood vessels of the central nervous system and here the cerebrospinal fluid takes the place of tissue fluid (lymph) found in other regions of the body. In the cervical and thoracic regions the space is annular and the distance between the arachnoid and the piamater, even in adult, is only about 3mm. The cord commonly finishes at the lower border of first lumbar vertebra so that below this level the subarachnoid space is no longer annular but is practically circular in cross section with a diameter of about 15mm, thus facilitating lumbar puncture in the lower lumbar region.

Cerebrospinal fluid [12]

Cerebrospinal fluid is an ultrafiltrate of the plasma with which it is in hydrostatic and osmotic equilibrium. It is a clear colorless fluid found in the spinal and cranial subarachnoid spaces and in the ventricles of the brain. At 37ºC, its specific gravity is 1.003 to 1.009, and its physiological pH is 7.4 to 7.6. The average total volume in adult ranges from 120 to 150 ml, of which 25 to 35 ml are in subarachnoid space. In horizontal position, the pressure of CSF ranges from 60 to 80 mm of H_2O.

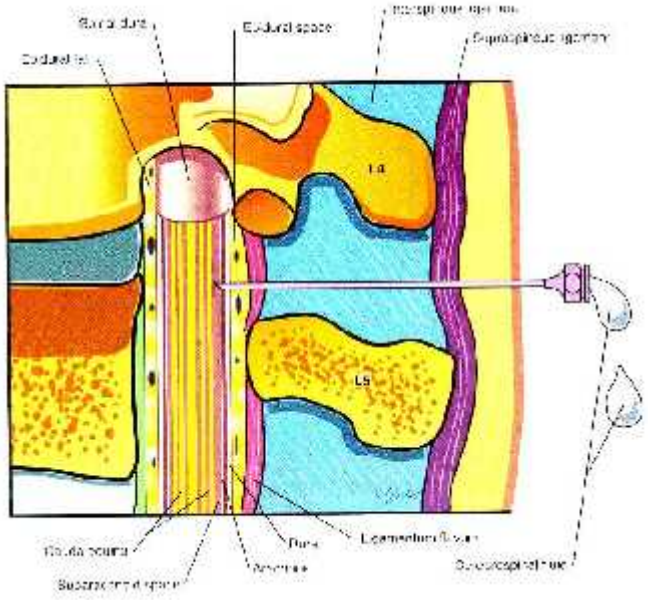


FIG 6 : SUBARACHNOID SPACE

Cerebrospinal fluid is formed by secretion or ultrafiltration from the choroid arterial plexuses of the lateral, third and fourth ventricles. Normal daily secretion is believed to be equal to the volume present (i.e. 150 ml). It has been shown that after removal of small volumes of CSF, it is re-formed at an increased rate of approximately 0.3 ml/min (432 ml /day).

Blood supply to the spinal cord :

Spinal cord is supplied by the anterior spinal artery and two posterior spinal arteries. The anterior spinal artery is formed between the pyramids of the medulla oblongata by the union of a root from the terminal part of each vertebral artery and descends in front of the anterior longitudinal sulcus of the spinal cord and the corresponding vein to the filum terminale .The posterior spinal arteries (two on each side) arise from the posterior inferior cerebellar arteries and descend medial to the posterior nerve roots , sending penetrating twigs to the posterior white columns and the remainder of the posterior grey columns.

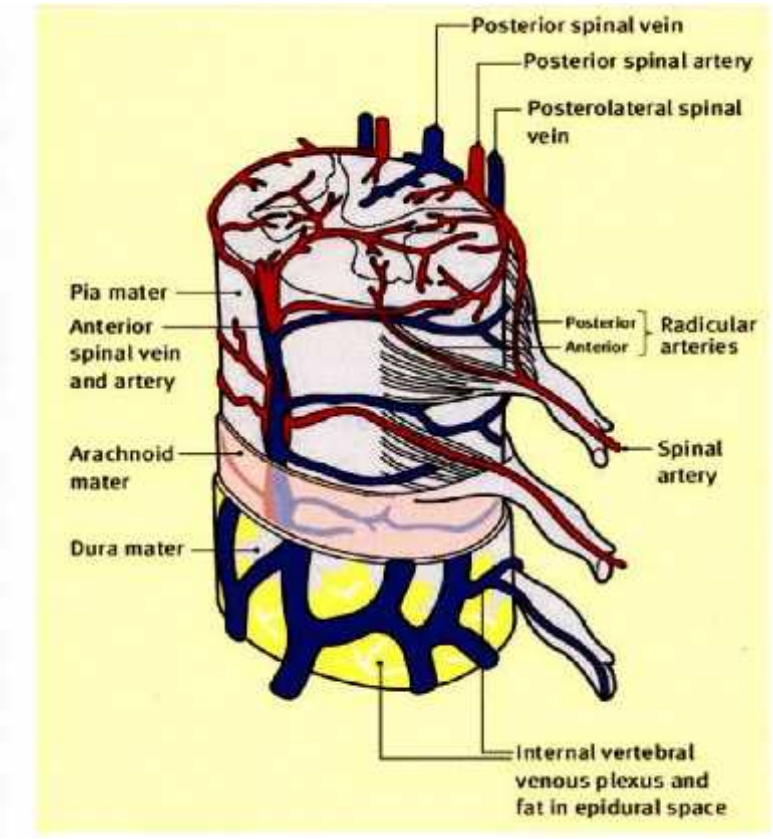


FIG 7: ARTERIAL AND VENOUS DRAINAGE OF SPINAL CORD

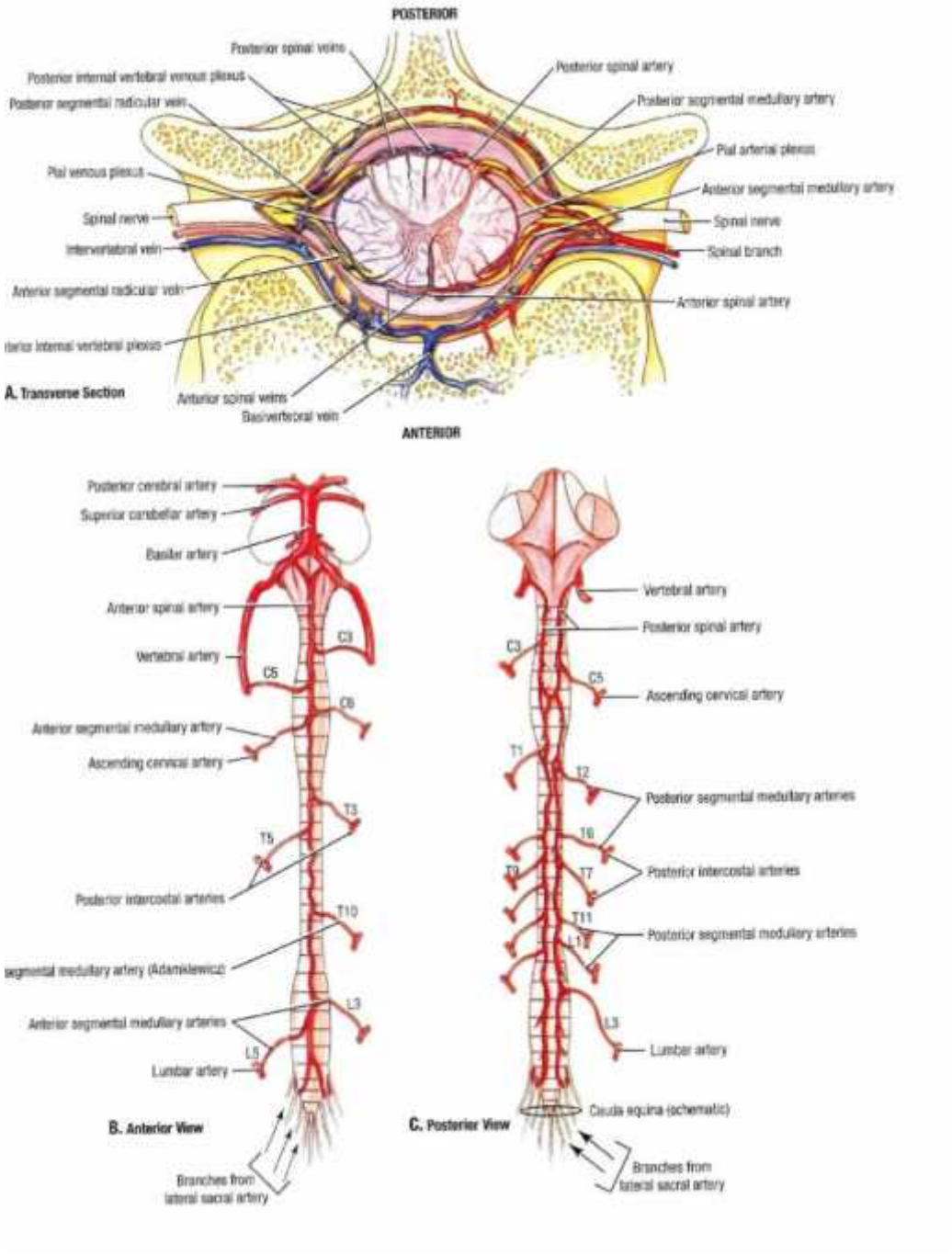


FIG 8: BLOOD SUPPLY OF SPINAL CORD

PHYSIOLOGY OF CENTRAL NEURAL BLOCKADE

Centrineuraxial blockade results in autonomic, sensory and motor blockade. At the upper end of the spinal block, a differential zone of anaesthesia exists. This is because weaker solutions are required to block the smaller autonomic fibers than the large sensory or motor fibers. The level of autonomic sympathetic block is two to four segments above the sensory level. Motor nerve blockade is usually one to four segments below the sensory level.

Sequence of Nerve modality block

- Vasomotor - dilation of skin vessels and increased cutaneous blood flow
- Cold temperature fibers
- Temperature discrimination
- Slow pain
- Fast pain
- Tactile sense
- Motor paralysis
- Pressure sense
- Proprioception and vibratory sense.

Following an intrathecal injection of a drug the extent of anaesthesia produced depends on various factors.

STOUT'S PRINCIPLES FOR SPREAD OF SOLUTION

- ❖ Height of anaesthesia varies directly with concentration.
- ❖ Extent of anaesthesia is inversely proportional to rapidity of fixation.
- ❖ Extent of anaesthesia is directly proportional to speed of injection
- ❖ Extent of anaesthesia is directly proportional to the volume of fluid (CSF).
- ❖ Extent of anaesthesia is directly proportional to spinal fluid pressure.

- ❖ Extent of anaesthesia is directly proportional to specific Gravity of Solutions
- ❖ With hyperbaric or hypobaric solutions extent depends on position of patient.

In practice control and spread of solution is obtained by observing the following: Amount of drug and type of drug, volume of solution, place of injection, rate of injection, specific gravity of solution, density and baricity, barbotage.

Effect of spinal anaesthesia on various organs:

1. **Cardiovascular system**

Paralysis of sympathetic vasoconstrictor fibers to the arterioles, capillaries and veins occur leading to vasodilatation and thus a fall in blood pressure. The systolic pressure falls and there is no proportional fall in diastolic pressure. In general the heart rate slows after spinal anaesthesia. Bradycardia in high spinal is probably due to some paralysis of the cardio accelerator nerves. In low spinal the Bainbridge reflex plays a role in the development of bradycardia. Cardiac output also decreases after subarachnoid block. After low spinal the reduction in cardiac output is to the tune of 16% and with a high spinal it is to the tune of 31 % of the resting level. Oxygen consumption is reduced but arterial oxygen saturation is not changed significantly.

2. **Respiratory system**

Spinal anaesthesia to the level of T4 does not affect pulmonary ventilation. Resting end tidal PCO2 decreases slightly. Sympathetic fibers to the bronchial musculature arise from the upper 5 or 6 thoracic segments. High spinal block may be accompanied by some bronchial spasm caused by predominant vagal activity. Apnea may be due to ischemia of the medullary respiratory centre following hypotension.

3. **Gastrointestinal tract**

Due to the dominant parasympathetic activity the gut will be contracted and the intestines are usually active and show segmental movements as well as slow peristalsis. If the stomach is full, in the presence of high spinal anaesthesia, regurgitation may occur. Subarachnoid block to the T5 level increases gastric emptying.

4. **Endocrine system**

Spinal anaesthetic block to the mid thoracic level is not associated with any major changes in plasma levels of cortisol, prolactin, luteal hormone, follicular stimulating hormone or growth hormone. Metabolic changes also do not occur. Spinal anaesthesia blocks the sympathetic stimulation caused by surgical stress. Blocks extending to levels of T5 and above will decrease plasma epinephrine and norepinephrine levels. Blocks extending to the midthoracic levels prevent significant changes in blood glucose, lactate, alanine, free fatty acids, glycerol or ketones caused by surgical trauma. Spinal anaesthesia extending to T4 – T6 will inhibit release of insulin. For upper abdominal surgeries a level of block extending to T4 will inhibit most of the endocrine and metabolic consequences of surgical stress. For lower abdominal surgeries a level of anaesthesia extending to upper thoracic levels achieves the same results.

5. **Renal system**

In spite of the decrease in blood flow to the kidneys there is no compromise in renal function. This is because of the wide physiologic reserve of the kidneys.

6. **Genitourinary system**

The bladder wall supplied by the parasympathetic system is paralysed during spinal anaesthesia. Urinary retention may outlast skin analgesia, as the slender parasympathetic fibers from S2-S4 are very susceptible to the analgesic solution.

PHYSIOLOGY OF PAIN

In 1979, the International association for the study of pain proposed a definition of pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.[43] Acute pain is caused by noxious stimulation due to injury, a disease process or abnormal function of muscle or viscera. It is nearly always nociceptive. Surgery is also a form of tissue injury producing nociceptive pain.

Pain is recognized by specific receptors called nociceptors.[44] They are free nerve endings. These nociceptors function as a transducer converting all forms of stimuli. The impulses from these receptors utilize separate pathways for transmitting acute sharp pain and chronic pain. The impulses are conducted along sensory afferent fibers; they are the Aδ myelinated large fibers, C unmyelinated small fibers, in peripheral nerves.

Nociceptors are present in both somatic and peripheral sites. Somatic nociceptors include those in skin (cutaneous) and deep tissues (muscles, tendons, fascia, and bone), while visceral nociceptors include those in internal organs. The cornea and tooth pulp are unique in they are almost exclusively innervated by nociceptive Aδ and C fibers. Nociceptive pain is due to activation or sensitization of peripheral nociceptors, i.e. specialized receptors that transduce noxious stimuli. Moderate to severe pain can affect nearly every organ function, regardless of site,and may adversely influence postoperative morbidity and mortality. Aδ fibers relay in thalamus and in the posterolateral nucleus.[45]They have conduction velocity of 12 – 20 meters per second. They form free nerve endings in the superficial layers of the dermis. They respond particularly well to pinching or pinprick. They conduct sharp pain produced by pinprick and are responsible for withdrawal reflex. Aδ fibres

conducted pain is felt quickly and well localized. C fibers are small fine non-myelinated with conduction velocity of 0.1 to 2.0 meters per second or less. They also form part of free nerve ending network of the skin. Their threshold for stimulation is higher, and is probably responsible for delayed noxious pain. Nociceptors are characterized by a high threshold for activation and encode the intensity of stimulation by increasing their discharge rates in a graded fashion. Noxious sensations can be broken down to components: a fast, sharp, and well localized (first pain), which is conducted with a short latency (0.1 s) by Aδ fibers (tested by pinprick). Duller, slower onset and often poorly localized (second pain), which is conducted by C fibers. There are other nociceptors which are also free nerve endings that sense heat, mechanical, and chemical tissue damage types are described: (1) mechanoreceptors, respond to pinch and pin prick, (2) silent nociceptive which respond only in the presence of inflammation and (3) polymodal mechano heat nociceptors. Polymodal nociceptors are slow to adapt to strong pressure and display heat sensitization. Specialized heat, cold and chemical nociceptors have also been described.

Pain Pathways

Pain is conducted along three neuron pathways that transmit noxious stimuli from the periphery to the cerebral cortex.[44] Primary afferent neurons are located in the dorsal root ganglia, which lie in the vertebral foramina at each spinal cord level. Each neuron has a single axon that bifurcates, sending one end to the peripheral tissues it innervates and the other into the dorsal horn of the spinal cord. In the dorsal horn, the primary afferent neuron synapses with a second order neuron whose axons cross the midline and ascend in the contra lateral spinothalamic tract to reach the thalamus. Second order neurons synapse in thalamic nuclei with third order neurons, which in

turn send projections through the internal capsule and corona radiata to the post-central gyrus of the cerebral cortex.

Majority of first order neurons send the proximal end of their axons into the spinal cord via the dorsal (sensory) spinal root at each cervical, thoracic, lumbar and sacral level. Some unmyelinated afferent (C) fibres have been shown to enter the spinal cord via the ventral nerve (motor) root. Once in the dorsal horn, in addition to synapsing with second order neurons, the axons of the first order neurons may synapse with inter neurons, sympathetic neurons and ventral horn neurons.

As afferent fibres enter the spinal cord, they segregate, according to size with large, myelinated fibres becoming medial, and small, unmyelinated fibres becoming lateral. Pain fibres may, ascend or descend one to three spinal, cord segments in Lissauers tract before synapsing with second order neurons in the gray matter of the ipsilateral dorsal horn.[44] Spinal cord gray matter was divided by Rexed into 10 laminae.

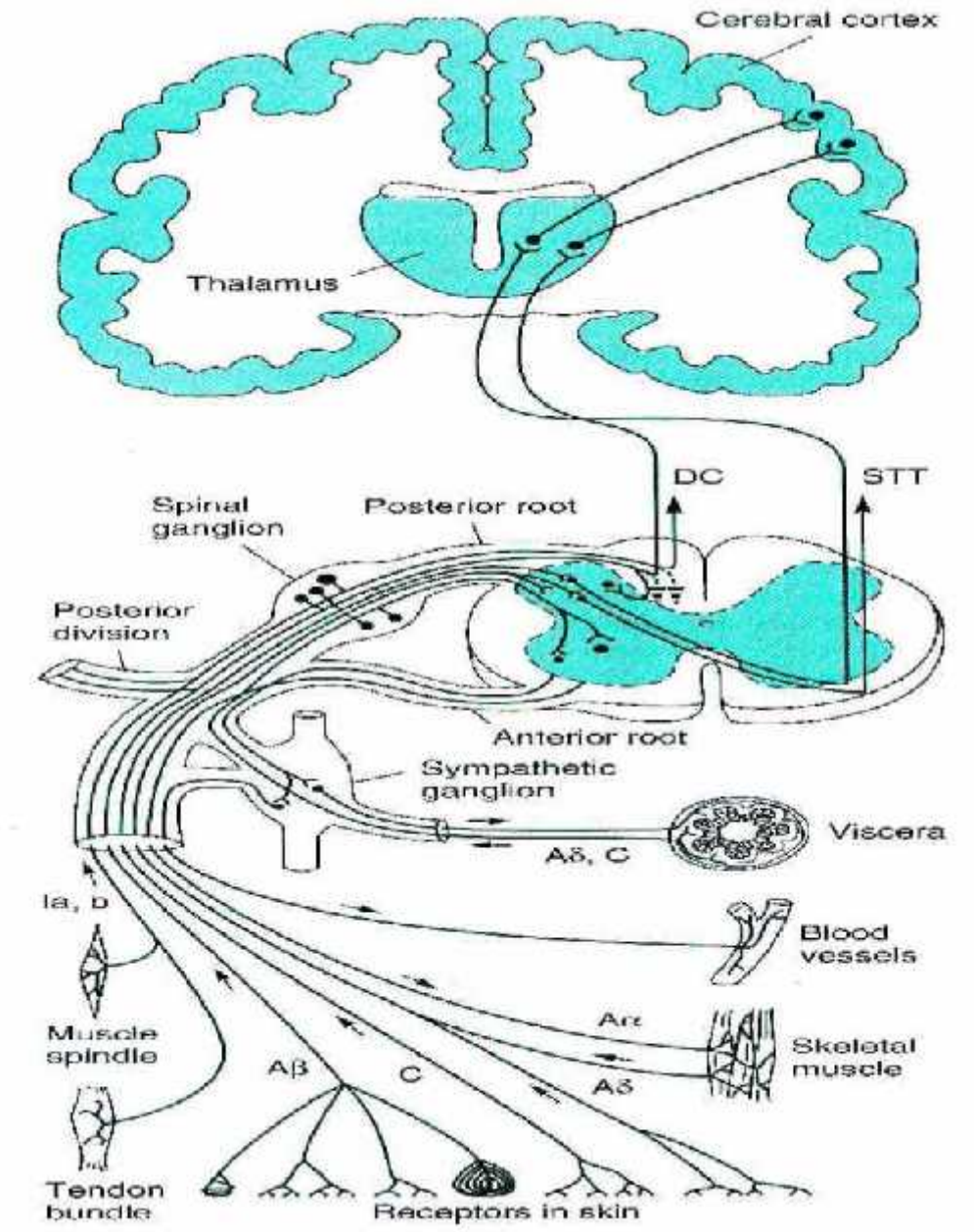


FIG 9: PAIN PATHWAYS

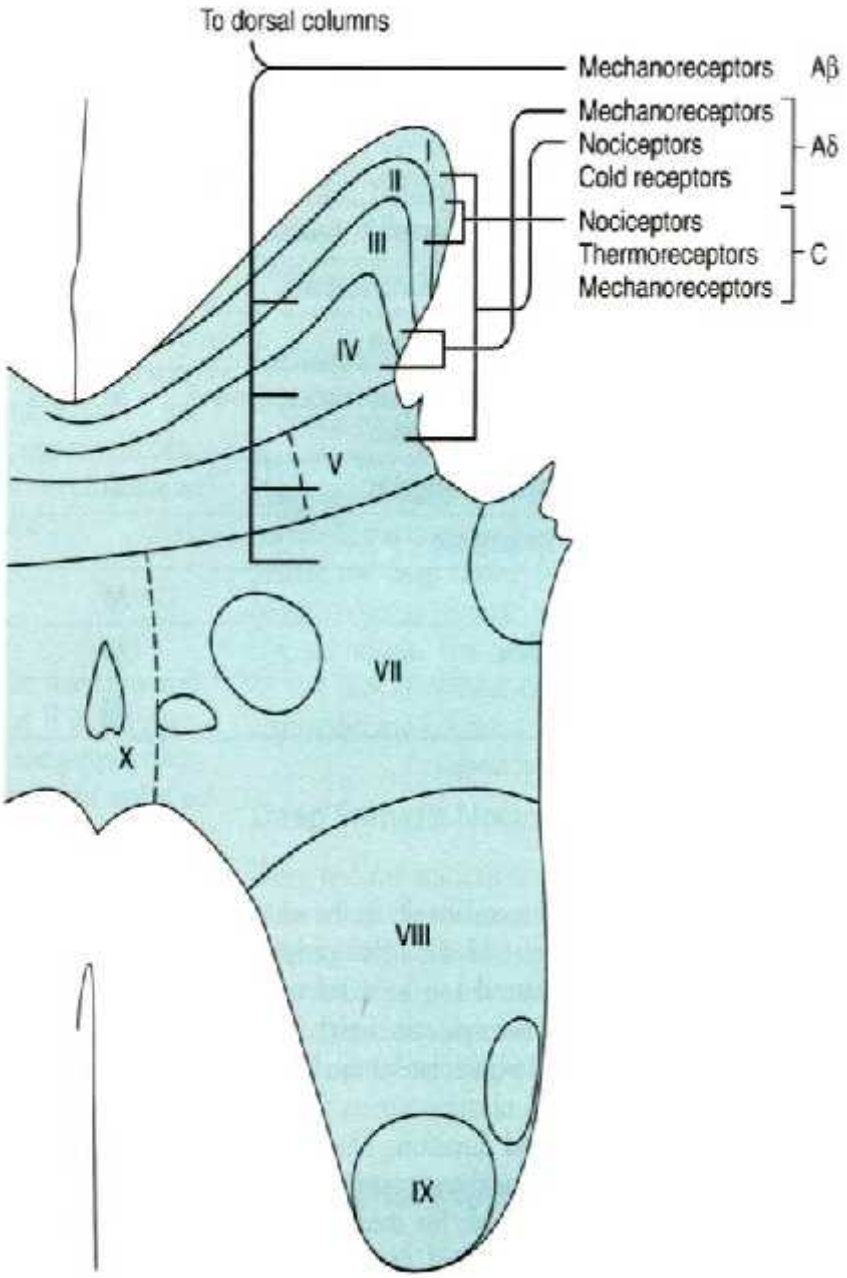


FIG 10: REXED'S LAMINA

First six laminae, which make up the dorsal horn, receive all afferent neural activity. Second order neurons are nociceptive - specific or wide dynamic range (WDR) neurons. Nociceptive specific neurons serve only noxious stimuli, but WDR neurons also receive non-noxious afferent input from Aβ, Aδ, and C fibres. Nociceptive-specific neurons are arranged somatotopically in lamina I and have

discrete, somatic receptive fields; they are normally silent and respond only to high-threshold noxious stimulation. WDR neurons are the most prevalent cell type in the dorsal horn. Though found throughout the dorsal horn, WDR neurons are most abundant in lamina V during repeated stimulation, WDR neurons characteristically increase their firing rate exponentially in a graded fashion, even with the same stimulus intensity. They also have large receptive fields compared with nociceptive-specific neurons. Most nociceptive C fibres send collaterals to, or terminate on second order neurons in laminas I, II, and to a lesser extent lamina V. Nociceptive Aδ fibres synapse mainly in laminas I and V. Lamina I responds primarily to noxious (nociceptive) stimuli from cutaneous and deep somatic tissues. Lamina II, the substantia gelatinosa, contains many interneurons and is believed to play a major role in processing and modulating nociceptive input from cutaneous nociceptors. Laminae III and IV receive primarily non nociceptive sensory input. Laminae VIII and IX make up the anterior (motor) horn. Lamina VII is called the inter-mediolateral column and contains the cell bodies of preganglionic sympathetic neurons. Lamina V responds to both noxious and non noxious sensory input and receives both visceral and somatic pain afferents. Compared with somatic fibres, visceral nociceptive fibres are fewer in number, more widely distributed, proportionately activate a larger number of spinal neurons, and are not organized somatotopically.

The axons of most second-order neurons cross the midline close to their level of origin (at the anterior commissure) to the contra lateral side of the spinal cord before they form the spinothalamic tract and send their fibres to the thalamus, the reticular formation, the nucleus raphe magnus, and the periaqueductal gray.

The spinothalamic tract, the major pain pathway, lies anterolaterally in the white matter of the spinal cord. This ascending tract can be divided as lateral and

medial spinothalamic tract. The lateral spinothalamic tract projects mainly to the ventral posterolateral nucleus of the thalamus and carries discriminative aspects of pain such as location, intensity and duration. The medial spinothalamic tract projects to the medial thalamus and is responsible for mediating the autonomic and unpleasant motional perception of pain. Some spinothalamic fibres also project to the periaqueductal gray and they may be an important link between the ascending and descending pathways. Collateral fibres project to the reticular activating system and the hypothalamus; these are likely responsible for the arousal response to pain.

The spino reticular tract, spino mesencephalic tract, spino hypothalamic tract and spino telencephalic tract are also other pathways, which help in pain perception.[46] Spinocervical tract ascends uncrossed to the lateral cervical nucleus, which relays the fibres to the contra lateral thalamus; this tract is likely a major alternative pathway. Some fibres in the dorsal columns which mainly carry light touch and proprioception are responsive to pain, they ascend medially and ipsilaterally. Somatic and visceral afferents are fully integrated with the skeletal motor and sympathetic systems in the spinal cord, brainstem, and higher centers. Afferent dorsal horn neurons synapse both directly and indirectly with anterior horn motor neurons. These synapses are responsible for reflex muscle activity that is normally associated with pain.

Chemical mediators of pain

Several neuro-peptides and excitatory amino acids function as neurotransmitters for afferent neurons subserving pain. The most important of these peptides are substance P[44, 47] and calcitonin gene-related peptide (CGRP). Glutamate is the most important excitatory amino acid. The other neurotransmitters that help in subserving pain are glutamate, aspartate and adenosine triphosphate (ATP) which are excitatory in function. Somatostatin,[46] acetylcholine, enkephalins, β endorphins, nor

epinephrine, adenosine, serotonin, Gamma amino butyric acid (GABA) and glycine which are inhibitory in function.

Modulation of pain

Modulation of pain occurs peripherally at the nociceptor, in the spinal cord, or in supraspinal structures. This modulation can either inhibit (suppress) or facilitate (aggravate) pain.

Peripheral modulation

a) Primary hyperalgesia

b) Secondary hyperalgesia

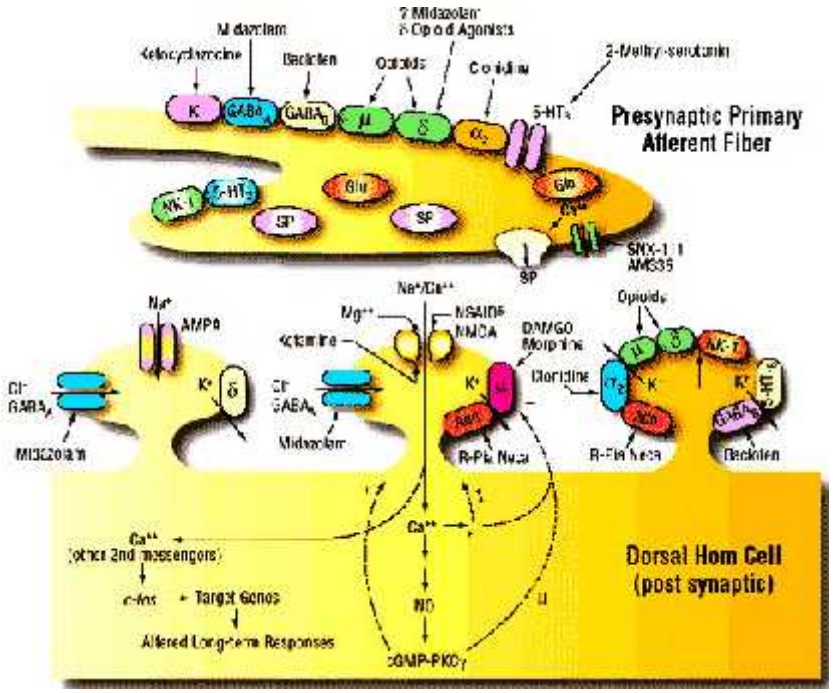


FIG 11: SYSTEMS OF PAIN RELIEF SHOWING THE VARIOUS RECEPTORS AND MEDIATORS OF PAIN

Central Modulation

A) Facilitation

B) Inhibition

Transmission of nociceptive input in the spinal cord can be inhibited by segmental activity in the cord itself, as well as descending neural activity from supraspinal centers.

Segmental inhibition: Activation of large afferent fibres subserving epicritic sensation inhibits WDR neuron and spinothalamic tract activity. Moreover, activation of noxious stimuli in noncontiguous parts of the body inhibits WDR neurons at other levels, i.e. pain in one part of the body inhibits pain in other parts. These two observations support a "gate theory" for pain processing in the spinal cord. Glycine and Gamma aminobutyric acid (GABA) are amino acids that function as inhibitory neurotransmitters. They likely play an important role in segmental inhibition of pain in the spinal cord. Antagonism of glycine and GABA results in powerful facilitation of WDR neurons and produces allodynia and hyperesthesia.

Sequelae to pain

Uncontrolled postoperative pain can result in several negative physiological effects that include disturbances of respiratory, cardiac,gastrointestinal, coagulation, renal, autonomic nervous system, endocrine and central nervous system function. Decreased mobility following orthopedic procedures, caused by severe pain impairs early ambulation and increases the risk of thrombo-embolism. Furthermore increased sympathetic activity results in peripheral vasoconstriction and production of a hypercoagulable state. These changes are associated with post operative inactivity leading to a significant reduction of blood flow in the lower limbs and can increase the risk of deep vein thrombosis. Pain produces an accelerated catecholamine response and increased concentrations of epinephrine and norepinephrine.[48] The resultant increase in systemic vascular resistance, cardiac work and myocardial oxygen consumption may be particularly harmful in patients with cardiac disease and

decreased cardiac reserve. Inadequately treated pain may result in cardiac arrhythmias, hypertension and myocardial ischemia. A decrease in the gastro intestinal motility and splanchnic circulation may be another detrimental effect of pain induced catecholamine response. Perioperative starvation of the patient also has important implications for fatigue, recovery of gastro intestinal function and impairment of postoperative rehabilitation. Many of these negative physiological effects can be reduced with improvements in postoperative pain management and postoperative rehabilitation efforts.

Complications of spinal anaesthesia

Complications associated with spinal anaesthesia can be due to effects of injected drugs, incorrect placement of needle, injection of organisms, spinal compromise due to ischemia or mass effect. Anticipation and prevention of complications along with their early diagnosis and treatment are the most important factors in dealing with regional anesthetic risks.

Complications of spinal anaesthesia may be considered as immediate or delayed.

Immediate Complications

1. Pain on injection
2. Hypotension[11]
3. Bradycardia[28]
4. Respiratory impairment [29]
5. Nausea, vomiting
6. Difficult spinal puncture

Late complications

1. Headache
2. Backache [30]

3. Urinary retention
4. Anterior spinal artery syndrome
5. Meningitis
6. Vascular injury
7. Nerve injury
8. Transient neurologic symptoms

PHARMACOLOGY

BUPIVACAINE

Bupivacaine is an amide group of local anaesthetic agent. A.F. Ekenstam and his colleagues synthesized Bupivacaine in 1957 at A B Bofors; Sweden. It was used clinically by Telivuo in 1963. Bupivacaine was the first local anaesthetic that combined the properties of an acceptable onset and profound conduction blockade and long duration of action. Bupivacaine is three to four times as potent as Lignocaine and considerably longer acting. Its speed of onset is sometimes to be marginally slower than that of Lignocaine.

Bupivacaine is an amino amide compound. It is derived from Mepivacaine. The chemical name is 1-n-butyl-DL-piperidine-2-carboxylic acid-2, 6 dimethylanilide hydrochloride, which differs from Mepivacaine in that a butyl group is substituted for a methyl group on the piperidine nitrogen.

Bupivacaine is thus a homologue of Mepivacaine, with a molecular formula of $C_{18}N_2OH_{28}HCl$.

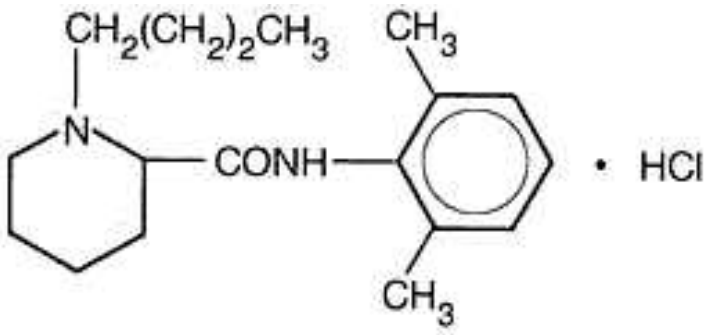


FIG 12 : CHEMICAL STRUCTURE

Mechanism of action

Bupivacaine binds to the intracellular portion of sodium channels and blocks sodium influx into nerve cells, which prevents depolarization. Since pain transmitting nerve fibres tend to be thinner and either unmyelinated or lightly myelinated, the agent can diffuse more readily into them than into thicker and more heavily myelinated nerve fibres like touch, proprioception, etc. (Myelin is non-polar / lipophilic).Bupivacaine also blocks specific potassium channels, an effect contributing to resting membrane potential depolarization.

Dosage

The maximum safe dose of Bupivacaine is in the region of 2mg kg^{-1} body weight. The concentration range currently available is 0.25%, 0.5% and 0.75% plain, 0.25% with Adrenaline1:400000 and 0.5% with Adrenaline 1:200 000 and 0.5% hyperbaric Bupivacaine.

Pharmacodynamics

The onset of action of Bupivacaine is between 4 and 6 minutes, maximum anaesthesia is obtained between 15 and 20 minutes. The duration of anaesthesia varies according to the type of block; the average duration for peripheral block is about 3.5 to 5 hours. For nerve blocks it is about 5 to 6 hours. In spinal anaesthesia, 0.75% Bupivacaine is equivalent to Tetracaine. The onset of action is about 3-4 minutes, and

complete anaesthesia occurs in 5 minutes and a subarachnoid dose of 15 to 20mg of 0.5% bupivacaine lasts for 3-4 hours The motor blockade is definitely inferior to Tetracaine.

Pharmacokinetics

Bupivacaine can be detected in the blood within 5 minutes of infiltration or following epidural or intercostals nerve blocks. Plasma levels are related to the total dose administered. It crosses the placental barrier by passive diffusion as any other local anaesthetic, but the lowest level of placental diffusion is reported for this drug due to high protein binding capacity. No effects on the fetus have been noted.

Plasma binding:

In plasma, the drug binds avidly with protein to the extent of 70% to 90%. Half life: the elimination half life is around 4-5 hours.

Metabolism

Since Bupivacaine is an amide, the liver is the primary site of metabolism. Most of the drug is partly metabolized by N-dealkylation. About 10% of the drug is excreted unchanged in urine within 24hours.[49]

Advantages of bupivacaine:

1. Less tachyphylaxis
2. Less cumulative effect
3. Selective, differential, segmental blockade
4. Less crossing of blood brain barrier
5. Less crossing of placenta
6. Less F/M ratio of 0.3, this helps in labour analgesia.

Adverse effects

No serious adverse effects have been reported following clinical doses. Hypotension and bradycardia are no greater than Mepivacaine or Lignocaine. Shivering is more frequent with Bupivacaine than with other local anaesthetics. Convulsions have followed accidental injection of large amounts of the drug into the blood vessels or after relative overdose. Nolte in 1982, in a follow up of more than 3000 cases of intradural anaesthesia, found no neurological sequelae related to use of Bupivacaine. Systemic toxicity of local anaesthetics is primarily a function of plasma levels. Local anaesthetics have the same membrane stabilizing effects on the brain and heart as on the peripheral nervous system. Commonest cause of acute systemic toxicity is accidental intra-vascular injection and this is a particular risk during epidural injection. However, continuous infusion can also lead to systemic toxicity. Toxicity is best avoided by the careful use of a dose known to be appropriate for a particular technique. Toxicity is primarily manifested as derangement of the central nervous system and cardiovascular system. Generally significantly lower doses and blood levels of local anaesthetics are required to produce central nervous system toxicity compared to those needed to disrupt the cardiovascular system.

Central nervous system

Bupivacaine can cause both excitation and depression of the central nervous system depending on the plasma level. A feeling of light headedness and dizziness followed by visual and auditory disturbances such as difficulty in focusing and tinnitus. Other subjective central nervous system symptoms include disorientation, feeling of drowsiness. Clinical signs of Bupivacaine toxicity include shivering, muscular twitching and tremors. These signs may progress to generalized convulsions of tonic clonic nature.

Cardiovascular System

Bupivacaine exerts direct effects on both cardiac muscle and vascular smooth muscle. Primary effects of Bupivacaine on cardiac muscle are electrophysiological due to their interaction with the fast sodium channels. Bupivacaine exerts a negative ionotropic effect, which is dose related. The more potent local anaesthetics like Bupivacaine tend to depress cardiac contractility at lower doses and concentration than their less potent counterparts. At concentrations of approximately 1 to 1.5 micrograms/ml Bupivacaine will depress ventricular contractility by about 25%. Bupivacaine is 16 times more potent than Lignocaine in inducing ventricular arrhythmias. Bupivacaine induced cardio vascular depression is more likely to be life threatening and management can be much more difficult.

CC/CNS ratio

Is the ratio of dosage required for irreversible cardiac collapse to the dosage, which will produce CNS toxicity. The CC/CNS ratio is lower for Bupivacaine 3.7 ± 5 as compared to Lignocaine 7.1 ± 1.1.[49]

USES

1. **Infiltration:** A concentration of 0.25% is used in healthy adults. 0.1% solution is satisfactory in debilitated patients & children.
2. **Nerve blocks:** The 0.5% solution is generally used up to 35ml of volume. This concentration is necessary to block large nerves and to produce complete motor block. A 0.25% solution is satisfactory for small peripheral nerves.
3. **Caudal block:** For obstetric analgesia and perineal surgery, the 0.25% solution is effective. A volume up to 30 ml may be used for the caudal technique. For surgery of the lower extremities, 0.5% solution must be used if good motor block is desired.
4. **Epidural block:** For obstetric analgesia and perineal surgery, 20 ml of 0.25% solution is effective. For lower extremity surgery, up to 20ml of the 0.5% solution is satisfactory.
5. **Subarachnoid block:** Bupivacaine has also become increasingly popular for spinal anaesthesia using either a hyper baric solution containing 5-8% dextrose or the commercial plain solution, which is slightly hypo baric. Concentrations of 0.5 to 0.75% are effective. 0.5% hyperbaric bupivacaine intradurally gives very good results for surgery to the lower limbs. The central neuraxial blockade produced is highly reliable and lasts between 2 to 4 hours.[49] Bupivacaine has currently established itself a place in the anaesthetists‘ armamentarium as a long acting agent producing less motor than sensory block. The sensory block gives good analgesia. It serves a useful function in central neuraxial blockade for general surgical, gynaecological and orthopedic procedures, for post operative and post traumatic analgesia, and is particularly useful for obstetric analgesia.[50]

Clonidine and Dexmedetomidine

Clonidine and Dexmedetomidine are α2 agonists. Clonidine acts as a selective partial agonist of the α2 receptor with a ratio of 200:1 (α2 to α1) whereas Dexmedetomidine is highly selective with a ratio of 1600:1.So an α1/ α2 selectivity ratio in Dexmedetomidine is eight time higher than Clonidine. These drugs are currently undergoing many clinical trials and experimentation due to their immense popularity for use in pain medicine.

The mechanism of action of these drugs involve activation of α2 adrenoreceptors which reduce peripheral Norepinephrine (NE) release by a negative feedback mechanism. Stimulation of central α2 receptors activate noradrenergic imidazoline receptors and also act on descending inhibitory tracts. The overall effect is sympatholysis resulting in analgesia, hypotension, bradycardia, and sedation.

Major differences in the pharmacology of clonidine and dexmedetomidine

Clonidine	**Dexmedetomidine**
Developed in the 1960s	Developed in the 1980s
Clinical practice: originally prescribed as a antihypertensive then as an analgesic in chronic pain (1983)	Clinical practice: tested in volunteers (1991) then used as a sedative in ICU (1999)
Ratio α2: α1 receptor binding is 200:1	Ratio α2: α1 receptor binding is 1600:1
Octanol/buffer partition coefficient: 0.8	Octanol/buffer partition coefficient: 2.8 More lipophilic (3.5-fold) than Clonidine
Plasmatic half-life t½: 9-12 hours	Plasmatic half-life t½: 2-2.5 hours
Protein binding: 50%	Protein binding: 94%

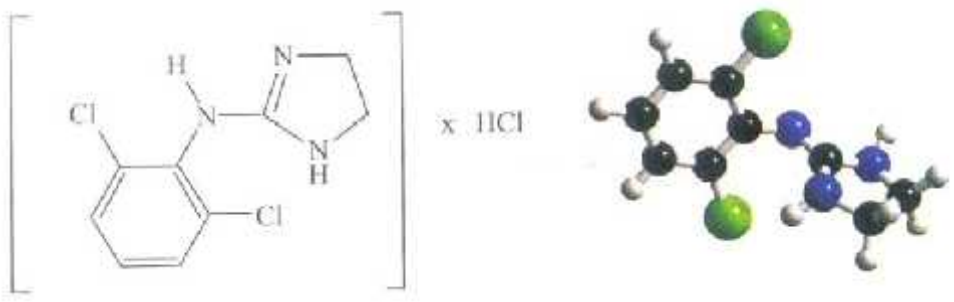
CLONIDINE[31, 32, 33, 34]

History and Chemistry:

Clonidine hydrochloride, an imidazoline derivative was originally developed as a nasal decongestant and vasoconstrictor. Its hypotensive and bradycardia effects were first appreciated in 1962. It is a centrally acting adrenergic agonist that lowers blood pressure by decreasing basal sympathetic nervous system activity. It was introduced first in Europe in 1966 and subsequently in the U.S. for use as an antihypertensive agent.

Clonidine hydrochloride is an imidazoline derivative and exists as a mesomeric compound. The chemical name is 2-(2,6-dichlorophenylamino)-2-imidazoline hydrochloride. The following is the structural formula: $C_9H_9C_{12}N_3$ HCl.

FIG 13&14: Molecular Structure and 3D View



The molecular weight of Clonidine is 266.56. Clonidine hydrochloride is an odorless, bitter, white, crystalline substance soluble in water and alcohol.

It was introduced in the early 1960's as a nasal decongestant. It was during its use a nasal decongestant that the anti hypertensive property of the

drug was found out. Subsequently more insight into the pharmacological properties has led to its use in clinical anaesthetic practice as well.

Mechanism of action:

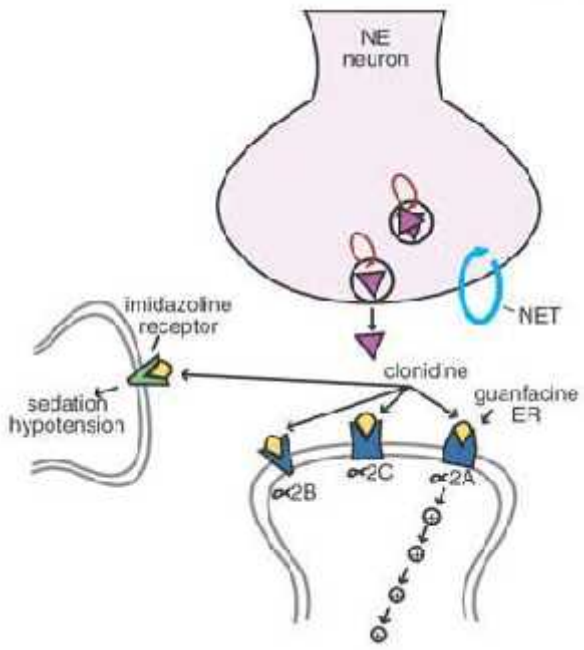


FIG 15: Mechanism of action of clonidine

Alpha-2 adrenergic agonists produce clinical effects by binding to alpha- 2 receptors of which there are 3 subtypes: alpha-2a, alpha-2b and alpha-2c. Alpha-2a receptors mediate sedation, analgesia and sympatholysis. Alpha-2b receptors mediate vasoconstriction and possibly anti-shivering mechanisms. The startle response reflects activation of alpha-2c receptors and it is the response of mind and body to a sudden unexpected stimulus, such as a flash of light, a loud noise (acoustic startle reflex), or a quick movement near the face.

In human beings, the reaction includes physical movement away from the stimulus, a contraction of the muscles of the arms and legs, blinking and it also includes blood pressure, respiration, and breathing changes. Clonidine is a centrally acting selective partial adrenergic agonist (alpha-2: alpha-1=220:1). Alpha-2 receptors are found densely in the pontine locus coeruleus which is an important

source of sympathetic nervous system innervation of the forebrain and a vital modulator of vigilance.

The sedative effects evoked by alpha-2 agonists most likely reflect inhibition of this nucleus. Clonidine also stimulates alpha-2 adrenergic inhibitory neurons in the medullary vasomotor centre. As a result, there is a decrease in the sympathetic nervous system outflow from the central nervous system (CNS) to the peripheral tissues. This causes central and peripheral attenuation of sympathetic outflow and central activation of non- adrenergic imidazoline preferring receptors. Decreased sympathetic nervous system activity is manifested as peripheral vasodilatation and a decrease in systolic blood pressure, heart rate and cardiac output. The ability of Clonidine to modify the potassium channels in the CNS and thereby hyperpolarize the cell membranes may be the mechanism for profound decrease in anaesthetic requirements produced by Clonidine. Neuraxial placement of Clonidine inhibits spinal substance P release and nociceptive neuron firing produced by the noxious stimulation. Alpha-2 afferent terminals are situated centrally and peripherally, in the superficial laminae of the spinal cord and several brain stem nuclei. This suggests that Clonidine's analgesic effects are more pronounced after neuraxial administration. Clonidine synchronously decreases the cold response threshold while slightly increasing the sweating threshold thus suggesting that it acts on the central thermoregulatory system rather than preventing shivering peripherally.

Pharmacological effects:

Intravenous Clonidine can cause a transient rise in blood pressure due to its ability to cause vasoconstriction via an alpha-2 agonist effect on vascular smooth muscle of skin and mucosa. This is followed by a decreased blood pressure

due presumably to activation of CNS alpha-2 receptors, resulting in a decreased central outflow of impulses in the sympathetic nervous system, although this is an area of intense current research interest, and some evidence suggests that different mechanisms may be more important. Some of the antihypertensive effect of Clonidine may also be due to diminished release of Norepinephrine at sympathetic postganglionic nerve terminals due to activation of presynaptic alpha-2 receptors.

Pharmacokinetics:

Clonidine is well absorbed orally, and is nearly 100% bioavailable. The mean half life of the drug in plasma is about 12 hours. It is excreted in an unchanged form by the kidney, and its half life can increase dramatically in the presence of impaired renal function. A transdermal delivery system is available in which the drug is released at a constant rate for about a week. Three or four days are required to achieve steady state concentrations.

Side Effects

1. **Body as a Whole:** Weakness, about 10 in 100 patients; fatigue, about 4 in 100; headache and withdrawal syndrome each about 1 in 100. Also reported were pallor; a weakly positive Coombs' test; increased sensitivity to alcohol; and fever.
2. **Cardiovascular :** Orthostatic symptoms, about 3 in 100 patients; palpitations and tachycardia, and bradycardia, each about 5 in 1000. Syncope, Raynaud's phenomenon, congestive heart failure, and electrocardiographic abnormalities (i.e., sinus node arrest, junctional bradycardia, high degree AV block and arrhythmias) have been reported rarely. Rare cases of sinus bradycardia and atrioventricular block have been reported, both with and without the use of concomitant digitalis.

3. **Central Nervous System :** Nervousness and agitation, about 3 in 100 patients; mental depression, about 1 in 100 and insomnia, about 5 in 1000. Other behavioral changes, vivid dreams or nightmares, restlessness, anxiety, visual and auditory hallucinations and delirium have rarely been reported.
4. **Dermatological :** Rash, about 1 in 100 patients; pruritus, about 7 in 1000; angioneurotic edema and urticaria, about 5 in 1000; alopecia, about 2 in 1000.
5. **Gastrointestinal :** Nausea and vomiting, about 5 in 100 patients; anorexia and malaise, each about 1 in 100; mild transient abnormalities in liver function tests, about 1 in 100; hepatitis, parotitis, constipation, pseudo-obstruction, and abdominal pain, rarely.
6. **Genitourinary :** Decreased sexual activity, impotence and loss of libido, about 3 in 100 patients; nocturia, about 1 in 100; difficulty in micturition, about 2 in 1000; urinary retention, about 1 in 1000.
7. **Hematologic :** Thrombocytopenia, rarely.
8. **Metabolic :** Weight gain, about 1 in 100 patients; gynecomastia, about 1 in 1000; transient elevation of blood glucose or serum creatine phosphokinase, rarely.
9. **Musculoskeletal :** Muscle or joint pain, about 6 in 1000 and leg cramps, about 3 in 1000.
10. **Oro-otolaryngeal :** Dryness of the nasal mucosa was rarely reported.
11. **Ophthalmologic:** Dryness of eyes, burning of the eyes and blurred vision were reported.

Drug Interactions :

Clonidine may potentiate the CNS-depressive effects of alcohol, barbiturates or other sedating drugs. If a patient receiving Clonidine hydrochloride is also taking tricyclic antidepressants, the hypotensive effect of Clonidine may be reduced, necessitating an increase in the Clonidine dose.

Due to a potential for additive effects such as bradycardia and AV block, caution is warranted in patients receiving Clonidine concomitantly with agents known to affect sinus node function or AV nodal conduction, e.g., digitalis, calcium channel blockers and beta-blockers.

Amitriptyline in combination with Clonidine enhances the manifestation of corneal lesions in rats (see Toxicology).

Toxicology :

In several studies with oral Clonidine hydrochloride, a dose-dependent increase in the incidence and severity of spontaneous retinal degeneration was seen in albino rats treated for six months or longer. Tissue distribution studies in dogs and monkeys showed a concentration of Clonidine in the choroid.

In view of the retinal degeneration seen in rats, eye examinations were performed during clinical trials in 908 patients before, and periodically after, the start of Clonidine therapy. In 353 of these 908 patients, the eye examinations were carried out over periods of 24 months or longer. Except for some dryness of the eyes, no drug-related abnormal ophthalmological findings were recorded and, according to specialized tests such as electroretinography and macular dazzle, retinal function was unchanged.

In combination with Amitriptyline, Clonidine hydrochloride administration led to the development of corneal lesions in rats within 5 days.

Carcinogenesis, Mutagenesis, Impairment of Fertility :

Chronic dietary administration of Clonidine was not carcinogenic to rats (132 weeks) or mice (78 weeks) dosed, respectively, at up to 46 or 70 times the maximum recommended daily human dose as mg/kg (9 or 6 times the MRDHD on a mg/m^2 basis). There was no evidence of genotoxicity in the Ames test for mutagenicity or mouse micronucleus test for clastogenicity.

Fertility of male or female rats was unaffected by Clonidine doses as high as 150 mcg/kg (approximately 3 times MRDHD). In a separate experiment, fertility of female rats appeared to be affected at dose levels of 500 to 2000 mcg/kg (10 to 40 times the oral MRDHD on an mg/kg basis; 2 to 8 times the MRDHD on an mg/m^2 basis.)

Over dosage :

Hypertension may develop early and may be followed by hypotension, bradycardia, respiratory depression, hypothermia, drowsiness, decreased or absent reflexes, weakness, irritability and miosis. The frequency of CNS depression may be higher in children than adults. Large overdoses may result in reversible cardiac conduction defects or dysrhythmias, apnea, coma and seizures. Signs and symptoms of overdose generally occur within 30 minutes to two hours after exposure. As little as 0.1 mg of Clonidine has produced signs of toxicity in children.

Antidote:

There is no specific antidote for Clonidine over dosage. Clonidine over dosage may result in the rapid development of CNS depression; therefore, induction of vomiting with Ipecac syrup is not recommended. Gastric lavage may be indicated following recent and/or large ingestions. Administration of

activated charcoal and/or a cathartic may be beneficial. Supportive care may include Atropine sulfate for bradycardia, intravenous fluids and/or vasopressor agents for hypotension and vasodilators for hypertension. Naloxone may be a useful adjunct for the management of Clonidine-induced respiratory depression, hypotension and/or coma; blood pressure should be monitored since the administration of naloxone has occasionally resulted in paradoxical hypertension. Tolazoline administration has yielded inconsistent results and is not recommended as first-line therapy. Dialysis is not likely to significantly enhance the elimination of Clonidine.

Available forms:

Clonidine is available as tablets, injections and transdermal patches as in table.

Available formulations of clonidine

Formulations	Generic / Brand	Available Dosage/ Strength
Oral tablets	Clonidine tablets	0.1, 0.2 and 0.3 mg
Transdermal patches	Clonidne-TTS(Catapress)	0.1, 0.2 and 0.3g
Combination tablets	Clonidine and chlorthalidone	0.1, 0.2 or 0.3 mg clonidine+15mg
Injection	Cloneon , Duraclon	500, 150, 100 mcg/ml

Various roots and doses of clonidine

Route	Dose
Intranasal	2-4 mcg/kg
Intramuscular	2mcg/kg
Oral	4-5 mcg/kg
Rectal	2.5-5 mcg/kg with atropine 40 mcg/kg
Intravevous	1-2 mcg/kg bolus or 0.18-3.16 mcg/kg/hr infusion.
Caudal anesthetic adjuvant	1-2 mcg/kg
Spinal anesthetic adjuvant	1-2 mcg/kg
Epidural anesthetic adjuvant	00.0625% Bupivacaine with fentanyl 1 mcg/ml and clonidine 0.6 mcg/ml
Sciatic block	0.2% Ropivacaine 0.4mg/kg/hr with clonidine 0.12 mcg/kg/hr infusion.

Anaesthetic use of Clonidine:

The anaesthetic use of an alpha-2 adrenergic receptor agonist has been of considerable and prolonged interest over the last 20 years. Clonidine is the archetype of this class of drugs. Though it is not the most selective acting drug, its use in anaesthetics is getting familiar by the day. The different sedative, hemodynamic

and analgesic action of the drug is however confusing. Presently there is a plethora of evidence available to us describing its use in clinical anaesthetic purpose. Based on this evidence it might be prudent to argue that it is a valuable agent available in the anaesthetic armamentarium.

1. **Premedication:** Clonidine causes sedation by stimulation of the locus ceruleus, a nucleus of the medulla involved in the sleep wake cycle. Sedation is by the stimulation of specific alpha-2 receptors coupled with a G protein, leading to cell membrane hyperpolarisation. The sedative effect can be useful when Clonidine is used as a premedicant. In addition it also has an anaesthesia- sparing effect. Alpha-2 adrenergic agonists reduce the dose of intravenous hypnotics and also reduce the MAC of the volatile anaesthetic agents. Clonidine has been recommended in doses of e in doses of 4 mcg/kg orally or intranasally and in doses of 5µg/kg rectally provides adequate sedation. Routine Atropine administration along with Clonidine negates the adverse effects like bradycardia and hypotension.

   However, one needs to cautious with the dosages of the IV induction agents when Clonidine has been used as a premedicant. Their dosages need to be reduced. Otherwise there is a propensity for the increased incidence of hypotension after induction and increased incidence of bradycardia during anaesthesia.

   Its use as a premedicant is particularly useful in certain subgroup of patients like

a) Drug addicts and alcoholics who give problems like withdrawal symptoms and risk of increased sympathetic activity especially in cocaine users.

b) Chronic pain and palliative care patients who often receive large doses of opioids and therefore have large perioperative opioid needs. This can be reduced with Clonidine premedication.

c) Hypertensive patients who are particularly vulnerable to blood pressure swings. Premedication with Clonidine is useful, though very underutilized means of reducing the haemodynamic hyperactivity.

2. **Control of haemodynamic response:**

The haemodynamic effects of alpha-2 adrenergic agonists are both central and peripheral. Stimulation of the peripheral sub endothelial receptor causes vasoconstriction. This action is however transient.

However, stimulation of the alpha -2 adrenergic receptors of the neurons in the nucleus tractus solitarius causes inhibition of the nucleus of the sympathetic neurons in the medulla. By this mechanism, alpha adrenergic agonists reduce the tonic activity of the baroreflex, decreasing atrial pressure and causing bradycardia. It is interesting to note that the phasic activity of the baroreflex is preserved or perhaps even improved, so that any decrease in arterial pressure is followed by a significant increase in heart rate. In addition alpha-2 adrenergic agonists depress presynaptic sympathetic neurons in the lateral horn of the thoracic spinal cord. It should be noted here that this effect is reversed by the local administration of cholinesterase inhibitor Neostigmine. It is a result of this modality of action that intrathecal administration of Clonidine causes more profound hypotension than after intravenous administration. Hypotension and bradycardia caused by Clonidine need to be reversed by fluids, vasoconstrictors (eg: Phenylephrine) and Atropine respectively. Large doses may be needed.

Clonidine prevents hypertension and tachycardia during laryngoscopy

and intubation as well as during surgical stimulation. During recovery from anaesthesia Clonidine also prevents tachycardia and hypertension, decrease the incidence of shivering and reduce VO_2 to control postoperative shivering it is given in 50mcg doses. Doses up to 150mcg have been reported to control postoperative shivering in 90% of patients within 5 minutes. Patients undergoing cardiac surgery and vascular surgery have superior control of haemodynamics and reduced incidence of myocardial ischemia in patients who have been pretreated with Clonidine. Patients with coronary artery disease undergoing major vascular surgical procedures, Clonidine has been found to decrease both morbidity and mortality.

3. **Postoperative analgesia and Regional Anaesthesia :**

Alpha -2 adrenergic agonists inhibit transmission of nociceptive stimuli in the dorsal horn of the spinal cord. Their effects mimic that of noradrenalin released by the inhibitory descending pathways. Noradrenaline inhibits the evoked activity of the wide dynamic range neurons and causes analgesia in laboratory animals. Clonidine increases the analgesic effect of opiates and interacts with cholinergic neurons to do so. They augment local anaesthetic blockade and prolong duration.

A. Central Neuraxis Blocks:

a) **Epidural:** Because of its action in the spinal cord, Clonidine has been given both intrathecally as well epidurally. If used as a sole agent to produce epidural analgesia large doses (up to 2 - 3000 mcg/ day) are needed to produce long term analgesia. At these doses significant sedation, bradycardia, hypotension are common. Thus its use as a sole is not popular at all. It is used more commonly as a combination with opioids and or local anesthetics to

provide good to excellent analgesia with minimal side effects. The dose in combination with other agents is limited to 10 - 15 mcg / hour.

b) **Spinal:** Compared to Morphine, intrathecal Clonidine produces analgesia of shorter duration but without the associated risk of respiratory depression or urinary retention. In association with local anesthetics the maximum dose of intrathecal Clonidine is 1-2 mcg/ kg. Giving Clonidine with local anesthetics improves the quality and duration of the block, minimizes the tourniquet pain during lower limb surgery, and prevents shivering.

c) **Caudal:** Caudal Clonidine combined with local anaesthetics in children potentially very useful and increases the duration of anaesthesia and analgesia by a factor of 2 or 3 without hemodynamic side effects. The dosage recommended in the caudal route is 1-2 mcg / kg.

Epidural Clonidine has also been suggested for use in labour analgesia. Clonidine has been given alone or in combination with Sufentanil and bupivacaine. Clonidine does cross the placental barrier but no adverse events have been documented in the newborns. To avoid hypotension and bradycardia in the foetus as well, the recommended dose of Clonidine has been suggested as 100 mcg during labour.

B. Peripheral Nerve Blocks:

Clonidine is commonly used as an adjuvant to local anaesthetics in peripheral nerve blocks where it prolongs the duration of anaesthesia as well analgesia. This effect is obtained at relatively small doses (2 - 3 mcg/kg) which obviously reduce the risks of side effects. Adding Clonidine gives very good quality of analgesia after lower limb surgery with the duration of analgesia

lasting beyond 24 hours.

The quality of intravenous regional anaesthesia (IVRA) or Bier's block produced by Lignocaine is improved by the addition of Clonidine. Addition of 150 mcg Clonidine has been found to enhance the tolerance of the tourniquet.

Intraarticular analgesia has also been shown to be improved with Clonidine. The results are similar to the ones found with intraarticular Morphine.

Clonidine thus has wide applications as an adjunct to local anaesthetics in peripheral regional blocks.

Other uses are:

1. **Prevention of emergence agitation:** In children who were given Clonidine had less perioperative sympathetic stimulation and postoperative pain as compared to children who were given Midazolam .
2. **Decreasing Minimum Alveolar Concentration (MAC) of sevoflurane:** Studies have found that oral Clonidine 4 mcg/kg given 105 minutes before induction decreased MAC values of Sevoflurane for LMA insertion.The combination of Clonidine and nitrous oxide lessened the MAC of Sevoflurane more than that achieved by either drug alone .
3. **Postoperative nausea and vomiting (PONV):** Studies has shown that premedication with 4mcg/kg of oral Clonidine 105 minutes before paediatric strabismus surgery enhances the antiemetic effect of Propofol when compared with oral Midazolam 0.4 mg/kg . Both oral and caudal Clonidine has been reported to reduce the incidence of postoperative vomiting in children.

4. **Controlled hypotension:** In adolescents aged 10 – 16 years, oral Clonidine 5 mcg/kg on the night before surgery and 90 minutes before a major oromaxillofacial surgery reduced the dose of anaesthetics, analgesics, hypotensive agents and provided faster recovery from anaesthesia. It also reduced the fluctuations in blood pressure and heart rate perioperatively .
5. **In cardiovascular surgery:** Intravenous Clonidine 0.18 to 3.16 mcg/kg/hr was found to be an effective analgesic, sedative and it ensured haemodynamic stability by decreasing withdrawal symptoms like CNS hyperactivation, hypertension, tachycardia and fever following surgery to correct congenital heart defects in infants aged 0–24 months. There was an age related normalized profile of the haemodynamic parameters with a reduction in heart rate and mean arterial pressure from the upper norm to the mean within 24 hours. In no case, was there a fall in blood pressure which required additional therapy to reach the target blood pressure.
6. **Post operative shivering:** Clonidine is effective in treating post operative shivering in children. In a study Clonidine prevented postoperative shivering when compared to Midazolam. Extrapolation from adult data revealed that a dose of 1.5 mcg/kg is required to stop shivering in 5 minutes after drug administration.
7. **Daycare Surgery:** Oral Clonidine premedication and new safer local anaesthetics like Ropivacaine and Levobupivacaine with adjunvants like Clonidine or Ketamine for regional blocks and single caudal shots prolong analgesia with minimal side effects.

8. **Attenuation of response to tracheal intubation and extubation:** It was found that children premedicated with rectal Clonidine 2.5 mcg/kg did not have a rise in neuropeptide Y, a marker of major adrenergic activation during tracheal intubation, compared to those who received Midazolam 300 mcg/kg. It was also found that oral Clonidine 4 mcg/kg given 105 minutes before induction attenuated hemodynamic changes associated with tracheal extubation
9. **Anaesthetic sparing effect:** Oral Clonidine premedication at a dose of 2-4 mcg/kg decreases the dose of intravenous barbiturate required for induction of anaesthesia and also reduces Halothane requirement for maintenance of anaesthesia.
10. **Treatment of spasticity:** Clonidine is used in children diagnosed with cerebral palsy or traumatic brain injury.

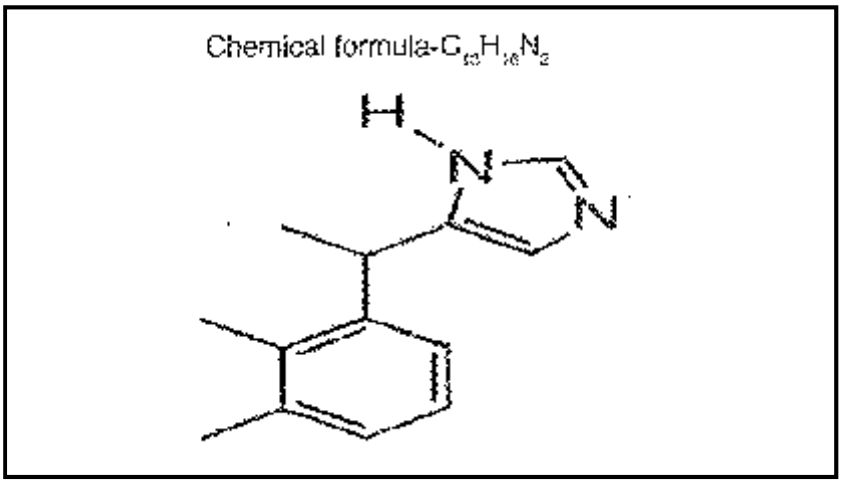
Contraindications to the use of Clonidine:

1. Hypovolemia,
2. A-V block,
3. Prolonged P-R interval and
4. Spontaneous bradycardia.

DEXMEDETOMIDINE[35, 36, 37, 38, 39, 40, 41, 42]

Dexmedetomidine, a highly selective and specific alpha 2 adrenergic agonist and was first synthesized in late 1980's. Dexmedetomidine is pharmacologically active S - enantiomer of medetomidine and is dextro isomer. Dexmedetomidine became α2 agonist of choice, due to its greatest α2 : α1 affinity (8 times greater than Clonidine).

Fig 16: Chemical structure of Dexmedetomidine



It is small molecule containing imidazole ring. It is chemically described as 4-[(1 S)--1 -(2,3-dimethylphenyl)ethyl]-1 H-imidazole monohydrochioride. Empirical formula is C13H16N2.HCL. It has a molecular weight of 236.7.

Mechanism of action:

Alpha 2 receptors are pre and post synaptic receptors found within central and peripheral nervous system. In CNS, the specific sites are locus coeruleus of upper brain stem and substantia gelatinosa in spinal cord. α2A receptors located in locus cerulus are responsible for sedation, anxiolysis and sympatholysis mediated by G- protein inhibition of L type calcium channels in post synaptic receptors. Dexmedetomidine appears to inhibit ion conductance through L- or P - type calcium channels and to facilitate conductance through voltage gated calcium activated

potassium channels. It is reversible by α2- adrenergic antagonists (e.g. Atipamezole). Effects are noncortical and sub cortical.

Dexmedetomidine produces analgesic effect by action on α2 receptor within locus coeruleus and spinal cord. Stimulation of α2 adrenergic receptors at this site reduces central sympathetic output, resulting in increased firing of inhibitory neurons. The presence of Dexmedetomidine at α2 adrenergic receptors in the dorsal horn of the ‘spinal cord modulates release of substance P to produce analgesic effects. Both α2B and α2C receptors are mostly post- synaptic.

These receptors are located mainly in dorsal horn of spinal cord and their activation inhibits nociception. Stimulation of α2B receptors post-synaptically mediates vasoconstriction in arterial and venous systems. Thus, it has dual mode of action- Central and peripheral. Centrally it acts on the postsynaptic α2 inhibitory receptors, resulting in sympatholysis and sedation.

Same action at the spinal cord results in analgesic effect. This antinociceptive effect may explain the prolongation of the sensory block when added to spinal anaesthetics. In the peripheral nerves and autonomic ganglia it reduces the release of catecholamine leading to sympatholytic effect. Alpha 2 receptors do not have an active role in the respiratory center, therefore, Dexmedetomidine throughout a broad range of plasma concentration (up to 8 mg/ml), has minimal effects on the respiratory system.

PHARMACOLOGICAL EFFECTS:

Dexmedetomidine is both potent and safe.

A. **Cardiovascular system:** It decreases heart rate, systemic vascular resistance and indirectly decreased myocardial contractility, cardiac output and systemic blood pressure. However, the hemodynamic effects of a bolus of

Dexmedetomidine are biphasic in a dose dependent manner. The initial hypertensive response is due to peripheral post- synaptic α2B stimulation with vasoconstriction and can be avoided by elimination or slow administration of the bolus dose.

Central pre-synaptic α2A stimulation decreases Norepinephrine through negative feedback mechanism which leads to hypotension (due to peripheral vasodilatation) and bradycardia. The beneficial effect on myocardial oxygen balance has been shown to decrease pen-operative myocardial ischaemia and infarction in cardiac as well as non cardiac surgery.

B. **CNS:** Dexmedetomidine decreases cerebral blood flow. It causes sedation, hypnosis, analgesia and anxiolysis. It ablates memory in dose dependent manner. Do not cause impairment of cognitive function.

C. **Gastrointestinal system:** Dexmedetomidine decreases gastro-intestinal secretion and motility. Thus may produce nausea and vomiting.

D. **Autonomic nervous system:**Dexmedetomidine effectively blocks the sympathetic stress response to surgical stimulation, thereby providing further hemodynamic stability.

E. **Respiratory system:** Dexmedetomidine produces sedation retaining the ventilatory response to increasing CO2. It enhances analgesia without causing further respiratory depression.

Pharmacokinetics

Following intravenous administration, it exhibits following pharmacokinetic characteristics: rapid distribution phase with distribution half life (t ½α) of about 6 minutes; and a terminal elimination half life (t ½) approximately 2 hours. It exhibits

linear pharmacokinetics in the dosage range of 0.2 to 0.7 mcg/kg/hr when administered by IV infusion for up to 24 hours.

Distribution

It is distributed widely throughout the body. The drug is initially distributed rapidly in high vascular organs such as the heart, lung and brain, then in skeletal muscle and finally in deeper fat compartments. The steady state volume of distribution of Dexmedetomidine after intravenous administration is approximately 118 liters. The average protein binding is 94%, and is significantly decreased in subjects with hepatic impairment.

Metabolism

Dexmedetomidine undergoes almost complete biotransformation with very little unchanged Dexmedetomidine excreted in urine and faeces.

Biotransformation involves both direct glucoronidation as well as cytochrome P450 mediated metabolism. Metabolites have no known clinical effects.

Elimination

The terminal elimination half life (t ½) is approximately 2 hours. The metabolites are eliminated in urine (95%) and faeces (4%). Clearance is estimated to be approximately 39 L/hour.

Factors affecting Dexmedetomidine pharmacokinetics

It is necessary to reduce the dose depending on the degree of hepatic impairment. Majority of metabolites excreted in urine, metabolites may accumulate upon long term infusion in patients with impaired renal function. Elderly may be more sensitive to the effects of Dexmedetomidine.

Clinical efficacy

Dexmedetomidine is used as an analgesic, as an adjunct to general or regional anaesthesia, and as an agent for premedication and maintenance of general anaesthesia. Preoperatively, Dexmedetomidine may be used for its analgesic action, to provide anxiolysis and sedation and as a supplement to anaesthesia. Also it is used for sedation of initially intubated and mechanically ventilated patients in an intensive care setting. Also used for sedation of non-intubated patients prior to and or during surgical and other procedures.

The use of Dexmedetomidine as adjuvant in regional anaesthesia is still not validated. But researchers have found that 3 µg Dexmedetomidine and 30 µg Clonidine are equipotent intrathecally. The addition of 5 µg of Dexmedetomidine prolonged the postoperative analgesic effect of bupivacaine by 8 hours.

Safety and tolerability:

Dexmedetomidine maintains spontaneous respiration and patency of the airway unrivaled by other sedatives. It has less likelihood of shivering. No risk of physical dependence. Mild or no amnesia. No tachyphylaxis or rebound hypertension.

Counter measures for adverse effects:

- Hypotension treated by decreasing or stopping infusion of drug, increases the rate of IV fluid administration, elevation of lower extremities, and use of pressor agents.
- Bradycardia treated by injection atropine.
- Reduced lacrimation treated by lubrication of patients eye to prevent corneal dryness.
- Transient hypertension treated by decreasing the dose infusion rate.
- Nausea and vomiting can be treated with antiemetic.

- Significant cardiovascular dysfunction treated by resuscitative measures.
- Parental drug products inspected visually for particulate matter and discoloration prior administration.

Dexmedetomidine: contraindication and cautions It should not be administered to patients in following categories.

- Those with desensitized autonomic nervous system control.
- Those with preexisting severe ventricular dysfunction.
- Those with preexisting advanced heart blocks.
- Those with renal or hepatic impairment
- Those with known hypersensitivity to Dexmedetomidine.
- Hypovoluaemic or shock patients
- Patients receiving concomitant Midazolam or other sedatives.
- Susceptibility to respiratory depression or disorder.
- Pregnant and lactating mother.

Dosage arid administration:

- Dexmedetomidine is available in 0.5 m1, l ml and 2 ml ampoules each ml of which contains Dexmedetomidine hydrochloride 100 mcg. (0.1 mg)
- Usually given by 1V injection for premedication, and or maintenance of anesthesia and sedation in ICU.
- Can also be used in spinal anesthesia and peripheral nerve blocks.
- Reduced doses are indicated in poor risk patients (with, cardiovascular and pulmonary disease, hepatic disease and liver dysfunction, geriatric patients).
- The compatibility depends upon several factors e.g. drug concentrations, diluents used, resulting pH, and temperature.

Recommended dosage regimen for Dexmedetomidine:

Adjunct to general anaesthesia: for adult patients

Loading dose of 1 mcg/kg over 10 to 20 mins followed by maintenance of 0.2 to 0.7 mcg/kg/hr intravenously.

Adjunct to regional anaesthesia:

- Epidural anesthesia: Recommended dose of Dexmedetomidine as adjuvant for epidural anesthesia is 1.5 - 2 µg/kg.
- Peripheral nerve blocks and intravenous regional anesthesia (IVRA): recommended dose is 0.5 µg/kg.

MATERIALS AND METHOD

This clinical study was conducted on 156 adult patients of ASA physical status I to III in the age group of 18-60years of either sex posted for elective lower abdominal or lower limb surgeries under spinal anaesthesia after taking informed consent at BLDE hospital Vijayapur.

Period Of Study : 18 MONTHS (October 2013-june 2015)

SAMPLE SIZE:

Estimation of sample size

According to study by KANAZ GE et al[8] ,

The mean time of sensory regression to S1 segment was

303+75 Min in goup D(DEXMEDETOMIDINE),

272+38 Min in group C(CLONIDINE)

190+48 Min in group B(NORMAL SALINE)

The mean time of motor regression to bromage 0 was

250+76 Min in group D(DEXMEDETOMIDINE)

216+35 in group C(CLONIDINE)

163+47 in group B(NORMAL SALINE)

Considering the average mean and standard deviation of time of sensory regression and motor regression 287+56, at alpha error 0.05 and beta error 0.20 the sample size is 52 for each group respectively

Following formula to be used to estimate the sample size for

$$n=\frac{(Z\alpha+Z\beta)^2 \times 2 \times S^2}{d^2}$$

Patients were randomly divided on an alternative basis into 3 groups of 52 each

Group-B: 0.5% Bupivacaine 15mg + 0.5 ml Normal saline (Test solution 3.5ml)

Group-C: 0.5% Bupivacaine 15mg + 50 µg Clonidine (Test solution was diluted with Normal saline to a total volume of 3.5ml)

Group-D : 0.5% Bupivacaine 15mg + 5 µg Dexmedetomidine(Test solution was diluted with Normal saline to a total volume of 3.5ml)

Inclusion Criteria

- Patients aged between 18-60 years
- ASA I-III
- Scheduled for elective lower abdomen and lower limb surgeries

Exclusion Criteria

- Patients using α_2-adrenergic receptors antagonists, calcium channel blockers, angiotensin converting enzyme inhibitors
- Dysrhythmia
- Body weight more than 120 Kg
- Height less than 140 cm,
- Post spinal surgeries, spinal deformity,
- History of allergy to study drugs,
- Pregnancy
- Coagulopathy
- Neurological disorder.

Method of Study

All patients examined properly in pre anaesthetic clinic one day prior to surgery. Routine investigations performed in each case including ECG, chest X-ray, serum electrolytes, Blood sugar, Blood Urea, Serum Creatinine, LFT.

Pre anaesthetic instruction,

1. Patients instructed to undergo over night fasting after 12 mid night.
2. All procedures explained in detail.

Anaesthetic technique

After arrival of patient in OT, an IV line secured with 20G IV cannula and standard monitoring inducing NIBP cuff, ECG lead, and pulse oximetry probe attached to patient. Baseline SBP and heart rate recorded by taking the mean of 3 consecutive reading taken 1 min apart.

Preloading done with Ringer lactate solution at a dose of 20 ml/kg/B.W. over 15 minute and no premedication given. The procedure of SAB was explained to the patient. Syringes of Inj Mephentermin (6mg/ml) and Inj. Atropine (.6mg/ml) loaded and kept ready for use. After taking all aseptic precautions and proper draping lumber interspace L3-L4 identified in lateral position. subarachnoid space identified by using a 25G Quinke spinal needle and once free flow of CSF appears, study solution injected with direction of bevel of needle cephaled. After completion of injection the patients immediately returned to supine position. The drug combinations were prepared by one anaesthetist and, various observations were made by a second anaesthesiologist who was involved after the procedure had been performed.

The following parameters were observed and recorded

1. Vital Parameters: Heart rate, mean arterial blood pressure and oxygen saturation monitored and recorded after the block every 3 minutes for half an hour then every 15 minutes upto 3 hour
2. Assessment of sensory blockade: Sensory level assessed by loss of pinprick sensation using a blunt 25-gauge needle along the mid-clavicular line bilaterally every minute till it reaches the highest level. In case of discrepancy level between left and right the higher level used for stastical analysis.. On achieving desired sensory blockade level, surgery was allowed. The time from intrathecal injection to two dermatome sensory regression, sensory regression to S1 dermatome were noted. The duration of sensory blockade was taken as time from onset to time of return of pinprick sensation to S1 dermatome is (lateral aspect of the calcaneus).
3. Assessment of Motor blockade This was assessed by BROMAGE SCALE. The time interval between injection of drug into subarachnoid space, to the patient's inability to lift the staright extended leg was taken as onset time(Br 3).The duration of motor block was taken from time of injection to complete regression of motor block.(ability to lift the extended leg)(Br 0)
4. Assessment of analgesia Pain was assessed by VISUAL ANALOGUE SCORE (VAS) FIRST ADVOCATED BY Revill and Robinson in 1976,VAS consists of a 10 cm line anchored at one end by a label such as" No pain'' and at the other end by a label such as the "Worst Pain Imaginable" or "Pain As Bad As CanBe". The patient simply marks the line to indicate the pain intensity and the provider then measures the length of the line to mark a point

scale. All the patients were instructed about the VAS and to point out the intensity of pain on the scale 0-no pain,10-worst pain

Visual analog scale*

Pain Intensity	Word Scale
0	No pain
1-2	Least pain
3-4	Mild pain
5-6	Moderate pain
7-8	Severe pain
9-10	Excruciating pain

Pain score >4 – supplementary analgesia given

Duration of pain relief (effective analgesia) was defined as the time from spinal injection to the first request for rescue analgesics or VAS was >4 was recorded. Rescue analgesics consisted of intravascular injection of diclofenac sodium 75 mg and repeated after 12h if needed with a maximum daily dose of 150mg.Rescue doses of diclofenac was recorded.

All durations were calculated in relation to the time of spinal injection. All duration calculated considering the time of spinal injection as time zero. Patients discharged from PACU after sensory regression to S1 dermatome and Bromage score 0.

Patients were shifted to the postoperative ward and observed till the administration of rescue analgesic (Diclofenac sodium 75mg intravenously, as per the patient demanded or VAS > 4) Occurrence of nausea and vomiting, pruritus, shivering, drowsiness, hypoxia (SO2<90%) dry mouth, bradycardia, hypotension or respiratory depression (RR <8/min) recorded to know undesirable side effects. The

incidence of hypotension(arterial B.P <20% of baseline or MAP <60mm HG was treated with inj.Mephentermin 6mg intravenous increments and bradycardia as HR <60/min was treated with atropine 0.6mg intravenous stat.Nausea and vomiting were treated with Inj. Ondansetron 4mg I.V. Shivering was treated with warm drapes and warm intravenous fluids.

OBSERVATION AND RESULTS

STATISTICAL TESTS USED: ANOVA ,CHI SQUARE TEST AND TUKEY TEST

DEMOGRAPHIC PROFILE

Table 1:

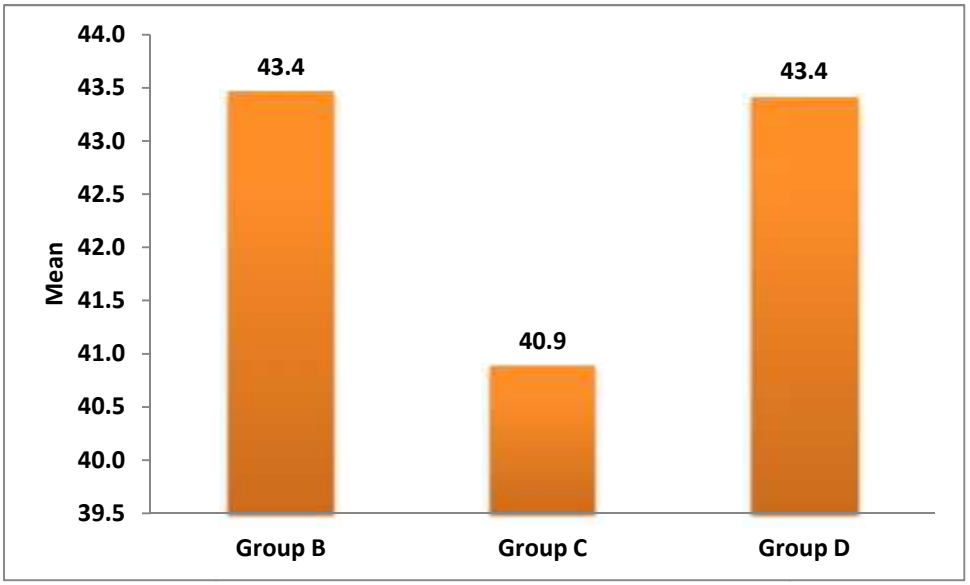
		N	Mean	SD	p value
Age (Ys.)	**Group B**	43.4	9.4	43.4	0.271
	Group C	40.9	9.9	40.9	
	Group D	43.4	8.5	43.4	
	Total	42.6	9.3	42.6	
Hight (cm.)	**Group B**	159.9	4.0	159.9	0.789
	Group C	160.5	6.9	160.5	
	Group D	160.7	7.3	160.7	
	Total	160.3	6.2	160.3	
Weight (kg.)	**Group B**	57.6	6.2	57.6	0.732
	Group C	57.2	6.7	57.2	
	Group D	56.5	8.2	56.5	
	Total	57.1	7.1	57.1	

Values are expressed as Mean ±SD.

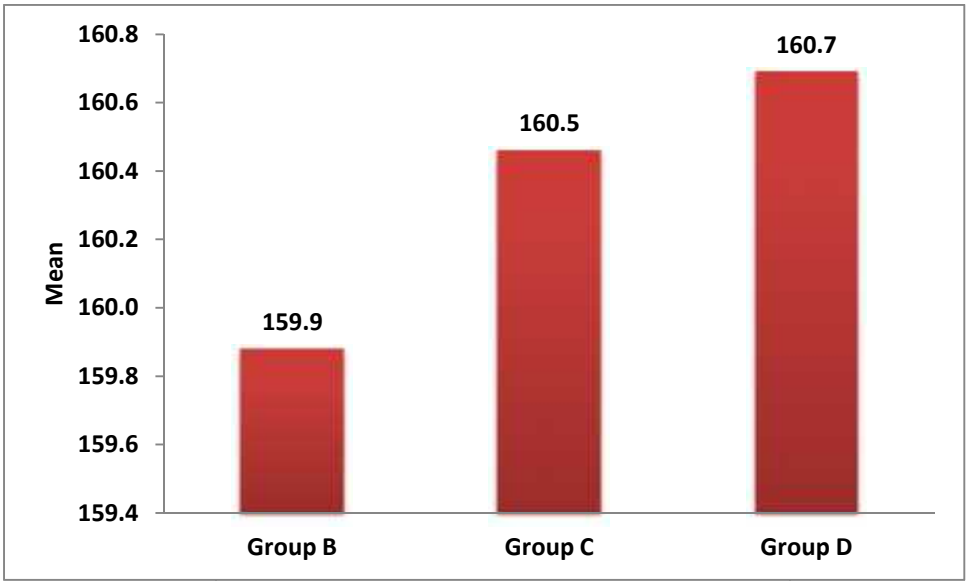
The mean age of the patient in group B was 43.4±9.4 years, in group c was 40.9±9.9 years and in group D was 43.4±8.5 years The mean height of the patient in centimetres in groupB was 159.9 ±4.0, in group C was 160.5±6.9 and in group D was 160.7±7.3.The mean weight of the patient in kilograms in group B was 57.6 ± 6.2, in group C was 57.2± 6.7 and in group D was 56.5±8.2 kgs (Table 1). There was no

statistically significant difference between the three groups with regards to age, height and weight (p>0.05).

Graph 1: Mean distribution of Age(Yrs) among Study groups



Graph 2: Mean distribution of Height (cm.) among Study groups



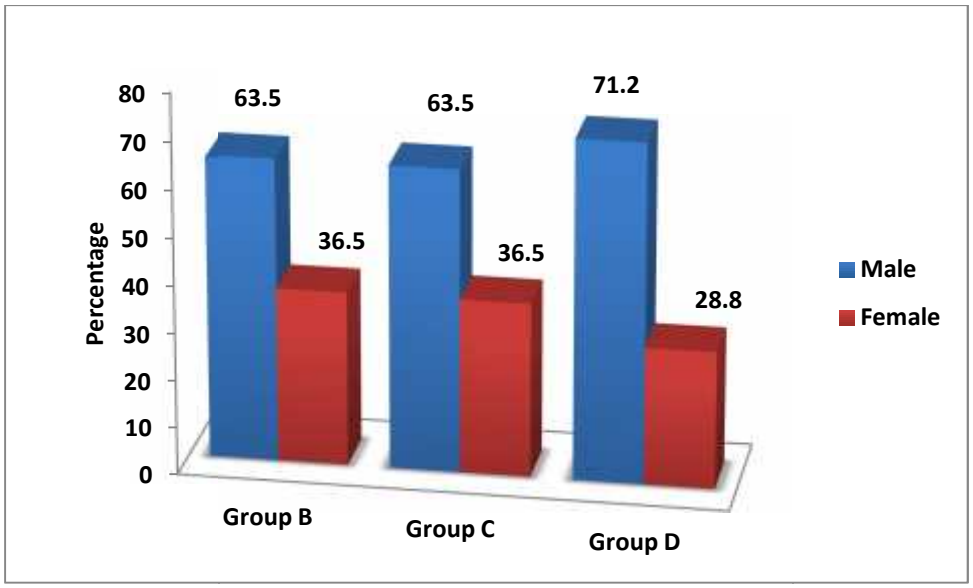
GENDER DISTRIBUTION

Table 2

Sex	Group B		Group C		Group D		Total		p value
	N	Percent	N	Percent	N	Percent	N	Percent	
Male	33	63.5	33	63.5	37	71.2	103	66	0.633
Female	19	36.5	19	36.5	15	28.8	53	34	

In group B, there were 33 males and 19 females, in group c there were 33 males and 19 females and in group D there were 37 males and 15 females. There was no statistically significant difference between the three groups in regard to sex.(p value >0.05)

Graph 3: Percent distribution of Sex among Study groups

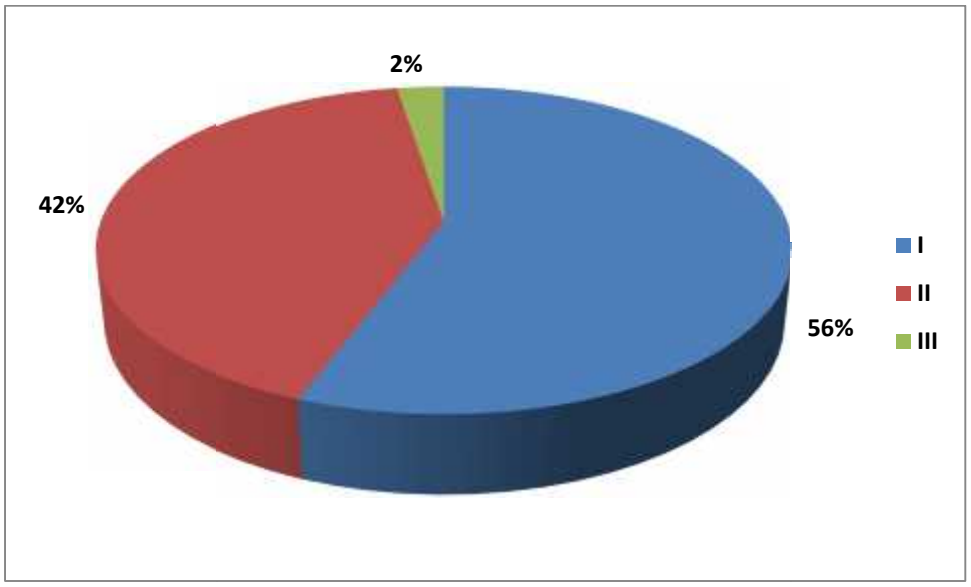


DISTRIBUTION OF PATIENTS ACCORDING TO THE ASA GRADE

Table 3

ASA Gd.	N	Percent
I	87	55.8
II	65	41.7
III	4	2.6
Total	156	100

Graph 4: ASA GRADE



The above table shows that patients in all three groups were incomparable with respect to their ASA physical status. Chi-square Test was performed on the above and p value >0.05 was taken as statistically not significant

TYPE OF SURGERY

Table 4: Distribution of Surgical Procedure among Study groups

Procedure	Group B		Group C		Group D		Total	
	N	Percent	N	Percent	N	Percent	N	Percent
AMP of NOF RT	0	0	1	1.9	0	0	1	0.6
Abdominal hysterectomy	4	7.7	3	5.8	4	7.7	11	7.1
Above Knee Amputation	0	0	0	0	1	1.9	1	0.6
Appendicetomy	3	5.8	1	1.9	3	5.8	7	4.5
CRIF of SOF RT	0	0	1	1.9	1	1.9	2	1.3
CRIF IL Nail SOF LT	0	0	1	1.9	1	1.9	2	1.3
CRIF IL Nail SOF RT	4	7.7	1	1.9	0	0	5	3.2
CRIF IL Nail Tibia LT	1	1.9	5	9.6	2	3.8	8	5.1
CRIF IL Nail Tibia RT	1	1.9	6	11.5	2	3.8	9	5.8
CRIF TFN of ITF RT	0	0	1	1.9	2	3.8	3	1.9
CRIF of ITF LT	1	1.9	0	0	0	0	1	0.6
CRIF of NOF LT	0	0	0	0	1	1.9	1	0.6
CRIF of SOF LT	3	5.8	3	5.8	0	0	6	3.8
CRIF of SOF RT	1	1.9	0	0	2	3.8	3	1.9
CRIF of Tibia LT	0	0	0	0	1	1.9	1	0.6
CRIF of Tibia RT	0	0	0	0	1	1.9	1	0.6
CRIF with Long TFN RT	1	1.9	0	0	0	0	1	0.6
Hernioplasty LT	5	9.6	6	11.5	4	7.7	15	9.6
Hernioplasty RT	5	9.6	1	1.9	6	11.5	12	7.7
ORIF + EF of Tibia RT	0	0	1	1.9	0	0	1	0.6

ORIF + IMIL of Tibia	3	5.8	0	0	0	0	3	1.9
ORIF +AMP NOF RT	2	3.8	1	1.9	1	1.9	4	2.6
ORIF IL Nail Tibia RT	2	3.8	0	0	0	0	2	1.3
ORIF IL Nail tibia LT	0	0	1	1.9	1	1.9	2	1.3
ORIF of ITF LT	1	1.9	1	1.9	2	3.8	4	2.6
ORIF of ITF RT	0	0	0	0	1	1.9	1	0.6
ORIF of NOF LT	0	0	0	0	2	3.8	2	1.3
ORIF of NOF RT	0	0	2	3.8	3	5.8	5	3.2
ORIF of SOF LT	0	0	1	1.9	1	1.9	2	1.3
ORIF of SOF RT	1	1.9	1	1.9	1	1.9	3	1.9
ORIF+AMP NOF LT	1	1.9	1	1.9	1	1.9	3	1.9
ORIF+DHS ITF LT	0	0	1	1.9	0	0	1	0.6
ORIF+DHS ITF RT	1	1.9	1	1.9	0	0	2	1.3
ORIF+DHS SOF RT	0	0	1	1.9	0	0	1	0.6
Pattelactomy LT	1	1.9	0	0	0	0	1	0.6
Skin Grafting Leg LT	3	5.8	1	1.9	2	3.8	6	3.8
Skin Grafting Leg RT	1	1.9	2	3.8	3	5.8	6	3.8
TBW of Patella LT	2	3.8	0	0	1	1.9	3	1.9
TBW of Patella RT	1	1.9	2	3.8	1	1.9	4	2.6
Tendon Repair RT	1	1.9	0	0	0	0	1	0.6
vaginal hysterectomy	3	5.8	5	9.6	1	1.9	9	5.8
Total	52	100	52	100	52	100	156	100

The above table shows distribution of patients according to type of sugery in three groups

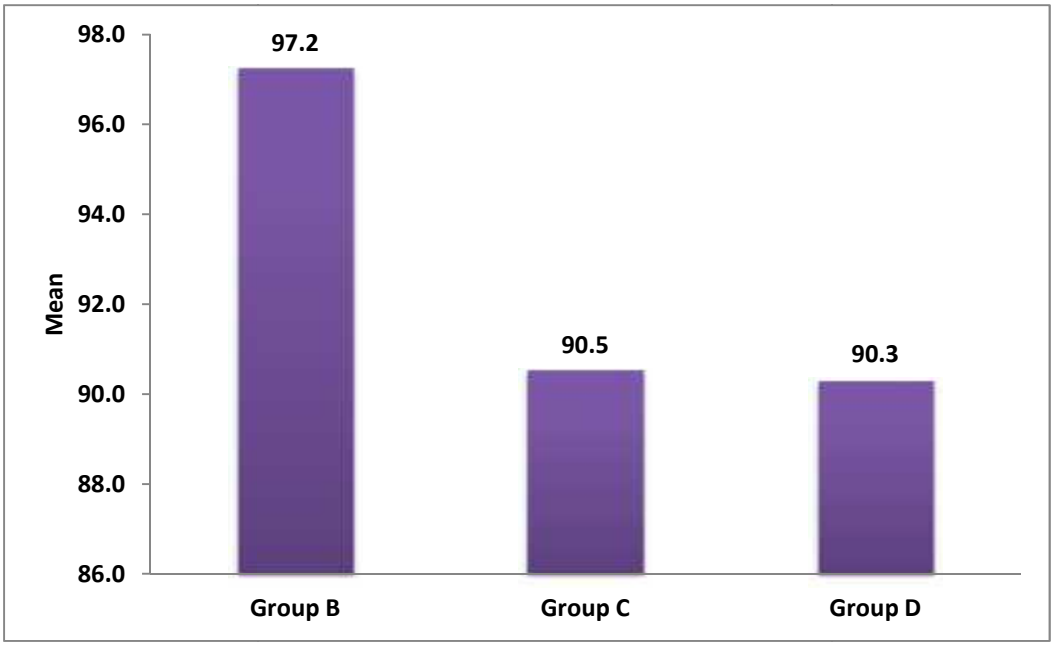
DISTRIBUTION OF PATIENTS ACCORDING TO DURATION OF SURGERY

Table 5: Mean Comparison of Duration of Surgery (min.) among Study groups

		N	Mean	SD	p value
Duration of Surgery (min.)	**Group B**	52	97.2	27.4	0.365
	Group C	52	90.5	27.9	
	Group D	52	90.3	29.3	
	Total	156	92.7	28.2	

Mean duration of surgery was 97.2±27.4 min in Group B , 90.5 ±27.9 min in Group C and 90.3 ±29.3 min in Group D (Table). The difference between the groups with regard to duration of surgery was not statistically significant.

Graph 5: Mean Comparison of Duration of Surgery (min.) among Study groups

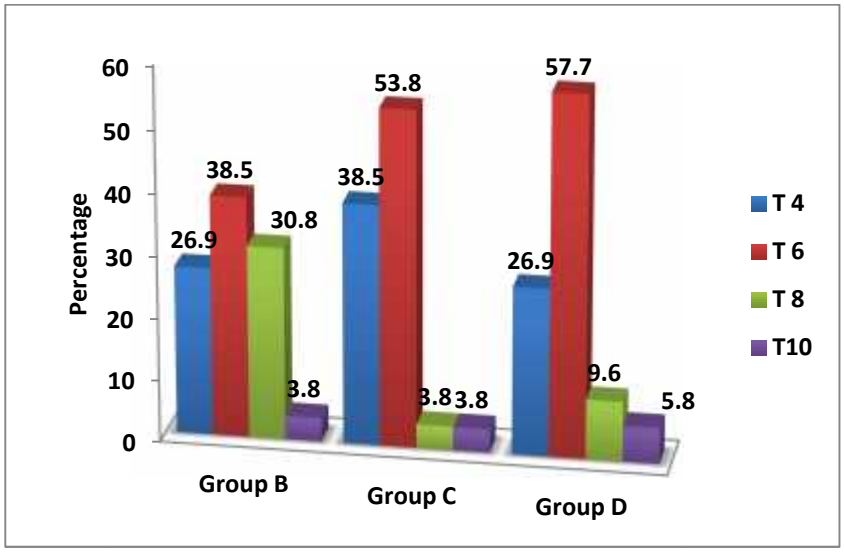


HIGHEST SENSORY LEVEL

Table 6: Percent distribution of Highest Sensory Level among Study groups

Hightest Sensory Level	Group B		Group C		Group D		Total	
	N	Percent	N	Percent	N	Percent	N	Percent
T 4	14	26.9	20	38.5	14	26.9	48	30.8
T 6	20	38.5	28	53.8	30	57.7	78	50
T 8	16	30.8	2	3.8	5	9.6	23	14.7
T10	2	3.8	2	3.8	3	5.8	7	4.5

Graph 6: Percent distribution of Highest Sensory Level among Study groups



With regard to the highest sensory level attained, patients of group B26.9% attained T4 level,38.5% achieved T6 level,30.8% achieved T8 level and 3.8% achieved T10 level. In group C 38.5% achieved T4 level,53.8 % achieved T6 level,3.8% attained T8 level and 3.8% achieved T10 level. In group D 26.9 % attained T4 level,57.7 % achieved T6 level,9.6% achieved T8 level and 5.8% patient had T10 level. This implied group C & Group D achieved highest level of sensory block. Difference between group B, C and group D was statistically insignificant.

Mean Comparison of Time to reach T10 Sensory level (min.) among Study groups.

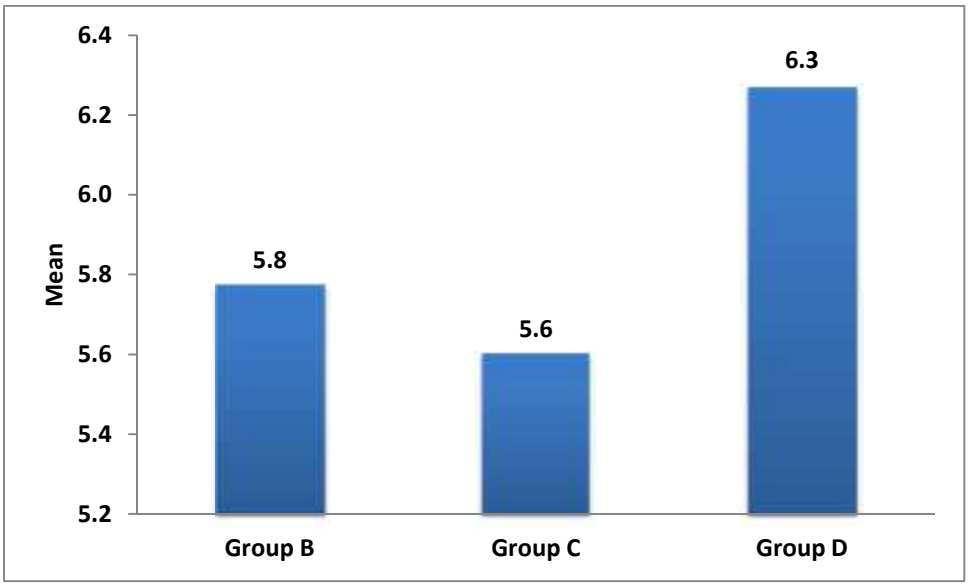
Table 7

		N	Mean	SD	p value
Time to reach T10 Sensory level (min.)	**Group B**	52	5.8	2.1	0.081
	Group C	52	5.6	1.4	
	Group D	52	6.3	1.1	
	Total	156	5.9	1.6	

MULTIPLE COMPARISONS

Time to reach T10 Sensory level (min.)	**Group B**	**Group C**	0.2	0.841
		Group D	-0.5	0.241
	Group C	**Group D**	-0.7	0.078

Graph 7: Mean Comparison of Time to reach T10 Sensory level (min.) among Study groups



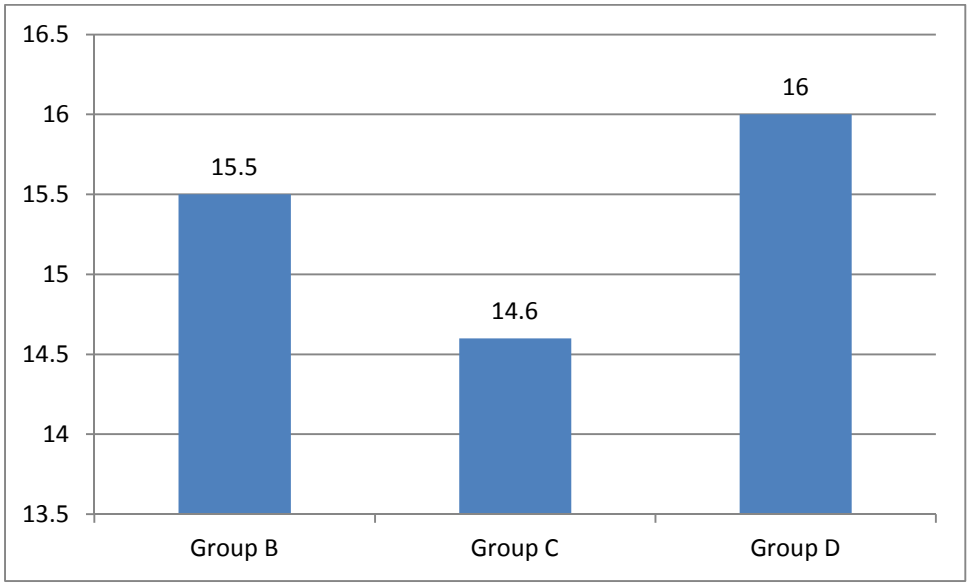
The time required to reach T10 sensory block level was 5.8±2.1 min. in Group B, 5.6±1.4 min. in Group C and 6.3±1.1 min. in Group D. (statistically insignificant). Intergroup comparison B to C , B to D and C to D P value was insignificant (more than 0.05).

TIME TO REACH HIGHEST SENSORY LEVEL (min).

Table 8

		N	Mean	SD	p value
Time to reach highest sensory level (min.)	**Group B**	52	15.5	3.2	0.328
	Group C	52	14.6	4.0	
	Group D	52	16.0	4.0	

Graph 8: Mean Comparison of Time to reach highest level (min.) among Study groups



The time to reach peak sensory block level was 15.5±3.2 min. in Group B , 14.6±4.0 min. in Group C and 16.0±4.0min. in Group D .P value is > 0.05 (statistically insignificant).

TIME TO REACH BROMAGE SCORE 3

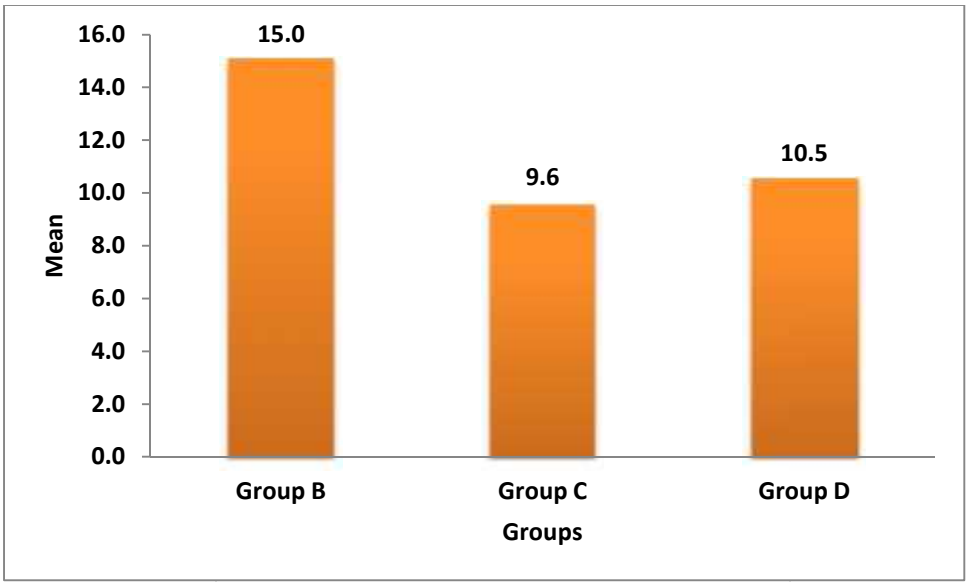
Table 9

		N	Mean	SD	p value
Time to reach Bromage Score 3 (min.)	**Group B**	52	15.0	3.4	0.000
	Group C	52	9.6	2.0	
	Group D	52	10.5	1.6	
	Total	156	11.7	3.4	

Time to reach Bromage Score 3 (min.)	**Group B**	**Group C**	5.4	0.000
		Group D	4.5	0.000
	Group C	**Group D**	1.9	0.049

The mean difference is significant at the 0.05 level

Graph 9: Mean Comparison of Time to reach Bromage Score 3 (min.) among Study groups



All patients achieved Bromage 3 motor block. The time to reach bromage scale 03 was 15± 3.4 min. in Group B, 9.6±2.0 min. in Group C and 10.5±1.6 min. in Group D. P value was < 0.001 (statistically significant).

Intergroup comparison B to C and B to D AND C to D ,P value was significant (less than 0.05). It was fastest in group C followed by group D and last was group B.

TIME REGRESSION TO BROMAGE 0

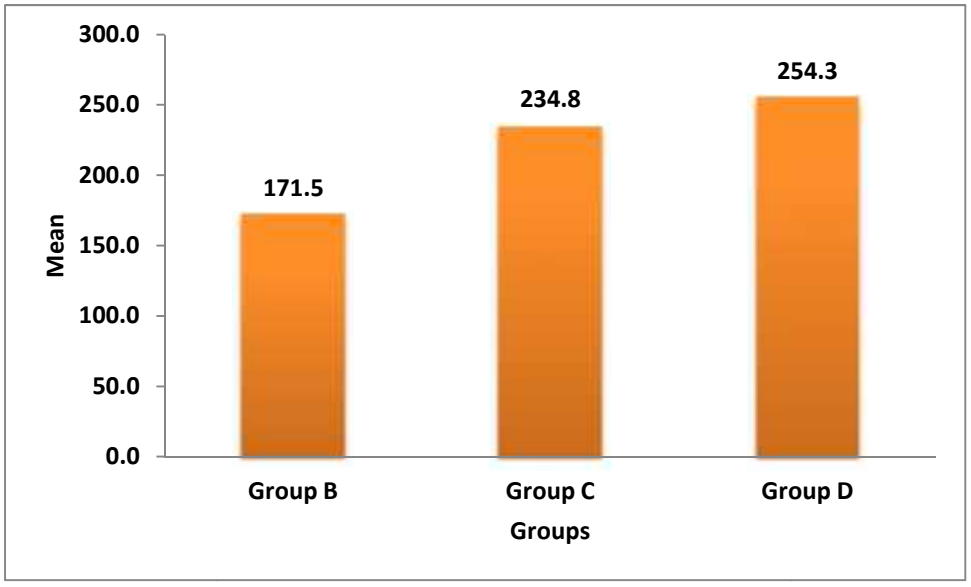
Table10

		N	Mean	SD	p value
Regression time to Bromage Score 0 (min.)	**Group B**	52	171.5	26.7	0.000
	Group C	52	234.8	44.6	
	Group D	52	254.3	36.9	
	Total	156	220.2	50.9	

Regression time to Bromage Score 0 (min.)	**Group B**	**Group C**	-63.2	0.000
		Group D	-82.7	0.000
	Group C	**Group D**	-19.5	0.021

The mean difference is significant at the 0.05 level.

Graph 10: Mean Comparison of Time to reach Bromage Score 0 (min.) among Study groups



The regression time to reach bromage scale 0 was 171.5±26.7 min. in Group B, 234.8±44.6 min. in Group C and 254.3±36.9 min. in Group D . P value was < 0.001 (statistically significant).

Intergroup comparison B to C, B to D an C to D , P value was significant (less than 0.05).It was longest in group D followed by group C and than group B.

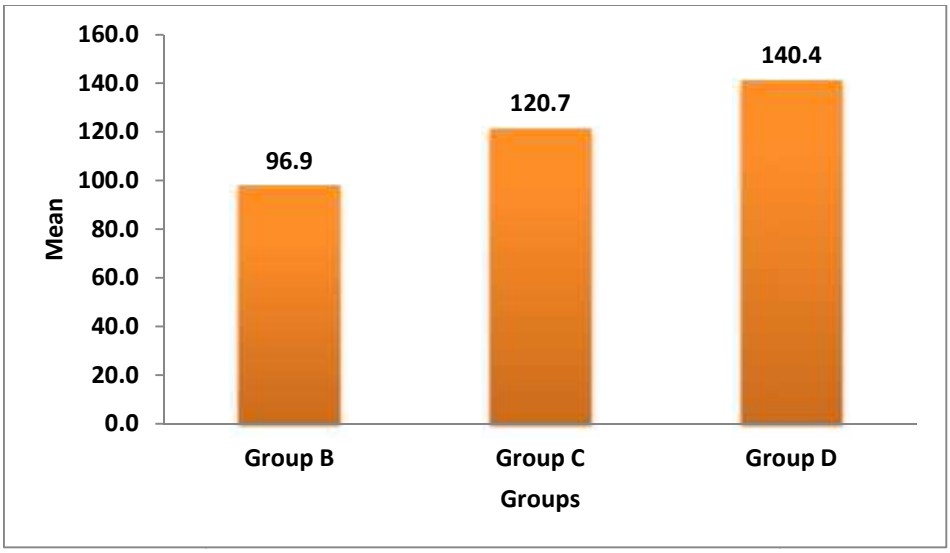
TIME TAKEN FOR 2 SEGMENT REGRESSION OF SENSORY BLOCK

Table11:		N	Mean	SD	p value
Time to 2 seg. Regression (min.)	Group B	52	96.9	27.9	0.000
	Group C	52	120.7	29.5	
	Group D	52	140.4	29.3	
	Total	156	119.3	33.8	

Time to 2 seg. Regression (min.)	Group B	Group C	-23.7	0.000
		Group D	-43.4	0.000
	Group C	Group D	-19.7	0.002

The mean difference is significant at the 0.05 level.

Graph 11: Mean Comparison of Time to 2 seg. Regression (min.) among Study groups



The two segments regression time was 96.9±27.9 min. in Group B, 120.7±29.5 min. in Group C and 140.4±29.3min. in Group D . P value was < 0.001 (statistically significant).

Intergroup comparison B to C, B to D and C to D was significant (less than 0.05).It was longest in group D followed by group C and B.

TIME TAKEN FOR REGRESSION TO S1 DERMATOME

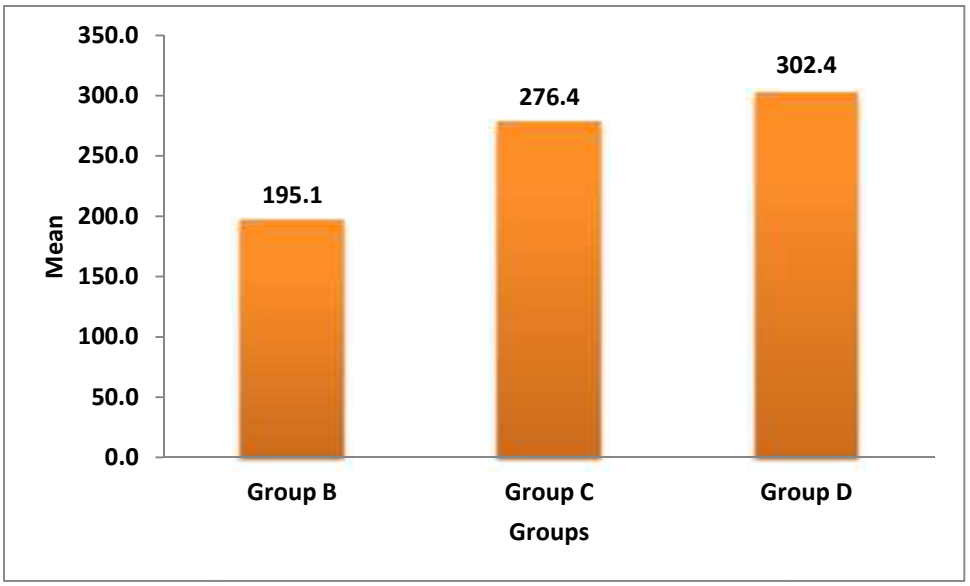
Table12

		N	Mean	SD	p value
Time to S1 Regression (min.)	**Group B**	52	195.1	30.3	0.000
	Group C	52	276.4	26.5	
	Group D	52	302.4	49.6	
	Total	156	258.0	58.7	

Time to S1 Regression (min.)	**Group B**	**Group C**	-81.2	0.000
		Group D	-107.3	0.000
	Group C	**Group D**	-26.0	0.001

The mean difference is significant at the 0.05 level.

Graph 12: Mean Comparison of Time to reach S1 Regression (min.) among Study groups



The time to regression time to S1 dermatome was 195.1± 30.2 min. in Group B, 276.4± 26.5 min. in Group C and 302.4±49.6 min. in Group D . P value was < 0.001 (statistically significant).Compete recovery of sensory function was observed in all studied patients.

Intergroup comparison B to C , B to D and C to D was significant (P less than 0.05).It was longest in group D followed by group C and than group B.

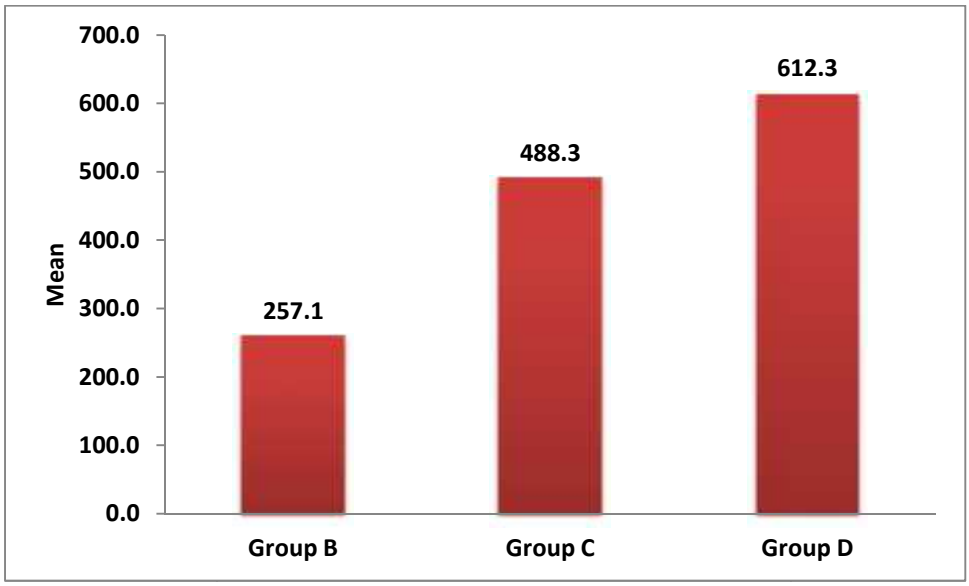
DURATION OF ANALGESIA

Table 13

		N	Mean	SD	p value
Time for first pain medication	**Group B**	52	257.1	49.0	<0.05
	Group C	52	488.3	56.3	
	Group D	52	612.3	77.0	
	Total	156	452.6	160.0	

Time for first pain medication	**Group B**	**Group C**	-231.2	0.000
		Group D	-355.2	0.000
	Group C	**Group D**	-124.0	0.000

Graph 13: Mean Comparison of Duration of analgesia [Time to first pain medication (min.)]among Study groups



The time of first rescue dose requested by patient was 257.1±49.0 min. in Group B, 488.3±56.3 min. in Group C and 612.3±77.0 min. in Group D . P value was < 0.001(statistically significant).

Intergroup comparison B to C, B to D and group Cto D was significant (less than 0.05).Duration was longest in group D followed by group C and than group B.

OCCURRENCE OF SIDE EFFECT

Table 14

Complications	Group B		Group C		Group D		Total	p value
	N	Percent	N	Percent	N	Percent		
NAUSEA & VOMITING	6	31.6	0	0.0	5	29.4	11	0.048
BRADYCARDIA	0	0.0	0	0.0	3	17.6	3	0.047
HYPOTENSION	3	15.8	7	77.8	5	29.4	15	0.413
PRURITES	0	0.0	0	0.0	0	0.0	0	NA
SHIVERING	10	52.6	2	22.2	4	23.5	16	0.027
RESPIRATORY DEPRESSION	0	0.0	0	0.0	0	0.0	0	NA

Three patients in group B, seven patients in group C and five patients in group D received one dose of Mephentermin .Three patients in group D required atropine.VAS values were less than 3 during the whole duration of the study and none of the patients required additional analgesics. The level of sedation scores were in the range 0–1 in all three groups with a median of zero. Intra-operative or post-operative nausea or vomiting occurred in six patients in group B and five patients in group D. Shivering in ten patients in group B, two patients in group C and four patients in group D.

HEART RATE

Table 15: Mean Comparison of Pulse rate among Study groups

Pulse rate		Mean	SD	ANOVA p value
Before spinal	**Group B**	106.8	6.6	0.000
	Group C	111.5	1.8	
	Group D	118.0	4.2	
	Total	112.1	6.5	
At The time of S.B.	**Group B**	116.4	3.9	0.000
	Group C	126.5	2.5	
	Group D	130.5	2.2	
	Total	124.5	6.6	
3 Min	**Group B**	120.9	2.3	0.000
	Group C	127.3	2.4	
	Group D	125.4	3.4	
	Total	124.5	3.9	
6 Min	**Group B**	117.1	4.5	0.000
	Group C	115.4	2.4	
	Group D	122.7	3.8	
	Total	118.4	4.8	
9 Min	**Group B**	111.6	2.8	0.000
	Group C	104.5	4.2	
	Group D	112.4	3.9	
	Total	109.5	5.1	
12 Min	**Group B**	102.2	4.6	0.050
	Group C	97.5	9.5	
	Group D	98.4	14.3	
	Total	99.4	10.4	
15 Min	**Group B**	97.7	3.2	0.000
	Group C	92.3	4.7	
	Group D	96.3	8.1	
	Total	95.4	6.1	

18 Min	**Group B**	96.1	1.9	0.000
	Group C	85.1	5.4	
	Group D	89.2	10.0	
	Total	90.1	8.0	
21 Min	**Group B**	93.1	1.9	0.000
	Group C	79.3	6.1	
	Group D	80.4	12.0	
	Total	84.3	10.0	
24 Min	**Group B**	91.6	1.3	0.000
	Group C	76.9	4.7	
	Group D	73.3	12.1	
	Total	80.6	10.9	
27 Min	**Group B**	88.6	3.3	0.000
	Group C	71.9	3.3	
	Group D	69.1	11.1	
	Total	76.5	11.1	
30 Min	**Group B**	84.7	1.6	0.000
	Group C	70.0	3.1	
	Group D	64.7	8.5	
	Total	73.2	10.0	
45 Min	**Group B**	81.3	2.1	0.000
	Group C	65.3	2.6	
	Group D	65.3	6.3	
	Total	70.7	8.6	
60 Min	**Group B**	86.2	4.0	0.000
	Group C	65.5	1.7	
	Group D	64.5	1.7	
	Total	72.1	10.4	
75 Min	**Group B**	82.6	3.7	0.000
	Group C	64.1	1.8	
	Group D	64.2	4.2	
	Total	70.3	9.4	

90 Min	**Group B**	96.8	2.1	0.000
	Group C	65.6	1.6	
	Group D	63.6	1.4	
	Total	75.3	15.4	
105 Min	**Group B**	106.6	4.7	0.000
	Group C	94.0	5.9	
	Group D	63.9	1.5	
	Total	88.2	18.5	
120 Min	**Group B**	92.3	1.3	0.000
	Group C	94.7	2.7	
	Group D	70.9	8.4	
	Total	85.9	11.9	
135 Min	**Group B**	94.1	3.1	0.000
	Group C	73.7	3.3	
	Group D	64.1	3.8	
	Total	77.3	13.0	
150 Min	**Group B**	86.2	4.0	0.000
	Group C	81.6	5.5	
	Group D	63.8	1.5	
	Total	77.2	10.5	
165 Min	**Group B**	89.3	3.4	0.000
	Group C	85.7	6.8	
	Group D	63.8	3.9	
	Total	79.6	12.3	
180 Min	**Group B**	104.8	3.8	0.000
	Group C	72.6	10.9	
	Group D	63.8	1.5	
	Total	80.4	18.9	

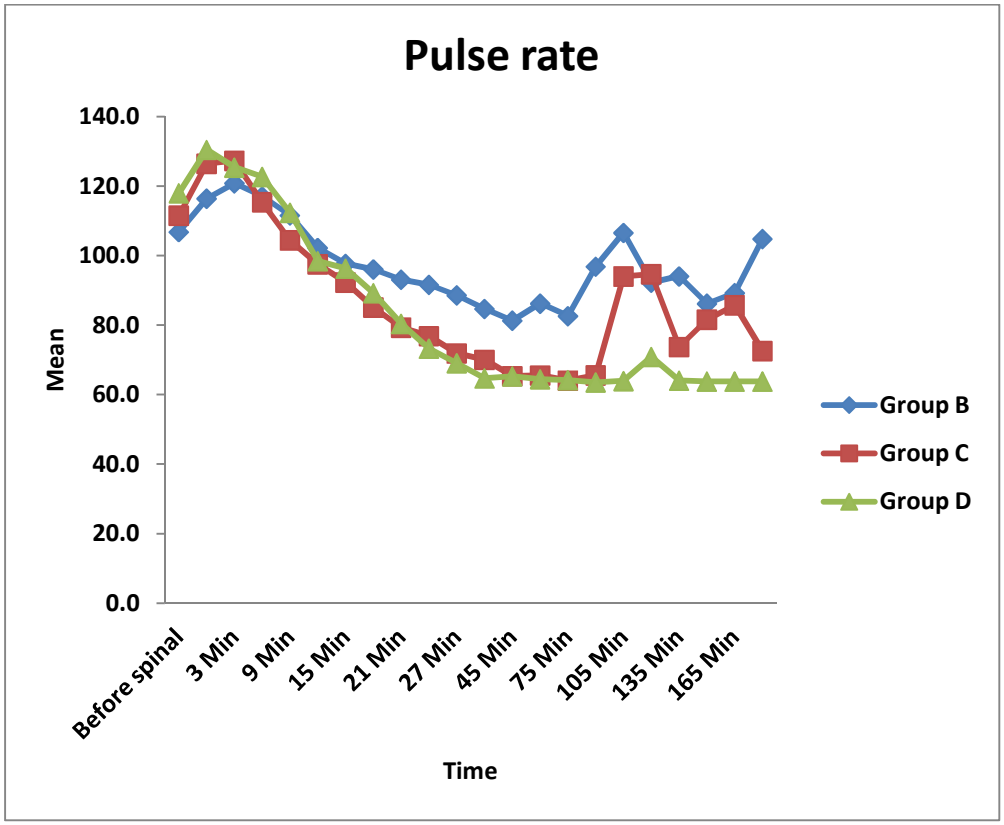
Table 17: Multiple Mean Comparison of Pulse rate among Study groups by Tukey HSD test

			Pulse	
	(I) Group	**(J) Group**	**Mean Difference (I-J)**	**p value**
Before spinal	**Group B**	**Group C**	-4.7	0.000
		Group D	-11.1	0.000
	Group C	**Group D**	-6.4	0.000
At The time of S.B.	**Group B**	**Group C**	-10.0	0.000
		Group D	-14.0	0.000
	Group C	**Group D**	-4.0	0.000
3 Min	**Group B**	**Group C**	-6.4	0.000
		Group D	-4.5	0.000
	Group C	**Group D**	1.9	0.001
6 Min	**Group B**	**Group C**	1.7	0.054
		Group D	-5.5	0.000
	Group C	**Group D**	-7.2	0.000
9 Min	**Group B**	**Group C**	7.1	0.000
		Group D	-0.8	0.508
	Group C	**Group D**	-7.9	0.000
12 Min	**Group B**	**Group C**	4.7	0.055
		Group D	3.8	0.149
	Group C	**Group D**	-0.9	0.895
15 Min	**Group B**	**Group C**	5.3	0.000
		Group D	1.3	0.457
	Group C	**Group D**	-4.0	0.001
18 Min	**Group B**	**Group C**	10.9	0.000
		Group D	6.8	0.000
	Group C	**Group D**	-4.1	0.006
21 Min	**Group B**	**Group C**	13.8	0.000
		Group D	12.7	0.000
	Group C	**Group D**	-1.1	0.757
24 Min	**Group B**	**Group C**	14.8	0.000
		Group D	18.3	0.000

	Group C	**Group D**	3.6	0.041
27 Min	**Group B**	**Group C**	16.7	0.000
		Group D	19.5	0.000
	Group C	**Group D**	2.8	0.101
30 Min	**Group B**	**Group C**	14.7	0.000
		Group D	20.0	0.000
	Group C	**Group D**	5.3	0.000
45 Min	**Group B**	**Group C**	16.0	0.000
		Group D	16.0	0.000
	Group C	**Group D**	0.0	0.999
60 Min	**Group B**	**Group C**	20.7	0.000
		Group D	21.8	0.000
	Group C	**Group D**	1.1	0.105
75 Min	**Group B**	**Group C**	18.6	0.000
		Group D	18.4	0.000
	Group C	**Group D**	-0.1	0.984
90 Min	**Group B**	**Group C**	31.3	0.000
		Group D	33.3	0.000
	Group C	**Group D**	2.0	0.000
105 Min	**Group B**	**Group C**	12.6	0.000
		Group D	42.6	0.000
	Group C	**Group D**	30.1	0.000
120 Min	**Group B**	**Group C**	-2.4	0.047
		Group D	21.4	0.000
	Group C	**Group D**	23.8	0.000
135 Min	**Group B**	**Group C**	20.3	0.000
		Group D	30.0	0.000
	Group C	**Group D**	9.7	0.000
150 Min	**Group B**	**Group C**	4.6	0.000
		Group D	22.4	0.000
	Group C	**Group D**	17.8	0.000
165 Min	**Group B**	**Group C**	3.5	0.001

		Group D	25.5	0.000
	Group C	**Group D**	21.9	0.000
180 Min	**Group B**	**Group C**	32.2	0.000
		Group D	41.0	0.000
	Group C	**Group D**	8.8	0.000

Graph 14: Mean heart rate



The above table shows the range intraoperative heart rate..In group B mean heart rate was between 120-83.In group C it was between 128-64.In group D it was between 125-63.The decrease in mean heart rate from 3 to 6 minutes until the end surgery was greater in group C and group D. P value <0.05

Intergroup comparison B to C and B to D was statistically significant. Between C and D it was significant only at 3,9,15,18,30,105,120,150 and 180 mins.None of the patients had bradycardia in group B and C. Decrease was more in group D.Three patients in group D had bradycardia.

TO INTRAOPERATIVE SYSTOLIC BLOOD PRESSURE

Table 16: Mean Comparison of SBP (mm hg) among Study groups

SBP (mm hg)		Mean	SD	p value
Before spinal	**Group B**	122.5	3.6	0.000
	Group C	125.5	4.2	
	Group D	117.7	8.2	
	Total	121.9	6.5	
At The time of S.B.	**Group B**	130.5	5.4	0.000
	Group C	134.3	3.3	
	Group D	136.3	4.7	
	Total	133.7	5.1	
3 Min	**Group B**	132.4	2.5	0.000
	Group C	127.3	2.3	
	Group D	136.2	3.5	
	Total	131.9	4.6	
6 Min	**Group B**	121.2	7.7	0.000
	Group C	114.2	2.4	
	Group D	85.3	5.1	
	Total	106.9	16.5	
9 Min	**Group B**	114.3	8.1	0.001
	Group C	110.2	2.1	
	Group D	111.8	5.5	
	Total	112.1	6.0	
12 Min	**Group B**	110.2	3.8	0.000
	Group C	107.2	3.9	
	Group D	100.6	6.1	
	Total	106.0	6.2	
15 Min	**Group B**	104.4	5.0	0.000
	Group C	104.0	4.5	
	Group D	93.9	1.3	
	Total	100.8	6.3	

18 Min	**Group B**	102.5	5.2	0.000
	Group C	99.3	3.5	
	Group D	90.8	1.6	
	Total	97.5	6.2	
21 Min	**Group B**	99.5	3.1	0.000
	Group C	94.6	3.6	
	Group D	88.4	3.5	
	Total	94.2	5.7	
24 Min	**Group B**	98.4	5.6	0.000
	Group C	90.8	3.5	
	Group D	86.2	2.5	
	Total	91.8	6.5	
27 Min	**Group B**	98.9	7.6	0.000
	Group C	87.5	3.5	
	Group D	82.2	2.6	
	Total	89.5	8.6	
30 Min	**Group B**	101.0	9.3	0.000
	Group C	84.7	2.0	
	Group D	80.7	1.5	
	Total	88.8	10.4	
45 Min	**Group B**	104.9	8.9	0.000
	Group C	82.7	2.2	
	Group D	80.9	2.1	
	Total	89.5	12.2	
60 Min	**Group B**	114.5	5.1	0.000
	Group C	87.3	3.3	
	Group D	87.8	1.5	
	Total	96.5	13.2	
75 Min	**Group B**	109.7	7.3	0.000
	Group C	83.9	3.4	
	Group D	84.4	0.8	
	Total	92.7	12.9	

90 Min	**Group B**	128.2	4.3	0.000
	Group C	88.5	3.9	
	Group D	88.5	2.8	
	Total	101.8	19.1	
105 Min	**Group B**	128.9	3.4	0.000
	Group C	115.9	9.2	
	Group D	87.8	1.5	
	Total	110.8	18.1	
120 Min	**Group B**	122.0	4.3	0.000
	Group C	115.4	18.3	
	Group D	90.4	2.7	
	Total	109.3	17.5	
135 Min	**Group B**	124.2	3.5	0.000
	Group C	98.5	5.3	
	Group D	84.4	0.8	
	Total	102.4	16.9	
150 Min	**Group B**	114.8	4.9	0.000
	Group C	102.7	6.0	
	Group D	87.8	1.5	
	Total	101.7	12.0	
165 Min	**Group B**	117.7	3.9	0.008
	Group C	142.1	162.3	
	Group D	84.4	0.8	
	Total	114.7	96.1	
180 Min	**Group B**	128.2	6.7	0.000
	Group C	95.7	10.2	
	Group D	87.7	1.6	
	Total	103.9	18.9	

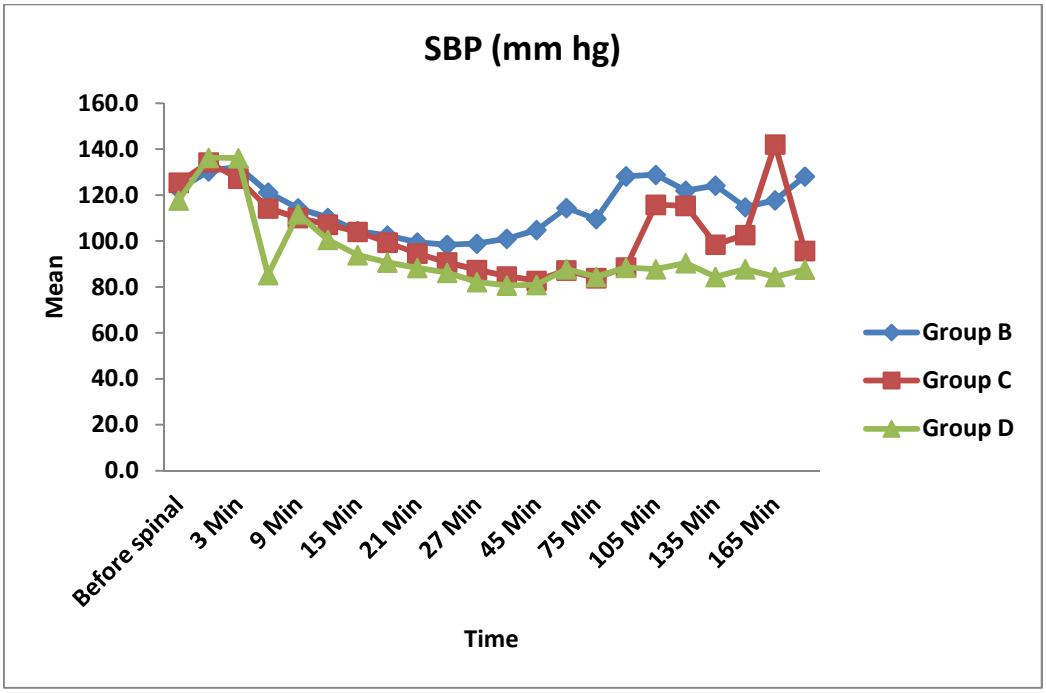
Table 19: Multiple Mean Comparison of Duration of SBP (mm hg) among Study groups by Tukey HSD test

			SBP (mm hg)	
	(I) Group	**(J) Group**	**Mean Difference (I-J)**	**p value**
Before spinal	**Group B**	**Group C**	-3.0	0.023
		Group D	4.7	0.000
	Group C	**Group D**	7.7	0.000
At The time of S.B.	**Group B**	**Group C**	-3.8	0.000
		Group D	-5.8	0.000
	Group C	**Group D**	-2.0	0.066
3 Min	**Group B**	**Group C**	5.1	0.000
		Group D	-3.8	0.000
	Group C	**Group D**	-8.8	0.000
6 Min	**Group B**	**Group C**	6.9	0.000
		Group D	35.9	0.000
	Group C	**Group D**	28.9	0.000
9 Min	**Group B**	**Group C**	4.1	0.001
		Group D	2.5	0.074
	Group C	**Group D**	-1.7	0.314
12 Min	**Group B**	**Group C**	3.0	0.004
		Group D	9.6	0.000
	Group C	**Group D**	6.6	0.000
15 Min	**Group B**	**Group C**	0.4	0.874
		Group D	10.5	0.000
	Group C	**Group D**	10.1	0.000
18 Min	**Group B**	**Group C**	3.1	0.000
		Group D	11.7	0.000
	Group C	**Group D**	8.6	0.000
21 Min	**Group B**	**Group C**	4.8	0.000
		Group D	11.1	0.000
	Group C	**Group D**	6.3	0.000

24 Min	**Group B**	**Group C**	7.6	0.000
		Group D	12.2	0.000
	Group C	**Group D**	4.5	0.000
27 Min	**Group B**	**Group C**	11.4	0.000
		Group D	16.7	0.000
	Group C	**Group D**	5.3	0.000
30 Min	**Group B**	**Group C**	16.4	0.000
		Group D	20.3	0.000
	Group C	**Group D**	4.0	0.001
45 Min	**Group B**	**Group C**	22.1	0.000
		Group D	23.9	0.000
	Group C	**Group D**	1.8	0.209
60 Min	**Group B**	**Group C**	27.2	0.000
		Group D	26.7	0.000
	Group C	**Group D**	-0.5	0.758
75 Min	**Group B**	**Group C**	25.8	0.000
		Group D	25.3	0.000
	Group C	**Group D**	-0.5	0.828
90 Min	**Group B**	**Group C**	39.7	0.000
		Group D	39.7	0.000
	Group C	**Group D**	0.0	0.998
105 Min	**Group B**	**Group C**	13.0	0.000
		Group D	41.1	0.000
	Group C	**Group D**	28.1	0.000
120 Min	**Group B**	**Group C**	6.6	0.007
		Group D	31.5	0.000
	Group C	**Group D**	25.0	0.000
135 Min	**Group B**	**Group C**	25.7	0.000
		Group D	39.8	0.000
	Group C	**Group D**	14.1	0.000
150 Min	**Group B**	**Group C**	12.1	0.000
		Group D	27.0	0.000

	Group C	**Group D**	14.9	0.000
165 Min	**Group B**	**Group C**	-24.4	0.383
		Group D	33.3	0.168
	Group C	**Group D**	57.7	0.006
180 Min	**Group B**	**Group C**	32.4	0.000
		Group D	40.5	0.000
	Group C	**Group D**	8.0	0.000

Graph 15: MEAN SYSTOLIC BLOOD PRESSURE



The SBP in group B decreased from 130 mmHg to 110 at 12 mins and to 99mmHg at 21 mins which increased gradually to 122mmHg at the end of 2hrs.In group C it decreased from 133mmHg to 107mmHg at 12mins to 94mmHg at 21mins,which increased gradually to 115mmHg at 2hrs and 95mmHg at 3hrs.In group D SBP decreased from 133mmHg to 100mmHg at 12mins to 88mmHg at 21mins.From 30mins to 3hrs it was maintained in the range of 80-90mmHg

Intergroup comparison B to C and B to D it was significant at ,6 ,9, 18, 21, 24, 27,30 ,45, 60, 75, 90,105,120,135,150,165,180 mins. In between C and D it was significant throughout except at 9 and 60 mins. Though intergroup SBP difference was significant between the 3 groups only 8 patients in group C and 4 patients in group D and group B had hypotension. In group B mean SBP never fell below 98mmHg and in group C and group D it never below 82mmHg and 80 mmHg respectively. Fall was more in group D followed by group C and than group B.

DIASTOLIC BLOOD PRESSURE

Table 17: Mean Comparison of DBP (mm hg) among Study groups

DBP (mm hg)		Mean	SD	p value
Before spinal	**Group B**	82.8	2.1	0.000
	Group C	81.3	2.4	
	Group D	75.7	4.5	
	Total	79.9	4.4	
At The time of S.B.	**Group B**	88.6	2.1	0.000
	Group C	90.3	3.1	
	Group D	86.8	4.5	
	Total	88.6	3.7	
3 Min	**Group B**	92.5	2.0	0.000
	Group C	82.4	3.4	
	Group D	87.6	3.8	
	Total	87.5	5.2	
6 Min	**Group B**	85.0	4.7	0.000
	Group C	75.7	4.9	
	Group D	82.6	4.3	
	Total	81.1	6.1	
9 Min	**Group B**	83.3	4.7	0.000
	Group C	73.3	3.2	
	Group D	76.8	3.9	
	Total	77.8	5.7	
12 Min	**Group B**	78.8	3.0	0.000
	Group C	71.8	4.4	
	Group D	69.0	2.6	
	Total	73.2	5.3	
15 Min	**Group B**	75.2	3.9	0.000
	Group C	70.2	3.4	
	Group D	67.6	3.8	
	Total	71.0	4.8	

18 Min	**Group B**	73.2	3.4	0.000
	Group C	68.2	5.4	
	Group D	65.5	2.5	
	Total	69.0	5.1	
21 Min	**Group B**	70.5	2.7	0.000
	Group C	68.0	2.7	
	Group D	62.0	2.8	
	Total	66.8	4.5	
24 Min	**Group B**	69.5	3.0	0.000
	Group C	64.9	3.2	
	Group D	61.4	2.4	
	Total	65.3	4.4	
27 Min	**Group B**	67.2	2.9	0.000
	Group C	62.4	1.9	
	Group D	60.5	0.9	
	Total	63.3	3.5	
30 Min	**Group B**	69.6	6.8	0.000
	Group C	60.1	1.7	
	Group D	60.5	2.3	
	Total	63.4	6.1	
45 Min	**Group B**	72.4	5.9	0.000
	Group C	61.0	1.6	
	Group D	60.7	1.8	
	Total	64.7	6.6	
60 Min	**Group B**	76.4	5.6	0.000
	Group C	66.8	3.1	
	Group D	64.7	2.3	
	Total	69.3	6.4	
75 Min	**Group B**	74.8	7.0	0.000
	Group C	64.0	2.3	
	Group D	63.3	1.8	
	Total	67.3	6.8	

90 Min	**Group B**	82.5	2.9	0.000
	Group C	67.3	3.4	
	Group D	63.0	1.7	
	Total	70.9	8.8	
105 Min	**Group B**	84.9	3.3	0.000
	Group C	81.3	5.0	
	Group D	64.8	2.3	
	Total	77.0	9.5	
120 Min	**Group B**	78.9	3.7	0.019
	Group C	116.0	164.3	
	Group D	64.5	4.3	
	Total	86.5	96.8	
135 Min	**Group B**	78.9	3.4	0.000
	Group C	74.2	5.5	
	Group D	62.9	1.8	
	Total	72.0	7.7	
150 Min	**Group B**	76.6	5.9	0.000
	Group C	76.1	4.5	
	Group D	64.8	2.4	
	Total	72.5	7.1	
165 Min	**Group B**	76.6	3.7	0.000
	Group C	80.1	5.3	
	Group D	63.0	1.8	
	Total	73.2	8.3	
180 Min	**Group B**	82.3	2.8	0.000
	Group C	68.5	4.4	
	Group D	64.7	2.3	
	Total	71.8	8.3	

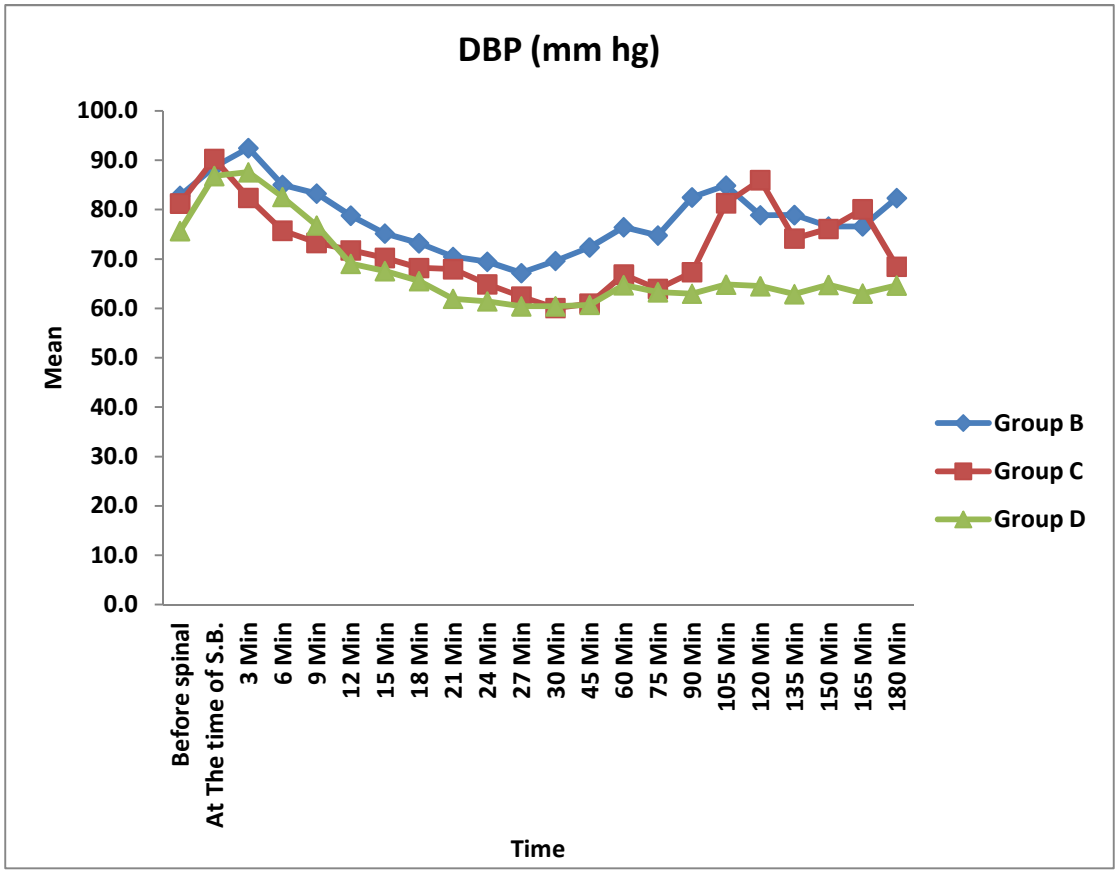
Table 21: Multiple Mean Comparison of Duration of DBP (mm hg) among Study groups by Tukey HSD test

			DBP (mm hg)	
	(I) Group	**(J) Group**	**Mean Difference (I-J)**	**p value**
Before spinal	**Group B**	**Group C**	1.5	0.038
		Group D	7.1	0.000
	Group C	**Group D**	5.5	0.000
At The time of S.B.	**Group B**	**Group C**	-1.6	0.038
		Group D	1.7	0.024
	Group C	**Group D**	3.4	0.000
3 Min	**Group B**	**Group C**	10.1	0.000
		Group D	4.8	0.000
	Group C	**Group D**	-5.1	0.000
6 Min	**Group B**	**Group C**	9.3	0.000
		Group D	2.4	0.021
	Group C	**Group D**	-6.8	0.000
9 Min	**Group B**	**Group C**	10.0	0.000
		Group D	6.4	0.000
	Group C	**Group D**	-3.5	0.000
12 Min	**Group B**	**Group C**	7.0	0.000
		Group D	9.7	0.000
	Group C	**Group D**	2.7	0.000
15 Min	**Group B**	**Group C**	4.9	0.000
		Group D	7.6	0.000
	Group C	**Group D**	2.7	0.001
18 Min	**Group B**	**Group C**	5.0	0.000
		Group D	7.7	0.000
	Group C	**Group D**	2.7	0.002
21 Min	**Group B**	**Group C**	2.5	0.000
		Group D	8.5	0.000
	Group C	**Group D**	6.0	0.000
24 Min	**Group B**	**Group C**	4.6	0.000

		Group D	8.0	0.000
	Group C	**Group D**	3.4	0.000
27 Min	**Group B**	**Group C**	4.8	0.000
		Group D	6.7	0.000
	Group C	**Group D**	1.9	0.000
30 Min	**Group B**	**Group C**	9.5	0.000
		Group D	9.2	0.000
	Group C	**Group D**	-0.4	0.889
45 Min	**Group B**	**Group C**	11.4	0.000
		Group D	11.7	0.000
	Group C	**Group D**	0.2	0.946
60 Min	**Group B**	**Group C**	9.6	0.000
		Group D	11.7	0.000
	Group C	**Group D**	2.1	0.018
75 Min	**Group B**	**Group C**	10.8	0.000
		Group D	11.5	0.000
	Group C	**Group D**	0.7	0.711
90 Min	**Group B**	**Group C**	15.2	0.000
		Group D	19.5	0.000
	Group C	**Group D**	4.3	0.000
105 Min	**Group B**	**Group C**	3.6	0.000
		Group D	20.1	0.000
	Group C	**Group D**	16.5	0.000
120 Min	**Group B**	**Group C**	-37.1	0.117
		Group D	14.4	0.720
	Group C	**Group D**	51.5	0.017
135 Min	**Group B**	**Group C**	4.8	0.000
		Group D	16.0	0.000
	Group C	**Group D**	11.3	0.000
150 Min	**Group B**	**Group C**	0.5	0.838
		Group D	11.8	0.000
	Group C	**Group D**	11.3	0.000

165 Min	**Group B**	**Group C**	-3.5	0.000
		Group D	13.6	0.000
	Group C	**Group D**	17.0	0.000
180 Min	**Group B**	**Group C**	13.9	0.000
		Group D	17.7	0.000
	Group C	**Group D**	3.8	0.000

Graph 16: MEAN DIASTOLIC BLOOD PRESSURE



The DBP in group B decreased from 82 mmHg (baseline) to 78 at 12 mins and to 73mmHg at 21 mins which increased gradually to 79mmHg at the end of 2hrs and to 82mmHg at the end of 3 hrs..In group C it decreased from 81mmHg to 71mmHg at 12mins to 67mmHg at 21mins,which increased gradually to 74mmHg at 2hrs and was maintained at 68mmHg at the end of 3hrs .In group D DBP decreased from 86mmHg to 69mmHg at 12mins to 62mmHg at 21mins.At the end of 3 hrs it was

maintained at 64 mmHg .

Intergroup comparison B to C and B to D it was significant at 3, 6 ,9, 18, 21, 24, 27, 30, 45 ,60, 75,90,105,120,135,150,165,180 mins. In between C and D it was significant throughout except at 30,45, 60 and 75 mins. Though intergroup SBP difference was significant between the 3 groups but mean DBP never fell below 71 mmHg in group B and 60mmHg in group C and D. Fall was more in group D followed by group C and B.

MEAN ARTERIAL PRESSURE

Table 18: Mean Comparison of MAP (mm hg) among Study groups

MAP (mm hg)		Mean	SD	p value
Before spinal	**Group B**	95.8	2.3	0.000
	Group C	92.8	8.5	
	Group D	88.5	6.0	
	Total	92.4	6.8	
At The time of S.B.	**Group B**	102.5	2.6	0.000
	Group C	104.4	2.7	
	Group D	101.0	5.3	
	Total	102.6	4.0	
3 Min	**Group B**	105.7	1.9	0.000
	Group C	97.1	2.7	
	Group D	102.8	10.3	
	Total	101.9	7.1	
6 Min	**Group B**	97.7	6.5	0.000
	Group C	89.2	4.1	
	Group D	96.3	3.4	
	Total	94.4	6.1	
9 Min	**Group B**	93.2	4.9	0.000
	Group C	86.1	2.4	
	Group D	88.3	3.6	
	Total	89.2	4.8	
12 Min	**Group B**	88.6	2.8	0.000
	Group C	83.0	3.3	
	Group D	79.0	1.6	
	Total	83.5	4.8	
15 Min	**Group B**	84.7	3.8	0.000
	Group C	81.1	2.2	
	Group D	75.9	2.3	
	Total	80.5	4.6	

18 Min	**Group B**	82.1	4.9	0.000
	Group C	77.9	2.4	
	Group D	73.3	1.6	
	Total	77.7	4.8	
21 Min	**Group B**	79.1	3.4	0.000
	Group C	76.8	2.2	
	Group D	71.0	2.2	
	Total	75.6	4.3	
24 Min	**Group B**	80.5	5.0	0.000
	Group C	72.8	2.5	
	Group D	69.4	2.0	
	Total	74.2	5.8	
27 Min	**Group B**	78.0	4.3	0.000
	Group C	70.0	2.3	
	Group D	67.3	1.0	
	Total	71.8	5.4	
30 Min	**Group B**	82.0	6.0	0.000
	Group C	67.5	1.5	
	Group D	66.5	0.9	
	Total	72.0	8.0	
45 Min	**Group B**	82.6	6.5	0.000
	Group C	68.4	2.0	
	Group D	66.9	1.6	
	Total	72.6	8.1	
60 Min	**Group B**	88.8	5.5	0.000
	Group C	73.1	3.6	
	Group D	71.8	1.8	
	Total	77.9	8.7	
75 Min	**Group B**	85.1	4.8	0.000
	Group C	70.4	3.0	
	Group D	68.8	3.6	
	Total	74.8	8.3	

90 Min	**Group B**	97.2	2.8	0.000
	Group C	73.3	3.1	
	Group D	69.5	1.5	
	Total	80.0	12.6	
105 Min	**Group B**	95.7	17.5	0.000
	Group C	90.1	8.8	
	Group D	72.3	2.3	
	Total	86.0	15.1	
120 Min	**Group B**	92.4	4.0	0.000
	Group C	93.3	5.3	
	Group D	72.8	2.6	
	Total	86.2	10.3	
135 Min	**Group B**	93.8	2.5	0.000
	Group C	80.7	4.0	
	Group D	69.7	1.3	
	Total	81.4	10.3	
150 Min	**Group B**	88.6	5.5	0.000
	Group C	85.4	6.5	
	Group D	72.2	2.0	
	Total	82.0	8.7	
165 Min	**Group B**	89.9	3.5	0.000
	Group C	90.9	6.6	
	Group D	69.7	2.7	
	Total	83.5	10.8	
180 Min	**Group B**	98.0	3.4	0.000
	Group C	75.9	5.7	
	Group D	71.8	1.8	
	Total	81.9	12.2	

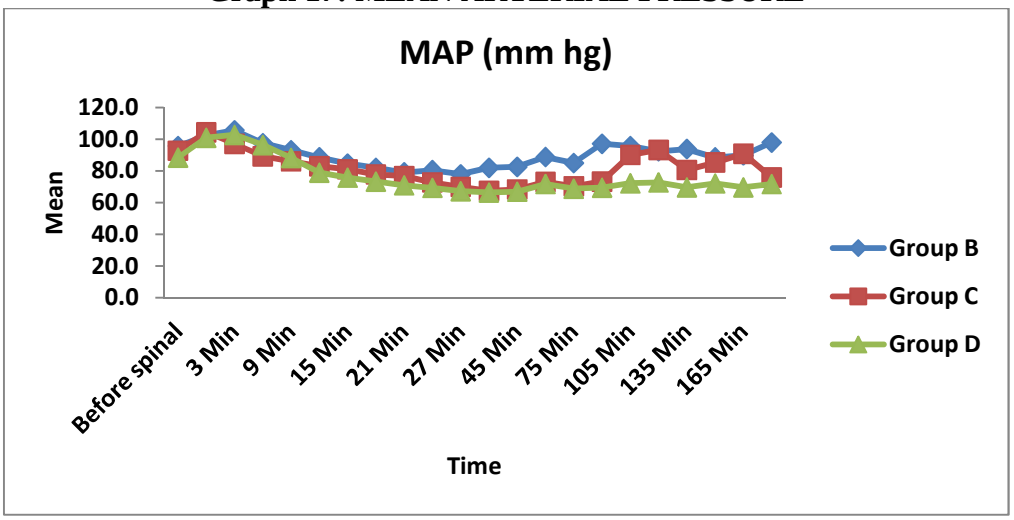
Table 23: Multiple Mean Comparison of Duration of MAP (mm hg) among Study groups by Tukey HSD test

			MAP (mm hg)	
	(I) Group	**(J) Group**	**Mean Difference (I-J)**	**p value**
Before spinal	**Group B**	**Group C**	3.0	0.035
		Group D	7.3	0.000
	Group C	**Group D**	4.3	0.001
At The time of S.B.	**Group B**	**Group C**	-1.8	0.034
		Group D	1.5	0.105
	Group C	**Group D**	3.3	0.000
3 Min	**Group B**	**Group C**	8.6	0.000
		Group D	2.9	0.048
	Group C	**Group D**	-5.7	0.000
6 Min	**Group B**	**Group C**	8.4	0.000
		Group D	1.4	0.327
	Group C	**Group D**	-7.0	0.000
9 Min	**Group B**	**Group C**	7.1	0.000
		Group D	4.9	0.000
	Group C	**Group D**	-2.1	0.011
12 Min	**Group B**	**Group C**	5.6	0.000
		Group D	9.6	0.000
	Group C	**Group D**	4.0	0.000
15 Min	**Group B**	**Group C**	3.6	0.000
		Group D	8.8	0.000
	Group C	**Group D**	5.2	0.000
18 Min	**Group B**	**Group C**	4.2	0.000
		Group D	8.8	0.000
	Group C	**Group D**	4.6	0.000
21 Min	**Group B**	**Group C**	2.3	0.000
		Group D	8.1	0.000
	Group C	**Group D**	5.8	0.000
24 Min	**Group B**	**Group C**	7.7	0.000
		Group D	11.2	0.000
	Group C	**Group D**	3.5	0.000

27 Min	**Group B**	**Group C**	8.0	0.000
		Group D	10.7	0.000
	Group C	**Group D**	2.7	0.000
30 Min	**Group B**	**Group C**	14.5	0.000
		Group D	15.5	0.000
	Group C	**Group D**	1.0	0.323
45 Min	**Group B**	**Group C**	14.2	0.000
		Group D	15.6	0.000
	Group C	**Group D**	1.5	0.156
60 Min	**Group B**	**Group C**	15.7	0.000
		Group D	17.0	0.000
	Group C	**Group D**	1.3	0.198
75 Min	**Group B**	**Group C**	14.7	0.000
		Group D	16.2	0.000
	Group C	**Group D**	1.6	0.097
90 Min	**Group B**	**Group C**	23.9	0.000
		Group D	27.7	0.000
	Group C	**Group D**	3.8	0.000
105 Min	**Group B**	**Group C**	5.5	0.038
		Group D	23.4	0.000
	Group C	**Group D**	17.9	0.000
120 Min	**Group B**	**Group C**	-0.9	0.516
		Group D	19.6	0.000
	Group C	**Group D**	20.5	0.000
135 Min	**Group B**	**Group C**	13.2	0.000
		Group D	24.1	0.000
	Group C	**Group D**	10.9	0.000
150 Min	**Group B**	**Group C**	3.2	0.004
		Group D	16.4	0.000
	Group C	**Group D**	13.2	0.000
165 Min	**Group B**	**Group C**	-1.0	0.478
		Group D	20.2	0.000

	Group C	**Group D**	21.2	0.000
180 Min	**Group B**	**Group C**	22.1	0.000
		Group D	26.2	0.000
	Group C	**Group D**	4.1	0.000

Graph 17: MEAN ARTERIAL PRESSURE



The MAP in group B decreased from 95 mmHg (baseline) to 88 at 12 mins and to 79mmHg at 21 mins which increased gradually to 92mmHg at the end of 2hrs and to 83mmHg at the end of 3 hrs..In group C it decreased from 92mmHg to 83mmHg at 12mins to 76mmHg at 21mins,which increased gradually to 93mmHg at 2hrs and was maintained at 75mmHg at the end of 3hrs .In group D MAP decreased from 88mmHg to 79mmHg at 12mins to 71mmHg at 21mins .At the end of 3 hrs it was maintained at 66 mmHg .

Intergroup comparison B to C it was significant throughout except at 120 mins. B to C was significant throughout except at 3 and 9 mins. And C to D was significant throughout except at 9,30,45,60 and 165 mins. Though intergroup MAP difference was significant between the 3 groups but mean of MAP never fell below 78 mmHg in group B and 66mmHg and 67 mmHg in group C and D.Fall was more in group D followed by group C and B.

DISCUSSION

Spinal anaesthesia is currently wide spread popular anaesthetic technique available today. It has the definitive advantage that profound nerve block can be produced in a large part of the body by the relatively simple injection of a small amount of local anaesthetic.[51] An ideal local anaesthetic agent used in spinal anaesthesia in lower limb surgeries should have rapid onset of action, intense analgesia, adequate motor blockade, long duration of action, adequate postoperative analgesia though for limited duration and minimal cardiovascular changes. Bupivacaine introduced by **"Ekenstam"** in 1957 seems to fulfil most of the requirements of an ideal local anaesthetic agent.

To address the problem of limited duration of action and to improve the quality of analgesia both intraoperative and postoperative, intrathecal opiates have been given in addition to Bupivacaine. However, this enthusiasm was soon tempered off by reports of side effects such as pruritis, urinary retention, nausea and vomiting and respiratory depression.

Although the endorphin system is well recognized, there are many other mechanisms involved in spinal antinociception and alpha$_2$ adrenergic agonists such as Clonidine and Dexmedetomidine have been shown to possess spinally mediated analgesic property. The mechanisms by which intrathecal α_2-adrenoceptor agonists prolong the motor and sensory block of local anaesthetics is not well understood. It is not a result of altered systemic absorption, as the plasma level of bupivacaine was not altered after the addition of intrathecal Clonidine to Bupivacaine spinal injection.[52] It may be an additive or synergistic effect secondary to the different mechanism of action local anaesthetic and the α_2-adrenoceptor agonist. The local anaesthetics act by blocking sodium channels, whereas the α_2-adrenoceptor agonist acts by binding to

pre-synaptic C-fibres and post-synaptic dorsal horn neurons. Intrathecal α_2-adrenoceptor agonists produce analgesia by depressing the release of C-fibre transmitters and by hyperpolarisation of post-synaptic dorsal horn neurons.[30, 53, 54, 55, 56] This antinociceptive effect may explain the prolongation of the sensory block when added to spinal anaesthetics. On the other hand, **Yaksh**[57] has shown that intrathecal α_2-adrenoceptor agonists can cause a dose-dependent decrease in motor strength in animals. The prolongation of the motor block of spinal anaesthetics may result from the binding of α_2-adrenoceptor agonists to motor neurons in the dorsal horn.[58] Most of the clinical experience gained in the use of intrathecal α_2-adrenoceptor agonists has been described with Clonidine. The use of intrathecal Clonidine has a well-established synergistic effect with local anesthetic.[7]Studies using a combination of intrathecal Dexmedetomidine and local anaesthetics are lacking and off label.

Dosage selection

Kalso *et al*,[59] and **Post** *et al*,[60] showed that a 1 : 10 dose ratio between intrathecal Dexmedetomidine and Clonidine produced a similar effect in animal models. **Asano** *et al*,[61] showed that the potency of epidurally administered α_2-adrenoceptor agonists was well correlated with their binding affinity to spinal α_2-adrenoreceptors. The binding affinity of Dexmedetomidine compared with Clonidine is approximately 1: 10. Thus, it hypothesized that 3 µg of intrathecal Dexmedetomidine might be equipotent to 30 µg of intrathecal Clonidine. Several studies have been done using different doses of Clonidine (15-300µg) and Dexmedetomidine in order to determine the most effective intrathecal administration with minimal side effects. In our study, 50µg of Clonidine and 5 µg of Dexmedetomidine were used, as it was found that the incidence of side effects increased with larger doses. In this clinical study, 156 patients in age group between

18-60 years, posted for various elective lower abdomen and lower limb surgeries belonging to ASA physical status I, II and III selected.

Group –B In this group, the patients received subarachnoid block with injection bupivacaine 0.5% (hyperbaric) 15 mg with added NS to make total volume of 3.5ml.

Group C- In this group, the patients received subarachnoid block with injection bupivacaine0.5% (hyperbaric) 15 mg with 50µg Clonidine with added NS to make total volume of 3.5ml.

Group-D-In this group, the patients received subarachnoid block with injection bupivacaine 0.5% (hyperbaric) 15 mg with 5 µg Dexmedetomidine (total volume of 3.5ml).

Jorm *et al* [62] found that Dexmedetomidine has an inhibitory effect on the locus coeruleus (A6 group) located at the brain stem. This supraspinal action could explain the prolongation of spinal anaesthesia after intravenous administration of Dexmedetomidine. The noradrenergic innervations of the spinal cord arises from the noradrenergic nuclei in the brain stem including the locus coeruleus, the A5, and the A7 noradrenergic nuclei. Neurons in the locus coeruleus are connected to the noradrenergic nuclei in the brain stem. Axon terminals of the noradrenergic nuclei reach lamina VII and VIII of the ventral horns of the spinal cord. The activity of the noradrenergic neurons is decreased by agonists acting at α2-adrenergic receptors on the locus ceruleus cell bodies. Therefore, inhibition of the locus coeruleus results in disinhibition of the noradrenergic nuclei and exerted descending inhibitory effect on nociception in the spinal cord. [24]

Highest dose of intrathecal Dexmedetomidine used in animal studies was 100µg.[51] **Konakci and colleagues**[64] reported white matter injury in rats when high dose epidural Dexmedetomidine (6 µg/kg) was used alone;

However, subsequently **Brummett and co-workers**[65] demonstrated no injury and a protective effect when doses of 26-40 µg/kg were used perineurally. Although no major neurological complications have been reported so far, larger studies are required to rule out any short term or long term adverse effects.

Strebel and coworkers[66] compared three doses of Clonidine (37.5, 75, 150 µg) and concluded that Clonidine produced dose-dependent prolongation of the effects of intrathecal Bupivacaine.

In a study conducted by **Hala E A Eid** *et al,*[24] where Dexmedetomidine was used in combination with Bupivacaine in patients undergoing anterior cruciate ligament reconstruction surgery, Intrathecal Dexmedetomidine in doses of 10 µg and 15 µg significantly prolong the anaesthetic and analgesic effects of spinal hyperbaric Bupivacaine in a dose-dependent manner.

We compared the onset and duration of sensory and motor block, hemodynamic effect and adverse effects of Dexmedetomidine or Clonidine given intrathecally with hyperbaric 0.5% Bupivacaine for lower abdomen and lower limb surgeries. In this clinical study, 156 patients in age group between 20-60 years, posted for various elective lower abdomen and lower limb surgeries belonging to ASA physical status I, II and III selected.

Group –B In this group, the patients received subarachnoid block with injection Bupivacaine 0.5% (hyperbaric) 15 mg with added NS to make total volume of 3.5ml.

Group C - In this group, the patients received subarachnoid block with injection Bupivacaine0.5% (hyperbaric) 15 mg with 50µg Clonidine with added NS to make total volume of 3.5ml.

Group-D - In this group, the patients received subarachnoid block with injection bupivacaine 0.5% (hyperbaric) 15 mg with 5 µg Dexmedetomidine (total volume 3.5ml).

DEMOGRAPHIC PROFILE

The mean age of the patient in group B was 43.4±9.4 years, in group C was 40.9±9.9 years and in group D was 43.4±8.5 years The mean height of the patient in centimetres in groupB was 159.9 ±4.0, in group C was 160.5±6.9 and in group D was 160.7±7.3.The mean weight of the patient in kilograms in groupB was 57.6 ± 6.2, in groupC was 57.2± 6.7 and in group D was 56.5±8.2 kgs (Table 1). There was no statistically significant difference between the three groups with regards to age, height and weight ($p>0.05$).

GENDER DISTRIBUTION

In group B, there were 33 males and 19 females, in group c there were 33 males and 19 females and in group D there were 37 males and 15 females. There was no statistically significant difference between the three groups in regard to sex.(p value >0.05)

CHARACTERISTICS OF SPINAL ANALGESIA

TIME REQUIRED TO REACH T10 SENSORY BLOCK: - In the present study, the time to reach T10 sensory block level was determined by pin prick test in mid clavicular line. The time required to reach T10 sensory block level was 5.8±2.1 min. in Group B, 5.6±1.4 min. in Group C and 6.3±1.1 min. in Group D. (statistically insignificant). Intergroup comparison B to C , B to D and C to D P value was insignificant (more than 0.05).

In the study conducted by **G.E.Kanazi** *et al* (2005)[14]reported that the mean time to reach T10 sensory block was 9.7 ±4.2 min in the control group (Bupivacaine 12 mg) , 7.6 ± 4.4 min in group C where bupivacaine supplemented with Clonidine 30 µg and 8.6 ± 3.7 min in group D where bupivacaine supplemented with Dexmedetomidine 3 µg. P value was >0.05 so it was statistically not significant. In an another study conducted by **Hala E A Eid** *et al*, (July 2011)[24] there was no significant difference observed in the time to reach T10 sensory block, 8.7 ± 3.3 min for group B (15 mg hyperbaric bupivacaine), 7.7± 3.6 min for group D1 (Dexmedetomidine 10 µg) and 8±2.5 min for group D2 (Dexmedetomidine 15 µg) with P value =0.67 [53]

B.S.Sethi *et al* (2007)[21] evaluated the effect of low dose 1 µg/kg intrathecal Clonidine as an adjuvant to 12.5mg hyperbaric bupivacaine and found that the onset of action was clinically and significantly faster that of group compared to bupivacaine group.

In the study conducted by **Hema Saxena** *et al* [23] mean times to reach T10 sensory block was 6.57±4.9 min. in Bupivacaine (13.5) mg group which almost concur with control group of present study

MAXIMUM HEIGHT OF SENSORY BLOCK:-

With regard to the highest sensory level attained,patients of group B26.9% attained T4 level,38.5% achieved T6 level,30.8% achieved T8 level and 3.8% achieved T10 level.In group C 38.5% achieved T4 level,53.8 % achieved T6 level,3.8% attained T8 level and 3.8% achieved T10 level.In group D 26.9 % attained T4 level,57.7 % achieved T6 level,9.6% achieved T8 level and 5.8% patient had T10 level.This implied group C & Group D achieved highest level of sensory block.Difference between group B, C and group D was statistically insignificant

Present study comparable with the study conducted by **G.E.Kanazi** *et al* (2005)[14].There was no difference between the groups in the median and range of the peak sensory level reached .The peak sensory level were T6 (T4-T10) in bupivacaine group , T6 (T3-T9) in Clonidine group and T6 (T2-T10) in Dexmedetomidine group. P value >0.3, so it was statistically not significant. **Hala E A Eid** *et al,* (July 2011)[24] also reported that there was no significant difference between the groups in the range of the peak sensory level reached. The peak sensory level reached were T6 (T3-T10) in group B (Bupivacaine 15mg), T5 (T3-T9) in group D1 (Dexmedetomidine10µg) and T7 (T4-T9) in group D 2 (Dexmedetomidine15µg).

Thus result of our study was almost similar to the studies done by these workers and it is concluded that there is no significant difference in maximum height of sensory block in three groups of study.

TIME TO REACH PEAK SENSORY BLOCK LEVEL:-

In the present study, the mean time taken to reach peak sensory block level was 15.5±3.2 min. in Group B, 14.6±4.0 min. in Group C and 16.0±4.0 min. in Group D .P value is > 0.05 (statistically insignificant).

In the study conducted by **G. E. Kanazi** *et al,* (2005)[16] reported that there was no difference among the groups in the time taken to achieve the peak sensory block. The time taken to achieve the peak sensory block was 20.2 ± 8.4 min in bupivacaine group, 18.7 ± 9.2 min in Clonidine group and 24.5 ± 14.8 min in Dexmedetomidine group (P value = 0.3). In an another study conducted by **Hema Saxena** *et al* [23] the mean time to reach the maximal sensory block level was 7.3 ± 1.125 min. in bupivacaine (13.5mg) group and 7.4 ± 1.131 min. in Clonidine (30 µg) group with no statistical different. The result of present study was similar to the studies done by these authors and concluded that the time taken to achieve the peak sensory blocked level among the groups was not significant

TIME TO REACH BROMAGE SCALE 03:--

All patients achieved Bromage 3 motor block. The time to reach bromage scale 03 was 15± 3.4 min. in Group B, 9.6±2.0 min. in Group C and 10.5±1.6 min. in Group D . P value was < 0.001 (statistically significant).

Intergroup comparison B to C and B to D AND C to D, P value was significant (less than 0.05). It was fastest in group C followed by group D and last was group B.

AUTHORS	CONTROLGROUP (Min)	CLONIDINE GROUP (Min)	DEX. GROUP (Min)	P value
G.E.Kanazi *et al*	20.7 ± 10.3.	11.7 ± 5.9	13.2 ± 5.6	0.002
Al-Mustafa MM *et al*	18±3.3 min	---	13.0±3.4	significant
Present study	15.± 3.4	9.6±2.0	10.5±1.6	<0.001

G.E.Kanazi *et al* (2005)[14]observed that the time to achieve Bromage 3 motor block was significantly shorter in Dexmedetomidine group (13.2 ± 5.6 min) and Clonidine group(11.7 ± 5.9 min) than in Bupivacaine group (20.7 ± 10.3 min, *P* = 0.002), whereas values C versus D was not significantly different. In the study conducted by **Al-Mustafa MM** *et al*,[22] to reach Bromage3 motor block was significantly shorter in Dexmedetomidine group (5 µg) (13.0±3.4 min.) compare to bupivacaine (12.5mg) group (18±3.3 min).

In the study conducted by **Ranjani Gupta** *et al* (2011)[25] the time to reach the bromage scale 03 was 11.6 ± 1.8 min in group D (Bupivacaine 12.5 mg plus Dexmedetomidine 5 µg) which almost concur with control group (group B) of present study .

The result of present study concluded that the time to achieve Bromage 3 motor block was significantly shorter in Dexmedetomidine group and Clonidine group than in Bupivacaine group.

REGRESSION TIME TO REACH BROMAGE SCALE 0:

The regression time to reach bromage scale 0 was 171.5 ± 26.7 min. in Group B, 234.8 ± 44.6 min. in Group C and 254.3 ± 36.9 min. in Group D. P value was < 0.001 (statistically significant).

Intergroup comparison B to C, B to D and C to D, P value was significant (less than 0.05).It was longest in group D followed by group C and than group B.

G. E. Kanazi *et al,* (2005) [14] observed that there was clinically and statistically significant difference between the groups in the median and range of the regression time to reach modified bromage 0 level. It was 163 ± 47min in Bupivacaine Group, 216 ± 35 min in Clonidine Group and 250 ± 76 min in Dexmedetomidine Group.

AUTHORS	CONTROL GROUP (Min)	CLONIDINE GROUP (Min)	DEX. GROUP (Min)	P value
G.E.Kanazi *et al*	163 ± 47	216 ± 35	250 ± 76	<0.001
B.S.Sethi *et al*	161 (range 90-270)	218 (range 150-240)	---	<0.05
Al-Mustafa MM *et al*	140.1 ±32.3	---	246.4 ±25.7	<0.05
Hala E A Eid *et al*	202±41.7	---	280±46	significant
HemaSaxena *et al*	153±19	220±47	---	significant
Present study	171.5±26.7	234.8±44.6	254.3±36.9	<0.001

B.S.Sethi *et al,* (2007)[21] observed significant difference in the duration of motor blockade which was 161 min. (range 90-270 min) in Bupivacaine group and205 min. (range 90-300min) in Clonidine group. **Hema Saxena et al**[23] observed that the regression time to reach modified bromage 0was 153±19 min in Bupivacaine (13.5 mg) group and 220±47 min in Clonidine group which was statistically significant.

Al-Mustafa MM *et al*,[22] also reported significant difference in the regression time to reach modified bromage 0level in Group NS (Bupivacaine 12.5 mg) or Group D5 (Dexmedetomidine 5 µg) or Group D10 (Dexmedetomidine 10 µg). The regression time to reach modified bromage 0level was 302.9 ±36.7 minutes in D10 Group, 246.4 ±25.7 minutes in D5 and 140.1 ±32.3 minutes in Group NS. P value is < 0.05.

Hala E A Eid *et al*, (July 2011)[24] also reported that there was significant difference observed in the regression time to reach modified bromage 0level . It was 202±41.7 min in group B (Bupivacaine 15 mg) and 280±46 min in group D1 (Dexmedetomidine 10 µg)and 335±58 min in group D2 (Dexmedetomidine 15 µg).

Present study almost correlates with the above studies. The regression time to reach modified bromage 0 levels was significantly longer in groups where Clonidine and Dexmedetomidine used as adjuvant.

TWO SEGMENTS SENSORY REGRESSION TIME:-

The two segments regression time was 96.9±27.9 min. in Group B, 120.7±29.5 min. in Group C and 140.4±29.3min. in Group D . P value was < 0.001 (statistically significant).

Intergroup comparison B to C, B to D and C to D was significant (less than 0.05).It was longest in group D followed by group C and B.

AUTHORS	CONTROL GROUP (Min)	CLONIDINE GROUP (Min)	DEX. GROUP (Min)	P value
G.E.Kanazi *et al*	80 ± 28	101 ± 37	122 ± 76	0.003
B.S.Sethi *et al*	136 (range 90-150)	218 (range 150-240)	-	<0.05
Hala E A Eid *et al*	76.9±41.7	---	103±28	Significant
HemaSaxena *et al*	89.9±14	192±142	---	Significant
Present study	96.9±27.9	120.7±29.5	140.4±29.3	<0.001

G.E.Kanazi *et al*, (2005)[14] observed that there was statistically significant difference between the Bupivacaine group and Dexmedetomidine group (P = 0.003) in the two segments regression time but not between Bupivacaine group and Clonidine group. Two segments regression time was 80 ± 28min in Bupivacaine group, 101 ± 37 min in Clonidine Group and 122 ± 76 min in Dexmedetomidine group.

B.S.Sethi *et al,* (2007) [21] observed that the two segments regression time was 136 min. (range 90-150 min) in Bupivacaine group and 218 min. (range 150-240 min) in Clonidine group which was significantly more (*P*<0.05) .

In the study conducted by **Hema Saxena** *et al.*[23] the two segments regression time was 89.9±14 min in Bupivacaine (13.5 mg) group and 192±142 min in Clonidine group which was significantly more.

Hala E A Eid *et al*, (July 2011)[24] also reported significant difference in the two segments regression time.It was 76.9±41.7 min in Bupivacaine group and 103±28 min in group D1 (Dexmedetomidine 10 µg) and 200.6±30.9 min in group D2 (Dexmedetomidine 15 µg)

Present study almost correlates with the above studies .The time for sensory regression by 2 segments significantly more in groups where Clonidine and Dexmedetomidine was used as adjuvant.

REGRESSION TIME TO REACH S1 DERMATOME:--

The time to regression time to S1 dermatome was 195.1± 30.2 min. in Group B, 276.4± 26.5 min. in Group C and 302.4±49.6 min. in Group D . P value was < 0.001 (statistically significant).Complete recovery of sensory function was observed in all studied patients.

Intergroup comparison B to C, B to D and C to D was significant (P less than 0.05).It was longest in group D followed by group C and than group B.

AUTHORS	CONTROL GROUP (Min)	CLONIDINE GROUP (Min)	DEX. GROUP (Min)	P value
G.E.Kanazi *et al.*	190±48	272±38	303±75	<0.001
Hala E A Eid *et al.*	238±57	---	320±65.8	<0.001
HemaSaxena *et al.*	99.75±21.9	264±44	---	<0.001
Al-Mustafa *et al.*	165±32	---	277±23	<0.001
Present study	195.1±30.2	276.4±26.5	302±49.6	<0.001

The result of our study was almost similar to the studies done by different authors. It is concluded that the difference in the regression time to reach S1 dermatome between the groups was significant.

DURATION OF ANALGESIA:

In our study mean time of first rescue dose requested by patient was 257.1±49.0 min. in Group B, 488.3±56.3 min. in Group C and 612.3±77.0 min. in Group D. P value was < 0.001(statistically significant).

Intergroup comparison B to C, B to D and group C to D was significant (less than 0.05).Duration was longest in group D followed by group C and than group B.

AUTHORS	CONTROL GROUP (Min)	CLONIDINE GROUP (Min)	DEX. GROUP (Min)	P value
B.S.Sethi *et al*	223 (range150-300)	614 (range480-1140)	---	<0.001
H.Saxena *et al*	99.75±21.9	264±44.3	---	<0.001
Solanki SL *et al*	406±119	678 ±178	824±244	<0.001
Present study	257.1±49.0	488.3±56.3	612.3±77.0	<0.001

B.S.Sethi *et al,*[21] used Clonidine 1 µg.kg-1with 12.5 mg 0.5% bupivacaine and compared duration of analgesia the Control group received an identical volume of saline mixed with 12.5mg0.5% bupivacaine. Author observed that duration of analgesia was significantly longer in Clonidine group (223 min) than Bupivacaine group (614 min). **H. Saxena** *et al,*[23] conducted a study, who used different doses of Clonidine as 15µg, 30µg and 37.5µg.It was observed that duration of analgesia was lesser for the group receiving 15µg of Clonidine than the group receiving 30µg, which was less than the 37.5µg of Clonidine group. It was concluded that duration of analgesia is dose dependent.

In a study conducted by **Hala E A Eid** *et al,* [24] shown significant prolongation of the duration of spinal blockade by intrathecal administration of Dexmedetomidine as an adjunct to hyperbaric Bupivacaine. Patients in the groups that received

Dexmedetomidine had reduced postoperative pain scores and a longer analgesic duration than those who received spinal bupivacaine alone. This effect appears to be dose dependent and more pronounced with the dose of 15 µg. Fifteen µg Dexmedetomidine but not 10 µg was associated with lower 24-hours analgesic requirements and desirable level of sedation.

Solanki SL *et al,*[26] Compared the duration of analgesia and adverse effects following intrathecal administration of Dexmedetomidine or Clonidine, both with Bupivacaine, All groups received hyperbaric Bupivacaine 0.5% 3 ml, to which was added saline 0.5 ml (Group B): Clonidine 50 µg (Group C) or Dexmedetomidine 5 µg (Group D) The time to analgesia was significantly prolonged in Group D (824±244 minutes) compared with Group C (678±178 minutes; P=0.01), the latter being longer than Group B (406±119 minutes; P=0.0001). Postoperative pain scores were lower in Groups C and D compared with group B. The requirement for rescue analgesia during the first 24 postoperative hours was significantly less in Groups C and D as compared to Group B (P=0.0001), but comparable between Groups C and D (P=0.203).

The result of our study was almost similar to the studies done by different authors.

.INTRAOPERATIVE HEART RATE AND BLOOD PRESSURE

Monitoring of heart rate, blood pressure, SpO2 and respiratory rate were done to assess the hemodynamic stability and respiratory effects of intrathecal Clonidine and Dexmedetomidine. In our study it was observed that patients in Group B had fall in the mean heart rate from the base line (108) to 84 compared to 111(baseline) to 70 in Group C and from 115(baseline) to 65 in group D, 30 minutes after the injection. None of the patients had bradycardia in group B and C. Decrease was more in group D. Three patients in group D had bradycardia.

Mean systolic pressure was significantly lower during the first 30-90 minutes after spinal injection in Group C and during 30-150 mins in group D than in Group B. Though intergroup SBP difference was significant between the 3 groups. In group B mean SBP never fell below 98mmHg and in group C and group D it never below 82mmHg and 80 mmHg respectively. Fall was more in group D followed by group C and than group B. Though intergroup MAP difference was also significant between the 3 groups but mean of MAP never fell below 78 mmHg in group B and 66mmHg and 67 mmHg in group C and D. Fall was more in group D followed by group C and B. Only 7 patients in group C and 5 patients in group D and 3 in group B had hypotension.

In a study by **Neimi L** *et al*[8] where 3µg/kg of Clonidine was added to 15 mg of 0.5% Bupivacaine for knee arthroscopy and reported significant hypotension in 10% of patients. Their values for mean arterial pressure were also significantly lower than control group after 45 minutes to 8 hours

. VAS values were less than 3 during the whole duration of the study and none of the patients required additional analgesics. The level of sedation scores were in the range 0–1 in all three groups with a median of zero. Intra-operative or post-operative nausea or vomiting occurred in 6 patients in group B and 5 patients in group D.

None of the patients had respiratory depression or pruritis seen in intraoperatively in any of the groups.

The addition of Dexmedetomidine or Clonidine to Bupivacaine did cause statistically significant decrease in the blood pressure when 3 groups were compared intra-operatively or post-operatively but incidence of hypotension and bradycardia were low.

Eisanach J C (1996) found that addition of a low dose of α_2-agonist to a high dose of local anaesthetics does not further affect the near-maximal sympatholysis.[30]

Strebel S, (2004) observed that Clonidine in the dose range 37.5–150 µg did not cause a significant decrease in blood pressure when added to 18 mg of Bupivacaine compared with Bupivacaine alone[66].

In contrast, **Klimscha W** (1995) [67] and **D'Angelo R**, **(**1999), [68] in different studies observed that more than 150 µg of Clonidine added to a low dose of Bupivacaine (5 mg) yielded a greater decrease in blood pressure than Bupivacaine alone.

CONCLUSION

Acute pain following surgical procedures is unique to the clinical practice of pain medicine. It is one of the few opportunities in which the cause of pain is known before its occurrence, the pain is reliably expected to occur and can be annulled effectively.

Despite advances in the knowledge of pathophysiology, pharmacology and the development of more effective techniques for the management of perioperative analgesia, many patients continue to experience distressing pain in the postoperative period. It is shown that relief of pain with neuraxial blockade with a local anaesthetic like Bupivacaine alone is limited to the initial postoperative period. When a combination of local anaesthetic and an alpha $_2$ adrenergic agonist like Clonidine is used, pain relief can be extended well into the post operative period. In conclusion, this study shows that the supplementation of bupivacaine spinal block with a low dose of intrathecal Dexmedetomidine (5 µg) or Clonidine (50 µg) produces a significantly shorter onset of motor and sensory block and a significantly longer sensory and motor block than bupivacaine alone. The 50µg of Clonidine or 5 µg of Dexmedetomidine dose provides maximum benefit and minimum side effects. These doses have an effect on sedation level, heart rate and mean arterial pressure which does not however require any therapeutic intervention and hence can be advocated as an adjuvant to bupivacaine in spinal anaesthesia for lower abdomen and lower limb surgeries. This approach to pain therapy may hold promise, that favourable outcomes such as successful analgesia may be achieved with minimal side effects.

SUMMARY

Spinal anaesthesia is effective in the management of perioperative pain which extends into the initial post operative period. In order to maximize post operative pain free period numerous techniques and newer drugs have been tried.

In this study, the anaesthetic properties of 15 mg of 0.5% hyperbaric Bupivacaine, 15 mg of 0.5% hyperbaric bupivacaine with 50µg of Clonidine and 15 mg of 0.5% hyperbaric Bupivacaine with 5µg of Dexmedetomidine given intrathecally were compared.

One hundred and fifty six patients ASA physical status I, II and III patients, posted for various elective lower abdomen and lower limb surgeries were studied.
The patients were divided into three groups of 52 each:

Group B - Received 0.5% hyperbaric bupivacaine 15 mg + NS 0.5 ml

Group C - Received 0.5% hyperbaric bupivacaine 15 mg + 50 µg of Clonidine.(total volume 3.5 ml with NS)

Group D - Received 0.5% hyperbaric bupivacaine 15 mg + 5µg of Dexmedetomidine (total volume 3.5 ml with NS)

Addition of 50 µg of Clonidine and 5µg of Dexmedetomidine to hyperbaric bupivacaine resulted in a statistically significant faster onset of the motor blockade The time to reach bromage scale 03 was (15.0± 3.4 min. in Group B, 9.6±2.0 min. in Group C and 10.5±1.6 min. in Group D) . P value was < 0.001 (statistically significant) . It was fastest in group C followed by group D and last was group B.

The time required to reach T10 sensory block level was shorter in group C and D as compared to group B (Mean time required to reach T10 sensory block level was 5.8±2.1 min. in Group B, 5.6±1.4 min. in Group C and 6.3±1.1 min. in Group D. P value was< 0.001 (statistically insignificant).

Intergroup comparison B to C and B to D P value was insignificant (less than 0.05).Whereas C to D was not significant > 0.05

The maximum level of sensory block achieved was shorter but it was statistically insignificant (mean time to reach peak sensory block level 14.6±4.0 min. in Group C and 16.0±4.0min. in Group D as compared to 15.5±3.2 min. in Group B).

Time for 2 segment regression was significantly prolonged in Group C and Group D (P < .001) with a mean duration of 120.70±29.5. min. in Group C and 140.4±29.30 min. in Group D as compared to 96.9±27.9 min. in Group B and was found to be statistically significant.

Intergroup comparison B to C, B to D and C to D was significant (less than 0.05).It was longest in group D followed by group C and B.

The time to regression time to S1 dermatome was 195.1± 30.30 min. in Group B, 274.4± 26.50 min. in Group C and 302.40±49.60 min. in Group D. P value was < 0.001 (statistically significant).Compete recovery of sensory function was observed in all studied patients.

Intergroup comparison B to C, B to D and C to D was significant (P less than 0.05).It was longest in group D followed by group C and than group B.

We found that duration of analgesia was significantly prolonged in Group C and Group D (P < .001) with a mean duration of 257.1±49.0 min. in Group B, 488.3±56.3 min. in Group C and 612.3±77.0 min.

Intergroup comparison B to C, B to D and group C to D was significant (less than 0.05).Duration was longest in group D followed by group C and than group B.

With the above findings it is evident that the use of 50µg of Clonidine and 5µg of Dexmedetomidine as an adjuvant to hyperbaric bupivacaine in lower abdomen and lower limb surgeries is beneficial in several aspects (shorter onset of motor and

sensory block and longer sensory and motor block) without any significant hemodynamic instability .and scored over the use of hyperbaric bupivacaine alone with minimal side effects.

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PHOTOGRAPHS

Spinal set

Spinal tray

Positioning

Procedure of spinal anaesthesia

Drugs Used

ANNEXURE I

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

Institutional Ethical Committee
BIJAPUR-586 103.
OUTWARD
No. 50/13
Date 14-11-13
B.L.D.E.U's Shri B.M. Patil Medical College

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2013 at 3-30pm to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.

Title "A comparative study of equipotent doses of intrathecal clonidine & dexmedetomidine on characterstics of bupivacaine subarachnoid block"

Name of P.G. student Dr. Vaibhav.
Department of Anaesthesiology

Name of Guide/Co-investigator Dr Ravindra. R. Kusugal.
Assoc Prof of Anaesthesiology.

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

ANNEXURE II

SAMPLE INFORMED CONSENT FORM

TITLE OF THE TOPIC	:	A COMPARATIVE STUDY OF EQUIPOTENT DOSES OF INTRATHECAL CLONIDINE AND DEXMEDETOMIDINE ON CHARACTERISTICS OF BUPIVACAINE SUBARACHNOID BLOCK
DURATION OF STUDY	:	October 2013 - June 2015(18 MONTHS)
PRINCIPAL INVESTIGATOR	:	Dr. VAIBHAV
PG GUIDE NAME	:	DR.R.R.KUSUGAL

PURPOSE OF STUDY

To compare the onset and duration of motor and sensory block, following intrathecal Bupivacaine with Clonidine vs intrathecal Bupivacaine with Dexmedetomidine in lower abdominal or lower limb surgeries

To compare hemodynamic changes and depth of sedation, following intrathecal Bupivacaine with Clonidine vs. intrathecal Bupivacaine with Dexmedetomidine in lower abdominal or lower limb surgeries.

PROCEDURE

I understand that I will be a part of this study. My history and physical findings will be recorded and evaluated in a systematic way. I may be asked for follow-up.

RISK AND DISCOMFORTS

I understand that this procedure is not expected to aggravate any side effect or cause any detrimental effect to me.

I have been briefed about the foregoing study being conducted by Dr.Vaibhav and it has been conveyed to me in my own language .I have had the opportunity to ask questions about it & all questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate in this study & understand that I have

the right to withdraw from the research at any time without in any way affecting my medical care.

CONFIDENTIALITY

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality and privacy regulation of BLDE University's Shri .B. M .Patil Medical College. Information of a sensitive and personal nature will not be a part of the medical records, but will be stored in the investigator's research file and will not be divulged to any peron .

If the data are used for publication in the medical literature or for teaching purpose no names will be used**.**

I understand that the relevant designated authority is permitted to have an access to

my medical record and to the data produced by the study for audit purpose only. However, they are required to maintain confidentiality**.**

STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr. Vaibhav has explained to me the purpose of study, the study procedure, that I will undergo and the possible discomforts as well as benefits that I may have. I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give consent to participate as a subject in this study.

_____ _____

(Participant)

_____ _____

(witness to signature) Date

ANNEXURE III

PROFORMA

A COMPARATIVE STUDY OF EQUIPOTENT DOSES OF INTRATHECAL CLONIDINE AND DEXMEDETOMIDINE ON CHARACTERISTICS OF BUPIVACAINE SUBARACHNOID BLOCK

Name :

Age/Gender :

IP. Number :

Ward/SU :

Date of surgery :

ASA Physical status :

Height (cm.) :

Weight (Kg.) :

Co morbidity :

Patient on any drugs :

(Being taken for prior co morbidity)

Group (Tick any one)

- Group-B: 0.5% Bupivacaine. 15mg + 0.5ml Normal saline
- Group-C: 0.5% Bupivacaine 15mg + 50 μg Clonidine
- Group -D: 0.5%Bupivacaine.15mg+ 5 μg Dexmedetomidine

Patient position:

Duration of surgery :

Medications : (to be given in case of Heart Rate Bp and Respiratory Changes)

Inj. Atropine 0.3-0.6mg i.v if PR< 50/min

Inj. Mephentermin 3 mg Intermittent bolus If MAP < 90 mmHg

Respiratory depression (RR <8 or SPo2<95%); Oxygen supplementation and respiratory support if required

OBSERVATIONS:

INTRAOPERATIVE HAEMODYNAMICS:

TIME	SpO_2	RR	SBP	DBP	MAP	Heart rate
Pre-Operative						
5 Min. after SAB						
10 Min. after SAB						
15 Min. after SAB						
20 Min. after SAB						
25 Min. after SAB						
30 Min. after SAB						
45 Min. after SAB						
1hr, after SAB						
1hr. 15 Min. after SAB						
1hr 30 Min. after SAB						
2hrs. after SAB						
2hrs. 30 Min. after SAB						
3hrs. after SAB						
3hrs30 Min. after SAB						
4hrs. after SAB						
4hrs30 Min. after SAB						
5hrs. after SAB						
5hrs 30 Min. after SAB						

SAB-sub Arachnoid Block

Post Operative Haemodynamics:

TIME	SpO_2	RR	SBP	DBP	MAP	Heart rate
Post Operative						
15Min.						
30min.						
45min.						
1hr						
2hrs						
3hrs						
4hrs						
5hrs						
6hrs						
7hrs						
8hrs						
12hrs						
24hrs						

Sensory blockade* :

Time	5 min	10 min	15 min	20 min
Sensory level				

*By loss of discrimination to pin prick every 5 minutes till it reaches the highest level

Motor blockade (Bromage scale)*:

Time	5 min	10 min	15 min	20 min
Motor level				

*By Bromage scale every 5 minutes till it reaches the grade 4

*Bromage scale

1- Free movement of legs / feet

2- Just able to flex knees with free movement of feet

3- Unable to flex knees, but with free movement of feet

4- unable to move legs/ feet

Sedation score:(Ramsay Sedation Scale (RSS)*:

Time	Depth of Sedation
Before surgery	
15 min. after SAB	
30 min. after SAB	
45 min. after SAB	
1hr after SAB	
2hrs after SAB	
3hrs after SAB	
4hrs after SAB	
5hrs after SAB	
6hrs after SAB	

SAB-sub arachnoid block

Ramsay Sedation Scale*

0- Fully awake

1- drowsy

2- drowsy but arousable to touch / call

3- drowsy but arousable on deep stimuli

Post operative pain score (Visual analog scale)*:

Time	Pain score
15 min.	
30 min.	
45 min.	
1 hour	
2 hour	
3 hour	
4 hour	
5 hour	
6 hour	
7 hour	
8 hour	
12 hour	
24 hour	

Visual analog scale*

Pain Intensity	Word Scale
0	No pain
1-2	Least pain
3-4	Mild pain
5-6	Moderate pain
7-8	Severe pain
9-10	Excruciating pain

Pain score >5 – supplementary analgesia given

DIFFERENT TIME INTERVALS AND REGRESSION OF SNSORY AND MOTOR BLOCKADE:

Time of sub arachnoid block	
Time to reach highest level of sensory blockade	
Time to obtain grade 4 motor block(Bromage scale)	
Time to reach 2-segment regression	
Time for Sensory regression to S1 dermatome	
Time for Motor block regression to S1 dermatome	
Time of rescue analgesia	

ANNEXURE-IV

KEY TO MASTER CHART

ASA	:	American Society of Anaesthesiologists
AMP	:	Austin moore prosthesis
CRIF	:	closed reduction internal fixation
DBP	:	Diastolic blood pressure
EF	:	External Fixation
GROUP B	:	Bupivacaine
GROUP C	:	Clonidine
GROUP D	:	Dexmedetomidine
Hr	:	HOUR
HR	:	Heart rate
IL	:	Interlocking
IMIL	:	Intramedullary interlocking
ITF	:	Inter trochanteric fracture of femur
LT	:	Left
Mins	:	Minutes
mmHg	:	Millimeter of mercury
MAP	:	Mean arterial pressure
NOF	:	Neck of femur
ORIF		Open reduction internal fixation
PFN	:	Proximal Femur Nailing
RT	:	Right
SAB	:	Sub arachnoid block
$SP0_2$	:	Oxygen saturation by pulseoximetry

Secs	:	Seconds
SBP	:	Systolic blood pressure
Sl. No	:	Serial number
SOF	:	Shaft of Femur
TBW	:	Tension Band Wiring
TFN	:	Teflon femur nailing
THR	:	Total Hip Replacement

Groups	S.No.	Name	Age (Ys.)	Sex	Reg. No.	Hight (cm.)	Weight (kg.)	Procedure	ASA Gd.	Duration of Surgery (min.)	Time to reach T10 Sensory level (min.)	Hightest Sensory Level	Time to reach hightest sensory level (min.)	Time to 2 seg. Regression (min.)	Time to S1 Regression (min.)	Time to reach Bromage Score 3 (min.)	Regression time to Bromage Score 0 (min.)	Time for first pain medication	Before spinal				At The time of S.B.					3 Min					6 Min					9 Min					12 Min					15 Min					18 Min					21 Min				
																			pulse(per min.)	SBP (mm hg)	DBP (mm hg)	MAP (mm hg)	SPO2(%)	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP
Group B	1		35	M	4927	165	64	CRIF IL Nail Tibia LT	11	155	5	T 6	13	95	180	16	165	295	102	118	84	98	100	110	138	90	106	100	118	136	94	108	100	122	130	90	106	100	114	124	86	98	100	108	114	80	89	100	92	110	80	88	100	98	108	76	86	100	94	104	68	76
Group B	2		40	F	15891	156	60	Abdominal hysterectomy	11	95	4	T 4	12	110	220	13	190	395	98	118	82	97	100	118	134	86	102	100	124	130	94	106	100	114	122	82	95	100	106	118	80	92	100	100	110	74	86	100	100	102	88	82	100	94	98	70	79	100	94	98	68	79
Group B	3		36	M	3375	165	62	CRIF IL Nail Tibia RT	11	105	5	T 6	15	80	165	10	160	320	110	124	78	97	100	118	126	86	99	100	120	132	92	105	100	110	120	84	96	100	112	104	80	88	100	96	108	78	88	100	100	102	74	83	100	94	100	72	81	100	90	98	70	82
Group B	4		50	F	16377	158	55	Abdominal hysterectomy	1	100	3	T 4	15	85	165	20	170	230	116	122	84	95	100	118	124	90	101	100	124	130	92	106	100	120	126	90	102	100	114	120	88	98	100	106	114	84	94	100	96	110	70	90	100	98	108	78	88	100	94	100	74	78
Group B	5		32	M	25429	152.5	60	CRIF of SOF LT	1	135	6	T 6	24	70	170	12	135	220	102	118	84	95	100	122	132	92	105	100	122	134	92	106	100	120	112	80	90	100	112	110	90	96	100	102	102	78	86	100	100	98	80	82	100	97	102	72	82	100	96	98	68	75
Group B	6		38	M	23029	162.5	64	Hernioplasty LT	1	60	8	T 4	13	75	190	14	150	295	98	128	82	91	100	118	128	88	102	100	120	130	88	102	100	116	108	78	88	100	108	106	76	86	100	98	108	76	86	100	92	98	74	79	100	94	94	68	76	100	92	98	68	72
Group B	7		35	F	24855	155	54	Appendicetomy	1	60	7	T 6	14	80	245	15	155	210	102	122	78	95	100	118	124	90	101	100	124	130	94	106	100	120	126	90	102	100	114	120	88	98	100	106	114	84	94	100	100	110	74	90	100	98	108	78	88	100	94	98	74	79
Group B	8		50	M	22560	165	62	Hernioplasty RT	11	70	5	T 6	17	85	205	20	170	310	102	120	84	97	100	118	126	86	99	100	120	132	92	105	100	110	120	84	96	100	112	104	80	88	100	96	108	78	88	100	96	102	70	83	100	94	100	72	81	100	90	100	70	78
Group B	9		60	M	27464	155	52	CRIF of SOF LT	111	115	4	T 4	12	165	240	12	160	340	100	120	82	95	100	122	132	92	105	100	122	134	92	106	100	120	112	80	90	100	112	110	90	96	100	102	102	78	86	100	100	98	78	82	100	97	102	72	82	100	96	98	68	75
Group B	10		45	M	22830	162.5	56	Skin Grafting Leg LT	1	55	8	T 8	20	95	180	16	165	205	100	122	80	91	100	118	128	88	102	100	120	130	88	102	100	116	108	78	88	100	108	106	76	86	100	98	108	76	86	100	100	98	72	79	100	94	94	68	78	100	92	104	68	84
Group B	11		44	F	16724	160	66	vaginal hysterectomy	11	90	7	T 4	13	80	165	14	160	295	98	118	78	91	100	118	128	88	102	100	120	130	88	102	100	116	108	78	88	100	108	106	76	86	100	98	108	76	86	100	100	98	70	79	100	94	94	68	76	100	92	98	68	75
Group B	12		38	F	27776	160	68	CRIF IL Nail SOF RT	111	105	8	T 8	14	120	195	20	235	380	112	124	84	97	99	118	134	86	102	98	124	130	94	106	100	114	122	82	95	100	106	118	80	92	100	100	110	74	86	100	100	102	72	82	100	94	98	70	79	100	94	94	68	76
Group B	13		31	M	26437	162.5	52	CRIF IL Nail SOF RT	1	95	8	T 4	16	65	250	20	160	225	102	128	84	98	99	110	138	90	106	99	118	136	94	108	100	122	130	90	106	100	114	124	86	98	100	108	114	80	89	100	98	110	78	88	100	98	108	76	86	100	94	104	74	84
Group B	14		32	M	27702	162.5	46	TBW of Patella LT	11	145	6	T 8	20	140	150	12	190	270	116	124	84	97	100	118	126	86	99	100	120	132	92	105	100	110	120	84	96	100	112	104	80	88	100	96	108	78	88	100	96	102	74	83	100	94	100	72	71	100	90	98	70	79
Group B	15		50	M	3893	162.5	62	ORIF + IMIL of Tibia	111	145	3	T 8	15	90	190	18	180	210	112	124	84	97	98	118	134	86	102	99	124	130	94	106	100	114	122	82	95	100	106	118	80	92	100	100	110	74	86	100	92	102	72	82	100	94	98	70	79	100	94	94	68	76
Group B	16		55	F	4171	157.5	55	Tendon Repair RT	11	90	13	T 6	16	145	175	12	205	230	98	118	78	91	100	118	128	88	102	100	120	130	88	102	100	116	108	78	88	100	108	106	76	86	100	98	108	76	86	100	100	98	70	79	100	94	94	68	76	100	92	98	68	75
Group B	17		59	F	30158	160	57	CRIF IL Nail SOF RT	1	100	8	T 8	15	85	165	20	170	230	116	122	84	97	100	118	126	86	99	100	120	132	92	105	100	110	120	84	96	100	112	104	80	88	100	96	108	78	88	100	100	102	74	83	100	94	100	72	81	100	90	98	70	79
Group B	18		25	M	85	170	49	Pattelactomy LT	1	90	4	T 8	18	80	165	14	160	210	110	128	84	95	100	118	124	90	101	100	124	130	94	106	100	120	126	90	102	100	114	120	88	98	100	106	114	84	94	100	100	110	80	90	100	98	108	78	88	100	94	98	74	82
Group B	19		45	M	27419	162.5	58	Skin Grafting Leg RT	1	85	8	T 6	14	120	195	20	235	300	102	128	82	95	98	122	132	92	105	99	122	134	92	106	100	120	112	80	90	100	112	110	90	96	100	102	102	78	86	100	100	98	74	82	100	97	102	72	82	100	96	100	68	78
Group B	20		35	M	3123	155	48	ORIF+DHS ITF RT	1	140	7	T 8	16	75	170	12	150	270	102	124	84	98	100	110	138	90	106	100	118	136	94	108	100	122	130	90	106	100	114	124	86	98	100	108	114	80	89	100	92	110	78	88	100	98	108	76	86	100	94	104	74	84
Group B	21		35	M	2032	157.5	54	CRIF of ITF LT	1	115	4	T 4	13	110	220	13	190	240	112	124	84	95	99	118	124	90	101	100	124	130	94	106	100	120	126	90	102	100	114	120	88	98	100	106	114	84	94	100	100	110	78	90	100	98	108	78	88	100	94	98	74	82
Group B	22		46	M	23207	160	45	Hernioplasty LT	11	85	6	T 6	20	70	170	12	135	270	116	118	84	97	100	118	126	86	99	100	120	132	92	105	100	110	120	84	96	100	112	104	80	88	100	98	108	78	88	100	100	102	72	83	100	94	100	72	81	100	90	98	70	79
Group B	23		48	F	17104	155	62	Abdominal hysterectomy	1	135	7	T 6	18	90	220	13	180	300	110	122	84	98	100	110	138	90	106	100	118	136	94	108	100	122	130	90	106	100	114	124	86	98	100	108	114	80	89	100	98	110	74	88	100	98	108	76	86	100	94	104	74	84
Group B	24		38	F	3375	157.5	65	ORIF IL Nail Tibia RT	1	90	8	T 6	12	150	165	20	240	210	102	118	84	98	100	110	138	90	106	100	118	136	94	108	100	122	130	90	106	100	114	124	86	98	100	108	114	80	89	100	92	110	80	88	100	98	108	76	86	100	94	104	68	76
Group B	25		37	M	1088	160	55	ORIF of SOF RT	1	135	7	T 8	13	80	165	10	160	220	102	128	84	98	99	110	138	90	106	99	118	136	94	108	100	122	130	90	106	100	114	124	86	98	100	108	114	80	89	100	98	110	78	88	100	98	108	76	86	100	94	104	74	84
Group B	26		35	M	4162	165	62	ORIF IL Nail Tibia RT	11	125	5	T 6	18	150	260	20	225	270	116	124	84	97	100	118	126	86	99	100	120	132	92	105	100	110	120	84	96	100	112	104	80	88	100	96	108	78	88	100	96	102	74	83	100	94	100	72	71	100	90	98	70	79
Group B	27		50	F	16857	155	55	vaginal hysterectomy	1	90	4	T 4	12	80	175	14	140	210	112	124	84	97	98	118	134	86	102	99	124	130	94	106	100	114	122	82	95	100	106	118	80	92	100	100	110	74	86	100	92	102	72	82	100	94	98	70	79	100	94	94	68	76
Group B	28		55	F	29703	152.5	60	CRIF of SOF LT	1	105	4	T10	13	100	205	12	160	270	98	118	78	91	100	118	128	88	102	100	120	130	88	102	100	116	108	78	88	100	108	106	76	86	100	98	108	76	86	100	100	98	70	79	100	94	94	68	76	100	92	98	68	75
Group B	29		45	M	23821	162.5	64	Hernioplasty LT	1	60	3	T 4	11	90	190	17	175	210	116	122	84	97	100	118	126	86	99	100	120	132	92	105	100	110	120	84	96	100	112	104	80	88	100	96	108	78	88	100	100	102	74	83	100	94	100	72	81	100	90	98	70	79
Group B	30		28	M	22354	155	54	Appendicetomy	1	85	7	T 4	12	90	240	20	170	180	110	128	84	95	100	118	124	90	101	100	124	130	94	106	100	120	126	90	102	100	114	120	88	98	100	106	114	84	94	100	100	110	80	90	100	98	108	78	88	100	94	98	74	82
Group B	31		42	M	22708	165	62	Hernioplasty RT	11	90	6	T 6	15	110	215	14	210	210	102	128	82	95	98	122	132	92	105	99	122	134	92	106	100	120	112	80	90	100	112	110	90	96	100	102	102	78	86	100	100	98	74	82	100	97	102	72	82	100	96	100	68	78
Group B	32		34	F	2509	155	52	ORIF of ITF LT	1	110	8	T 6	16	85	205	20	170	210	102	124	84	98	100	110	138	90	106	100	118	136	94	108	100	122	130	90	106	100	114	124	86	98	100	108	114	80	89	100	92	110	78	88	100	98	108	76	86	100	94	104	74	84
Group B	33		50	M	21707	162.5	56	Skin Grafting Leg LT	1	55	4	T 8	12	165	240	12	160	210	112	124	84	95	99	118	124	90	101	100	124	130	94	106	100	120	126	90	102	100	114	120	88	98	100	106	114	84	94	100	100	110	78	90	100	98	108	78	88	100	94	98	74	82
Group B	34		44	F	17005	160	66	Abdominal hysterectomy	11	105	3	T 4	15	95	180	16	165	225	116	118	84	97	100	118	126	86	99	100	120	132	92	105	100	110	120	84	96	100	112	104	80	88	100	98	108	78	88	100	100	102	72	83	100	94	100	72	81	100	90	98	70	79
Group B	35		45	F	27471	160	68	CRIF with Long TFN RT	11	130	7	T 8	22	80	165	14	160	255	110	122	84	98	100	110	138	90	106	100	118	136	94	108	100	122	130	90	106	100	114	124	86	98	100	108	114	80	89	100	98	110	74	88	100	98	108	76	86	100	94	104	74	84
Group B	36		60	F	26785	156.5	52	CRIF of SOF RT	111	125	8	T 4	14	120	195	20	235	295	102	118	84	98	100	110	138	90	106	100	118	136	94	108	100	122	130	90	106	100	114	124	86	98	100	108	114	80	89	100	92	110	80	88	100	98	108	76	86	100	94	104	68	76
Group B	37		50	M	30334	162.5	46	TBW of Patella LT	11	70	4	T 8	16	75	170	12	150	295	102	118	84	98	100	110	138	90	106	100	118	136	94	108	100	122	130	90	106	100	114	124	86	98	100	108	114	80	89	100	92	110	80	88	100	98	108	76	86	100	94	104	68	76
Group B	38		35	F	4082	160.5	62	ORIF + IMIL of Tibia	11	100	4	T 8	14	65	250	14	140	330	110	118	84	95	100	118	124	90	101	100	124	130	94	106	100	120	126	90	102	100	114	120	88	98	100	106	114	84	94	100	100	110	80	90	100	98	108	78	88	100	94	98	74	82
Group B	39		52	M	28937	157.5	55	Hernioplasty RT	11	65	3	T 6	22	90	190	18	180	210	100	120	80	93	100	120	130	90	103	100	120	132	90	104	100	118	110	80	90	100	110	108	78	88	100	100	108	78	88	100	98	100	72	81	100	98	96	70	78	100	95	100	66	77
Group B	40		26	F	2774	152.5	60	ORIF+AMP NOF LT	1	150	9	T 6	16	145	175	12	205	240	98	118	78	91	100	118	128	88	102	100	120	130	88	102	100	116	108	78	88	100	108	106	76	86	100	98	108	76	86	100	100	98	70	79	100	94	94	68	76	100	92	98	68	75
Group B	41		58	M	24584	162.5	64	Hernioplasty LT	1	90	8	T 4	15	85	165	20	170	270	112	124	84	97	99	118	134	86	102	98	124	130	94	106	100	114	122	82	95	100	106	118	80	92	100	100	110	74	86	100	100	102	72	82	100	94	98	70	79	100	94	94	68	76
Group B	42		38	M	22559	165	54	Appendicetomy	1	85	4	T 6	12	70	170	12	135	330	102	128	84	98	99	110	138	90	106	99	118	136	94	108	100	122	130	90	106	100	114	124	86	98	100	108	114	80	89	100	98	110	78	88	100	98	108	76	86	100	94	104	74	84
Group B	43		56	M	22814	165	62	Hernioplasty RT	11	60	5	T 6	20	75	190	14	150	210	116	124	84	97	100	118	126	86	99	100	120	132	92	105	100	110	120	84	96	100	112	104	80	88	100	96	108	78	88	100	96	102	74	83	100	94	100	72	71	100	90	98	70	79
Group B	44		35	M	2741	155	52	ORIF +AMP NOF RT	1	100	4	T 6	14	80	245	15	155	210	112	124	84	97	98	118	134	86	102	99	124	130	94	106	100	114	122	82	95	100	106	118	80	92	100	100	110	74	86	100	92	102	72	82	100	94	98	70	79	100	94	94	68	76
Group B	45		45	M	22832	162.5	56	Skin Grafting Leg LT	1	60	8	T 8	20	75	190	14	150	295	98	118	78	91	100	118	128	88	102	100	120	130	88	102	100	116	108	78	88	100	108	106	76	86	100	98	108	76	86	100	100	98	70	79	100	94	94	68	76	100	92	98	68	75
Group B	46		44	F	17439	160	66	vaginal hysterectomy	11	100	4	T 6	17	80	245	15	155	210	116	122	84	97	100	118	126	86	99	100	120	132	92	105	100	110	120	84	96	100	112	104	80	88	100	96	108	78	88	100	100	102	74	83	100	94	100	72	81	100	90	98	70	79
Group B	47		48	F	2082	160	68	ORIF +AMP NOF RT	11	110	5	T 8	16	85	205	20	170	270	110	128	84	95	100	118	124	90	101	100	124	130	94	106	100	120	126	90	102	100	114	120	88	98	100	106	114	84	94	100	100	110	80	90	100	98	108	78	88	100	94	98	74	82
Group B	48		50	M	5287	162.5	52	CRIF IL Nail SOF RT	1	115	4	T10	12	165	240	12	160	240	102	128	82	95	98	122	132	92	105	99	122	134	92	106	100	120	112	80	90	100	112	110	90	96	100	102	102	78	86	100	100	98	74	82	100	97	102	72	82	100	96	100	68	78
Group B	49		32	M	3109	162.5	46	TBW of Patella RT	11	60	4	T 8	16	75	170	12	150	300	102	124	84	98	100	110	138	90	106	100	118	136	94	108	100	122	130	90	106	100	114	124	86	98	100	108	114	80	89	100	92	110	78	88	100	98	108	76	86	100	94	104	74	84
Group B	50		53	M	4680	162.5	62	ORIF + IMIL of Tibia	11	75	4	T 8	12	110	220	13	190	285	112	124	84	95	99	118	124	90	101	100	124	130	94	106	100	120	126	90	102	100	114	120	88	98	100	106	114	84	94	100	100	110	78	90	100	98	108	78	88	100	94	98	74	82
Group B	51		55	M	28933	157.5	55	Hernioplasty RT	11	65	7	T 6	14	80	165	10	160	210	116	118	84	97	100	118	126	86	99	100	120	132	92	105	100	110	120	84	96	100	112	104	80	88	100	98	108	78	88	100	100	102	72	83	100	94	100	72	81	100	90	98	70	79
Group B	52		55	M	29088	157.5	55	Hernioplasty LT	11	75	5	T 4	22	80	165	10	160	240	110	122	84	98	100	110	138	90	106	100	118	136	94	108	100	122	130	90	106	100	114	124	86	98	100	108	114	80	89	100	98	110	74	88	100	98	108	76	86	100	94	104	74	84

Groups	S.No.	Name	Age (Ys.)	Sex	Reg. No.	Hight (cm.)	Weight (kg.)	Procedure	ASA Gd.	Duration of Surgery (min.)	Time to reach T10 Sensory level (min.)	Hightest Sensory Level	Time to reach hightest sensory level (min.)	Time to 2 seg. Regression (min.)	Time to S1 Regression (min.)	Time to reach Bromage Score 3 (min.)	Regression time to Bromage Score 0 (min.)	Time for first pain medication	Before spinal				At The time of S.B.					3 Min					6 Min					9 Min					12 Min					15 Min					18 Min					21 Min				
																			pulse(per min.)	SBP (mm hg)	DBP (mm hg)	MAP (mm hg)	SPO2(%)	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP
Group C	1		30	M	22687	170	52	Appendicetomy	11	70	7	T 4	12	150	295	10	260	445	112	126	84	93	100	126	130	92	106	100	128	130	82	98	100	118	116	74	88	100	102	112	72	84	100	98	110	68	83	100	90	108	68	82	100	82	102	66	74	100	76	90	70	79
Group C	2		28	M	22995	173	68	Hernioplasty RT	1	85	6	T 6	16	160	270	16	300	420	112	120	80	92	100	124	132	88	102	100	128	124	82	96	100	118	112	70	84	100	110	112	70	90	100	106	110	60	82	100	96	108	64	81	100	90	104	64	80	100	80	98	66	76
Group C	3		29	F	27252	155	70	ORIF of NOF RT	1	135	4	T 6	12	90	290	8	190	570	110	122	78	96	100	124	132	88	102	100	124	126	78	94	100	112	112	70	84	100	98	108	70	85	100	54	108	80	74	100	86	104	74	77	100	78	98	70	78	100	72	98	64	75
Group C	4		55	F	25942	158	78	Skin Grafting Leg LT	1	60	3	T 6	10	145	230	9	290	510	108	128	80	99	100	132	138	94	106	100	126	126	90	102	100	114	118	88	98	100	108	110	80	87	100	100	100	70	89	100	96	104	74	84	100	84	100	70	80	100	80	94	70	80
Group C	5		35	F	28723	160	68	CRIF IL Nail SOF RT	1	145	7	T10	14	90	240	9	300	480	112	130	84	98	100	124	138	90	106	100	128	126	80	95	100	114	112	78	89	100	106	108	74	85	100	100	110	74	80	100	96	98	72	82	100	88	94	86	78	100	82	97	70	76
Group C	6		42	F	28238	155	55	CRIF TFN of ITF RT	11	100	4	T 6	15	120	275	9	235	450	114	128	84	99	100	124	138	94	108	100	130	132	84	100	100	118	118	76	90	100	104	114	74	85	100	100	100	70	86	100	92	112	74	85	100	84	104	70	78	100	78	90	72	81
Group C	7		38	F	18760	153	65	Abdominal hysterectomy	11	105	7	T 6	12	150	295	10	260	510	112	130	84	99	100	126	138	90	106	100	128	126	82	95	100	114	112	78	89	100	106	108	74	89	100	100	100	70	80	100	96	98	74	82	100	88	94	70	76	100	83	100	70	76
Group C	8		26	M	269	175	68	TBW of Patella RT	11	70	6	T 4	16	160	270	16	300	600	112	130	84	99	100	128	138	92	106	100	130	126	82	95	100	114	112	78	89	100	106	108	74	83	100	100	106	74	80	100	96	98	70	82	100	88	94	68	80	100	82	90	70	76
Group C	9		53	M	4680	172	59	ORIF + EF of Tibia RT	1	120	7	T 4	22	120	300	10	180	540	114	130	80	74	100	124	134	92	106	100	126	128	86	100	100	118	116	80	92	100	110	112	78	90	100	104	110	70	84	100	98	100	68	80	100	94	98	64	78	100	90	90	64	74
Group C	10		42	F	19118	162	56	vaginal hysterectomy	11	80	6	T 4	12	130	295	8	260	510	110	124	80	96	100	126	132	92	104	100	126	128	80	96	100	114	114	72	96	100	100	110	70	89	100	96	108	80	83	100	88	106	74	80	100	80	100	70	82	100	74	90	68	77
Group C	11		45	M	5183	173	58	ORIF+DHS ITF RT	11	130	5	T 4	20	80	310	10	220	450	114	120	80	92	100	130	130	86	100	100	134	124	84	97	100	120	118	80	92	100	110	110	76	87	100	100	108	74	85	100	98	100	64	80	100	96	102	70	74	100	94	94	68	76
Group C	12		30	F	18965	158	60	Abdominal hysterectomy	11	65	4	T 4	12	110	265	8	225	465	110	122	78	98	100	126	132	88	102	100	124	126	78	94	100	112	112	70	84	100	98	108	70	84	100	94	110	70	83	100	86	104	72	77	100	78	98	62	80	100	72	98	64	75
Group C	13		53	M	30433	170	60	Skin Grafting Leg RT	1	50	5	T 6	10	160	280	7	300	570	114	128	84	93	100	132	138	96	108	100	130	132	84	100	100	118	118	76	90	100	104	114	74	85	100	100	110	74	86	100	92	112	68	85	100	84	104	68	77	100	78	94	72	82
Group C	14		32	F	1756	157	50	AMP of NOF RT	1	80	7	T 4	16	90	290	9	175	480	112	120	80	92	100	126	130	88	102	100	128	124	82	96	100	118	112	70	84	100	110	112	70	83	100	106	110	68	82	100	96	108	70	81	100	90	104	64	82	100	80	100	66	76
Group C	15		50	M	29589	160	52	ORIF of SOF LT	11	105	5	T 4	22	120	270	8	200	510	108	120	78	74	100	128	128	80	96	100	124	130	90	103	100	114	114	82	92	100	104	108	78	86	100	92	104	74	84	100	82	106	68	82	100	80	102	72	76	100	72	98	68	77
Group C	16		45	M	24685	165	58	Hernioplasty LT	1	65	7	T 4	12	150	300	12	195	450	110	124	80	74	100	130	134	90	104	100	126	128	80	96	100	114	114	72	86	100	100	110	70	85	100	96	110	70	83	100	88	106	68	80	100	80	100	64	76	100	74	96	68	77
Group C	17		58	F	18266	158	60	vaginal hysterectomy	11	80	5	T 6	20	80	210	10	275	450	110	124	80	98	100	124	136	90	104	100	126	128	80	96	100	114	114	72	86	100	100	110	70	85	100	96	110	70	83	100	88	106	70	80	100	80	100	64	78	100	74	96	68	77
Group C	18		40	M	2717	155	55	CRIF IL Nail Tibia RT	11	60	6	T 4	22	110	280	9	160	510	112	126	84	99	100	130	138	92	106	100	128	130	82	98	100	118	116	74	88	100	102	112	72	85	100	98	110	70	83	100	90	108	74	82	100	82	102	66	76	100	76	96	70	79
Group C	19		40	M	26401	158	52	CRIF of SOF RT	1	90	6	T 6	11	70	295	10	200	480	112	130	84	98	100	126	136	90	106	100	128	126	80	95	100	114	112	78	89	100	106	108	74	84	100	100	100	70	80	100	96	98	70	82	100	88	94	70	77	100	85	98	70	76
Group C	20		31	F	4753	153	58	CRIF IL Nail Tibia LT	11	145	5	T10	12	140	255	12	255	555	112	126	84	93	100	126	130	92	106	100	128	130	82	98	100	118	116	74	88	100	102	112	72	84	100	98	110	68	83	100	90	108	68	82	100	82	102	66	74	100	76	90	70	79
Group C	21		19	F	1303	155	50	CRIF IL Nail Tibia LT	11	95	7	T 6	13	120	310	9	240	525	112	120	80	92	100	124	132	88	102	100	128	124	82	96	100	118	112	70	84	100	110	112	70	90	100	106	110	60	82	100	96	108	64	81	100	90	104	64	80	100	80	98	66	76
Group C	22		42	M	2059	157	62	CRIF IL Nail Tibia RT	1	110	8	T 6	18	160	270	8	225	510	110	122	78	96	100	124	132	88	102	100	124	126	78	94	100	112	112	70	84	100	98	108	70	85	100	54	108	80	74	100	86	104	74	77	100	78	98	70	78	100	72	98	64	75
Group C	23		43	M	28622	155	58	ORIF+DHS ITF LT	11	125	5	T 4	14	85	240	10	180	450	108	128	80	99	100	132	138	94	106	100	126	126	90	102	100	114	118	88	98	100	108	110	80	87	100	100	100	70	89	100	96	104	74	84	100	84	100	70	80	100	80	94	70	80
Group C	24		38	F	28047	151	48	CRIF of SOF LT	1	120	6	T 6	10	160	310	8	195	600	112	130	84	98	100	124	138	90	106	100	128	126	80	95	100	114	112	78	89	100	106	108	74	85	100	100	110	74	80	100	96	98	72	82	100	88	94	86	78	100	82	97	70	76
Group C	25		44	M	24953	155	50	Hernioplasty LT	1	80	7	T 6	12	150	290	9	250	510	114	128	84	99	100	124	138	94	108	100	130	132	84	100	100	118	118	76	90	100	104	114	74	85	100	100	100	70	86	100	92	112	74	85	100	84	104	70	78	100	78	90	72	81
Group C	26		37	F	19863	157	65	vaginal hysterectomy	11	145	5	T 6	20	75	295	8	220	480	112	130	84	99	100	126	138	90	106	100	128	126	82	95	100	114	112	78	89	100	106	108	74	89	100	100	100	70	80	100	96	98	74	82	100	88	94	70	76	100	83	100	70	76
Group C	27		25	M	4012	175	68	TBW of Patella RT	11	60	8	T 4	11	145	300	12	195	570	112	130	84	99	100	128	138	92	106	100	130	126	82	95	100	114	112	78	89	100	106	108	74	83	100	100	106	74	80	100	96	98	70	82	100	88	94	68	80	100	82	90	70	76
Group C	28		45	M	3314	172	59	CRIF IL Nail Tibia RT	1	120	7	T 6	14	90	240	9	300	420	114	130	80	74	100	124	134	92	106	100	126	128	86	100	100	118	116	80	92	100	110	112	78	90	100	104	110	70	84	100	98	100	68	80	100	94	98	64	78	100	90	90	64	74
Group C	29		35	F	19820	162	56	vaginal hysterectomy	11	90	4	T 4	15	120	275	9	235	450	110	124	80	96	100	126	132	92	104	100	126	128	80	96	100	114	114	72	96	100	100	110	70	89	100	96	108	80	83	100	88	106	74	80	100	80	100	70	82	100	74	90	68	77
Group C	30		40	M	24828	173	58	ORIF of SOF RT	11	115	5	T 6	20	80	310	10	220	450	112	130	84	98	100	124	138	90	106	100	128	126	80	95	100	114	112	78	89	100	106	108	74	85	100	100	110	74	80	100	96	98	72	82	100	88	94	86	78	100	82	97	70	76
Group C	31		34	F	19187	158	60	Abdominal hysterectomy	11	60	4	T 4	12	110	265	8	225	420	114	128	84	99	100	124	138	94	108	100	130	132	84	100	100	118	118	76	90	100	104	114	74	85	100	100	100	70	86	100	92	112	74	85	100	84	104	70	78	100	78	90	72	81
Group C	32		36	M	33139	170	60	Skin Grafting Leg RT	1	55	5	T 6	10	160	280	7	300	540	112	130	84	99	100	126	138	90	106	100	128	126	82	95	100	114	112	78	89	100	106	108	74	89	100	100	100	70	80	100	96	98	74	82	100	88	94	70	76	100	83	100	70	76
Group C	33		48	M	999	167	50	ORIF of NOF RT	1	125	7	T 4	16	90	290	9	175	420	112	130	84	99	100	128	138	92	106	100	130	126	82	95	100	114	112	78	89	100	106	108	74	83	100	100	106	74	80	100	96	98	70	82	100	88	94	68	80	100	82	90	70	76
Group C	34		40	M	709	160	52	ORIF+DHS SOF RT	11	135	5	T 6	22	120	270	8	200	495	114	130	80	74	100	124	134	92	106	100	126	128	86	100	100	118	116	80	92	100	110	112	78	90	100	104	110	70	84	100	98	100	68	80	100	94	98	64	78	100	90	90	64	74
Group C	35		50	M	25060	165	58	Hernioplasty LT	1	60	7	T 4	12	150	300	12	195	480	110	124	80	96	100	126	132	92	104	100	126	128	80	96	100	114	114	72	96	100	100	110	70	89	100	96	108	80	83	100	88	106	74	80	100	80	100	70	82	100	74	90	68	77
Group C	36		58	F	18355	158	60	vaginal hysterectomy	11	85	5	T 6	20	80	210	10	275	405	114	130	80	74	100	124	134	92	106	100	126	128	86	100	100	118	116	80	92	100	110	112	78	90	100	104	110	70	84	100	98	100	68	80	100	94	98	64	78	100	90	90	64	74
Group C	37		57	M	3735	155	55	CRIF IL Nail Tibia RT	11	65	6	T 4	22	110	280	9	160	510	110	124	80	96	100	126	132	92	104	100	126	128	80	96	100	114	114	72	96	100	100	110	70	89	100	96	108	80	83	100	88	106	74	80	100	80	100	70	82	100	74	90	68	77
Group C	38		48	M	3153	158	52	ORIF +AMP NOF RT	1	70	8	T 6	11	145	300	12	195	450	112	120	80	93	100	126	130	88	102	100	128	124	82	96	100	118	112	70	84	100	110	112	70	84	100	106	110	68	82	100	96	108	64	81	100	90	104	64	77	100	80	98	66	76
Group C	39		23	F	277	153	58	CRIF IL Nail Tibia LT	11	80	7	T 8	14	90	240	9	300	435	110	122	78	92	100	126	132	88	102	100	124	126	78	94	100	112	112	70	84	100	98	108	70	84	100	94	110	70	83	100	86	104	64	77	100	78	98	62	74	100	72	94	64	74
Group C	40		41	F	13377	155	50	CRIF IL Nail Tibia LT	11	65	4	T 6	15	120	275	9	235	540	110	112	78	92	100	126	132	88	102	100	124	126	78	94	100	112	112	70	84	100	98	108	70	84	100	94	110	70	83	100	86	104	64	77	100	78	98	62	74	100	72	94	64	74
Group C	41		45	M	4125	157	62	CRIF IL Nail Tibia RT	1	90	7	T 6	12	150	295	10	260	540	110	122	78	96	100	126	132	88	102	100	124	126	78	94	100	112	112	70	84	100	98	108	70	84	100	94	110	70	83	100	86	104	74	77	100	78	98	62	74	100	72	94	64	74
Group C	42		54	M	24784	155	58	ORIF+AMP NOF LT	11	75	6	T 4	16	160	270	16	300	450	109	128	80	99	100	124	132	94	106	100	126	126	90	102	100	114	118	88	98	100	108	110	80	90	100	100	108	80	89	100	96	104	70	84	100	84	100	70	78	100	80	94	70	80
Group C	43		42	M	25682	161	48	CRIF of SOF LT	1	110	4	T 6	12	90	290	8	190	600	114	130	84	93	100	126	138	90	106	100	130	128	86	100	100	118	116	80	92	100	110	112	78	89	100	104	106	74	94	100	98	100	70	80	100	94	98	68	80	100	90	96	64	74
Group C	44		40	M	25771	155	50	Hernioplasty LT	1	60	3	T 6	10	145	230	9	290	420	114	120	80	92	100	130	130	86	100	100	134	124	84	97	100	120	118	80	92	100	110	110	76	87	100	100	108	74	85	100	98	100	64	80	100	96	102	70	74	100	94	94	68	76
Group C	45		35	M	2149	153	58	ORIF IL Nail tibia LT	1	85	7	T 8	12	150	290	9	250	390	110	122	78	98	100	126	132	88	102	100	124	126	78	94	100	112	112	70	84	100	98	108	70	84	100	94	110	70	83	100	86	104	72	77	100	78	98	62	80	100	72	98	64	75
Group C	46		28	M	3005	165	50	CRIF IL Nail Tibia LT	1	75	5	T 6	20	75	295	8	220	570	114	128	84	93	100	132	138	96	108	100	130	132	84	100	100	118	118	76	90	100	104	114	74	85	100	100	110	74	86	100	92	112	68	85	100	84	104	68	77	100	78	94	72	82
Group C	47		41	M	5059	157	62	CRIF IL Nail Tibia RT	1	65	7	T 6	22	120	300	10	180	510	112	120	80	92	100	126	130	88	102	100	128	124	82	96	100	118	112	70	84	100	110	112	70	83	100	106	110	68	82	100	96	108	70	81	100	90	104	64	82	100	80	100	66	76
Group C	48		60	F	25912	155	58	CRIF IL Nail SOF LT	11	90	6	T 4	12	130	295	8	260	435	108	120	78	74	100	128	128	80	96	100	124	130	90	103	100	114	114	82	92	100	104	108	78	86	100	92	104	74	84	100	82	106	68	82	100	80	102	72	76	100	72	98	68	77
Group C	49		55	M	24925	161	48	CRIF of SOF LT	1	80	4	T 4	12	90	290	8	190	495	110	124	80	74	100	130	134	90	104	100	126	128	80	96	100	114	114	72	86	100	100	110	70	85	100	96	110	70	83	100	88	106	68	80	100	80	100	64	76	100	74	96	68	77
Group C	50		34	M	25840	158	50	Hernioplasty LT	1	65	3	T 6	10	145	230	9	290	390	110	124	80	98	100	124	136	90	104	100	126	128	80	96	100	114	114	72	86	100	100	110	70	85	100	96	110	70	83	100	88	106	70	80	100	80	100	64	78	100	74	96	68	77
Group C	51		35	M	23635	151	48	ORIF of ITF LT	1	145	4	T 6	12	90	290	8	190	540	112	126	84	99	100	130	138	92	106	100	128	130	82	98	100	118	116	74	88	100	102	112	72	85	100	98	110	70	83	100	90	108	74	82	100	82	102	66	76	100	76	96	70	79
Group C	52		51	M	26721	165	50	Hernioplasty LT	11	65	3	T 6	10	145	230	9	290	435	112	130	84	98	100	126	136	90	106	100	128	126	80	95	100	114	112	78	89	100	106	108	74	84	100	100	100	70	80	100	96	98	70	82	100	88	94	70	77	100	85	98	70	76

Groups	S.No.	Name	Age (Ys.)	Sex	Reg. No.	Hight (cm.)	Weight (kg.)	Procedure	ASA Gd.	Duration of Surgery (min.)	Time to reach T10 Sensory level (min.)	Hightest Sensory Level	Time to reach hightest sensory level (min.)	Time to 2 seg. Regression (min.)	Time to S1 Regression (min.)	Time to reach Bromage Score 3 (min.)	Regression time to Bromage Score 0 (min.)	Time for first pain medication	Before spinal				At The time of S.B.					3 Min					6 Min					9 Min					12 Min					15 Min					18 Min					21 Min				
																			pulse(per min.)	SBP (mm hg)	DBP (mm hg)	MAP (mm hg)	SPO2(%)	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP
Group D	1		50	F	29439	168	64	CRIF of SOF RT	11	75	7	T 6	16	100	300	9	265	740	120	110	80	96	100	130	140	90	106	100	124	136	90	105	100	128	88	88	100	100	110	108	80	89	100	96	90	70	80	100	90	92	68	76	100	80	90	70	72	100	70	80	66	73
Group D	2		46	M	1627	160	72	CRIF IL Nail Tibia LT	1	90	6	T 4	14	140	245	11	300	600	120	128	80	94	100	134	136	90	106	100	130	136	88	104	100	120	80	80	96	100	118	116	78	90	100	114	100	70	80	100	110	94	70	78	100	106	90	64	74	100	100	80	60	76
Group D	3		25	M	6023	170	86	Above Knee Amputation	1	90	5	T 6	18	110	300	12	295	570	118	124	76	83	100	128	128	88	96	100	126	140	90	96	100	118	84	84	97	100	110	118	78	91	100	96	110	70	76	100	94	94	60	72	100	86	94	64	72	100	80	92	60	70
Group D	4		41	M	4694	174	64	CRIF IL Nail Tibia RT	1	110	3	T 8	15	170	375	10	310	690	110	110	80	94	100	130	136	78	94	100	120	130	80	96	100	120	86	76	90	100	108	104	70	81	100	94	100	64	80	100	92	96	70	78	100	85	90	64	72	100	72	90	60	70
Group D	5		35	M	3413	160	50	CRIF IL Nail SOF LT	11	95	6	T 6	22	110	250	8	270	685	118	124	80	96	100	128	140	88	96	100	126	140	90	96	100	128	84	84	97	100	110	118	78	91	100	96	110	70	79	100	94	94	68	76	100	86	90	64	76	100	80	92	60	70
Group D	6		42	F	4093	153	52	ORIF+AMP NOF LT	11	80	7	T 6	14	110	345	12	240	740	120	128	76	83	100	134	140	90	106	100	130	136	88	104	100	124	80	80	96	100	118	118	78	90	100	114	100	70	80	100	110	94	70	77	100	106	90	64	75	100	100	88	60	66
Group D	7		47	M	26293	158	56	Hernioplasty LT	11	60	6	T 4	13	150	265	11	300	660	120	110	80	83	100	130	136	90	106	100	124	136	90	105	100	126	88	88	100	100	110	108	80	89	100	96	90	70	80	100	90	92	70	73	100	89	90	68	73	100	70	88	66	73
Group D	8		32	M	30040	162	45	Hernioplasty RT	11	65	7	T 6	13	165	265	9	280	600	124	110	80	96	100	130	140	86	102	100	126	140	90	106	100	128	86	86	99	100	112	110	80	90	100	98	90	72	76	100	90	94	68	76	100	82	90	64	75	100	72	88	66	73
Group D	9		35	M	18406	150	52	ORIF +AMP NOF RT	11	145	7	T 4	24	145	250	12	235	630	120	128	70	83	100	134	128	90	106	100	130	136	88	96	100	118	80	80	96	100	118	116	78	90	100	114	100	70	80	100	110	94	60	72	100	106	94	64	72	100	100	88	60	69
Group D	10		45	M	30092	180	49	Hernioplasty RT	1	70	6	T 6	15	170	290	10	240	570	110	110	70	94	100	128	140	78	94	100	120	130	80	96	100	120	76	76	90	100	108	104	70	81	100	94	100	64	80	100	92	96	70	78	100	84	90	64	72	100	72	90	60	70
Group D	11		40	M	34107	170	68	Skin Grafting Leg RT	1	50	8	T 8	15	80	360	16	240	660	124	110	70	83	100	130	140	86	102	100	126	140	90	106	100	124	86	86	99	100	112	110	80	90	100	98	98	72	80	100	90	94	70	78	100	82	90	68	72	100	72	88	66	73
Group D	12		57	M	29606	170	52	CRIF of SOF RT	1	70	8	T10	16	170	275	12	275	570	120	110	70	83	100	130	140	90	106	100	124	136	90	105	100	128	88	88	100	100	110	108	80	89	100	96	98	70	80	100	90	92	68	77	100	80	90	70	76	100	70	88	66	73
Group D	13		42	F	17106	160	48	Abdominal hysterectomy	1	145	7	T 6	14	145	250	12	235	540	120	128	70	83	100	134	140	90	106	100	130	136	88	104	100	124	80	80	96	100	118	116	78	90	100	115	100	70	79	100	110	94	70	76	100	106	90	64	72	100	100	88	60	69
Group D	14		42	M	27309	154	45	Hernioplasty LT	1	70	6	T10	15	170	290	10	240	510	120	110	80	94	100	130	136	90	106	100	124	136	90	105	100	120	88	88	100	100	110	108	80	89	100	96	98	70	80	100	90	92	70	78	100	80	90	70	74	100	70	88	66	73
Group D	15		40	M	5471	162	58	CRIF of Tibia LT	11	70	7	T 6	14	160	375	8	200	600	118	124	76	83	100	128	128	88	96	100	126	140	90	96	100	118	84	84	97	100	110	118	78	91	100	96	110	70	76	100	94	94	60	72	100	86	94	64	72	100	80	92	60	70
Group D	16		56	F	24108	155	60	Abdominal hysterectomy	1	145	6	T 6	22	100	290	11	205	540	110	110	80	94	100	130	136	78	94	100	120	130	80	96	100	120	96	76	90	100	118	104	70	81	100	94	100	64	80	100	92	96	70	78	100	84	90	64	76	100	72	90	60	70
Group D	17		42	M	23262	160	55	Appendicetomy	1	60	7	T 6	14	170	375	9	230	410	118	124	70	83	100	128	140	88	96	100	126	140	90	96	100	124	84	84	97	100	110	118	78	91	100	96	110	70	79	100	94	94	70	77	100	86	90	64	72	100	80	92	60	70
Group D	18		42	M	23170	156	64	Hernioplasty RT	1	80	6	T 4	15	165	275	11	285	540	120	110	80	96	100	130	140	90	106	100	124	136	90	105	100	128	88	88	100	100	110	108	80	89	100	96	90	70	80	100	90	92	68	76	100	80	90	70	72	100	70	80	66	73
Group D	19		40	F	23631	158	52	ORIF of NOF LT	11	110	7	T 6	16	170	250	8	200	510	120	128	80	94	100	134	136	90	106	100	130	136	88	104	100	120	80	80	96	100	118	116	78	90	100	114	100	70	80	100	110	94	70	78	100	106	90	64	74	100	100	80	60	76
Group D	20		42	F	28238	155	58	Skin Grafting Leg LT	1	55	4	T 4	14	135	255	11	305	570	118	124	76	83	100	128	128	88	96	100	126	140	90	96	100	118	84	84	97	100	110	118	78	91	100	96	110	70	76	100	94	94	60	72	100	86	94	64	72	100	80	92	60	70
Group D	21		58	F	23666	157	65	vaginal hysterectomy	1	145	6	T 4	20	90	375	12	250	585	120	128	80	96	100	134	140	90	106	100	130	136	88	140	100	128	80	80	96	100	118	116	78	90	100	114	100	70	80	100	110	94	68	76	100	106	90	64	72	100	100	88	60	69
Group D	22		53	F	24444	153	52	CRIF TFN of ITF RT	1	110	5	T 6	12	180	250	12	305	600	110	110	76	83	100	130	128	78	94	100	120	130	80	96	100	118	96	76	90	100	108	104	70	81	100	94	100	64	76	100	92	96	60	72	100	84	94	64	74	100	72	90	60	70
Group D	23		35	M	24385	153	48	ORIF of ITF RT	11	120	6	T10	12	130	360	10	250	570	110	110	76	83	100	130	128	78	94	100	120	130	80	96	100	118	96	76	90	100	108	104	70	81	100	94	100	64	76	100	92	96	60	72	100	84	90	64	73	100	72	90	60	70
Group D	24		33	M	12647	160	59	TBW of Patella LT	1	75	7	T 6	20	160	375	12	250	710	118	124	80	94	100	128	136	88	96	100	126	140	90	96	100	120	84	84	97	100	110	118	78	91	100	96	110	70	80	100	94	94	70	78	100	86	94	64	72	100	80	92	60	70
Group D	25		33	F	912	160	65	CRIF IL Nail Tibia RT	1	70	6	T 6	14	120	340	10	200	720	110	110	76	83	100	130	128	78	94	100	120	130	80	96	100	118	96	76	90	100	108	104	70	81	100	94	100	64	76	100	92	96	68	72	100	84	90	64	74	100	72	90	60	70
Group D	26		40	M	30281	150	52	CRIF of NOF LT	11	80	7	T 4	17	180	365	11	210	690	120	128	80	96	100	134	140	90	106	100	130	136	88	140	100	128	80	80	96	100	118	116	70	90	100	14	100	70	80	100	110	94	68	76	100	106	90	64	72	100	100	88	60	69
Group D	27		48	M	28939	180	49	Hernioplasty RT	1	70	8	T 6	12	115	260	12	190	540	120	128	70	96	100	134	140	90	106	100	130	136	88	140	100	124	80	80	96	100	118	116	70	90	100	114	100	70	80	100	110	94	70	76	100	106	90	64	72	100	100	88	60	69
Group D	28		60	M	4495	170	68	Skin Grafting Leg RT	1	55	6	T 8	15	110	250	8	270	660	120	110	70	83	100	130	136	90	106	100	124	136	90	105	100	126	88	88	100	100	110	108	80	89	100	96	98	70	79	100	90	92	70	77	100	80	90	70	76	100	70	88	66	73
Group D	29		55	M	2672	170	52	CRIF TFN of ITF RT	1	90	7	T 6	14	110	345	12	240	540	124	110	70	83	100	130	140	86	102	100	126	140	90	106	100	124	86	86	99	100	112	110	80	90	100	98	98	72	80	100	90	94	70	78	100	82	90	68	72	100	72	88	66	73
Group D	30		42	F	17706	160	48	Abdominal hysterectomy	1	70	6	T 6	14	150	265	11	300	510	120	110	70	83	100	130	140	90	106	100	124	136	90	105	100	128	88	88	100	100	110	108	80	89	100	96	98	70	80	100	90	92	68	77	100	80	90	70	76	100	70	88	66	73
Group D	31		42	M	28175	159	45	Hernioplasty LT	1	65	7	T 4	13	165	265	9	280	540	120	128	70	83	100	134	140	90	106	100	130	136	88	104	100	124	80	80	96	100	118	116	78	90	100	115	100	70	79	100	110	94	70	76	100	106	90	64	72	100	100	88	60	69
Group D	32		42	M	1775	162	58	ORIF IL Nail tibia LT	11	70	7	T 6	14	160	375	8	200	600	120	110	80	94	100	130	136	90	106	100	124	136	90	105	100	120	88	88	100	100	110	108	80	89	100	96	98	70	80	100	90	92	70	78	100	80	90	70	74	100	70	88	66	73
Group D	33		34	F	2509	155	60	ORIF of ITF LT	1	145	6	T 6	14	100	290	11	205	570	118	124	76	83	100	128	128	88	96	100	126	140	90	96	100	118	84	84	97	100	110	118	78	91	100	96	110	70	76	100	94	94	60	72	100	86	94	64	72	100	80	92	60	70
Group D	34		42	M	24211	160	55	Appendicetomy	1	60	7	T 4	13	170	375	9	230	510	110	110	80	94	100	130	136	78	94	100	120	130	80	96	100	120	96	76	90	100	118	104	70	81	100	94	100	64	80	100	92	96	70	78	100	84	90	64	76	100	72	90	60	70
Group D	35		42	M	23269	156	64	Hernioplasty RT	1	80	6	T 4	15	165	275	11	285	510	118	124	70	83	100	128	140	88	96	100	126	140	90	96	100	124	84	84	97	100	110	118	78	91	100	96	110	70	79	100	94	94	70	77	100	86	90	64	72	100	80	92	60	70
Group D	36		48	M	1736	158	52	ORIF of NOF RT	11	110	7	T 6	16	170	250	8	200	540	120	110	80	96	100	130	140	90	106	100	124	136	90	105	100	128	88	88	100	100	110	108	80	89	100	96	90	70	80	100	90	92	68	76	100	80	90	70	72	100	70	80	66	73
Group D	37		30	M	2766	155	58	Skin Grafting Leg LT	1	55	4	T 4	14	135	255	11	305	600	120	128	80	94	100	134	136	90	106	100	130	136	88	104	100	120	80	80	96	100	118	116	78	90	100	114	100	70	80	100	110	94	70	78	100	106	90	64	74	100	100	80	60	76
Group D	38		39	F	1766	157	65	ORIF of NOF RT	1	145	6	T 6	15	90	375	12	250	710	118	124	76	83	100	128	128	88	96	100	126	140	90	96	100	118	84	84	97	100	110	118	78	91	100	96	110	70	76	100	94	94	60	72	100	86	94	64	72	100	80	92	60	70
Group D	39		60	M	23842	163	52	ORIF of NOF LT	11	125	7	T 6	16	100	300	9	265	600	110	110	80	94	100	130	136	78	94	100	120	130	80	96	100	120	86	76	90	100	108	104	70	81	100	94	100	64	80	100	92	96	70	78	100	85	90	64	72	100	72	90	60	70
Group D	40		50	M	15144	153	48	ORIF of SOF LT	11	110	6	T 8	14	140	245	11	300	600	118	124	80	96	100	128	140	88	96	100	126	140	90	96	100	128	84	84	97	100	110	118	78	91	100	96	110	70	79	100	94	94	68	76	100	86	90	64	76	100	80	92	60	70
Group D	41		58	M	24138	160	59	TBW of Patella RT	1	90	5	T 6	18	110	300	12	295	720	120	128	76	83	100	134	140	90	106	100	130	136	88	104	100	124	80	80	96	100	118	118	78	90	100	114	100	70	80	100	110	94	70	77	100	106	90	64	75	100	100	88	60	66
Group D	42		52	M	6455	160	65	CRIF IL Nail Tibia LT	1	110	3	T 6	13	170	375	10	310	720	120	110	80	83	100	130	136	90	106	100	124	136	90	105	100	126	88	88	100	100	110	108	80	89	100	96	90	70	80	100	90	92	70	73	100	89	90	68	73	100	70	88	66	73
Group D	43		52	M	3876	160	52	CRIF of SOF RT	11	105	6	T 4	22	110	250	8	270	585	124	110	80	96	100	130	140	86	102	100	126	140	90	106	100	128	86	86	99	100	112	110	80	90	100	98	90	72	76	100	90	94	68	76	100	82	90	64	75	100	72	88	66	73
Group D	44		38	M	26630	180	49	ORIF of ITF LT	1	120	7	T 6	14	110	345	12	240	660	120	128	70	83	100	134	128	90	106	100	130	136	88	96	100	118	80	80	96	100	118	116	78	90	100	114	100	70	80	100	110	94	60	72	100	106	94	64	72	100	100	88	60	69
Group D	45		30	M	21073	170	68	Skin Grafting Leg RT	1	50	6	T 8	14	150	265	11	300	740	110	110	70	94	100	128	140	78	94	100	120	130	80	96	100	120	76	76	90	100	108	104	70	81	100	94	100	64	80	100	92	96	70	78	100	84	90	64	72	100	72	90	60	70
Group D	46		60	F	16502	160	52	ORIF of SOF RT	11	115	7	T 6	13	165	265	9	280	585	124	110	70	83	100	130	140	86	102	100	126	140	90	106	100	124	86	86	99	100	112	110	80	90	100	98	98	72	80	100	90	94	70	78	100	82	90	68	72	100	72	88	66	73
Group D	47		42	F	17962	160	48	Abdominal hysterectomy	1	85	7	T 6	14	145	250	12	235	570	120	110	70	83	100	130	140	90	106	100	124	136	90	105	100	128	88	88	100	100	110	108	80	89	100	96	98	70	80	100	90	92	68	77	100	80	90	70	76	100	70	88	66	73
Group D	48		42	M	28294	154	45	Hernioplasty LT	1	80	6	T 4	15	170	290	10	240	660	120	128	70	83	100	134	140	90	106	100	130	136	88	104	100	124	80	80	96	100	118	116	78	90	100	115	100	70	79	100	110	94	70	76	100	106	90	64	72	100	100	88	60	69
Group D	49		34	F	3113	155	58	CRIF of Tibia RT	11	70	7	T 6	14	160	375	8	200	685	120	110	80	94	100	130	136	90	106	100	124	136	90	105	100	120	88	88	100	100	110	108	80	89	100	96	98	70	80	100	90	92	70	78	100	80	90	70	74	100	70	88	66	73
Group D	50		38	M	2223	155	60	ORIF of NOF RT	1	145	6	T 6	22	100	290	11	205	710	118	124	76	83	100	128	128	88	96	100	126	140	90	96	100	118	84	84	97	100	110	118	78	91	100	96	110	70	76	100	94	94	60	72	100	86	94	64	72	100	80	92	60	70
Group D	51		42	M	24285	160	55	Appendicetomy	1	60	7	T 6	14	170	375	9	230	690	110	110	80	94	100	130	136	78	94	100	120	130	80	96	100	120	96	76	90	100	118	104	70	81	100	94	100	64	80	100	92	96	70	78	100	84	90	64	76	100	72	90	60	70
Group D	52		42	M	23513	156	64	Hernioplasty RT	1	80	6	T 4	15	165	275	11	285	675	118	124	70	83	100	128	140	88	96	100	126	140	90	96	100	124	84	84	97	100	110	118	78	91	100	96	110	70	79	100	94	94	70	77	100	86	90	64	72	100	80	92	60	70

24 Min					27 Min					30 Min					45 Min					60 Min					75 Min					90 Min					105 Min					120 Min					135 Min					150 Min					165 Min					180 Min					Intraop. Complication								
SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	NAUSEA & VOMITING	BRADYCARDIA	INJ. ATROPINE	HYPOTENSION	INJ. MEPHENTERMIN	PRURITES	INJ. ANTIHISTAMINIC	SHIVERING	RESPIRATORY DEPRESSION
100	92	100	70	88	100	90	96	68	77	100	86	94	64	78	100	84	98	66	76	100	92	110	70	83	100	88	104	68	80	100	96	124	80	94	100	100	126	82	96	100	92	118	74	88	100	90	126	78	92	100	92	116	70	83	100	88	120	72	86	100	104	136	84	101	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	90	90	66	74	100	90	94	62	76	100	84	100	70	80	100	80	104	70	76	100	84	116	76	89	100	80	110	74	86	100	100	130	86	101	100	108	128	88	101	100	92	124	80	84	100	98	122	74	98	100	84	110	76	89	100	90	114	78	92	100	104	126	84	98	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	92	100	66	78	100	88	96	68	73	100	84	98	64	75	100	80	100	68	81	100	88	110	72	84	100	84	104	70	81	100	96	126	84	98	100	112	128	82	97	100	92	118	78	98	100	94	126	72	95	100	88	114	72	84	100	88	120	74	87	100	108	132	80	97	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	94	94	68	79	100	90	92	72	86	100	86	94	74	90	100	80	100	78	78	100	82	114	82	92	100	78	108	80	89	100	100	138	86	100	100	104	134	90	104	100	94	128	84	98	100	98	132	72	96	100	82	122	82	92	100	82	126	80	93	100	110	128	86	100	YES	NIL	NIL	YES	YES	NO	NIL	NIL	NIL
100	90	112	72	84	100	92	116	68	81	100	84	122	76	91	100	82	122	82	85	100	84	122	86	98	100	82	126	80	95	100	96	138	82	100	100	112	124	88	100	100	94	128	84	92	100	96	124	78	93	100	84	122	86	98	100	88	118	82	96	100	102	118	82	100	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	92	96	70	76	100	88	108	68	76	100	82	112	72	85	100	78	118	78	95	100	82	122	82	95	100	80	118	78	91	100	94	130	78	94	100	108	132	84	100	100	90	122	78	98	100	92	126	74	90	100	82	114	82	95	100	88	120	78	91	100	98	118	78	91	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	90	94	66	79	100	90	92	62	73	100	86	94	74	90	100	82	100	78	91	100	82	114	82	92	100	78	108	80	89	100	100	126	86	100	100	104	134	90	104	100	94	128	84	91	100	98	122	78	96	100	82	110	82	92	100	90	114	80	93	100	110	128	86	100	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	94	100	72	78	100	88	96	72	86	100	84	98	64	75	100	78	122	68	85	100	84	110	72	84	100	82	104	70	81	100	96	138	84	98	100	112	128	82	97	100	92	118	78	98	100	94	132	78	95	100	88	122	72	84	100	82	126	84	87	100	108	132	80	97	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	92	112	68	84	100	92	116	68	81	100	84	122	76	91	100	84	118	82	78	100	88	122	86	98	100	80	126	80	95	100	96	128	82	94	100	112	124	88	100	100	94	128	84	92	100	96	124	76	93	100	84	122	86	98	100	88	118	82	96	100	102	118	82	100	NIL	NIL	NIL	NIL	NO	NO	NIL	YES	NIL
100	94	96	70	76	100	88	108	68	77	100	82	112	72	85	100	82	98	78	95	100	84	124	82	95	100	78	118	78	91	100	94	124	78	94	100	108	132	84	100	100	90	118	78	88	100	92	120	76	90	100	82	110	82	85	100	94	114	78	91	100	98	118	78	91	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	90	96	66	76	100	88	108	68	81	100	82	112	72	85	100	78	118	78	91	100	82	122	82	95	100	80	118	78	91	100	94	128	78	94	100	108	132	84	10	100	90	122	78	92	100	92	124	74	90	100	82	122	82	95	100	88	120	78	91	100	98	118	78	91	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	92	90	66	74	100	90	94	68	76	100	84	100	70	80	100	80	104	70	81	100	84	116	76	89	100	80	110	74	86	100	100	130	86	101	100	108	128	88	101	100	92	124	80	94	100	98	126	84	98	100	84	116	76	89	100	94	114	78	92	100	104	126	84	98	NIL	NIL	NIL	NIL	NO	NO	NIL	YES	NIL
100	92	100	70	88	100	90	96	68	77	100	86	94	64	78	100	84	98	66	78	100	92	110	70	83	100	88	104	68	80	100	96	124	80	94	100	100	126	82	96	100	92	118	74	88	100	90	120	78	92	100	92	110	70	83	100	90	114	72	86	100	104	136	84	101	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	90	100	68	78	100	88	96	62	73	100	84	98	64	75	100	80	100	68	76	100	88	110	72	84	100	84	104	70	81	100	96	126	84	98	100	112	128	82	97	100	92	118	78	91	100	94	122	82	95	100	88	110	72	84	100	88	120	74	87	100	108	132	80	97	NIL	NIL	NIL	NIL	NO	NO	NIL	YES	NIL
100	92	90	66	74	100	90	94	68	76	100	84	100	70	80	100	80	104	70	78	100	84	116	76	89	100	80	110	74	86	100	100	130	86	101	100	108	128	88	101	100	92	124	80	94	100	98	126	84	98	100	84	116	76	89	100	88	118	78	92	100	104	126	84	98	YES	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	90	96	66	76	100	80	108	62	81	100	82	112	72	85	100	78	118	78	81	100	82	122	82	95	100	80	118	78	91	100	94	128	78	94	100	108	132	84	100	100	90	122	78	92	100	92	124	74	90	100	82	122	82	95	100	90	114	78	91	100	98	118	78	91	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	90	100	68	78	100	80	96	68	73	100	84	98	64	75	100	80	100	68	91	100	88	110	72	84	100	84	104	70	81	100	96	126	84	98	100	112	128	82	97	100	92	118	78	91	100	94	126	82	95	100	88	110	72	84	100	88	120	74	87	100	108	132	80	97	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	92	94	72	79	100	90	92	72	76	100	86	94	74	90	100	80	100	78	78	100	82	114	82	92	100	78	108	95	89	100	100	130	86	100	100	104	134	90	104	100	94	128	84	98	100	98	132	82	96	100	82	114	82	92	100	82	126	80	93	100	110	128	86	100	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	94	112	70	84	100	92	116	68	86	100	84	122	76	91	100	82	122	82	85	100	84	122	83	98	100	83	126	80	85	100	96	138	82	100	100	112	124	88	100	100	94	128	84	98	100	96	120	78	93	100	84	122	86	98	100	94	114	82	96	100	102	118	82	100	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	92	100	70	88	100	90	96	68	77	100	86	94	64	78	100	84	98	66	95	100	92	110	70	83	100	88	104	68	80	100	96	124	80	94	100	100	126	82	96	100	92	118	74	88	100	90	126	78	92	100	92	110	70	83	100	88	120	72	86	100	104	136	84	101	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
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100	90	100	78	78	100	88	96	68	73	100	84	98	64	75	100	82	100	68	85	100	88	110	72	84	100	84	104	70	81	100	96	126	84	98	100	112	128	82	97	100	92	118	78	91	100	94	120	82	95	100	88	110	72	84	100	94	114	74	87	100	108	132	80	97	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
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24 Min					27 Min					30 Min					45 Min					60 Min					75 Min					90 Min					105 Min					120 Min					135 Min					150 Min					165 Min					180 Min					Intraop. Complication								
SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	NAUSEA & VOMITING	BRADYCARDIA	INJ. ATROPINE	HYPOTENSION	INJ. MEPHENTERMIN	PRURITES	INJ. ANTIHISTAMINIC	SHIVERING	RESPIRATORY DEPRESSION
100	74	88	66	74	100	72	90	64	73	100	70	86	62	66	100	62	82	62	70	100	66	90	68	75	100	64	84	66	73	100	66	90	66	75	100	98	104	88	70	100	96	114	92	99	100	76	96	72	82	100	82	104	72	89	100	98	112	82	97	100	66	92	68	74	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	74	92	60	70	100	70	92	64	69	100	66	84	60	68	100	66	84	60	69	100	66	84	64	70	100	64	83	62	67	100	66	94	68	70	100	100	118	74	102	100	98	134	70	83	100	76	102	70	79	100	88	98	72	80	100	84	100	70	80	100	68	88	68	70	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	72	90	62	70	100	68	88	60	72	100	70	86	58	70	100	68	84	60	70	100	64	86	68	74	100	64	80	64	68	100	64	83	64	71	100	94	108	84	85	100	90	110	88	100	100	72	98	78	78	100	78	100	84	82	100	76	108	78	85	100	62	88	62	70	NIL	NIL	NIL	YES	YES	NO	NIL	NIL	NIL
100	78	88	68	75	100	74	90	64	68	100	72	84	60	68	100	68	82	60	68	100	63	88	60	79	100	62	82	64	70	100	62	88	68	69	100	82	110	80	84	100	95	126	78	88	100	68	98	78	77	100	72	100	72	81	100	88	104	76	85	100	64	90	62	70	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
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100	84	100	68	74	100	74	82	62	68	100	72	84	60	68	100	62	86	60	66	100	66	88	66	73	100	66	84	64	70	100	66	88	72	73	100	90	110	80	107	100	94	124	82	92	100	74	90	76	82	100	80	100	80	86	100	84	108	84	92	100	88	114	72	70	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	75	88	68	74	100	74	82	62	68	100	66	80	60	68	100	64	80	64	66	100	66	88	66	73	100	64	84	66	70	100	66	88	66	72	100	90	124	80	90	100	94	114	82	92	100	74	90	76	82	100	80	100	80	86	100	98	108	84	92	100	88	114	72	70	NIL	NIL	NIL	YES	YES	NO	NIL	NIL	NIL
100	72	88	68	70	100	70	84	60	71	100	68	84	58	65	100	66	80	60	71	100	68	92	70	77	100	64	88	64	73	100	68	92	66	77	100	100	120	86	89	100	98	114	84	98	100	68	108	80	89	100	94	114	84	94	100	86	120	88	98	100	74	96	74	78	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
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24 Min					27 Min					30 Min					45 Min					60 Min					75 Min					90 Min					105 Min					120 Min					135 Min					150 Min					165 Min					180 Min					Intraop. Complication								
SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	SpO2	Pulse	SBP	DBP	MBP	NAUSEA & VOMITING	BRADYCARDIA	INJ. ATROPINE	HYPOTENSION	INJ. MEPHENTERMIN	PRURITES	INJ. ANTIHISTAMINIC	SHIVERING	RESPIRATORY DEPRESSION
100	64	84	60	70	100	62	80	62	68	100	80	80	58	66	100	62	82	60	67	100	62	88	68	74	100	64	84	64	70	100	63	98	62	70	100	64	88	62	73	100	68	90	64	74	100	60	84	64	69	100	62	88	62	74	100	64	84	62	69	100	62	88	68	74	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
100	94	84	63	68	100	90	80	60	66	100	60	84	60	68	100	76	78	60	66	100	64	86	64	71	100	70	84	66	62	100	64	90	62	72	100	66	86	66	71	100	66	90	70	70	100	64	84	62	69	100	64	86	68	71	100	70	84	62	69	100	64	86	64	71	NIL	NIL	NIL	NIL	NO	NO	NIL	NIL	NIL
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