"A COMPARATIVE STUDY OF EPIDURAL BUPIVACAINE WITH FENTANYL AND BUPIVACAINE WITH DEXMEDETOMIDINE FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES"

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A COMPARATIVE STUDY OF EPIDURAL BUPIVACAINE WITH FENTANYL AND BUPIVACAINE WITH DEXMEDETOMIDINE FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES

ABSTRACT

Background:

Epidural anaesthesia with catheter insertion offers a useful technique of anaesthesia for lower abdominal and lower limb surgeries, in that prolonged surgeries can be performed with either continuous infusion of drug via epidural catheter or by intermittent top up doses. Further it can also be used to offer effective post operative analgesia to the patients. Using adjuvants to epidural anaesthetics, the dose of local anesthetics can be reduced and an effective and prolonged anaesthesia with good post-operative analgesia can be provided. This study was conducted to study the effects of dexmedetomidine and fentanyl as adjuvants to hyperbaric bupivacaine.

Materials and Methods:

This randomized prospective study involved 60 adult patients of either sex belonging to ASA Grade I and Grade II aged between 18 to 50 years undergoing elective lower abdominal and lower limb surgeries under epidural anaesthesia. Group D received 18ml of 0.5% bupivacaine with dexmedetomidine 1 microgram per kilogram made up to 2ml by adding sterile water. Group F received 18ml of 0.5% bupivacaine with fentanyl 1microgram per kilogram made upto 2ml by adding sterile water. The hemodynamic variability with onset and duration of sensory and motor blocks were assessed. Post operative requirement of rescue analgesia and other side effects were also recorded.

Results:

Onset of sensory blockade and motor blockade was (8.80±1.13min), (15.40±1.89min) in group D and (10.70±1.26min), (16.97±1.40min) in group F. Duration of sensory and motor blockade was (295.17±23.02 min), (213.97±17.98min) in group D and (263.00±16.90min), (165.73±13.85min) in group F. Two segment regression time was prolonged with group D (164.23±15.18min) compared to group F (124.60±15.98min).

CONCLUSION:

Epidural Dexmedetomidine with bupivacaine is associated with faster onset of sensory and motor blockade, with significantly prolonged sensory and motor blockade and less requirement of rescue analgesia compared to Fentanyl with bupivacaine.

Key words:

Epidural, Bupivacaine, Dexmedetomidine, Fentanyl, Analgesia.

INTRODUCTION

Neuraxial anesthesia is the term used for all central blocks involving spinal, epidural and caudal space.[1] Regional anesthesia in the form of spinal/ epidural is common for lower abdominal and lower limb surgeries.[2]

The main benefit of epidural anesthesia is to provide post operative analgesia. An ideal local anesthetic in the epidural space provides quick onset sufficient motor block for surgical relaxation and prolonged sensory block for providing post operative analgesia. Longer-acting local anesthetics used for epidural blockade are either bupivacaine or ropivacaine in varying concentrations. Greater concentrations of either will produce a greater motor block in addition to the sensory block.[1]

Bupivacaine is one of the common drug used for epidural anesthesia. Bupivacaine hydrochloride, a long-acting local anesthetic agent in concentrations of 0.25% and 0.5% is satisfactory in caudal, epidural, and peripheral nerve block for pain relief of labor, vaginal delivery, perineal surgery and extremity surgery. Since epidural anesthesia is a volume dependent block, bupivacaine has to be given in larger doses to achieve the analgesic and anesthetic effects, the use of adjuvants with

bupivacaine have shown to reduce its dose requirements in epidural anaesthesia with reduced incidence of side effects.[3]

Fentanyl, an opioid, has been regularly used as adjuvant to local anaesthetics in epidural anaesthesia with faster onset and prolonged duration of action compared to sole local anaesthetics.[4] Fentanyl rapidly transverses the dura and penetrates the spinal cord to produce analgesic effect.[5]

The addition of adjuvants like opioids or α-2agonist provide a dose-sparing effects of local anesthetics and accelerates the onset of sensory blockade of epidural anesthesia and decrease the effective dose of local anesthetic. Fentanyl acts as agonist at μ-opioid receptors to enhance the analgesia, while dexmedetomidine acts on pre and post-synaptic sympathetic nerve terminal and central nervous system to decrease the sympathetic outflow and nor-epinephrine release causing sedation, analgesia, sympatholytic and hemodynamic effects. Motor blockade tends to be denser with dexmedetomidine. Dexmedetomidine is also devoid of respiratory depression, pruritus, nausea, and vomiting.[6]

As there are not many studies comparing efficacy of bupivacaine with fentanyl & dexmedetomidine, this study is to compare the effects of these two drugs.

MATERIALS AND METHODS

The study was conducted at R.L. Jalappa hospital and research centre, Tamaka, Kolar from December 2013 to May 2015. This was a prospective randomized double blind study which involved 60 adult patients posted for lower limb and lower abdominal surgeries. Institutional ethical committee clearance and informed consent was obtained from the patients. Patients were randomly divided into two groups of 30 each using computer generated random numbers.

Group ‘D’ – BUPIVACAINE with DEXMEDETOMIDINE.

Group ‘F’- BUPIVACAINE with FENTANYL.

Inclusion criteria:

Patients of ASA Grade I and II in the age group of 18 years to 50years, of either sex with weight 50 to 80 kg and height 150-170 cm, posted for elective lower abdominal & lower limb surgeries .

Exclusion criteria

1. Patients physically dependant on opioids.
2. Patients with history of drug allergy (local anesthetics, fentanyl, dexmedetomidine).
3. Patients with gross spinal abnormality, localized skin sepsis, hemorrhagic diathesis, neurological involvement / diseases.
4. Head injury cases.
5. Patients with cardiac, pulmonary, hepatic or renal disorders.(h/o angina, previous myocardial ischemia)
6. Patients with peripheral neuropathy.
7. Patients with psychiatric disease

In the operation theatre, after sterile preparation the epidural space was identified in sitting position in L_{2-3} or L_{3-4} space with 18 gauge Touhy needle using loss of resistance technique and a epidural catheter was secured. After insertion of epidural catheter, a test dose was given with 3ml of 2% lignocaine with adrenaline 1:2,00,000 through the catheter and observed for any intravascular or intrathecal injection. After confirming correct placement of the catheter, epidural anesthesia was activated with 18ml of 0.5% bupivacaine with dexmedetomidine 1 microgram per kilogram made

upto 2ml by adding sterile water in group “D” while the patients in group “F” received 18ml of 0.5% bupivacaine with fentanyl 1 microgram per kilogram made upto 2ml by adding sterile water. Epidural catheter was secured 3-5cm into the epidural space.

Surgical procedure was initiated after establishment of adequate surgical anaesthesia.

The bilateral pin prick method was used to evaluate and check the sensory level while the modified Bromage scale was used to measure motor blockade.

The following block characteristics was observed and recorded: onset of analgesia, the highest dermatomal level of sensory blockade, time to achieve highest sensory level, the complete establishment of motor blockade, time to two segment regression and time to complete motor recovery. Time for rescue analgesia was assessed by VAS score. Sedation was assessed using Ramsay Sedation score.

Standard monitoring was carried out in the form of pulse oximetry, ECG and non invasive arterial blood pressure. Pulse rate, respiratory rate, arterial blood pressure and oxygen saturation were recorded every 5mins for first 20 mins, then every 15 mins intra operatively.

A note was made of blood loss, urine output, IV fluid input. Patients were observed for hypotension (defined as >20% decrease in SBP from baseline and were treated with IV fluids and IV mephenteramine 3-6 mg in incremental boluses), bradycardia (pulse <50 beats/min were treated with IV atropine sulphate 0.6mg bolus doses) and other adverse effects such as anxiety, nausea, vomiting, pruritus, urinary

retention, shivering, etc., recorded and the need for additional medications also attended.

Duration of analgesia was assessed by VAS scores, more than 4 was considered for requirement of rescue analgesia. The onset of pain was managed with top up doses of 10ml 0.125% bupivacaine through epidural catheter.

At the end of the surgery, the vitals were recorded and sedation assessed.

STATISTICAL METHODS :

At the end of study, all data were compiled and the results were expressed as mean ± SD for the statistical analysis. For continuous data- Student's t-test and for categorical data- Chi-Square test and Mann-Whitney U test were used. A $P<0.05$ was considered statistically significant.

RESULTS

60 adult patients belonging to ASA grade I and II, of either sex, in age group between 15- 50 years, posted for elective lower abdominal and lower limb surgeries in general surgery, orthopedics, gynecology and urology under epidural anaesthesia were selected for the study. They were randomly allocated to two groups with 30 patients in each group using computer generated random numbers.

Time to attain adequate sensory block was faster in Group D when compared to Group F ($p<0.001$) which is statistically significant as shown in table 10.

Establishment of complete motor blockade was faster in Group D when compared to Group F ($p<0.001$) which is statistically significant as shown in table 11.

Onset of Sensory blockade (min)	Group D		Group F	
	No	%	No	%
6-10	29	96.7	15	50.0
11-15	1	3.3	15	50.0
Total	30	100.0	30	100.0
Mean ± SD	8.80±1.13		10.70±1.26	

P<0.001**

Table 10: Onset of Sensory block in two groups of patients studied

Onset of Motor blockade (min)	Group D		Group F	
	No	%	No	%
11	2	6.7	0	0.0
12	1	3.3	0	0.0
13	1	3.3	0	0.0
14	3	10.0	2	6.7
15	7	23.3	1	3.3
16	8	26.7	8	26.7
17	4	13.3	8	26.7
18	4	13.3	9	30.0
20	0	0.0	2	6.7
Total	30	100.0	30	100.0
Mean ± SD	15.40±1.89		16.97±1.40	

P=0.001**

Table 11: Onset of Motor blockade in two groups of patients studied

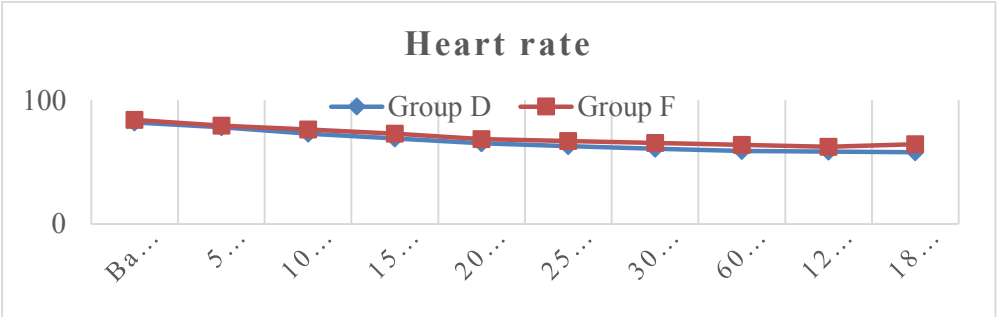
The fall in heart rate was statistically significant in Group D when compared to Group F between 10 min and 180 min(p value being significant) as shown in graph 3.

It was observed that there was bradycardia (PR<50) in 7 patients in group D ,which required a single dose of Inj Atropine 0.6mg IV, and further no doses of atropine were required as shown in table 12. None of the patients in Group F had bradycardia.

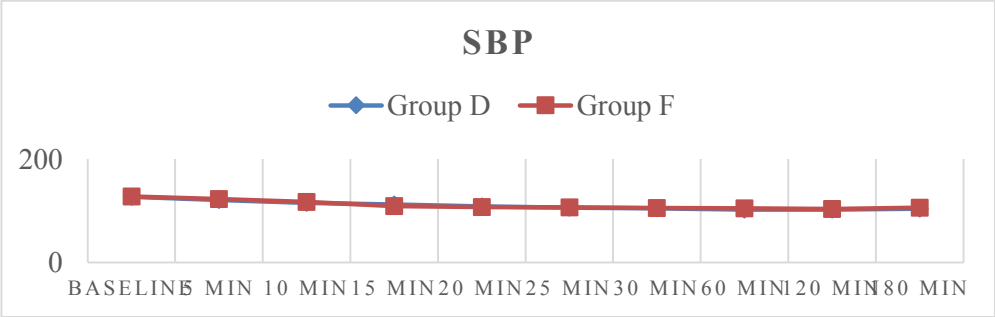
The systolic blood pressure showed suggestive significant difference (p=0.074) in between Group D and Group F at 15min as shown in graph 4.

The incidence of diastolic hypotension was more in Group D when compared to Group F(p<0.001) at 5, 10, 120 and 180 min as shown in graph 5.

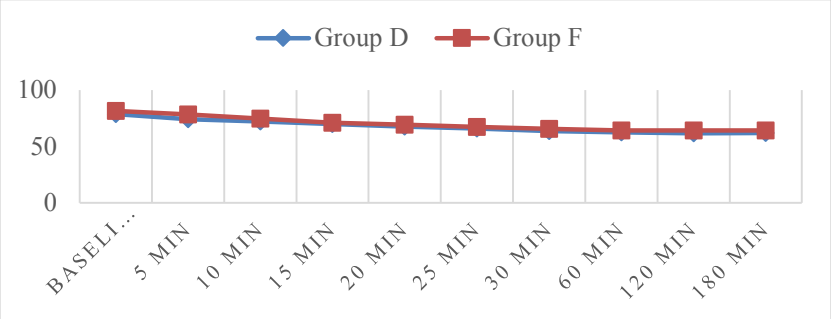
With similar statistically significant difference in mean arterial blood pressure in between Group D and Group F at 5,10,120 and 180 mins as shown in graph 6. The hypotension was treated with incremental doses of mephenteramine 3mg bolus doses, but the total dose did not cross 18mg in any of the groups.



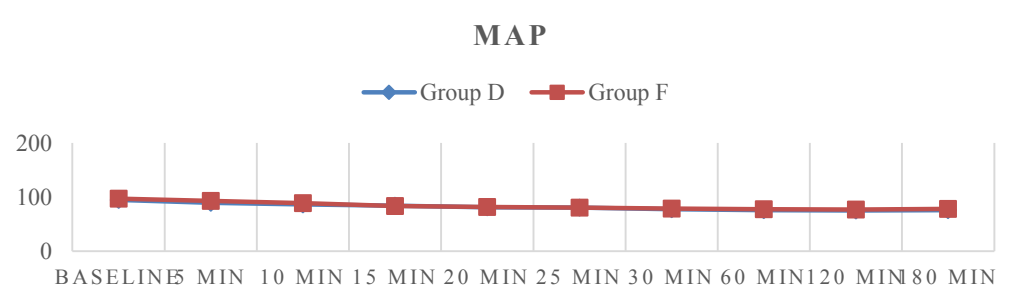
Graph 3: COMPARISON OF HEART RATE BETWEEN TWO GROUPS



Graph 4 : COMPARISON OF SBP BETWEEN TWO GROUPS



Graph 5: COMPARISON OF DBP BETWEEN TWO GROUPS



Graph 6: COMPARISON OF MAP BETWEEN TWO GROUPS

Two segment regression, the duration of analgesia and time to complete motor recovery was prolonged in Group D when compared to Group F with statistically significant difference as shown in table 16.

	Group D	Group F	P value
Time to two segment regression(min)	164.23±15.18	124.60±15.98	<0.001**
Effective duration of analgesia(min)	295.17±23.02	263.00±16.90	<0.001**
Time for complete motor recovery (min)	213.97±17.98	165.73±13.85	<0.001**

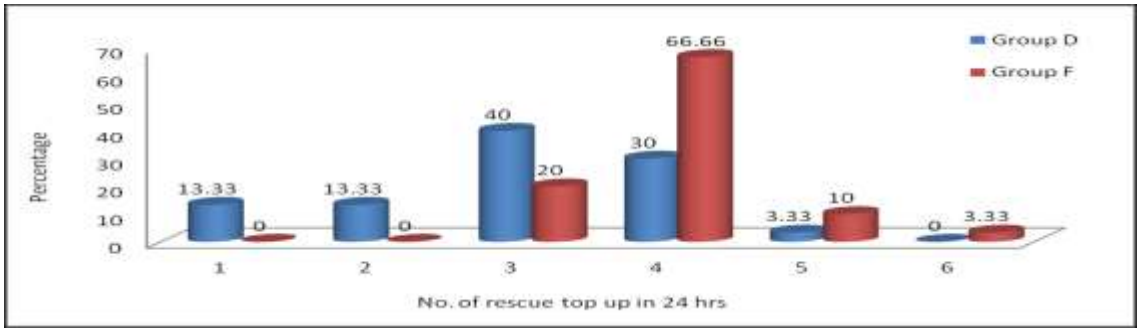
Table 16: Comparision of study variables in two group of patients

Maximum number of patients in group D had sedation score of 3. Maximum number of patients in group F had sedation score of 2. Patients in both the groups maintained saturation above 90% and none of them required oxygen support.

Side effects	Group D (n=30)		Group F (n=30)	
	No	%	No	%
No	23	76.7	19	63.3
Yes	7	23.3	11	36.7
Bradycardia	7	23.3	3	10.0
Pruritis	0	0.0	3	10.0
Dry mouth	0	0.0	3	10.0
Nausia/Vomiting	0	0.0	2	6.7
Shivering	0	0.0	0	0.0

Table 18: Side effects in two groups of patients studied

Number of rescue top up given in 24 hours was less in Group D in comparison to F group which is statistically significant (P<0.001) as shown in graph 11.



Graph 11- No. of rescue top up in 24 hr in two groups of patients studied

DISCUSSION

Epidural anesthesia with insertion of catheter has emerged as a safe technique of anesthesia for lower abdominal and lower limb surgeries, in that the stress response of general anesthesia can be totally avoided. Further epidural anesthesia with catheter can be used for prolonged surgeries. An additional advantage of epidural catheter insertion is for providing postoperative analgesia.[1]

The present study involved comparision of epidural bupivacaine with dexmedetomidine and bupivacaine with fentanyl for lower abdominal and lower limb surgeries.

Demographic profile (age, sex) is comparable in all three groups.

In our study the mean time to attain adequate sensory level was 8.80±1.13min in Group D and 10.70±1.26min in Group F(p<0.001) which is statistically significant.

The time for onset of motor blockade in Group D was 15.40±1.89min and in Group F was 16.97±1.40min($p<0.001$) which is statistically significant.

Similar results were obtained in studies by Kumkum Gupta and her colleagues in which time for onset of sensory block in LD group was 7.25±2.3 min and in LF group was 9.27±2.79 min. Mean duration to complete motor block was 19.27±4.7min in LD group and 22.78±5.5min in LF group.[6]

It was observed that there was bradycardia (PR<50) in 7 patients in Group D, which required a single dose of Inj Atropine 0.6mg IV, and further no doses of atropine were required. None of the patients in Group F had bradycardia.

In our study likely significant difference in mean arterial blood pressure between Group D and Group F at 5,10, 120 and 180mins was observed. The hypotension was treated with incremental doses of mephenteramine 3mg bolus doses, but the total dose did not cross 18mg.

In a study conducted by Mohamed Fouad Selim, MAP decreased significantly at T20 in both epidural groups. MAP showed non significant degree of decrease in Bupivacaine with Dexmedetomidine group compared with Bupivacaine with Fentanyl group.[41]

In our study mean Duration of analgesia (in min) was 295.17±23.02 in Group D and 263.00±16.90 in Group F($p<0.001$). Time to two segment regression (in min) was 164.23±15.18 in Group D and 124.60±15.98 in Group F. Time to complete motor recovery (in min) was 213.97±17.98 in Group D and 165.73±13.85 in Group F.

Our results are in correlation with studies conducted by Mohamed Fouad Selim and his colleagues, where it was seen that duration of analgesia in group

Bupivacaine with Dexmedetomidine was 155.6±28.1 compared to 129±18.7 in group Bupivacaine with Fentanyl.[41]

Sedation score of 1 was observed in 10% patients in Group F. Sedation score of 2 was seen in 23.3% patients in Group D and 70% patients in Group F. Sedation score of 3 was observed in 63.3% patients in Group D and 20% patients in Group F. Sedation score of 4 was observed in 13.3% patients in Group D. It is clear that sedation was more in Group D in comparison to Group F.

Our results are in agreement with studies by Bajwa S J and his colleagues, in which 38% and 42% of patients in group Ropivacine with Dexmedetomidine exhibited grade II and grade III sedation as compared to 16% and 2% of patients in the Ropivacaine with Fentanyl group, respectively. Only 12% of the patients in the Ropivacine with Dexmedetomidine group had sedation scores of 1 as compared to 82% wide and awake patients in Ropivacaine with Fentanyl group which was a highly significant statistical entity.[54]

In our study bradycardia was observed in 23.3% of patients of group D, whereas 10% of patients in Group F had bradycardia. The incidence of dry mouth was 10 % in Group F. Nausea, vomiting and pruritis was observed in Group F. None of the patients in any group had respiratory depression.

In a similar study with Bajwa SJ and his colleagues, comparative evaluation of dexmedetomidine and fentanyl in epidural anaesthesia, the side effect profile of both these drugs were quite favourable as none of the patients in either group had profound deep sedation or respiratory depression. Higher incidence of nausea and vomiting was observed despite a low dose of fentanyl used epidurally.[54]

CONCLUSION

The present study concludes that:

1. Onset of sensory and motor blockade was faster with dexmedetomidine compared with fentanyl when used with epidural bupivacaine.
2. Time to two segment regression and recovery of motor power were prolonged with dexmedetomidine compared with fentanyl when used with epidural bupivacaine.
3. The duration of analgesia was prolonged with dexmedetomidine compared with fentanyl when added to epidural bupivacaine.
4. The patient in epidural dexmedetomidine bupivacaine group received lesser number of rescue analgesics compared to fentanyl bupivacaine group.
5. Epidural dexmedetomidine-bupiv acaine was associated with increased incidence of bradycardia, hypotension and sedation compared to fentanyl-bupivacaine group.

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INTRODUCTION

Neuraxial anesthesia is the term used for all central blocks involving spinal, epidural and caudal space.[1] Regional anesthesia in the form of spinal/ epidural is common for lower abdominal and lower limb surgeries.[2]

Epidural anesthesia is a versatile technique widely used in anesthetic practice. Its potential to decrease postoperative morbidity and mortality has been demonstrated in numerous studies. Epidural anesthesia is an invaluable adjunct and is a safe and effective alternative to general anesthesia.With epidural anesthesia a decrease stress response has been noted with positive cardiac benefits such as reduced perioperative and postoperative ischemia. The main benefit of epidural anesthesia is to provide post operative analgesia. An ideal local anesthetic in the epidural space provides quick onset sufficient motor block for surgical relaxation and prolonged sensory block for providing post operative analgesia. The choice of which local anesthetic agent to use can be selected on desired length of action. Longer-acting local anesthetics used for epidural blockade are either bupivacaine or ropivacaine in varying concentrations. Greater concentrations of either will produce a greater motor block in addition to the sensory block .[1]

Bupivacaine is one of the common drug used for epidural anesthesia. Bupivacaine hydrochloride, a long-acting local anesthetic agent in concentrations of 0.1%, 0.25%, 0.5%, and 0.75% is used in caudal, epidural, and peripheral nerve block. Bupivacaine in 0.25% and 0.5% is satisfactory in caudal, epidural, and peripheral nerve block for pain relief of labor, vaginal delivery, perineal surgery and extremity surgery. Since epidural anesthesia is a volume dependent block, bupivacaine has to be given in larger doses to achieve the analgesic and anesthetic

effects, the use of adjuvants with bupivacaine have shown to reduce its dose requirements in epidural anaesthesia with reduced incidence of side effects.[3]

Fentanyl, an opioid has been regularly used as adjuvant to local anaesthetics in epidural anaesthesia with faster onset and prolonged duration of action compared to sole local anaesthetics.[4] Fentanyl is a short-acting lipophilic opioid analgesic. It is structurally related to drug pethidine for opioid activity. There has been attempts to improve the quality of epidural opioid analgesia by the addition of low concentration of local anesthetic to reduce the incidence of side-effects. Fentanyl rapidly transverses the dura and penetrates the spinal cord to produce analgesic effect.[5]

Maintainance of stable hemodynamic and an ability to provide prolonged postoperative analgesia are the main desirable qualities of an epidural adjuvant. The addition of adjuvants like opioids or α-2agonist provide a dose-sparing effects of local anesthetics and accelerates the onset of sensory blockade of epidural anesthesia and decrease the effective dose of local anesthetic. Fentanyl acts as agonist at μ-opioid receptors to enhance the analgesia, while dexmedetomidine acts on pre and post-synaptic sympathetic nerve terminal and central nervous system to decrease the sympathetic outflow and nor-epinephrine release causing sedation, analgesia, sympatholytic and hemodynamic effects. Motor blockade tends to be denser with dexmedetomidine. Dexmedetomidine is also devoid of respiratory depression, pruritus, nausea, and vomiting.[6]

As there are not many studies comparing efficacy of bupivacaine with fentanyl & dexmedetomidine, this study is to compare the effects of these two drugs.

OBJECTIVES OF THE STUDY

To compare the effects of Dexmedetomidine with bupivacaine (group D) and Fentanyl with bupivacaine (group F) in epidural anesthesia in terms of:

1. Time of onset and duration of sensory blockade .
2. Time of onset and duration of motor blockade .
3. Time to two segment regression.
4. Time to rescue analgesia.
5. Monitoring of hemodynamic parameters like heart rate, mean arterial blood pressure and SpO_2.
6. Side effects like bradycardia, respiratory depression, pruritis, nausea and vomiting.

ANATOMICAL ASPECTS:

ANATOMY OF THE VERTEBRAL COLUMN.[7]

Knowledge of the anatomy of vertebral column and of the lumbar vertebrae in particular is important for anaesthesiologists.

A typical vertebra consists of two parts:

1. BODY, anteriorly, which bears the weight.
2. THE ARCH, surrounding the cord laterally and posteriorly consisting of lamina and pedicles.

There are seven processes :

- Three muscular processes– one spinous and two transverse.
- Four articular processes – two upper and two lower.

LUMBAR VERTEBRAE:-

The bodies of lumbar vertebrae are kidney shaped and large. The foramina are triangular in shape and intermediate in size between those in the thoracic and cervical regions. The pedicles are thick. The transverse processes are slender, increasing in length from L_1 to L_3 and then become shorter again. The laminae are short and the lumbar spines are horizontal and oblong, which do not overlap each other. Lumbosacral angle is produced by the fifth vertebra. Its transverse processes are short, thick and strong and arise from the arch and from the side of the vertebral body.

Articulation of the vertebrae is by ligamentous connections, but there are certain recognized gaps in between the vertebrae:

1. **The lateral intervertebral gap**.

2. **The posterior interlaminar gap.**

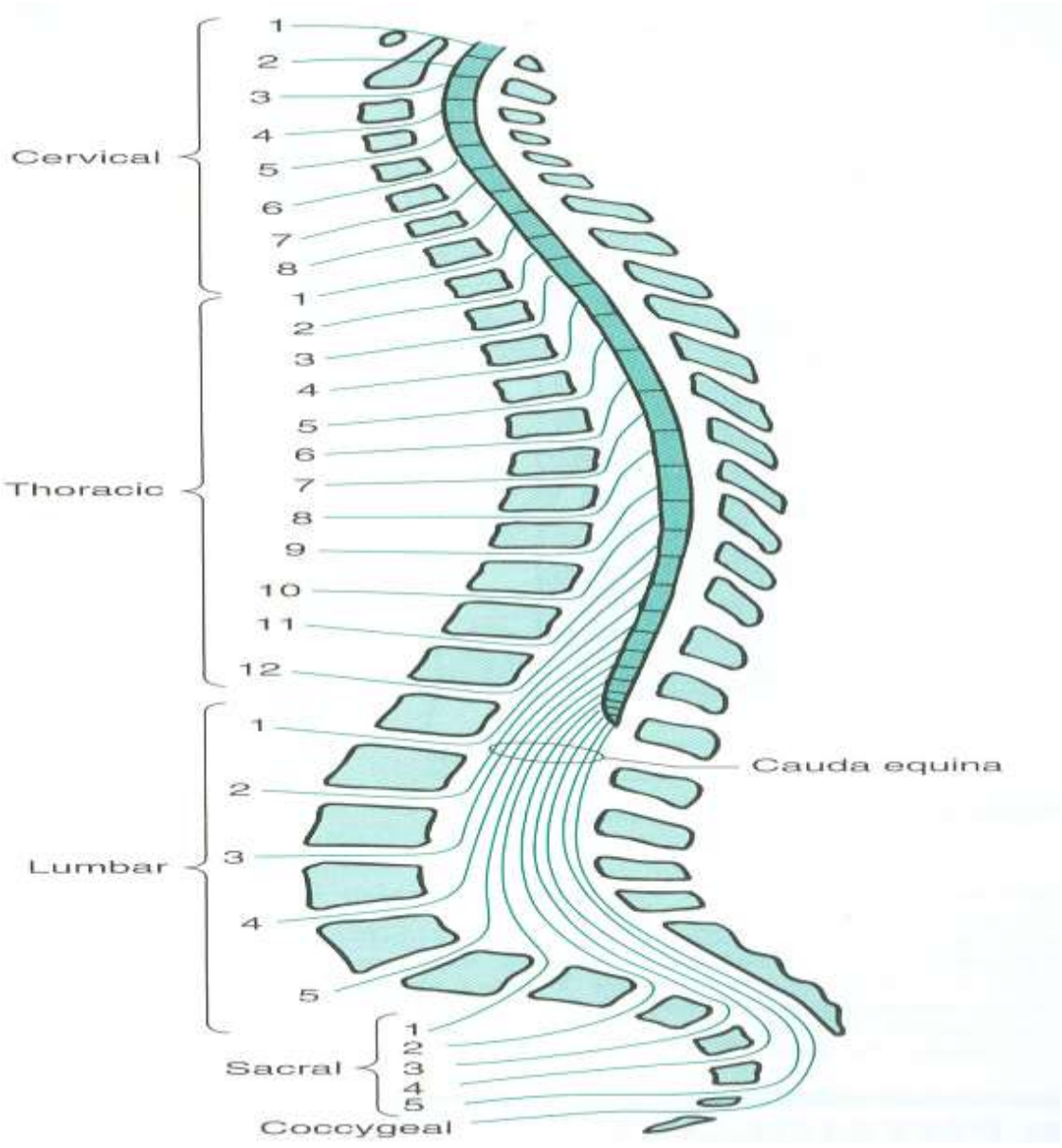


Figure 1: Vertebral column

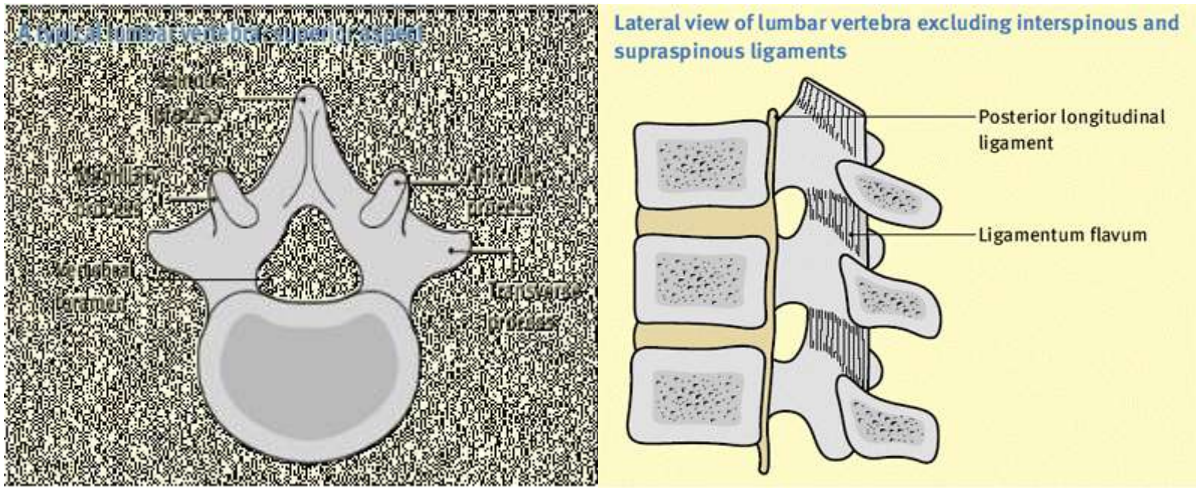


Figure 2. LUMBAR VERTEBRAE

INTERVERTEBRAL LIGAMENTS: - from anterior to posterior

1)Anterior longitudinal ligament.

2)Posterior longitudinal ligament.

Supraspinous ligament: - It is a thick fibrous band connecting the apices of spines from seventh cervical vertebrae to the sacrum. This may be ossified in old age and render penetration with a thin needle impossible.

Interspinous ligament: - It is a thin fibrous band connecting the shafts of the adjacent spines.

Ligamentum flavum: - It stretches from the lower border and inner surface of the upper lamina to the upper border and outer surface of the lower lamina.

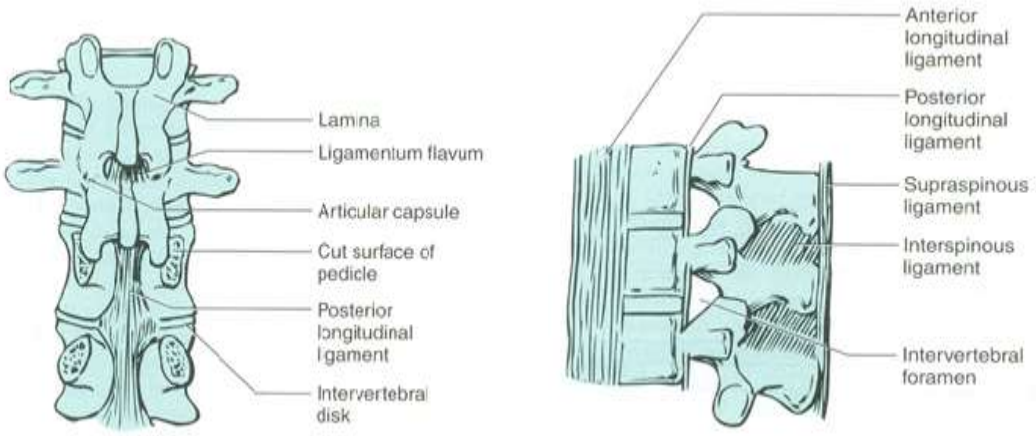


Figure 3: VERTEBRAL LIGAMENTS

SPINAL CORD.[7]

The spinal cord extends from the foramen magnum and continues through to the conus medullaris near the second lumbar vertebrae terminating in a fibrous extension known as the filum terminale.

The vertebral level of termination of spinal cord in adults may be as follows: -

Lower border of L_1 vertebra 50%

Upper border of L_2 vertebra 40%

Lower border of L_3 vertebra 3%

THE MENINGES.[7]

The spinal cord is protected by three covering membranes.

From outward to inward :

1) Duramater

2) Arachnoid mater

3) Piamater

The dural sac of the spinal duramater is firmly attached to the circumference of foramen magnum above, while the lower extent of dural sac may be as follows: -

S_2 vertebra	35%
Below S_2 vertebra	40%
Above S_2 vertebra	25%

Below this it continues as the covering of filum terminale.

SPINAL SEGMENTS:-

The cord is divided into segments by the 31 pair of spinal nerves, which arises from it:-

Cervical	8
Thoracic	12
Lumbar	5
Sacral	5
Coccygeal	1 rudimentary

There is no epidural sheath of the nerve roots within the dura and are therefore easily affected by doses of analgesic drugs brought into contact with them.

SPINAL NERVES:-

Anterior and posterior root fuse together to form spinal nerves. The posterior root is larger than anterior and efferent impulses from whole body including the

viscera passes through these roots. Sympathetic preganglionic axons arise from cells in the inter mediolateral horn of the spinal cord from T_1 to L_2.

Posterior root conveys fibres of pain, touch, temperature, deep sensation from joints, muscles and tendons, efferent from viscera (accompanying sympathetic) and vasodilator fibres.

BLOOD SUPPLY OF SPINAL CORD: -

The principle arterial supply of the spinal cord is derived from one anterior and two posterior spinal arteries.

The anterior spinal artery is the largest of vessels and supplies a large anterior portion of the cord. It is formed at the foramen magnum by the union of branches from each vertebral artery. There are two posterior spinal arteries, one on either side. They are derived from each vertebral artery at the base of brain. They supply posterior $1/3^{rd}$ of the spinal cord. Blood supply is also derived from spinal branches of the vertebral, ascending cervical, posterior intercostals, lumbar and lateral sacral arteries, which pass through inter vertebral foramina.

Venous drainage of spinal cord is through a plexus of anterior and posterior veins in the neck, the azygous vein in thorax, lumbar veins in abdomen and lateral sacral veins in the pelvis.

EPIDURAL SPACE.[8, 9,10,11]

It is a potential space that lies between the dura and the periosteum lining the inside of the vertebral canal.

Boundaries of the Epidural Space.[8,9]

The epidural space surrounds the dural sac. The space communicates freely with the paravertebral space through the intervertebral foramina. Superiorly, the space is anatomically closed at the foramen magnum. The boundaries are :-

Upper: the foramen magnum where the spinal dura attaches with the endosteal dura of the cranium.

Caudally: the epidural space ends at the sacral hiatus, which is closed by the sacrococcygeal ligament.

Anteriorly: The posterior longitudinal ligament covering the posterior aspect of the vertebral bodies and the intervertebral discs.

Posteriorly: The periosteum of the anterior surface of the vertebral lamina and the ligamentum flavum.

Laterally: Intervertebral foramina and vertebral pedicles.

Contents of Epidural Space:

1. Dural sac.
2. Spinal nerve roots as they exit the dural sac and pass through the intervertebral foramina.
3. Epidural Vessels: arteries and an extensive plexus of veins.
4. Semi liquid fat: appeared to be the principal epidural tissue.
5. Lymphatics.
6. Loose areolar connective tissue.

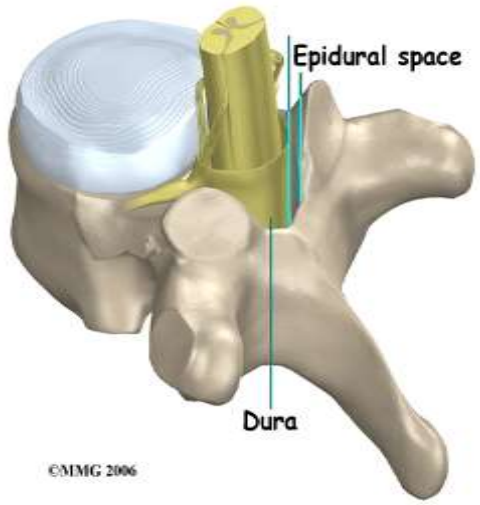
To reach the epidural space in the midline sagittal plane, the following structures are penetrated:

Skin and subcutaneous tissue.

Supraspinous ligament.

Interspinous ligament.

Ligamentum flavum



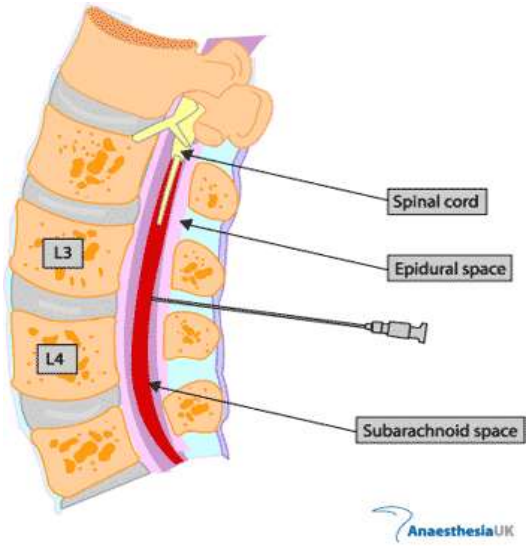


Fig 4: Anatomy of epidural space **Fig 5: Approach to epidural space**

The shape of the epidural space in cross-section is of considerable clinical importance. The shape of vertebral canal and the dural sac determines it. The former is nearly circular in the cervical and upper thoracic region and becoming triangular with the descent to the lumbar segments and the articular processes indent the triangle. The epidural space narrows posterolaterally and then widens again laterally

towards the intervertebral foramina. Thus, the safest point of entry into the epidural space is in the midline for entering the lumbar epidural space.

Regional dural thickness.[9,10]

The dura is thinnest in the lumbar and thickest in the cervical region. The increased thickness of the duramater in the upper segments gives added protection against accidental dural puncture and spinal cord injury.

It varies along the length of the vertebral column

Site	**Regional dural thickness**
Cervical	1.5-2 mm
Upper thoracic	1 mm.
Lower thoracic	1 mm.
Lumbar	0.33 – 0.66 mm

Table 1: Regional dural thickness

Regional epidural space width.[10,11]

It is not uniform throughout. Epidural space is widest in the lumbar region and narrowest in the cervical region.

Regional epidural space width	
Cervical	1-1.5 mm
Upper thoracic	2.5-3 mm
Lower thoracic	4-5 mm
Lumbar	5-6 mm

Table 2: Regional epidural space width

Characteristics of Ligamentum flavum at different vertebral levels.[Michael j cousins]

Site	Skin to ligament (cm)	Thickness of ligament (mm)
Cervical	-	1.5-3.0
Thoracic	-	3.0-5.0
Lumbar	3.0 – 8.0	5.0-6.0
Caudal	Variable	2.0-6.0

Table 3: Characteristics of Ligamentum flavum

IDENTIFICATION OF EPIDURAL SPACE.[7, 8,9]

a) Negative pressure techniques:

1) Hanging drop sign.

2) Capillary tube method.

3) Manometer technique.

b) Disappearance of resistance techniques:

1) Syringe technique.

2) Spring loaded syringe.

3) Balloon technique.

4) Brooks device.

5) Vertical tube of Dawkins.

c) Others:

1) Ultrasonic localization.

2) The oxford epidural space indicator.

RECENT TECHNIQUES:

Use of auditory amplificationof the sound made by the epidural needle as it transverses the intraspinous ligament and ligamentum flavum.

1. Doppler guidance. 2. Pressure transducer guided method.

PHYSIOLOGIC CONSIDERATIONS:

Negative pressure in epidural space is greatest at firm attachment points. It is greatest in the thoracic region, less in the lumbar area and least in the sacral area. Two theories explain this negative pressure:

1) The cone theory*:* considers that the dura is depressed when needle is introduced into the epidural space, consequently creating a larger epidural space. It thus is considered an artifact caused by indentation of the dura, by the advancing needle.

2) The transmission theory*:* considers that the transmission of the intrapleural negative pressure through the intervertebral foramina to the peridural space causes the negative pressure in the epidural space is.

PHYSIOLOGY.[8,9,10]

Effects on organ systems:

1.Cardiovascular system: Drop in blood pressure occurs due to vasodilatation of resistance and capacitance vessels, causing relative hypovolaemia and

tachycardia. It is exacerbated by blockade of the sympathetic nerve supply to the adrenal glands, preventing the release of catecholamines. Bradycardia may occur if blockade is as high as T2 when sympathetic supply to the heart (T2-5) is also interrupted. This may result in inadequate perfusion of vital organs and measures are required to restore the blood pressure and cardiac output, such as fluid administration and the use of vasoconstrictors.

2. **Respiratory system:** Usually not affected unless blockade is high enough to affect intercostal muscle nerve supply (thoracic nerve roots) leading to reliance on diaphragmatic breathing alone. It may cause distress to the patient, as they may feel inability to breathe adequately.

3. **Gastrointestinal system:** Sympathetic outflow blockade (T5-L1) to the Gastrointestinal tract leads to predominance of parasympathetic (vagus and sacral parasympathetic outflow) causing active peristalsis and relaxed sphincters, and a small contracted gut which enhances surgical access. Splenic enlargement occurs about 2-3 fold.

4. **Endocrine system:** Reduction in the release of catecholamines occur due to blocked nerve supply to the adrenals.

5. **Genitourinary tract:** A severe drop in blood pressure may affect glomerular filtration in the kidney if sympathetic blockade extends high enough to cause significant vasodilatation. Urinary retention is a common problem with epidural anesthesia.

HISTORICAL REVIEW OF LITERATURE:

Corning first described the epidural space in 1901 and Fidel Pages first used epidural anaesthesia in humans in 1921. Epidural anaesthesia is a type of central neuraxial block with many applications.

The discovery of the cocaine's local analgesic effect by Carl Koller in 1884 made possible the vast array of peripheral local and regional analgesic therapy, whereas previously brain was thought to be the only major site of pain control.[12]

Many historians consider the *father of modern epidural anaesthesia* to be AM Dogliotti of Turin, an Italian surgeon. He described the anatomy and physiology of epidural space in detail and developed the modern "*loss of resistance*" technique for epidural space location.[12]

Walter Wyner in England (February 1889) and Heinrich Quincke in Keil, Germany (December 1890) introduced lumbar dural puncture independently . Until May 1891, as Wyner did not report these cases, in *The Lancet,* usually Quincke is credited with the performance of first lumbar puncture.[12,13]

In 1885 Leonard J Corning, a New York neurologist performed the first epidural analgesia inadvertently, by injecting cocaine between the spinous process of the inferior dorsal vertebrae, for treating his patient's complaint of masturbation.[14]

In 1931, Dogliotti, in Italy and Massey Dawkins, in Britain popularized clinical use of epidural analgesia in obstetric practice particularly for labour analgesia.[15,16]

In 1942, Hingson and Edwards introduced a malleable and flexible steel needle for continuous caudal analgesia and in 1943 reported 1000 cases of continuous caudal analgesia.[17]

Hingson and Southworth, introduced a small 4F ureteric catheter into the lumbar epidural space with a spinal needle, and reported their experience of continuous lumbar epidural analgesia.[17]

Epidural needles:

In 1944, Tuohy, passed no.4 ureteric silk catheter into subarachnoid space using 15G Barker needle. Huber RL, a Seattle dentist, invented hypodermic needle, with a long sharp and curved tip to lessen the pain on injection.[18]

Tuohy recognised this curved tip (Huber point) would facilitate placement of epidural catheter and applied this design to his needle in 1945. He added a stylet to this, to decrease the risk of skin plugging. Sprotte, in 1987 introduced pencil- point epidural needle, to minimize tissue trauma.[19,20]

Epidural catheters:

The first indwelling catheter to be used was silk 3.5 to 4F ureteric catheters for continuous epidural anaesthesia. The use of plastic catheters was described by Flowers in 1949. Polyethylene was the first material to be used , this was replaced by polyvinyl chloride (PVC). Recently teflon, nylon, polyurethane and silicone materials are being used to produce thin, yet kink resistant catheter with good stiffness and tensile strength.

HISTORY OF ALPHA 2 AGONISTS:

The first α-2 adrenoceptor agonist was synthesized in the early 1960's to be used as nasal decongestant. Early application of the new substance now known as clonidine, showed unexpected side effects, with sedation for 24 hours & symptoms of severe cardiovascular depression. Subsequent testing led to the introduction of clonidine as an antihypertensive drug in 1966.[21]

Dexmedetomidine is a selective α-2 agonist approved for use in 1999, it is a imidazole compound, dextroisomer of medetomidine that demonstrates selective α-2 agonist action because of its pharmacological activity. α-2 agonist produce sedation ,anxiolysis, sympatholysis and possess some analgesic properties. These characteristics of dexmedetomidine have made this drug particularly useful in the perioperative period and for sedation of patients in the intensive care unit.[22]

PHARMACOLOGY OF DRUGS

PHARMACOLOGY OF BUPIVACAINE.[7,23,24,25]

Bupivacaine is an amino amide local anesthetic. It is chemically known as 1-butyl 2-piperidyl formo-2'6'-xylidine hydrochloride. It was first synthesized by Swedish investigator Boaf Ekenstam et al.

Structure:

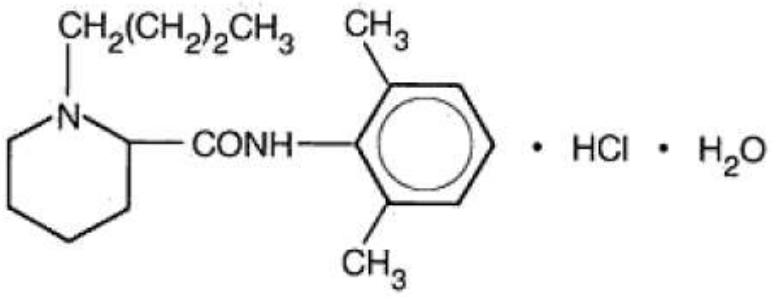


Figure 6- Structure of Bupivacaine

Chemical name: l-n-butyl-DL-piperidine-2-carboxylic acid-2, 6 dimethylanilide hydrochloride.

Physicochemical properties

Molecular weight	- 288 (base)
	325 (chloride salt)
pKa	- 8.1
Plasma protein binding	- 95%
Elimination half life	- 2.7 hrs
Maximum dose	- 2mg/kg

Solubility: Although the base is sparingly soluble, the hydrochloride is readily soluble in water.

Stability and sterilization: Bupivacaine is highly stable and withstands repeated autoclaving.

Melting point: 258˚C.

Potency: Bupivacaine is approximately three to four times more potent than lignocaine.

Bupivacaine, is a chiral drug because its molecule possesses an asymmetric carbon atom and it is available for clinical use as racemic mixture of the enantiomers.

Mechanism of action

Local anaesthetics prevent transmission of nerve impulses by inhibiting passage of sodium ions through ion selective sodium channels in nerve membranes. Occlusion of open sodium channels contributes little to overall inhibition of sodium permeability. Failure of sodium ion channel permeability to increase slows the rate of depolarization so that threshold potential is not reached and an action potential is not propagated.

Pharmacokinetics

Local anaesthetics are weak bases that have pKa values little higher than physiologic pH. As a result at physiologic pH ,<50% of the local anaesthetic exists in a lipid soluble non-ionized form.

Pharmacodynamics:

Bupivacaine is slower in onset of action than other local anaesthetics, but has the longest duration of action of the existing local anaesthetics. With increasing concentration, the degree of motor block increases.

Dosage for spinal anesthesia:

Weight in kgs	0-5 kgs	5-15 kgs	>15kgs
Bupivacaine 0.5% hyperbaric dose	0.5mg/kg	0.4mg/kg	0.3mg/kg

Table 4- Bupivacaine dosage for spinal anesthesia

Not more than 150mg i.e 30ml of 0.5% solution should be given at one time or in any 4 hour period.

Bupivacaine is available in injectable form in 0.25%, 0.5%, and 0.75% concentrations

Peripheral nerve block: 0.25-0.5% solution, 5-20ml for a dose of 12.5-50mg results in blockade duration of 180-360 min.

Caudal block: 0.25-0.5% solution. 30-50 ml for a maximum dose of 225mg results in blockade duration of 360-720minutes.

Epidural block: 0.25-0.75% solution. 15-30 ml for a dose of 37.5-225 mg results in block duration of 180-300 minutes.

Spinal block: 0.5% solution. 3-4ml for a dose of 15-20mg results in block duration of 75-150 minutes. 0.75% solution, 2-3 ml for a dose of 15-22.5mg results in block duration of 75-150min.

These doses may be repeated in 3-4 hours but the maximum dose in 24 hours is 400 mg. Bupivacaine can be used with or without epinephrine. The addition of Vasoconstrictor produces slight increase in the duration of action. However, the peak blood level is significantly reduced, minimizing the system toxicity.

Absorption and distribution

Absorption of local anesthetic from site of injection into the systemic circulation is influenced by the site of injection, dosage, use of epinephrine, and pharmacologic characteristics of the drug. The ultimate plasma concentration of a local anesthetic is determined by the rate of tissue distribution and the rate of drug clearance.

Lipid solubility is primary determinant of intrinsic local anesthetic potency and also important in redistribution. The local anesthetic is eliminated from the plasma by metabolism and excretion. Protein binding of local anesthetic has influence on their distribution and excretion.

The first pass pulmonary extraction for bupivacaine is dose dependent, suggesting that the uptake process becomes saturated rapidly. Clinically significant trans-placental transfer of local anesthetic between the mother and fetus may be there. Plasma protein binding influences the rate and degree of diffusion of local anesthetics across the placenta. Bupivacaine, is highly protein bound (approximately 95%) and has an umbilical vein-maternal arterial concentration ratio of about 0.32.

Metabolism

Local anaesthetics undergo varying rates of metabolism by microsomal enzymes located primarily in the liver. Bupivacaine undergoes the slowest metabolism among the amide local anesthetics by aromatic hydroxylation, N-dealkylation, amide hydrolysis and conjugation.

Systemic toxicity

Systemic toxicity of local anesthetics is due to an excess plasma concentration of the drug. Plasma concentration is determined by the rate of drug entering into the systemic circulation relative to their redistribution to inactive tissue sites and clearance by metabolism.

Central Nervous System toxicity

Early signs are tinnitus, light headedness, confusion and numbness.

Intermediate signs are shivering, muscle twitching, tremors, and tonic clonic convulsions.

Late signs are unconsciousness, generalized CNS depression and respiratory arrest.

Skeletal muscle twitching is often first seen in the face and extremities and signals the imminence of tonic-clonic seizures. Seizures are classically followed by CNS depression which may be accompanied with hypotension and apnea.

The typical plasma concentration of 4.5 to 5.5 μg/ml is associated with seizures.

Selective cardiac toxicity

After accidental intravenous injection of bupivacaine the protein binding sites (alpha1 acid glycoprotein and albumin) are quickly saturated, leaving a significant mass of unbound drug available for diffusion into the conducting tissue of the heart. It may result in precipitous hypotension, cardiac dysrhythmias and atrioventricular heart block.

Cardiotoxic plasma concentration of bupivacaine is 8 to 10 μg/ml. The threshold for cardiac toxicity produced by bupivacaine may be lowered in patients being treated with drugs that inhibit myocardial impulse propagation (beta adrenergic blockers, digitalis preparations, calcium channel blockers).

It depresses the maximal depolarization rate of cardiac action potential (Vmax) by virtue of their ability to inhibit sodium ion influx via sodium channels. Bupivacaine depresses Vmax considerably more than lidocaine. The resulting slowed conduction of the cardiac action potential manifest as prolongation of the P-R and QRS intervals on the electrocardiogram and reentry ventricular cardiac dysrhythmias. R enantiomer of bupivacaine is more toxic than the S enantiomer.

Hepatotoxicity

Continuous or intermittent epidural administration of bupivacaine has been associated with increased plasma concentration of liver transaminase enzymes that normalizes when bupivacaine infusion was discontinued.

PHARMACOLOGY OF DEXMEDETOMIDINE.[21,22]

Dexmedetomidine is an imidazole compound and is pharmacologically active s-enantiomer of medetomidine, a veterinary anesthetic agent. At the end of 1999, Dexmedetomidine was approved by Food & Drug Administration for use in humans as a short term medication (<24hrs) for analgesia & sedation in the intensive care unit. Its unique properties render it suitable for sedation & analgesia during the perioperative period.

Chemistry :

Dexmedetomidine is chemically (+)-4-(s)[2 3 –(dimethylphenyl) ethyl]-1H-imidazole monohydrochloride. Its empirical formula is C13H16N2HCl and its molecular weight is 236.7.

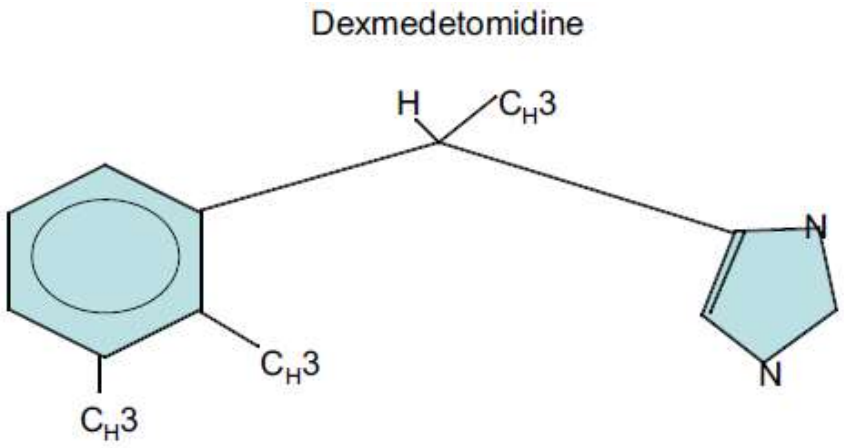


Fig 7. Chemical structure of dexmedetomidine

Mechanism of action :

Dexmedetomidine is the dextro enantiomer of medetomidine which is the methylated derivative of etomidine, its specificity for the alpha-2 receptor is 8 times that of clonidine, with an α-2 /α-1 binding affinity ratio of 1620:1 and its effects are dose dependently reversed by administration of a selective alpha-2 antagonist, such as Atipamezole.

Dexmedetomidine is considered as the full agonist at alpha-2 receptors compared to clonidine which is considered as a partial agonist at alpha-2 adrenoceptors. The selectivity of Dexmedetomidine to alpha-2 receptors compared to alpha-1 receptors is 1620:1, whereas with clonidine it is 200:1. The selectivity is dose dependant; at low to medium doses & on slow infusion, high levels of alpha-2 selectivity is observed, while high doses or rapid infusions of low doses are associated with both alpha-1 & alpha-2 activities.

1. Sedation, anxiolysis, hypnosis & amnesia

Dexmedetomidine provides dose dependant increases in anxiolysis & sedation. However, the quality of sedation appears to be unique in comparison with GABAnergic agents such as midazolam or propofol. Arousability is maintained at deep levels of sedation, with relevant correlation between the level of sedation and the bispectral EEG (BIS)..

Dexmedetomidine induced sedation qualitatively resembles normal sleep. It induces sleep by activating endogenous non-rapid eye movement pathways. Stimulation of alpha-2A receptors in the nucleus ceruleus causes inhibition of nor adrenergic neurons and disinhibition of gamma-aminobutyric acid (GABAneregic) neurons in the ventrolateral preoptic nucleus(VLPO). In contrast, propofol or

benzodiazepines , the GABAneregic agents, directly enhance the inhibitory effects of the GABAnergic system at the VLPO and as such norepinephrine release remains unaffected , thus leading to less restful sleep.

The involvement of non-rapid eye movement sleep pathways seems to explain why patients who appear to be deeply asleep from Dexmedetomidine are relatively easily aroused in much the same way as occurs with natural sleep. This type of sedation is called “co-operative or arousable”, to distinguish it from sedation induced by drugs acting on the GABA system, such as midazolam or propofol which produce a clouding of consciousness. Patients can cooperate with ICU nursing, radiologic and even airway procedures and sophisticated neurologic testing during craniotomies for tumour dissection or stereotactic implantations can be undertaken. Sedation with Dexmedetomidine is dose dependant, however even low doses might produce sedation. Dexmedetomidine may lack amnestic properties; many patients who received Dexmedetomidine for postoperative sedation were able to recall their ICU stay when compared to those who received propofol for sedation. With dexmedetomidine amnesia is achieved only at high plasma levels(>1.9ng/ml) without retrograde amnesia.

2. Analgesia

Dexmedetomidine appears to exert analgesic effects at the spinal and at supraspinal sites. However there has been a debate as to whether its analgesic effects are primary or simply opioid sparing. In comparison with hypnotic agents like propofol or postoperative opioids used alone, Dexmedetomidine significantly decreases opioid requirement.

Dexmedetomidine may also provide antinociception through nonspinal mechanisms –intra articular administration during knee surgery improves postoperative analgesia, with less sedation than IV route. Suggested mechanisms are activation of alpha-2A receptors, inhibition of the conduction of nerve signals through C &Aδ fibres and the local release of encephalin.

3. Respiratory effects.

Dexmedetomidine is able to achieve its sedative, hypnotic & analgesic effects without causing any clinically relevant respiratory depression unlike opioids. The changes in ventilation appeared similar to those observed during natural sleep. It also exhibited a hypercarbic arousal phenomenon, which has been described during normal sleep & is a safety feature. It has been reported to have episodes of obstructive apnea in a group of patients who received high doses of the drug, the effects were seen more common with doses of 1 to 2μg/kg given over 2 minutes, doses that provide rapid sedation. The obstructive respiration pattern & irregular breathing seen with such doses are mostly related more to deep sedation & anatomical features of the patient and this could be easily overcome by insertion of an oral airway.

In contrast to infusions of opioids, benzodiazepines or propofol, Dexmedetomidine can safely be infused through tracheal extubation in patients who had previously failed extubation because of excessive agitation. Dexmedetomidine is effective in achieving excellent sedation without respiratory depression during fibreoptic intubation and other difficult airway procedures. Intubating conditions are further enhanced because Dexmedetomidine decreases saliva production and airway secretions.

4. Cardiovascular effects

Dexmedetomidine does not appear to have any direct effects on the heart. A biphasic cardiovascular response has been described after the application of dexmedetomidine. The administration of a bolus of 1μg/kg, initially causes transient increase of the blood pressure & a reflex decrease in heart rate, especially in younger healthy patients. The initial reaction can be explained by the peripheral alpha 2B adrenoceptor stimulation of vascular smooth muscle and can be attenuated by a slow infusion over 10 or more minutes. However, even at slower infusion rates the increase in mean arterial pressure over the first 10 minutes was shown to be in the range of 7% with a decrease in heart rate between 16% & 18%. The initial response lasts for 5-10 minutes and is followed by a decrease in blood pressure of approximately 10%-20% below the baseline values. Both these effects are caused by the inhibition of the central sympathetic outflow overriding the direct stimulant effects. Another possible explanation for the subsequent heart rate decrease is the stimulation of presynaptic alpha-2 adrenoceptors, causing decreased norepinephrine release.

Dexmedetomidine can result in cardiovascular depression i.e bradycardia & hypotension. The incidence of postoperative bradycardia has been reported to be as high as 40% in healthy surgical patients who received Dexmedetomidine, especially high doses. Usually these temporary effects were successfully treated with atropine or ephedrine and volume infusions. There are clinical situations in which the sympatholytic on alpha-2 adrenoceptors agonists may be deleterious especially in hypovolemic patients or patients with fixed stroke volume.

5. Effect on renin release

Renin release is stimulated by β-adrenoceptors, whereas alpha-2 adrenoceptor agonists directly inhibit rennin release.

6. **Effect on insulin release.**

Stimulation of alpha-2 adrenoceptors on islet cells directly inhibits insulin release; this effect has unproven clinical importance, because hyperglycemia has never been reported to be significant in patients receiving clonidine.

7. **Effect on thermoregulation.**

Like Clonidine, Dexmedetomidine is also associated with lower rates of shivering. Intravenous infusion of Dexmedetomidine reduces the vasoconstriction and the shivering threshold. It did not change the sweating threshold and decreased the concentration response curves for vasoconstriction and shivering in a linear fashion. Therefore with Dexmedetomidine, thermoregulatory responses were inhibited within a wider range of temperatures. Dexmedetomidine and other alpha-2 agonists suppress shivering, possibly by their activity at alpha-2B receptors in the hypothalamic thermoregulatory centre of the brain. Low dose Dexmedetomidine has an additive effect with Meperidine on increasing the shivering threshold, when these drugs are combined. Dexmedetomidine may be beneficial in decreasing patient discomfort from postanaesthetic shivering.

8. **Effect on renal function.**

Dexmedetomidine produces a complex effect on renal function. Alpha-2 agonists exert a diuretic effect by causing inhibition of the antidiuretic action of arginine vasopressin (AVP) at the collecting duct, resulting in decreased expression of

aquaporin-2 receptors and decreased salt and water reabsorption. There is experimental evidence that Dexmedetomidine attenuates radiocontrast nephropathy by preserving cortical blood flow. This mechanism is supported by the observation that the renal cortical release of norepinephrine is decreased by Dexmedetomidine.

Pharmacokinetics :

- Intravenous administration of dexmedetomidine exhibits a rapid distribution phase with a distribution half life – 6 mins.
- Elimination half life – 2hours. It follows linear or zero order kinetics.
- Distribution : the steady state volume of distribution of dexmedetomidine is approximately 118L. Protein binding is reported to be approximately 94% and remains constant despite various concentrations of the drug.
- Metabolism : the biotransformation of dexmedetomidine is nearly complete glucuronidation and cytochrome P450 media metabolism .

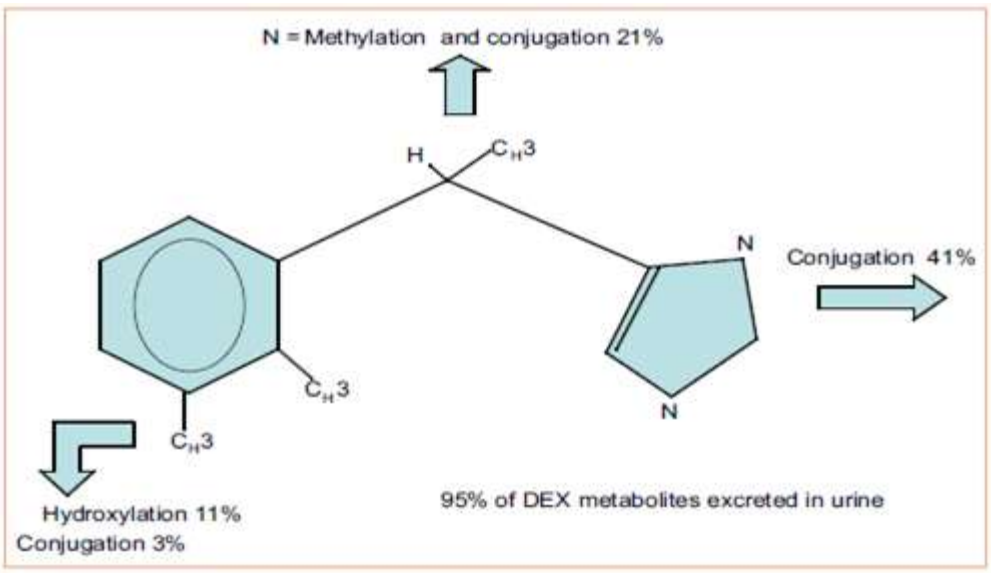


Figure 8- The pathways in the metabolism of dexmedetomidine

Perioperative uses

1. Premedication .

As a premedicant, Dexmedetomidine, at intravenous doses 0.33 to 0.67μg/kg given 15 minutes before surgery, seems efficacious, while minimizing the cardiovascular side effects of hypotension and bradycardia. Dexmedetomidine has also been used intranasally as premedicant for children in the dose of 1μg/kg and found that it attained more significant and satisfactory sedation at parenteral separation and at induction of anaesthesia compared to the children premedicated with 0.5mg/kg oral midazolam.

2. As an adjunct to general anaesthesia

The use of Dexmedetomidine may provide haemodynamic stability because of attenuation of the stress induced sympathoadrenal responses to intubation during surgery and during emergence from anesthesia. Administration of Dexmedetomidine intraoperatively produces an anesthetic sparing effect.

3. **Use for regional anaesthesia.**

Studies have explored the effect of epidural Dexmedetomidine on the incidence of postoperative shivering in patients undergoing orthopaedic surgery. It was found that patients who received Dexmedetomidine at a dose of 100μg added to 20ml 0.5% bupivacaine showed lower incidence in postoperative shivering, when compared to patients who received epidural bupivacaine alone(10% vs 36%).

4. In Monitored anaesthesia care.

Dexmedetomidine produces arousable sedation with ease of orientation, anxiolysis, mild analgesia lack of respiratory depression and haemodynamic stability at moderate doses. These properties makes dexmedetomidine as almost an ideal agent for MAC despite its lack of amnesia and poor controllability because of its slow onset and offset.

5. In Intensive care unit

Dexmedetomidine showed advantages over propofol for sedation in mechanically ventilated patients when both drugs were titrated to equal sedation as assessed by the BIS(approximately 50) and Ramsay sedation score (5), dexmedetomidine patients required significantly less narcotics.

PHARMACOLOGY OF FENTANYL.[26,27,28]

Figure 9- Structure of Fentanyl

Fentanyl citrate is a synthetic phenylpiperidine opioid analgesic and chemical congener of the reversed ester of pethidine. Fentanyl was first synthesized by Dr. Paul Jannsen in 1960 and released into clinical practice in 1963. It is a powerful, safe and rapidly acting analgesic.

Fentanyl has a low molecular weight and is highly lipid soluble. Fentanyl is widely available for parenteral use. It is also available in buccal, transdermal and aerosolized formulation. Fentanyl provides analgesia and relaxation.

Fentanyl is 1000 times more potent than meperidine, 50-100 times more potent than morphine. 100mcg fentanyl is equal to 10mg morphine.

Presentation:

- As a clear, colorless solution for injection containing 50mcg/ml of fentanyl citrate.

- Transdermal patches which delivers 25/50/75/100 mcg/hr fentanyl over a 72 hour period.

- Fentanyl lollipop- dissolves slowly in mouth, and is available in 6 dosages 200-1600 micrograms in 200mcg increments excluding 1000 and 1400 mcg.

Physiochemical properties:

- pK 8.4 % non-ionized 8.5% at pH 7.5
- Protein binding 84%
- Effect site equilibrium 6.8 min
- Elimination half time 3.1-6.6hrs
- Context sensitive half life 260 min

Routes of administration:

1. Oral as syrup or lozenges
2. Intravenous route
3. Epidural route
4. Intrathecal route

PHARMACOKINETICS

After intravenous administration, the onset of action of fentanyl is 1-2 minutes with duration of action for about 60 minutes. After epidural route duration is 3-4 hours.

After intrathecal administration, onset is within 5 minutes and duration is of 60 minutes.

METABOLISM AND ELIMINATION

Fentanyl is eliminated from body predominantly by the biotransformation in the liver and is metabolized by N dealkylation to Norfentanyl, which is inactive pharmacologically .

Fentanyl is mainly excreted in urine as metabolites, less than 8% is excreted as unchanged drug.

MECHANISM OF ACTION

Fentanyl is mainly a μ receptor agonist with an analgesic potency greater than morphine, pethidine and alfentanyl. Analgesia is produced principally at supraspinal sites through interaction with μ receptors. It also binds to kappa receptors, though to a lesser degree located within the spinal cord. There is also evidence now that, the gray matter of the spinal cord contains opioid receptors and most of them are located in substantia gelatinosa. ie 50% kappa, 40% μ and 10% Delta.

PHARMACOLOGICAL ACTION

1. CARDIOVASCULAR SYSTEM

A. **Heart Rate**

There is a decrease in the heart rate due to stimulation of central vagus nucleus. This decrease in heart rate is dependent on dose and speed of injection. It can

be prevented effectively by premedication with parasympatholytic agent such as glycopyrolate or atropine. Fentanyl blocks sympathetic stress response that includes increase in heart rate by decreasing in CNS sympathetic vasoregulatory flow. At a dose of 1mcg/kg , no significant effect on papillary muscle function 7mcg/kg, at induction decreases heart rate, but no change in MAP 10mcg/kg, myocardial contractility reduced by 50% 20-25mcg/kg, decreases heart rate, MAP, systemic and pulmonary vascular resistance and pulmonary capillary wedge pressure by 15% in patients with coronary artery disease.

B. **Blood pressure**

Minor reductions in blood pressure are seen due to a reduction in systematic vascular resistance through centrally mediated reduction in sympathetic tone and is often associated with bradycardia.

C. **Cardiac electrophysiological effects**

Fentanyl slows AV conduction, prolongs RR interval, AV node refractory period. The duration of Purkinjie fiber action potential isalso prolonged.

2. RESPIRATORY SYSTEM

Dose related depression of breathing is seen with fentanyl. Resting minute volume, tidal volume and respiratory rate is decreased. The ventilatory responses to hypoxia and hypercapnia are blunted.

1-2mcg/kg, decreases respiratory rate and increase tidal volume

>3mcg/kg, deceases respiratory rate, tidal volume and also the ventilatory response to hypoxia and hypercarbia.

3. RIGIDITY

Occurs frequently during intravenous induction of anaesthesia with larger doses. But is not seen with intrathecal fentanyl. In fact fentanyl was used earlier to

relieve the spasticity with intrathecal Baclofen. Wooden chest phenomenon or chest wall rigidity is due activation of μ receptors located at GABAnergic interneurons. This can be controlled by early use of muscle relaxants.

4. CEREBRAL BLOOD FLOW AND INTRACRANIAL PRESSURE

Fentanyl produces almost no change or modest reduction in cerebral blood flow and cerebral metabolic oxygen consumption.

5. GASTROINTESTINAL TRACT

Fentanyl causes decrease in intestinal motility and constipation can be a problem. It can increase the tone of sphincter of Oddi and produce increased pressure in biliary ducts, occasionally leading to pain. The effects are produced by combination or peripheral actions.

Intrathecal action: —Selective Spinal Analgesia

Intrathecal fentanyl produces selective spinal analgesia by acting on opioid receptors in the substantia gelatinosa of the spinal cord. The major advantage of selective blockade of pain lie in the absence of sympathetic blockade and postural hypotension potentially allowing early ambulation of the patient and avoidance of cardiovascular collapse or convulsion, which are one the major complications of spinal anesthetic blockade.

Intrathecal dose- 10-25μgm.

Duration of action- 2-6 hrs

1. Drug distribution:

a) After drug administration, fentanyl is lost into the epidural space and epidural fat, and thus unavailable at the target tissue site in the spinal cord.

b) The transfer rate constant for CSF to epidural space is same as meningeal permeability co-efficient. Fentanyl octonol: buffer distribution co-efficient is 955 i.e. intermediate hydrophobicity which is less than morphine.

c) Estimated apparent volume of distribution at spinal cord Vcord applies to unbound, freely diffusible opioid in CSF. Vcord parallels the drug's octonal: buffering distribution co-efficient and it is 23.58.

d) Vepi-fat –Fentanyl highest 45.88ml

Vcsf - 11.08 ml

So fentanyl's low non ionized fraction compared to sufentanyl may lead to great ion trapping.

2. Potency:

It is 4 times more potent than morphine when administered intrathecally compared to intra venous administration. It is a less hydrophobic and has little rostral spread which causes less respiratory depression compared to morphine. Fentanyl because of its high volume of distribution in spinal cord and epidural space results in very low integral exposure within the spinal cord. Addition of vasoconstrictors would be modestly beneficial to exposure as most of the dose is lost into the epidural space.

Relationship between fentanyl plasma concentration and effect.

Plasma Fentanyl concentration (ng/ml)	Pharmacological effect
>1	Slight analgesia, minimal ventilatory depression
1-3	Analgesia; 50% decrease in the ventilatory response to carbon dioxide
4-10	Analgesia for surgery if combined with nitrous oxide
>20	Unconsciousness, satisfactory anesthesia if used as sole agent

Table 5- Relationship between fentanyl plasma concentration and effect

6. DRUG INTERACTIONS

Neuraxial administration of opioids in conjunctions with local anesthetics improves the quality of intraoperative analgesia and also prolongs the duration of post-operative analgesia.

Uses:

- Provide analgesic component of balanced anaesthesia for short surgical procedures, dose 2mcg/kg.

- High dose fentanyl anaesthesia (50-100mcg/kg) with nitrous oxide and oxygen or oxygen alone for cardiac surgeries or long surgical procedures. With continued post op ventilation.

- Post-operative pain relief in the loading dose of 50-150mcg and maintenance infusion of 0.5-1.5mcg/kg/hr.

- For sedation and analgesia in the dose of 1-4mcg/kg iv for patient on mechanical ventilation

- Analgesia for labor and delivery

- As a component of neuroleptanalgesia with droperidol.

ADVERSE EFFECTS:

Adverse effects seen with fentanyl can be bradycardia, hypotension, pruritus, urinary retention, respiratory depression (Dose related), hyperalgesia, neonatal morbidity, sexual dysfunction, ocular dysfunction, anaphylaxis, shivering, nausea and vomiting.

The four classical side effects are:

1. Pruritus: Incidence 0-100% . It may be generalized or more likely over face, neck and thorax. The cephalad spread of the drug in the CSF and the interaction of opioid in the substantia trigeminal initiates the itch reflex by indirect action on trigeminal nucleus.

2. Nausea and vomiting: Incidence 30%. Seen more in women compared to men

Mechanism:

-Activation of opioid receptors located in area postrema due to cephalad spread of the drug.

-Sensitization of vestibular system to motion

-Decreased gastric emptying time.

3. Urinary retention: Incidence 0-80%. Seen more in young males and is related to dose of opioid dose administered.

Activation of opioid receptors in the sacral spinal cord causes inhibition of sacral parasympathetic nerves causing detrusor muscle relaxation, increased urine accumulation and retention of urine.

4. Respiratory depression:

Early onset respiratory depression is seen within 2 hrs of injection, delayed respiratory depression occurs 2 hrs after the administration which is dose dependent and synergistic with concomitant use of other sedatives or respiratory depressant drugs.

THERAPEUTIC EFFICACY

Fentanyl is both safe and potent. It has a therapeutic index of 323, which is much greater than that of morphine (69) and pethidine (4.8)

CONTRA INDICATION AND CAUTIONS

1. Fentanyl should not be administered to patients who have taken mono amine oxidase inhibitors within previous 24 hrs.

2. Bronchial Asthma

3. Myasthenia gravis

COUNTER MEASURES FOR ADVERSE EFFECTS

- Respiratory depression is usually treated with Naloxone and by mechanical ventilation.
- Pruritis, nausea and urinary retention can also be reversed by Naloxone and antihistaminic, antiemetic and by catheterization.
- Bradycardia by Atropine or Glycopyrolate.

REVIEW OF CLINICAL STUDIES

Regional anesthesia in the form of spinal or epidural block is commonly used for lower abdominal and lower limb surgeries.[2]

Neuraxial anesthesia is an invaluable adjunct and even occasionally an alternative to general anesthesia. Epidural anesthesia is a versatile technique widely used in anesthetic practice. Neuraxial blocks have even been shown to reduce the incidence of venous thrombosis and pulmonary embolism while also minimizing

transfusion requirements and respiratory compromise following thoracic and upper abdominal surgery. A decreased stress response has also been noted which may have positive cardiovascular benefits such as reduced perioperative and postoperative ischemia. Its potential to decrease postoperative morbidity and mortality has been demonstrated by numerous studies.[1]

Epidural anaesthesia is more effective than spinal anesthesia for post operative analgesia and sedation with lesser side effects.[29]

Visser WA and his colleagues in their study on the factors affecting the spread and distribution of neural blockade by local anesthetics in epidural anesthesia, compared lumbar epidural with thoracic epidural anaesthesia concluded that specifically for thoracic epidural anesthesia, the total mass of LA appeared to be the most important factor in determining the extent of sensory, sympathetic, and motor neural blockade, whereas the site of epidural needle/catheter placement governed the pattern of distribution of blockade relative to the injection site. Based on these results, they formulated and suggested epidural insertion sites that may optimize both analgesia and sympatholysis for various surgical indications.[30]

Bupivacaine hydrochloride, a long-acting local anesthetic agent in concentrations of 0.1%, 0.25%, 0.5%, and 0.75% is used in caudal, epidural, and peripheral nerve block. Bupivacaine in 0.125%,0.25% and 0.5% is satisfactory in caudal, epidural, and peripheral nerve block for pain relief of labor, vaginal delivery, perineal surgery and extremity surgery.[3]

In a study done on rats, it was seen that epidural Bupivacaine significantly decreased the cytokine, malondialdehyde, and myeloperoxidase levels and also increased the antioxidant enzyme levels. It attenuates the mesenteric ischemia/reperfusion related inflammatory response and intestinal damage.[31]

Opioids like fentanyl has been used traditionally in epidural anesthesia as adjuvant to bupivacaine and produces a rapid onset of sensory block and motor block.[4]

Continuous infusion of epidural fentanyl results in nonsegmental analgesia (suggesting relevant opioid binding in the brain) where as segmental analgesia (suggesting relevant opioid binding in the spinal cord) results after bolus administration.[32]

Addition of 50 µg fentanyl to epidural 0.5% bupivacaine has been shown to significantly reduce the VAS score. It also reduces intra-operative analgesia supplementation and prolongs the duration of postoperative analgesia without altering the other block characteristics.[33]

Fentanyl 5.0 µg/ml when combined with ropivacaine 0.2% when used in thoracic epidural, provides optimal balance between postoperative pain relief and sedation for thoracotomy.[5]

In a study done to compare the analgesic efficacy and the safety profile of different concentrations of sufentanil and fentanyl as an adjuvant to bupivacaine for postoperative lumbar epidural analgesia, it was found that the quality of postoperative analgesia of all combinations of bupivacaine-sufentanil were equivalent to bupivacaine-fentanyl . Pruritus was found to be significantly less with bupivacaine – sufentanil 0.5µg/ml.[34]

Fentanyl and Butorphanol as epidural adjuvants are equally safe and provide comparable stable hemodynamics, early onset and establishment of sensory anesthesia. Post-operative analgesia was significantly prolonged with butorphanol.[35]

In a study done to compare the efficacy of sufentanil and fentanyl with low-concentration bupivacaine for combined spinal epidural labour analgesia, it was found that combined spinal epidural using sufentanil and fentanyl achieved high patient satisfaction and excellent labour analgesia without serious maternal or neonatal side-effects. Sufentanil provided a significantly longer duration of labour analgesia compared with fentanyl.[36]

The clinical profile of epidural 0.75% Ropivacaine with fentanyl was better as compared to 0.5% Bupivacaine with fentanyl for hemiarthroplasty in elderly patients.[4]

The combinations of ropivacaine or bupivacaine with fentanyl achieve equally effective and excellent labour analgesia with no motor blockade and without any significant side effects on mother and foetus and, hence, are recommended for labour analgesia.[37]

There was no significant difference in bupivacaine-fentanyl and ropivacaine-fentanyl when used in epidural anesthesia in terms of quality of block which was assessed by taking into account the rating of comfort by the patients.[38]

Bupivacaine 0.125% in combination with Fentanyl 2 mcg/ml and Fentanyl 4 mcg/ml are safe for providing labour analgesia via epidural route.[39]

In hip surgery patients, combination of Bupivacaine-Clonidine was found to be a better option than Bupivacaine-Fentanyl for postoperative epidural analgesia.[40]

Dexmedetomidine is a highly selective alpha 2 adrenergic agonist with sedative and analgesic properties. It is shown that when dexmedetomidine is added as adjuvant to bupivacaine, it produces earlier onset and longer duration of action with fewer side effects than when fentanyl is added as adjuvant in parturients.[41]

Neuraxial administration of dexmedetomidine produces spinal analgesia as efficiently as clonidine. Epidural dexmedetomidine exhibits synergism with local anesthetics and results in intense motor block, prolongs the sensory/motor block duration time, postoperative analgesia without any additional morbidity.[42]

Neuraxial Dexmedetomidine is a favorable local anesthetic adjuvant with better and longer analgesia. Bradycardia is the greatest concern.[43]

In patients undergoing total knee arthroplasty, Dexmedetomidine seems to be an ideal adjuvant to epidural bupivacaine for postoperative analgesia.[44]

Dexmedetomidine is a better adjuvant than clonidine in epidural anaesthesia as far as patient comfort, stable cardio-respiratory parameters, intra-operative and post-operative analgesia is concerned. [45]

Addition of dexemedetomidine can be advantageous than magnesium sulfate when added to epidural bupivacaine with respect to increased duration of motor and sensory blockade and arousable sedation.[46]

In major abdominal surgeries, dexmedetomidine is a good alternative to morphine as an adjuvant to levobupivacaine in epidural anesthesia .[47]

Dexmedetomidine when added to caudal bupivacaine was found to reduce the response to hernial sac traction. It also prolonged the duration of postoperative analgesia in children undergoing inguinal hernia repair.[48]

The administration of dexmedetomidine may prevent the incidence of postoperative shivering, although there was no difference compared with other anti-shivering drugs, such as meperidine, fentanyl, tramadol, and clonidine.[49]

Dexmedetomidine when added to regular mixture of epidural anesthetics in women undergoing elective cesarean section was found to improve intraoperative

conditions and quality of postoperative analgesia without significant maternal or neonatal significant side effects.[50]

For pediatric lower abdominal surgeries, when caudal dexmedetomidine (2 μg/kg) with 0.25%Ropivacaine (1 ml/kg) was used, it was shown to provide significant postoperative pain relief and better quality of sleep and a prolonged duration of arousable sedation.[51]

For the safe regional anaesthesia practice in patients receiving alpha 2 agonists (dexmedetomidine, clonidine) as adjuvants to local anesthetic agents, monitoring for bradycardia, hypotension, possible excess sedation and subsequent fall in haemoglobin saturation should be done.[52]

For patients undergoing vaginal hysterectomy, dexmedetomidine was found to be better than fentanyl as an epidural adjuvant for providing early onset of sensory analgesia, adequate sedation with no respiratory depression and prolonged postoperative analgesia.[6]

Dexmedetomidine produces a dose dependant increase in the duration of sensory and motor blocks induced by local anesthetics, regardless of the neuraxial route of administration (spinal, epidural or caudal) without any evidence of neurotoxicity in human volunteers.[53]

Dexmedetomidine seems to be a better alternative to fentanyl as an epidural adjuvant as it provides comparable stable hemodynamics, early onset, and establishment of sensory anesthesia, prolonged post-op analgesia, lower consumption of post-op local anesthetics for epidural analgesia, and much better sedation levels.[54]

Dexmedetomidine is a potent and more selective a2-adrenergic agonist than clonidine. Cellular effects mediated by signalling pathways other than through a2-

adrenoceptors have a role in neuroprotection. In mechanically ventilated patients in the ICU, it does not significantly depress ventilator drive and may preserve physiological sleep better than any other sedative. It may also reduce mortality in sepsis via attenuation of immunosuppression.[55]

In a study conducted on 60 pediatric patients scheduled for lower abdominal surgeries. After sevoflurane in oxygen anaesthesia, all patients received one dose of caudal bupivacaine 0.25% 1ml/kg. Then they were randomized to receive either dexmedetomidine 2µg/kg in normal saline 1ml, clonidine 2µg/kg in normal saline 1ml or corresponding volume of normal saline epidurally. It was concluded that addition of dexmedetomidine or clonidine to caudal bupivacaine significantly promoted analgesia with no significant advantage of dexmedetomidine over clonidine.[56]

MATERIALS AND METHODS

The study was conducted at R.L. Jalappa hospital and research centre, Tamaka, Kolar from December 2013 to May 2015. This was a prospective randomized double blind study which involved 60 adult patients posted for lower limb and lower abdominal surgeries. Institutional ethical committee clearance and informed consent was obtained from the patients. Patients were randomly divided into two groups of 30 each using computer generated random numbers.

Group 'D' – BUPIVACAINE with DEXMEDETOMIDINE.

Group 'F'- BUPIVACAINE with FENTANYL.

Inclusion criteria:

Patients of ASA Grade I and II in the age group of 18 years to 50years, of either sex with weight 50 to 80 kg and height 150-170 cm, posted for elective lower abdominal & lower limb surgeries .

Exclusion criteria

1. Patients physically dependant on opioids.
2. Patients with history of drug allergy (local anesthetics, fentanyl, dexmedetomidine).
3. Patients with gross spinal abnormality, localized skin sepsis, hemorrhagic diathesis, neurological involvement / diseases.
4. Head injury cases.
5. Patients with cardiac, pulmonary, hepatic or renal disorders.(h/o angina, previous myocardial ischemia)
6. Patients with peripheral neuropathy.
7. Patients with psychiatric disease

Pre- anesthetic evaluation:

Patients were visited on the previous day of the surgery, a detailed clinical history was taken, General and Systemic examinations were done. Basic laboratory investigations like complete haemogram, bleeding time, clotting time, blood sugar, blood urea, serumcreatinine and urine analysis were carried out routinely on all patients. ECG was done in patients more than 40 years of age and chest x-ray when indicated.

The patients were explained about the epidural technique with catheter in situ, its advantages and disadvantages. All the patients were provided with a written information sheet about procedure, drugs and voluntary participation was sought. Afterwards written informed consent was taken from each patient.

Premedication:

To allay the anxiety and apprehension all patients were given tab. Alprazolam 0.5mg orally along with tab. Ranitidine 150mg orally the night before the procedure. Patients were kept nil orally for 10 hrs before surgery.

On the day of surgery in the pre operative room, an intravenous line was secured and the patients were preloaded with 15 ml/kg Ringer's lactate, 30 minutes prior to epidural anaesthesia. On the OT table, patients basal pulse rate and blood pressure, respiratory rate, SpO_2 were recorded.

Anesthetic technique:

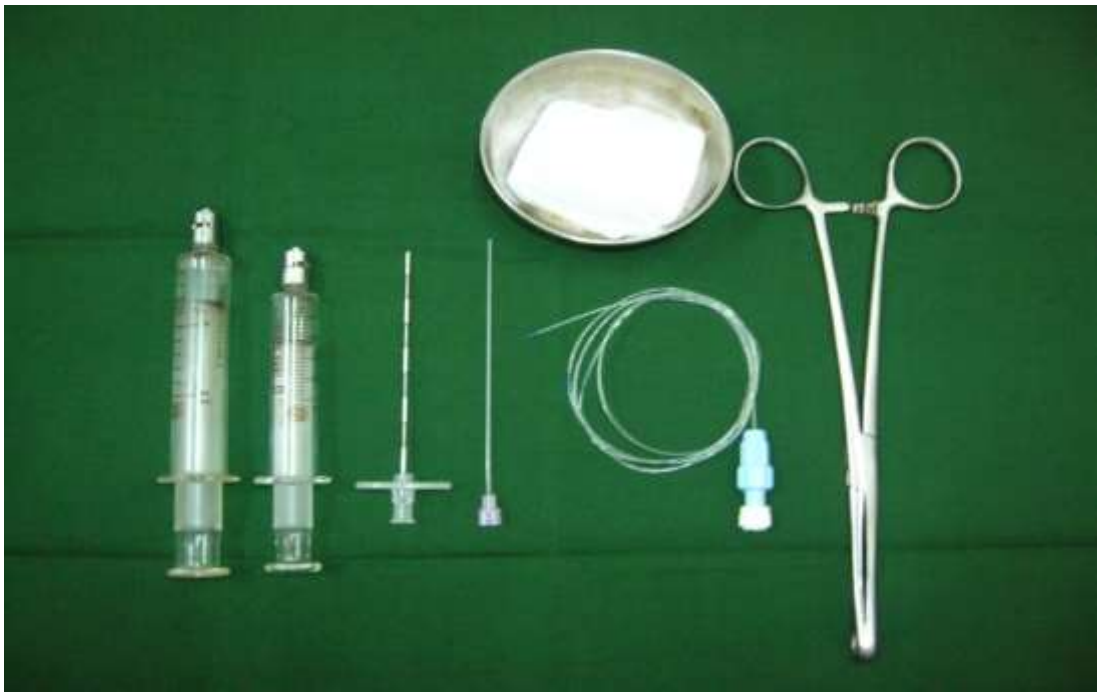


Figure 10: **Epidural Tray**

Figure 11: **Fentanyl**

Figure 12: **Dexmedetomidine**

After sterile preparation the epidural space was identified in sitting position in L_{2-3} or L_{3-4} space with 18 gauge Touhy needle using loss of resistance technique and a epidural catheter was secured. After insertion of epidural catheter, a test dose was given with 3ml of 2% lignocaine with adrenaline 1:2,00,000 through the catheter and observed for any intravascular or intrathecal injection. After confirming correct placement of the catheter, epidural anesthesia was activated with 18ml of 0.5% bupivacaine with dexmedetomidine 1 microgram per kilogram made upto 2ml by adding sterile water in group "D" while the patients in group "F" received 18ml of

0.5% bupivacaine with fentanyl 1 microgram per kilogram made upto 2ml by adding sterile water. Epidural catheter was secured 3-5cm into the epidural space.

Surgical procedure was initiated after establishment of adequate surgical anaesthesia.

The bilateral pin prick method was used to evaluate and check the sensory level while the modified Bromage scale was used to measure motor blockade.

Modified Bromage scale (0 -3):

0 No power impairment and able to raise straight leg against resistance

1 Unable to raise straight leg but able to flex knee

2 Unable to flex knee but able to move ankle joint

3 Unable to move hip, knee, or ankle

The following block characteristics was observed and recorded: onset of analgesia, the highest dermatomal level of sensory blockade, time to achieve highest sensory level, the complete establishment of motor blockade, time to two segment regression and time to complete motor recovery. Time for rescue analgesia was assessed by VAS score. Sedation will be assessed using Ramsay Sedation score.

DEFINITIONS:

1. **Onset of analgesia** (sensory block): is defined as the time interval between administration of local anesthetic epidurally to the loss of pinprick sensation at the site of surgical incision.

2. **Maximum level of sensory blockade**: is the maximum sensory dermatome level after 30 minutes of administering the local anesthetic in the epidural space. The local

anesthetics usually get fixed to their respective receptors by 20 minutes and regression of 2 dermatome usually occurs after 30 minutes.

3. **Time to attain maximum sensory level**: is defined as the time in minutes at which maximum sensory level was attained after administering the drug epidurally.

4. **Time to complete motor blockade**: is defined as time interval between administering of drug epidurally to complete loss of motor activity (modified bromage scale score of 0-3).

5. **Time for two segment regression**: is defined as interval between onset of analgesia epidurally to regression of two segments from maximum sensory level attained.

6. **Duration of motor block**: Duration of motor block was recorded from onset time to time when the patient was able to lift the extended leg.

7. **Duration of analgesia**: The duration of analgesia was taken from the time of epidural drug administration to the time of first supplementation with rescue analgesic.

Standard monitoring was carried out in the form of pulse oximetry, ECG and non invasive arterial blood pressure. Pulse rate, respiratory rate, arterial blood pressure and oxygen saturation were recorded every 5mins for first 20 mins, then every 15 mins intra operatively.

A note was made of blood loss, urine output, IV fluid input. Patients were observed for hypotension (defined as >20% decrease in SBP from baseline and were treated with IV fluids and IV mephenteramine 3-6 mg in incremental boluses), bradycardia (pulse <50 beats/min were treated with IV atropine sulphate 0.6mg bolus

doses) and other adverse effects such as anxiety, nausea, vomiting, pruritus, urinary retention, shivering, etc., recorded and the need for additional medications also attended.[57]

Ramsay Sedation Scale[58]

1 Anxious and agitated, restless

2 Co-operative, oriented, tranquil

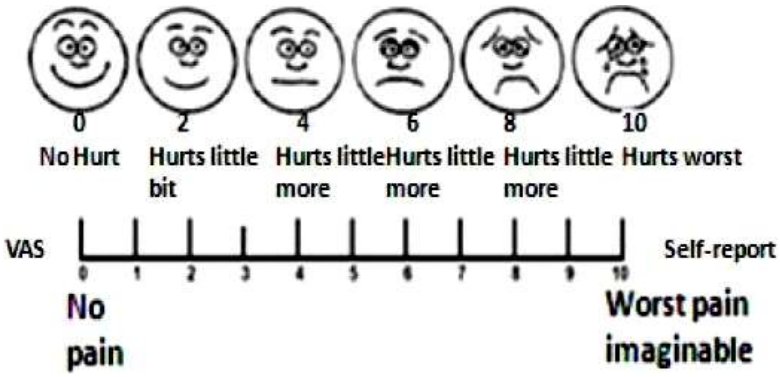
3 Responsive to verbal commands, drowsy

4 Asleep, responsive to light stimulation (loud noise, tapping)

5 Asleep, slow response to stimulation

6 No response to stimulation

Post operative pain was assessed by Visual Analogue Scale (VAS)[59]



Duration of analgesia was assessed by VAS scores, more than 4 is considered for requirement of rescue analgesia.

The onset of pain was managed with top up doses of 10ml 0.125% bupivacaine through epidural catheter.

At the end of the surgery, the vitals were recorded and sedation assessed.

All the observations and particulars of each patient were recorded in a proforma, a copy of which is enclosed.

STATISTICAL ANALYSIS

The sample size was determined by power analysis based on previous literature. Keeping the mean difference of 5.1 and standard deviation in group 1 as 6.9 and group 2 as 3.7, a sample size of 26 patients per group was required. Considering 10% of non compliance, a sample size of 30 patients were selected for each group in our study. Results are expressed as the means and standard deviations, medians and ranges, or numbers and percentages.

STATISTICAL METHODS :

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, **Ass**umptions: 1**.**Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent

Data was analyzed using following statistical tests:

For continuous data- Student's t-test

For categorical data- Chi-Square test and Mann-Whitney U test.

Significant figures

+ Suggestive significance (P value: $0.05<P<0.10$)

* Moderately significant (P value:$0.01<P \leq 0.05$)

** Strongly significant (P value: $P \leq 0.01$)

Statistical software: The Statistical software SPSS 15.0 was used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

RESULTS

60 adult patients belonging to ASA grade I and II, of either sex, in age group between 15- 50 years, posted for elective lower abdominal and lower limb surgeries in general surgery, orthopedics, gynecology and urology under epidural anaesthesia were selected for the study. They were randomly allocated to two groups with 30 patients in each group using computer generated random numbers.

Group "D" received 18ml of 0.5% bupivacaine with dexmedetomidine 1 microgram per kilogram made upto 2ml by adding sterile water.

Group "F" received 18ml of 0.5% bupivacaine with fentanyl 1 microgram per kilogram made upto 2ml by adding sterile water.

Age in years	**Group D**		**Group F**	
	No	**%**	**No**	**%**
<20	1	3.3	2	6.7
21-30	11	36.7	5	16.7
31-40	6	20.0	13	43.3
41-50	12	40.0	10	33.3
Total	30	100.0	30	100.0
Mean ± SD	36.37±9.59		37.37±9.61	

Samples are age matched with P=0.688

Table 6: Age distribution of patients studied

Gender	Group D		Group F	
	No	%	No	%
Female	17	56.7	19	63.3
Male	13	43.3	11	36.7
Total	30	100.0	30	100.0

Samples are gender matched with P=0.598

Table 7: Gender distribution of patients studied

	Group D	Group F	P value
Weight (kg)	55.77±4.46	55.30±3.96	0.670
Height (cm)	163.77±4.60	160.70±5.84	0.028*

Table 8: Weight and Height distribution in two groups studied

ASA Grade	Group D		Group F	
	No	%	No	%
ASA I	28	93.3	26	86.7
ASA II	2	6.7	4	13.3
Total	30	100.0	30	100.0

Table 9: ASA Grade in two groups of patients studied

The two groups were comparable with regard to demographic data as shown in tables 6,7,8 and 9. There was no statistically significant variation between the two groups with respect to age, gender, weight, ASA grading($p>0.05$).

Onset of Sensory blockade (min)	Group D		Group F	
	No	%	No	%
6-10	29	96.7	15	50.0
11-15	1	3.3	15	50.0
Total	30	100.0	30	100.0
Mean ± SD	8.80±1.13		10.70±1.26	

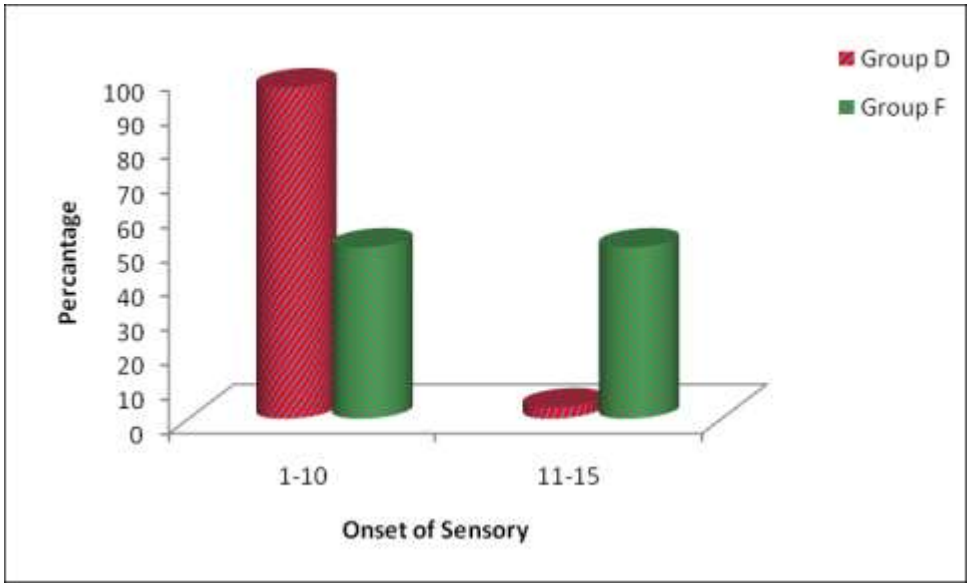
P<0.001**

Table 10: Onset of Sensory block in two groups of patients studied

Onset of Motor blockade (min)	Group D		Group F	
	No	%	No	%
11	2	6.7	0	0.0
12	1	3.3	0	0.0
13	1	3.3	0	0.0
14	3	10.0	2	6.7
15	7	23.3	1	3.3
16	8	26.7	8	26.7
17	4	13.3	8	26.7
18	4	13.3	9	30.0
20	0	0.0	2	6.7
Total	30	100.0	30	100.0
Mean ± SD	15.40±1.89		16.97±1.40	

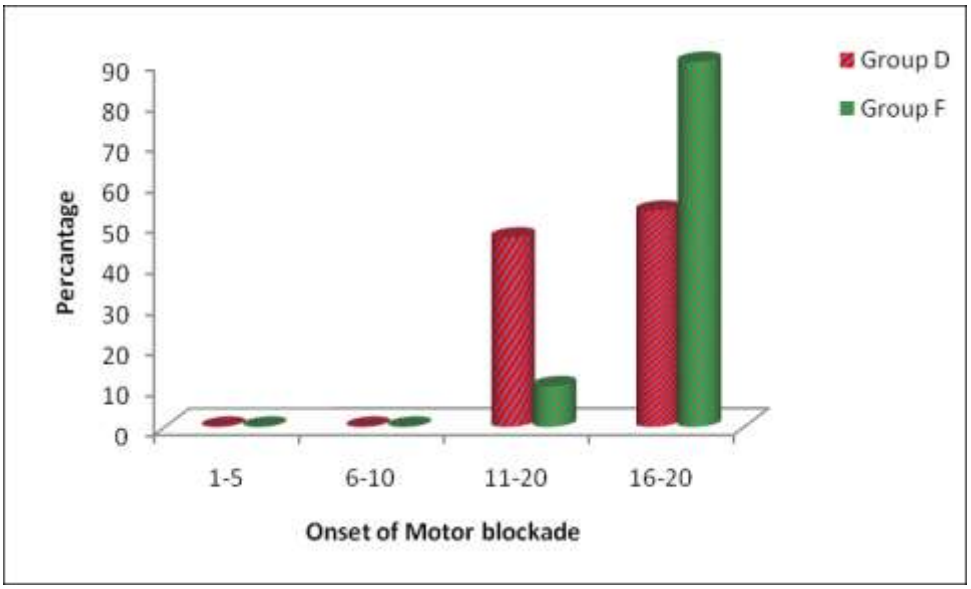
P=0.001**

Table 11: Onset of Motor blockade in two groups of patients studied



Graph 1:COMPARISON OF ONSET OF SENSORY BLOCK IN TWO GROUPS

Time to attain adequate sensory block was faster in Group D when compared to Group F ($p<0.001$) which is statistically significant as shown in table 10.

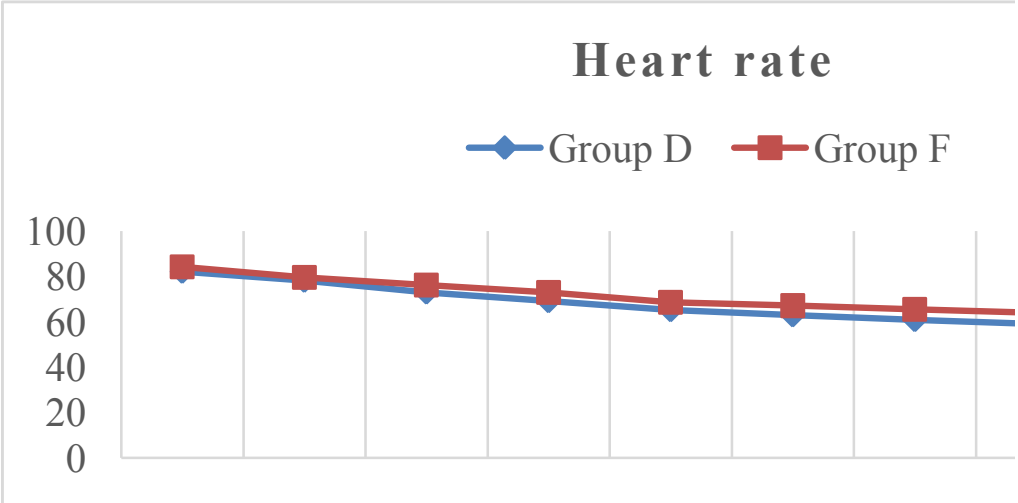


Graph 2: COMPARISON OF TIME TO ATTAIN COMPLETE MOTOR BLOCK

Establishment of complete motor blockade was faster in Group D when compared to Group F ($p<0.001$) which is statistically significant as shown in table 11.

Heart rate (bpm)	Group D	Group F	P value
Baseline	82.07±5.55	84.13±4.98	0.134
5 min	78.10±4.57	79.47±4.33	0.239
10 min	72.93±4.75	76.17±4.51	0.009**
15 min	69.10±4.21	72.97±3.41	<0.001**
20 min	65.13±3.43	68.57±4.28	0.001**
25 min	62.87±3.35	67.10±4.38	<0.001**
30 min	60.77±2.99	65.47±5.12	<0.001**
60 min	59.00±1.91	64.00±3.15	<0.001**
120 min	58.53±3.33	62.40±3.11	<0.001**
180 min	58.00±5.11	64.40±3.59	<0.001**

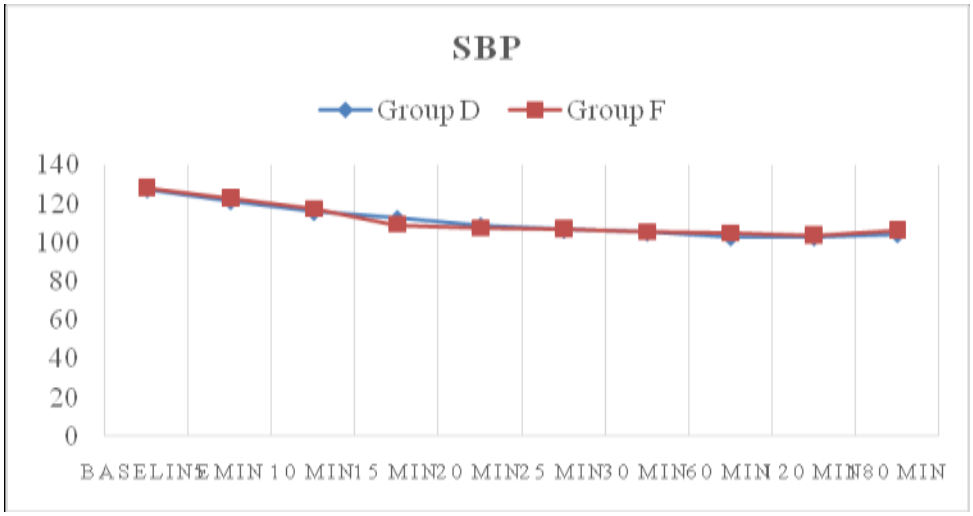
Table 12: Comparison of Heart rate (bpm) in two groups of patients studied



Graph 3: COMPARISON OF HEART RATE BETWEEN TWO GROUPS

SBP (mm Hg)	Group D	Group F	P value
Baseline	127.20±8.86	128.00±7.28	0.704
5 min	121.13±8.28	122.80±5.96	0.375
10 min	115.57±8.57	117.17±6.10	0.408
15 min	112.47±7.73	109.13±6.40	0.074+
20 min	108.77±7.90	107.33±6.73	0.452
25 min	106.33±7.50	106.87±5.58	0.756
30 min	104.87±6.34	105.20±4.77	0.819
60 min	102.53±6.56	104.53±4.07	0.161
120 min	102.47±6.66	103.53±5.35	0.497
180 min	104.13±5.20	106.27±4.86	0.106

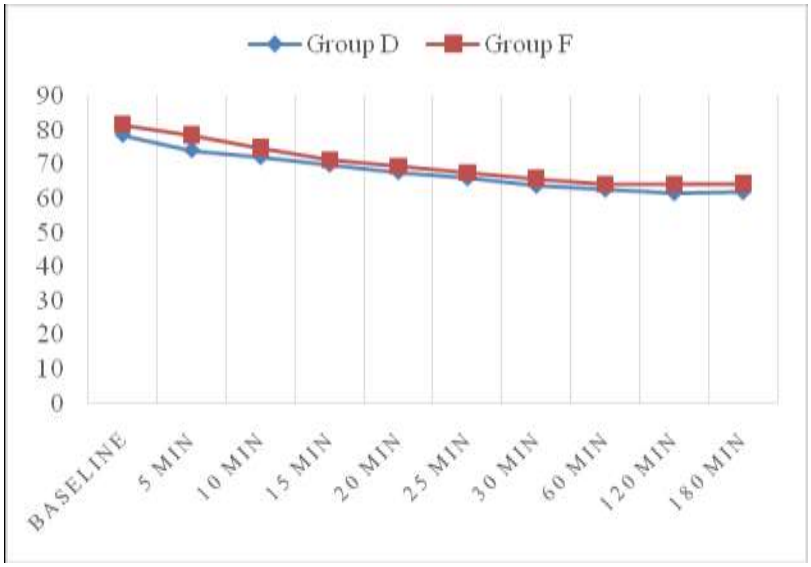
Table 13:Comparison of SBP (mm Hg) in two groups of patients studied



Graph 4 : COMPARISON OF SBP BETWEEN TWO GROUPS

DBP (mm Hg)	Group D	Group F	P value
Baseline	78.60±5.10	79.20±4.47	0.702
5 min	74.13±4.26	78.47±4.38	<0.001*
10 min	72.13±3.60	74.80±4.54	0.014*
15 min	69.87±3.64	71.13±4.02	0.206
20 min	67.67±3.97	69.27±4.05	0.128
25 min	65.87±3.71	67.40±4.11	0.135
30 min	63.67±3.83	65.73±4.45	0.059+
60 min	62.53±3.86	64.07±4.56	0.165
120 min	61.47±3.19	64.07±5.00	0.020*
180 min	61.80±2.85	64.13±4.93	0.028*

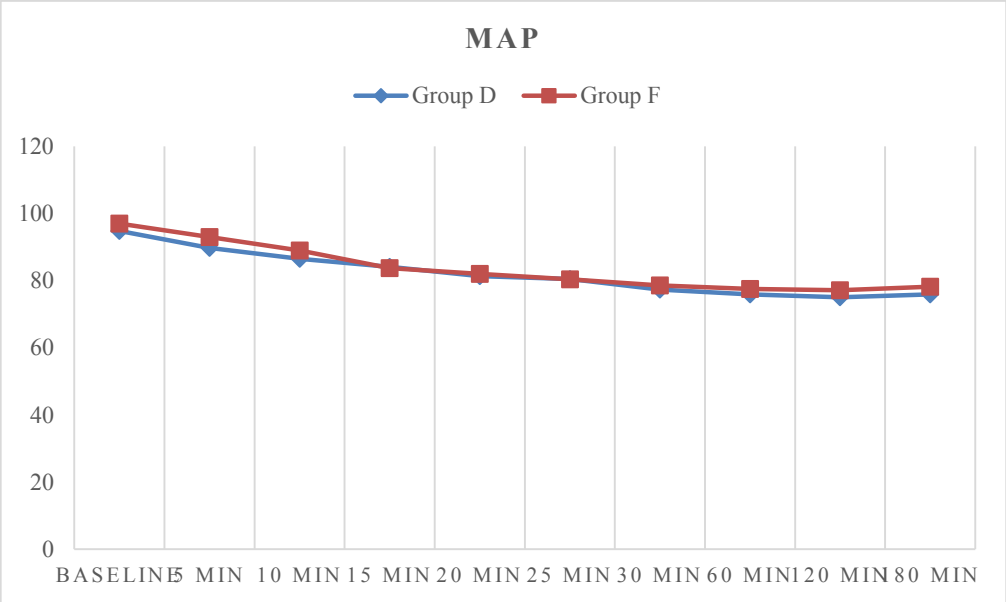
Table 14: Comparison of DBP (mm Hg) in two groups of patients studied



Graph 5: COMPARISON OF DBP BETWEEN TWO GROUPS

MAP (mm Hg)	Group D	Group F	P value
Baseline	94.77±5.59	95.03±3.23	0.692
5 min	89.73±4.71	92.97±3.64	0.004*
10 min	86.53±3.95	88.97±3.45	0.014*
15 min	84.07±3.81	83.77±3.78	0.761
20 min	81.30±3.94	81.97±3.81	0.508
25 min	80.47±7.19	80.40±3.62	0.964
30 min	77.30±4.09	78.60±4.06	0.222
60 min	75.93±3.66	77.50±3.62	0.101
120 min	75.03±3.07	77.17±4.04	0.025*
180 min	75.87±2.85	78.23±4.16	0.013*

Table 15: Comparison of MAP (mm Hg) in two groups of patients studied



Graph 6: COMPARISON OF MAP BETWEEN TWO GROUPS

Hemodynamic Variables:

The fall in heart rate was statistically significant in Group D when compared to Group F between 10 min and 180 min(p value being significant) as shown in table 12.

It was observed that there was bradycardia (PR<50) in 7 patients in group D ,which required a single dose of Inj Atropine 0.6mg IV, and further no doses of atropine were required as shown in table 12. None of the patients in Group F had bradycardia.

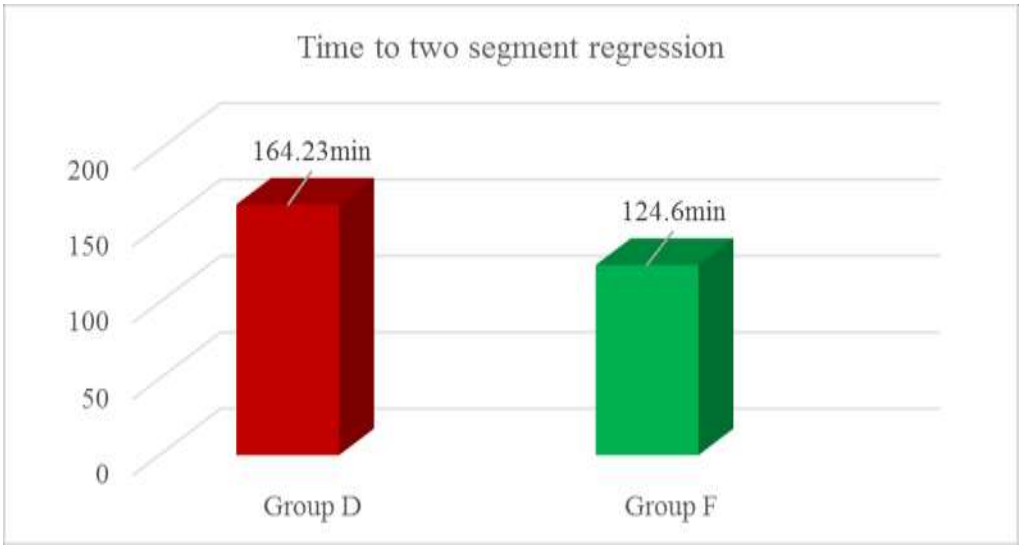
The systolic blood pressure showed suggestive significant difference (p=0.074) in between Group D and Group F at 15min as shown in table 13.

The incidence of diastolic hypotension was more in Group D when compared to Group F(p<0.001) at 5, 10, 120 and 180 min as shown in table 14.

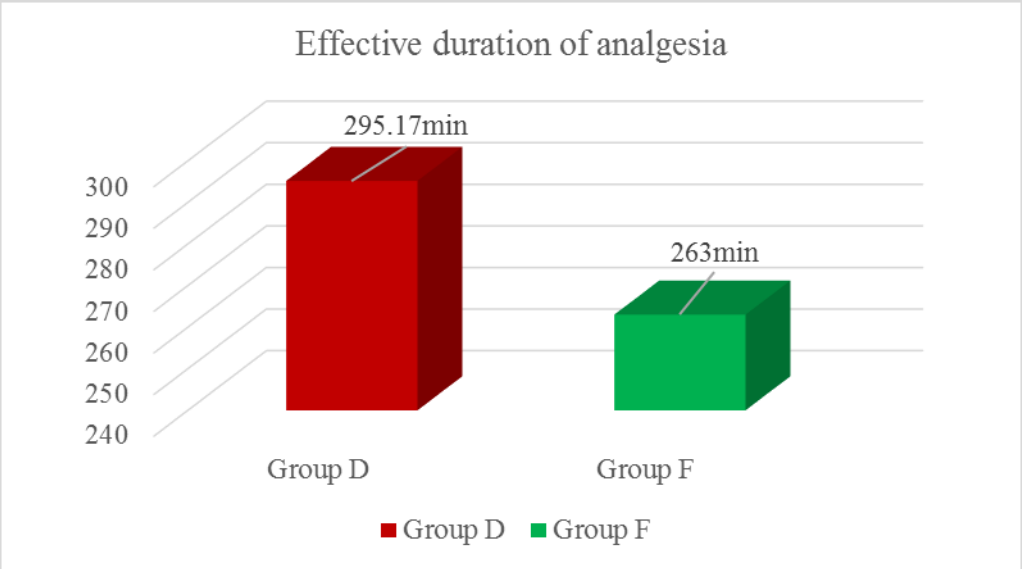
With similar statistically significant difference in mean arterial blood pressure in between Group D and Group F at 5,10,120 and 180 mins as shown in table 15. The hypotension was treated with incremental doses of mephenteramine 3mg bolus doses, but the total dose did not cross 18mg in any of the groups.

	Group D	**Group F**	**P value**
Time to two segment regression(min)	164.23±15.18	124.60±15.98	<0.001**
Effective duration of analgesia(min)	295.17±23.02	263.00±16.90	<0.001**
Time for complete motor recovery (min)	213.97±17.98	165.73±13.85	<0.001**

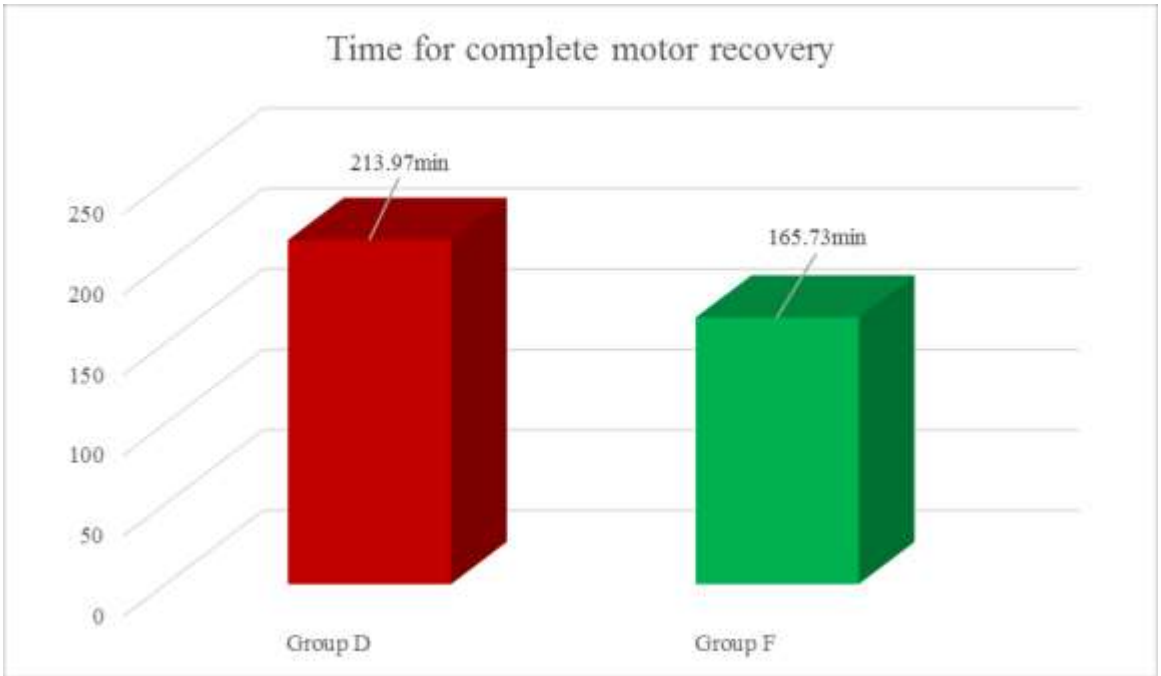
Table 16: Comparision of study variables in two group of patients



Graph 7: COMPARISON OF TIME TO TWO SEGMENT REGRESSION BETWEEN TWO GROUPS.



Graph 8: COMPARISON OF EFFECTIVE DURATION OF ANALGESIA BETWEEN TWO GROUPS.



Graph 9: COMPARISON OF COMPLETE MOTOR RECOVERY BETWEEN TWO GROUPS.

Two segment regression was prolonged in Group D when compared to Group F with statistically significant difference as shown in table 16.

The duration of analgesia was significantly longer in Group D when compared to Group F ($p<0.001$), as seen in Table 16. Thus denoting that addition of additives like fentanyl and dexmedetomidine prolongs the duration of analgesia which is more in dexmedetomidine group.

Time to complete motor recovery was significantly longer in Group D when compared to Group F ($P<0.001$) as shown in table 16. However from this it is observed that addition of additives intensifies the motor blockade, while dexmedetomidine has more influence on duration of motor blockade.

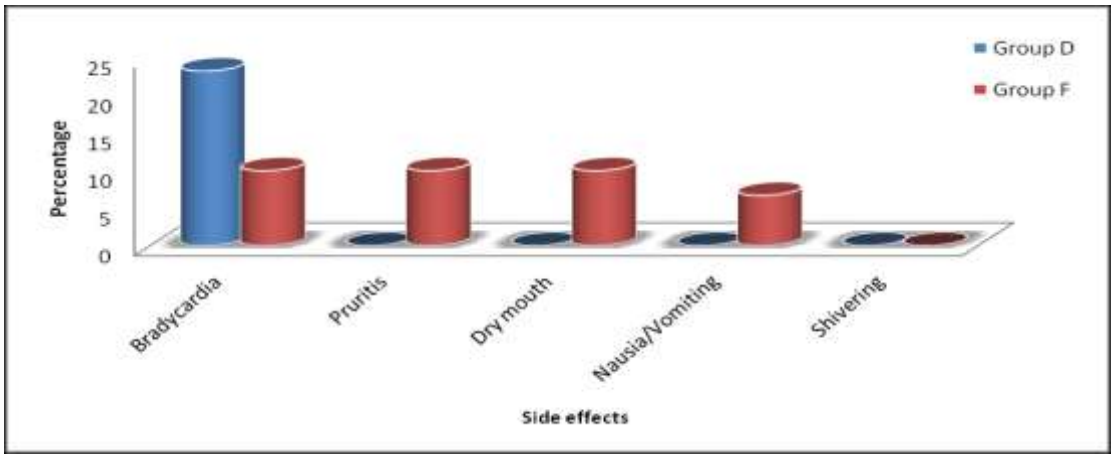
Sedation Score	Group D (n=30)		Group F (n=30)	
	No	%	No	%
1	0	0	3	10.0
2	7	23.3	21	70.0
3	19	63.3	6	20.0
4	4	13.3	0	0
5	0	0	0	0
6	0	0	0	0

Table 17: Sedation score in two groups of patients studied

From Table 17 it is clear that, maximum number of patients in group D had sedation score of 3 (Responsive to verbal commands, drowsy). Four patients had sedation score of 4 (Asleep, responsive to light stimulation). Maximum number of patients in group F had sedation score of 2 (Co-operative, oriented, tranquil). Patients in both the groups maintained saturation above 90% and none of them required oxygen support.

Side effects	Group D (n=30)		Group F (n=30)	
	No	%	No	%
No	23	76.7	19	63.3
Yes	7	23.3	11	36.7
Bradycardia	7	23.3	3	10.0
Pruritis	0	0.0	3	10.0
Dry mouth	0	0.0	3	10.0
Nausia/Vomiting	0	0.0	2	6.7
Shivering	0	0.0	0	0.0

Table 18: Side effects in two groups of patients studied

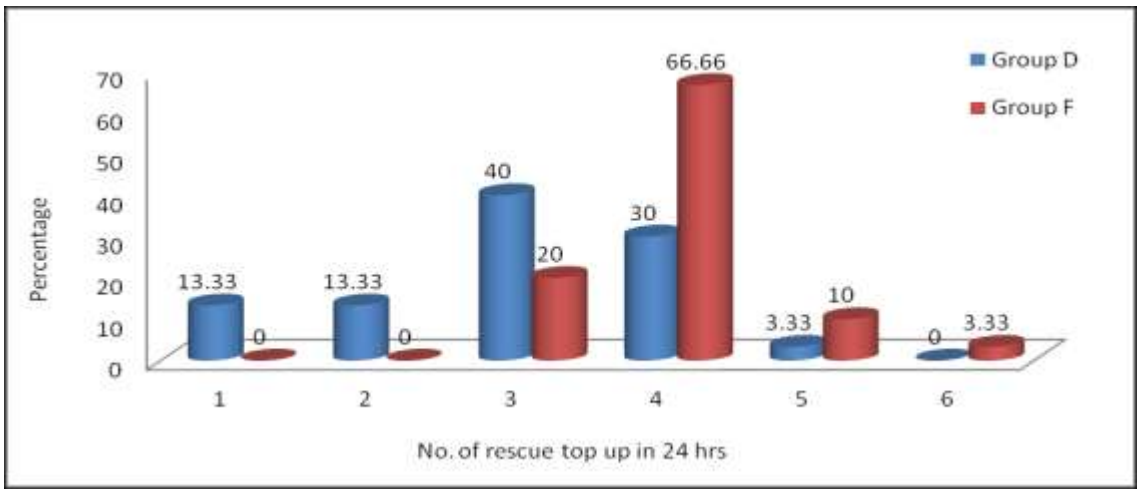


Graph 10: COMPARISON OF EACH SIDE EFFECT BETWEEN TWO GROUPS.

Table 18 shows the incidences of side effects in various groups. Bradycardia was observed in 23.3% of patients in Group D and 10% of patients in Group F . The incidence of pruritis and dry mouth was 10 % in Group F. Nausea, vomiting was observed in 6.7% in Group F. Shivering was not observed in patients of both the group.

No. of rescue top up in 24 hr	**Group D**		**Group F**	
	No	**%**	**No**	**%**
1	4	13.33	0	0
2	4	13.33	0	0
3	12	40	6	20
4	9	30	20	66.66
5	1	3.33	3	10
6	0	0	1	3.33

Table 19: No. of rescue top up in 24 hr in two groups of patients studied



Graph 11- No. of rescue top up in 24 hr in two groups of patients studied

From Table 19 it is clear that number of rescue top up given in 24 hours was less in Group D in comparison to F group which is statistically significant (P<0.001).

DISCUSSION

Epidural anesthesia with insertion of catheter has emerged as a safe technique of anesthesia for lower abdominal and lower limb surgeries, in that the stress response of general anesthesia can be totally avoided. Further epidural anesthesia with catheter can be used for prolonged surgeries. An additional advantage of epidural catheter insertion is for providing postoperative analgesia.[1]

The present study involved comparision of epidural bupivacaine with dexmedetomidine and bupivacaine with fentanyl for lower abdominal and lower limb surgeries.

Local anesthetics popularily used for offering epidural anesthesia have been lidocaine and bupivacaine. Bupivacaine has been shown by authors to offer prolonged duration of anesthesia and post operative analgesia as well when used during epidural anesthesia. Hence in our study we have used Bupivacaine 0.5% as the local anesthetic for epidural anesthesia.[3]

Many adjuvants have been studied by various authors for prolonging epidural anesthesia as well as during post operative analgesia. Among them are opioids, alpha 2 agonists, non opioid like tramadol and neostigmine. Among them opiods have been a popular choice like fentanyl in that they offer faster onset and prolongs the duration of analgesia. Recently alpha 2 agonists like clonidine and dexmedetomidine have also been used in prolonging the duration of epidural analgesia. Hence our study involved comparision of epidural bupivacaine 0.5% plus dexmedetomidine and bupivacaine plus fentanyl for lower abdominal and lower limb surgeries with major emphasis on onset of sensory blockade, onset of motor blockade, time to two segment regression, total duration of analgesia, time to complete motor recovery, hemodynamic variables.

Fentanyl an opioid analgesic is a lipid-soluble, strong μ-receptor agonist and phenyl piperidine derivative with a rapid onset and short duration of action. It has been commonly used as adjunct to local anesthetics in epidural anesthesia from a varying dose of 50 microgram to 100 microgram with minimal side effects. They hasten the onset, improve the quality of the block and prolong the duration of analgesia.[33,35, 38]

Alpha 2 adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anesthesia. Dexmedetomidine is a highly selective alpha 2 agonist when compared to clonidine. It exerts its analgesic effects at the spinal and supraspinal sites. Various studies have stated that the dose of clonidine is 1.5-2 times higher than dexmedetomidine when used in epidural route. A dose upto 1.5microgram per kilogram body wt has been used in epidural anesthesia in various studies without any significant side effect. The stable hemodynamics and decreased oxygen demand due to enhanced sympathoadrenal stability makes it a very useful pharmacologic agent.[45]

We did not include patients more than 50yr as it was shown in a study conducted by Mischa J. G. Simon and colleaguesin their study on the effects of Age on neural blockade and hemodynamic changes after epidural anaesthesia with ropivacaine studied the influence of age on the neural blockade and hemodynamic changes after the epidural administration of ropivacaine 1.0% and concluded that age influences the clinical profile of ropivacaine 1.0%. The hemodynamic effects in older patients were caused by the high thoracic spread of analgesia, although a diminished hemodynamic homeostasis may contribute.[60]

Demographic profile (age, sex) is comparable in all three groups.

Time to attain sensory block (min)

In our study the mean time to attain adequate sensory level was 8.80±1.13 in Group D and 10.70±1.26 in Group F. This shows that time to attain adequate sensory level was faster in Group D when compared to Group F ($p<0.001$) which is statistically significant.

Similar results were obtained in studies by Kumkum Gupta and her colleagues , time for onset of sensory block in Levobupivacaine with Dexmedetomidine group was 7.25±2.3 min and in Levobupivacaine with Fentanyl group was 9.27±2.79 min.[6]

In a study by Mohamed Fouad Selim and his colleagues, similar results were shown, mean being 5.9±2.7min in Bupivacaine with Dexmedetomidine group and 9.1±1.9min in Bupivacaine with Fentanyl group.[41]

Time to complete motor blockade:

In our study mean time for onset of motor blockade in Group D was 15.40±1.89min and in Group F was 16.97±1.40min. It was found that establishment of complete motor blockade was faster in Group D when compared to Group F ($p<0.001$) which is statistically significant.

Our study can be correlated with other two studies, Kumkum Gupta and her colleagues, where mean duration to complete motor block was 19.27±4.7min in Levobupivacaine with Dexmedetomidine group and 22.78±5.5min in Levobupivacaine with Fentanyl group, where dexmedetomidine and fentanyl were studied for epidural in hysterectomy.[6]

In a similar study by Bajwa SJ and his colleagues, time to attain complete motor block level with Ropivacaine with Dexmedetomidine group was 18.16±4.52min and

22.98±4.78min with Ropivacaine with Fentanyl group. This shows that addition of dexmedetomidine hastens the maximum motor block compared to fentanyl.[54]

Hemodynamic variables :- heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, SpO_2

Heart Rate:

In our study the fall in heart rate was statistically significant in Group D when compared to Group F between 10 min and 180min (p value being significant).

It was observed that there was bradycardia (PR<50) in 7 patients in Group D, which required a single dose of Inj Atropine 0.6mg IV, and further no doses of atropine were required. None of the patients in Group F had bradycardia.

Systolic blood pressure:

In our study the systolic blood pressure showed statistically mild significant difference (p<0.074+) in between Group D and Group F with hypotension commoner in Group D.

Diastolic blood pressure:

In our study incidence of diastolic hypotension was more in Group D when compared to Group F (p<0.001) at 5,10,120 and 180 min.

Mean blood pressure:

In our study likely significant difference in mean arterial blood pressure between Group D and Group F at 5,10, 120 and 180mins was observed. The hypotension was treated with incremental doses of mephenteramine 3mg bolus doses, but the total dose did not cross 18mg.

In a study conducted by Mohamed Fouad Selim, MAP decreased significantly at T20 in both epidural groups. MAP showed non significant degree of decrease in Bupivacaine with Dexmedetomidine group compared with Bupivacaine with Fentanyl group.[41]

In a similar study by Kumkum Gupta and her colleagues, mean arterial blood pressure was decreased from baseline in both groups Levobupivacaine with Dexmedetomidine and Levobupivacaine with Fentanyl with maximum decline at 30-35 minutes after the epidural injection but it never went beyond acceptable physiological limit of 65 mmHg.[6]

SpO_2

In our study similarly pulse oximetry trends did not show any significant variation in patient saturation in patients of both groups. Patients in both the groups maintained a saturation above 90%.

Two segment regression, duration of analgesia and recovery of motor blockade:

In our study mean Duration of analgesia (in min) was 295.17±23.02 in Group D and 263.00±16.90 in Group F. This shows that duration of analgesia was significantly longer in D when compared to Group F ($p<0.001$). Thus denoting that addition of dexmedetomidine prolongs the duration of analgesia compared to fentanyl.

Our results are in correlation with studies conducted by Mohamed Fouad Selim and his colleagues, where it was seen that duration of analgesia in group Bupivacaine with Dexmedetomidine was 155.6±28.1 compared to 129±18.7 in group Bupivacaine with Fentanyl.[41]

In our study mean time to two segment regression (in min) was 164.23±15.18 in Group D and 124.60±15.98 in Group F. This shows that two segment regression was prolonged in Group D when compared to group F with statistically significant difference.

In our study mean time to complete motor recovery (in min) was 213.97±17.98 in Group D and 165.73±13.85 in Group F. This shows that time to complete motor recovery was significantly longer in Group D when compared to Group F($P<0.001$). From this it is observed that addition of dexmedetomidine intensifies the motor blockade when compared to fentanyl.

In a similar study with with Kumkum gupta and her colleagues, duration of sensory analgesia between groups was statistically significant with187.7 min in group Levobupivacaine with Dexmedetomidine and 146.7 min in group Levobupivacaine with Fentanyl. Duration of motor block (min) in group Levobupivacaine with Dexmedetomidine was 167.4±21 where as in group Levobupivacaine with Fentanyl, it was found to be 125.6±36.[6]

Sedation:

Sedation score of 1 was observed in 10% patients in Group F. Sedation score of 2 was seen in 23.3% patients in Group D and 70% patients in Group F. Sedation score of 3 was observed in 63.3% patients in Group D and 20% patients in Group F. Sedation score of 4 was observed in 13.3% patients in Group D. It is clear that sedation was more in Group D in comparison to Group F.

Our results are in agreement with studies by Bajwa S J and his colleagues, in which 38% and 42% of patients in group Ropivacine with Dexmedetomidine exhibited grade II and grade III sedation as compared to 16% and 2% of patients in

the Ropivacaine with Fentanyl group, respectively. Only 12% of the patients in the Ropivacine with Dexmedetomidine group had sedation scores of 1 as compared to 82% wide and awake patients in Ropivacaine with Fentanyl group which was a highly significant statistical entity.[54]

Side effects:

In our study bradycardia was observed in 23.3% of patients of group D, whereas 10% of patients in Group F had bradycardia. The incidence of dry mouth was 10 % in Group F. Nausea, vomiting and pruritis was observed in Group F. None of the patients in any group had respiratory depression.

In a similar study with Bajwa SJ and his colleagues, comparative evaluation of dexmedetomidine and fentanyl in epidural anaesthesia, the side effect profile of both these drugs were quite favourable as none of the patients in either group had profound deep sedation or respiratory depression. Higher incidence of nausea and vomiting was observed despite a low dose of fentanyl used epidurally.[54]

In a study by Mohamed Fouad Selim and his colleagues, nausea and pruritis were significantly higher in group Bupivacaine with Fentanyl compred to group Bupivacaine with Dexmedetomidine. The incidence of respiratory depression was nil in all groups.[41]

CONCLUSION

The present study concludes that:

1. Onset of sensory and motor blockade was faster with dexmedetomidine compared with fentanyl when used with epidural bupivacaine.
2. Time to two segment regression and recovery of motor power were prolonged with dexmedetomidine compared with fentanyl when used with epidural bupivacaine.
3. The duration of analgesia was prolonged with dexmedetomidine compared with fentanyl when added to epidural bupivacaine.
4. The patient in epidural dexmedetomidine bupivacaine group received lesser number of rescue analgesics compared to fentanyl bupivacaine group.
5. Epidural dexmedetomidine-bupivacaine was associated with increased incidence of bradycardia, hypotension and sedation compared to fentanyl-bupivacaine group.

SUMMARY

This prospective randomized double blinded clinical comparative study "**A COMPARATIVE STUDY OF EPIDURAL BUPIVACAINE WITH FENTANYL AND BUPIVACAINE WITH DEXMEDETOMIDINE FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES "** was conducted in 60 adult patients belonging to ASA grade I and II, of either sex, in age group between 15- 50 years, posted for elective lower abdominal and lower limb surgeries in general surgery, orthopedics, gynecology and urology under epidural anaesthesia who were admitted to R.L .Jalappa Hospital and Research Centre, Tamaka, Kolar.

They were randomly allocated to three groups with 30 patients in each group.

Group "D" received 18ml of 0.5% bupivacaine with 2 ml of 1micro gram per kilogram of dexmedetomidine, diluted using normal saline.

Group "F" received 18ml of 0.5% bupivacaine with 2 ml of 1micro gram per kilogram of fentanyl, diluted using normal saline.

The following parameters were studied:

Onset time of sensory blockade level, time to complete motor blockade, time to two segment regression, duration of analgesia, time to complete motor recovery, changes in vital parameters like heart rate, mean arterial blood pressure and SpO2 and incidence of side effects.

Demographic profile (age, sex) was comparable in both groups. The data collected from all the patients was compared using student t test, chi square test and paired t test. The p value was calculated and $P < 0.05$ was considered statistically significant.

Our study concluded that Epidural dexmedetomidine- bupivacaine was associated with faster onset of sensory and motor blockade and less requirement of rescue analgesia compared to fentanyl- bupivacaine.

Epidural dexmedetodine-bupivacaine was associated with increased incidence of bradycardia, hypotension and sedation compared to fentanyl-bupivacaine.

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PROFORMA

A COMPARATIVE STUDY OF EPIDURAL BUPIVACAINE WITH FENTANYL AND BUPIVACAINE WITH DEXMEDETOMIDINE FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES.

NAME: **DATE:**

AGE: **I.P.NO:**

SEX:

PRE-OPERATIVE EVALUATION:

GENERAL PHYSICAL EXAMINATION:

PR	BP	RR	Temp	Wt	Ht	Spine

AIRWAY:

SYSTEMIC EXAMINATION:

RS:

CVS:

OTHERS:

INVESTIGATIONS:

Hb%: BLOOD SUGAR: URINE ANALYSIS:

ECG: CHEST X-RAY: BT: CT:

B.UREA: S.CREATININE: OTHERS:

DIAGNOSIS:

PROPOSED SURGERY:

PREMEDICATION: Tab.Alprazolam 0.5 mg, Tab.Ranitidine 150 mg.

ASA CLASS:

DRUGS USED IN EPIDURAL ANAESTHESIA:

GROUP D: BUPIVACAINE (0.5%) 18.0cc AND 2ml of DEXMEDETOMIDINE (1µg per kg)

GROUP F: BUPIVACAINE (0.5%) 18.0cc AND 2ml of FENTANYL (1µg per kg)

PARAMETERS NOTED DURING EPIDURAL ANAESTHESIA:

a) Time of administration:

b) Onset of block:

Sensory level attained(segment):

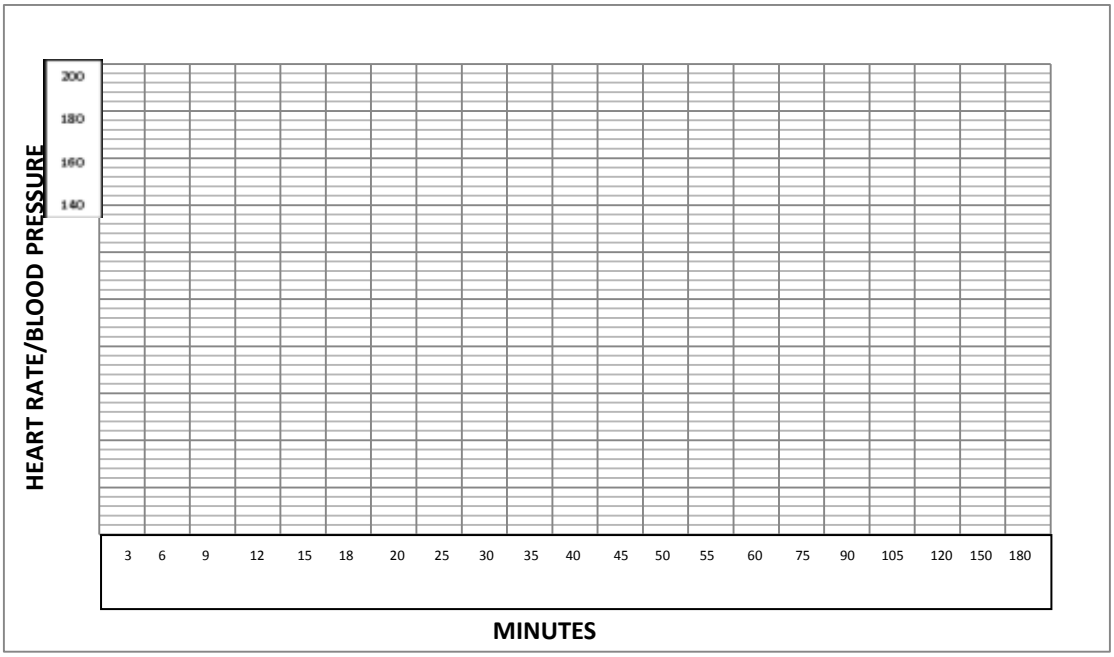
Motor: Modified Bromage scale 0:

Modified Bromage scale 1:

Modified Bromage scale 2:

Modified Bromage scale 3:

c) INTRAOPERATIVE OBSERVATION:



• Pulse • Systolic BP • Diastolic BP

c) TIME TO TWO SEGMENT REGRESSION OF SENSORY LEVEL:

d) EFFECTIVE DURATION OF ANALGESIA:

e)TIME FOR COMPLETE MOTOR RECOVERY:

ASSESSEMENT OF SEDATION:

Ramsay Sedation Scale

1 Anxious and agitated, restless

2 Co-operative, oriented, tranquil

3 Responsive to verbal commands, drowsy

4 Asleep, responsive to light stimulation (loud noise, tapping)

5 Asleep, slow response to stimulation

6 No response to stimulation

POST OPERATIVE VITALS:

HR(bpm): BP(mm of Hg): SpO_2:

SIDEEFFECTS: DRY MOUTH, NAUSEA, VOMITING, BRADYCARDIA, HYPOTENSION, BRADYCARDIA, RESPIRATORY DEPRESSION, SHIVERING, HEADACHE.

ANNEXURE –2

Patient Information Sheet:

Title: A COMPARATIVE STUDY OF EPIDURAL BUPIVACAINE WITH FENTANYL AND BUPIVACAINE WITH DEXMEDETOMIDINE FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES.

We are carrying out a study comparing epidural bupivacaine with fentanyl and bupivacaine with dexmedetomidine in lower abdominal and lower limb surgeries. The study has been reviewed by the local ethical review board and has been started only after their formal approval.

Epidural anesthesia with insertion of catheter has emerged as a safe technique of anesthesia for lower abdominal and lower limb surgeries, in that the stress response of general anaesthesia can be totally avoided. Dexmedetomidine seems to be a better alternative to fentanyl as an epidural adjuvant as it provides comparable stable hemodynamics, early onset and establishment of sensory anesthesia, prolonged postop analgesia, lower consumption of postop local anesthetics for epidural analgesia, and much better sedation levels. Both dexmedetomidine and fentanyl in the concentration being used in this study have been found to be safe without significant side effects.

In this study we aim to investigate the influence of Dexmedetomidine added to Bupivacaine in lower abdominal and lower limb surgeries for onset and duration of both sensory and motor blockade under epidural anaesthesia and reduction in need for postoperative rescue analgesia.

Participation in this study doesn't involve any cost for the patient. This study is beneficial in maintaining stable hemodynamics of the patient for epidural anaesthesia and also provides post operative analgesia.

All the information collected from the patient will be strictly confidential and will not be disclosed to any outsider unless compelled by law. This information collected will be used only for research.

I request you to kindly give consent for the procedure i.e epidural anesthesia.

There is no compulsion to participate in this study. You will be no way affected if you don't wish to participate in this study. You are required to sign only if you voluntarily agree to participate in this study. Further, you are at a liberty to withdraw from the study at any time, if you wish to do so. Be assured that your withdrawal will not affect your treatment by the concerned surgeon in any way. It is up to you to decide whether to participate. This document will be stored in the safe locker in the department of Anaesthesia in the college and a copy is given to you for information.

ANNEXURE –3

INFORMED WRITTEN CONSENT

I, Mr/Mrs/Ms, exercising my own free will, power of choice, hereby give consent for my self as a subject in the clinical study "A comaparitive study of epidural bupivacaine with fentanyl and bupivacaine with dexmedetomidine for lower abdominal and lower limb surgeries".

The attending doctors have informed me, to my satisfaction and in a language best understood by me, the purpose of this study, the materials to be used during the course of this study as well as the side effects/complications associated with the drug/tools to be used. I shall not hold the doctors or the staff responsible for any untoward consequences. I am also aware of my right to opt out of the study without prejudice to further treatment at any time during the course of the study without having to give any reasons to do so.

Signature of attending doctor:

Signature/Left thumb impression of patient

Date:

Signature of two witnesses

1.

2.

ANNEXURE –4

KEY TO MASTER CHART

M	Male
F	Female
Yrs	Years
Min	Minutes
mm	Millimeters
Hg	Mercury
B	Bradycardia
H	Headache
S	Shivering
N	Nausea
V	Vomiting
RD	Respiratory depression
DM	Dry mouth

ANNEXURE –5

MASTER CHART

S. NO	GROUP	AGE	SEX	IP No.	SURGERY	WEIGHT	HEIGHT	ASA grade	ONSET OF SENSORY BLOCKADE	ONSET OF MOTOR BLOCKADE	BASAL				5min				10min				15min				20min			
		(yrs)				(Kgs)	(cms)		(min)	(min)	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP
1	D	42	Female	4079	TAH	51	162	I	8	14	82	130	84	99	78	126	80	95	74	120	78	92	72	116	76	89	68	112	74	87
2	D	42	Female	14303	EXPLORATORY LAP	50	165	I	9	15	78	128	80	96	76	124	78	93	70	122	74	90	68	118	72	87	64	116	70	85
3	D	50	Female	1018434	TAH	50	156	I	10	18	90	134	86	102	84	130	80	97	80	118	76	90	76	116	72	87	72	114	70	85
4	D	48	Female	22781	VH	52	158	I	8	15	90	130	74	93	82	128	70	89	76	120	68	85	70	116	66	83	64	110	64	79
5	D	26	Male	20479	PFN FEMUR	57	170	I	9	17	84	120	80	93	80	124	72	89	72	120	74	89	68	110	72	85	62	104	70	81
6	D	24	Male	44058	MESHPLASTY	56	170	I	10	16	80	126	78	94	78	126	70	89	70	122	70	87	68	120	68	85	66	106	68	81
7	D	30	Male	44057	IMIL TIBIA	57	166	I	9	17	78	130	80	97	76	128	74	92	72	104	72	83	70	110	70	83	64	110	66	81
8	D	25	Male	35829	DHS FEMUR	56	169	I	8	15	74	124	78	93	70	120	72	88	70	116	70	85	70	110	68	82	70	106	68	81
9	D	25	Male	5326	LCP FEMUR	60	168	I	8	16	80	126	82	97	78	118	74	89	72	110	70	83	68	108	66	80	64	110	64	79
10	D	45	Female	34069	MYOMECTOMY	52	160	I	9	16	92	138	86	103	84	130	80	97	80	124	78	93	74	118	76	90	70	108	74	85
11	D	40	Female	404312	ABD HYSTERECTOMY	51	154	II	8	14	90	140	88	105	86	136	80	99	82	130	76	94	76	126	70	89	64	120	64	83
12	D	42	Female	1018905	TAH	53	157	I	9	16	88	138	86	103	80	124	78	93	76	120	74	89	70	114	72	86	68	105	68	80
13	D	45	Female	25308	EXPLORATORY LAP	55	160	I	10	16	92	134	84	101	88	128	80	96	80	122	76	91	74	110	70	83	60	108	66	80
14	D	27	Male	52802	DHS FEMUR	64	167	I	11	15	78	128	78	95	76	120	74	89	70	104	76	85	64	112	74	87	64	110	72	85
15	D	45	Male	52421	PFN FEMUR	60	168	I	10	18	76	140	76	97	74	114	72	86	70	124	70	88	63	126	70	89	63	130	68	89
16	D	50	Male	35250	TKR	62	160	I	9	11	84	136	80	99	78	128	76	93	72	124	70	88	68	120	68	85	64	118	66	83
17	D	26	Female	50028	IMIL TIBIA	56	163	I	7	15	90	138	82	101	84	128	78	95	78	120	76	91	75	122	74	90	66	120	72	88
18	D	28	Female	13642	FEMUR ORIF	55	168	II	8	17	80	132	80	97	76	120	78	92	70	118	74	89	64	110	72	85	64	100	72	81
19	D	22	Male	49425	PFN FEMUR	51	170	I	10	16	78	120	74	89	70	116	70	85	66	100	68	79	66	98	64	75	67	98	62	72
20	D	38	Female	46351	TAH	52	159	I	8	15	76	126	70	89	74	120	68	85	68	110	64	79	64	108	62	77	64	105	60	75
21	D	40	Female	46270	TAH	56	163	I	10	17	74	114	74	87	70	110	70	83	68	107	72	84	66	104	70	81	64	100	68	79
22	D	43	Female	45188	EXPLORATORY LAP	52	164	I	10	16	78	130	78	95	80	114	74	87	76	118	72	87	70	114	70	85	65	110	70	83
23	D	40	Male	48648	DHS FEMUR	63	168	I	8	18	74	110	80	90	71	110	76	87	64	100	72	81	62	98	72	81	60	96	68	77
24	D	30	Female	1021070	VH	60	167	I	9	15	80	118	80	93	78	100	74	83	70	98	74	82	66	96	72	80	62	94	70	78
25	D	40	Female	1019816	VH	50	161	I	10	16	86	114	72	86	80	120	70	87	68	114	70	85	64	110	68	82	60	108	66	80
26	D	28	Male	130847	IMIL TIBIA	61	160	I	7	11	84	140	76	97	80	136	70	92	82	130	68	89	76	126	66	86	70	120	64	83
27	D	18	Male	119242	MESHPLASTY	55	170	I	10	18	80	120	70	87	78	118	70	86	74	112	68	83	73	110	66	81	71	108	62	77
28	D	45	Female	84997	TAH	52	165	I	7	14	84	114	68	83	80	110	64	79	76	118	66	83	74	110	64	79	70	108	60	76
29	D	48	Female	78080	MYOMECTOMY	60	162	I	7	13	82	120	74	89	78	116	74	88	72	112	72	85	66	110	70	83	64	100	70	80
30	D	40	Male	141107	EXPLORATORY LAP	64	163	I	8	12	80	118	80	93	76	112	78	89	70	110	76	87	68	108	76	87	60	109	74	86
31	F	40	Female	2674	EXPLORATORY LAP	54	158	I	9	16	84	130	88	102	78	126	84	98	75	122	82	95	72	118	80	93	70	114	72	86
32	F	45	Male	36289	PFN FEMUR	52	164	I	12	18	80	128	86	100	76	124	86	99	75	120	84	96	72	112	80	91	72	110	78	89
33	F	40	Female	10973	VH	55	162	I	10	18	90	120	78	92	74	116	74	88	72	115	72	86	70	106	68	81	72	108	68	81
34	F	40	Female	9055	TAH	55	151	II	11	15	78	134	84	101	76	130	82	98	72	126	78	94	70	116	74	88	70	110	72	85
35	F	35	Female	10833	MYOMECTOMY	61	157	I	10	17	80	120	88	99	76	116	80	92	76	118	80	93	74	106	74	85	72	106	72	83
36	F	40	Female	10082	MYOMECTOMY	57	165	II	10	14	80	130	84	99	80	128	82	97	78	120	70	87	74	110	68	82	70	106	70	82
37	F	42	Female	20925	EXPLORATORY LAP	53	154	I	9	18	88	120	82	95	76	120	82	95	70	110	78	89	68	104	74	84	68	104	72	83
38	F	50	Female	22856	WERTHEIMS	50	166	I	10	16	88	130	84	99	86	126	84	98	82	124	80	95	78	120	74	89	78	122	74	90
39	F	40	Female	27133	IMIL TBW	57	150	II	12	18	78	128	74	92	74	120	70	87	70	116	72	87	70	118	66	83	70	118	68	85
40	F	39	Female	38883	LCP FEMUR	58	163	I	10	16	80	130	76	94	72	126	74	91	70	120	70	87	72	110	70	83	72	110	70	83
41	F	19	Female	38894	EXPLORATORY LAP	55	156	I	10	17	74	128	84	99	74	120	82	95	72	118	80	93	70	110	74	86	66	100	70	80
42	F	20	Male	29778	LCP FEMUR	62	170	I	9	18	80	130	80	97	78	122	78	93	74	116	72	87	72	114	70	85	68	114	72	86
43	F	35	Male	125048	MESHPLASTY	51	168	I	13	17	80	124	88	100	78	120	84	96	74	118	80	93	72	110	76	87	64	108	74	84
44	F	44	Male	127594	THR	52	155	I	11	18	84	120	74	89	82	118	74	89	80	110	68	82	74	100	64	76	74	100	64	76
45	F	40	Female	45355	TAH	51	168	I	11	16	78	124	78	93	76	120	76	91	73	116	72	87	68	110	70	83	66	112	66	81
46	F	35	Female	35987	TAH	57	155	I	10	17	90	130	80	97	84	128	78	95	82	120	74	87	80	112	72	85	74	104	74	84
47	F	40	Female	51839	TAH	54	158	I	11	18	88	128	86	100	80	124	80	95	78	118	78	91	74	106	76	86	72	106	74	85
48	F	50	Female	47956	ABD HYSTERECTOMY	57	152	I	10	16	86	124	88	100	82	118	84	95	80	110	80	90	76	110	76	87	74	108	72	84
49	F	42	Female	54959	VH	64	162	I	8	16	92	126	84	98	80	120	80	93	78	116	76	89	74	112	70	84	70	110	72	85
50	F	35	Female	55015	EXPLORATORY LAP	52	157	I	10	17	88	120	86	97	84	116	80	92	80	108	70	87	75	110	68	82	63	112	68	83
51	F	35	Female	53203	EXPLORATORY LAP	51	161	I	10	18	90	110	86	94	78	106	82	90	70	100	80	87	72	98	72	81	70	94	70	78
52	F	48	Female	109796	TAH	60	159	I	13	20	88	120	84	96	86	114	80	91	82	110	76	84	72	100	70	80	64	98	68	78
53	F	22	Male	134657	PFN FEMUR	53	167	I	11	17	88	140	80	100	84	130	78	95	78	124	74	91	74	110	70	83	62	110	60	77
54	F	50	Male	128478	TKR	51	170	I	12	18	78	130	78	95	74	130	70	90	70	128	68	88	68	124	66	85	64	120	64	83
55	F	21	Male	78748	LCP FEMUR	63	165	I	11	16	88	138	74	95	82	128	72	91	80	120	72	88	74	110	68	82	60	110	66	81
56	F	24	Male	107269	PFN FEMUR	57	168	II	10	16	90	136	76	96	88	130	74	83	84	122	70	87	80	106	68	81	68	100	64	76
57	F	50	Male	119187	THR	60	159	I	12	17	84	140	80	100	84	126	78	94	82	120	74	89	80	110	72	85	62	106	68	81
58	F	48	Female	1019844	TAH	52	158	I	11	14	86	138	80	99	82	130	76	94	78	124	70	88	72	104	68	80	70	100	64	76
59	F	28	Male	140357	MESHPLASTY	53	167	I	13	20	88	124	78	93	84	122	74	90	80	110	72	85	74	100	66	77	66	104	64	77
60	F	40	Female	141084	MYOMECTOMY	52	156	I	12	17	78	140	80	100	76	130	76	94	70	116	72	87	68	98	70	79	66	96	68	77

25min				30min				60min				120min				180min				TIME TO TWO SEGMENT REGRESSION	EFFECTIVE DURATION OF ANALGESIA	TIME FOR COMPLETE MOTOR RECOVERY	SEDATION SCORE	VAS SCORE	NO. OF RESCUE TOP UP IN 24 HR	SPO2
HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	(min)	(min)	(min)				
64	110	70	83	60	104	68	80	60	100	68	79	62	100	64	76	60	108	68	81	150	340	230	2	5	4	99
60	114	68	83	56	104	66	79	58	98	64	75	60	104	58	73	62	104	60	75	175	280	220	4	5	3	100
70	112	68	83	60	110	66	81	58	102	60	74	52	98	58	71	50	100	60	73	160	330	220	3	7	5	100
60	108	60	76	56	104	58	73	58	100	60	73	56	100	62	75	48	104	64	77	170	320	218	2	5	4	98
58	100	68	79	60	100	64	76	60	98	62	74	58	100	60	73	60	102	64	77	180	340	220	3	5	4	99
60	100	66	77	58	98	60	73	62	96	70	79	62	98	66	77	64	100	60	73	190	310	224	3	8	3	99
60	108	64	79	60	106	62	77	56	104	62	76	60	102	60	74	62	104	58	73	172	300	220	4	6	4	99
66	106	66	79	64	108	64	79	60	110	60	77	60	106	60	75	56	98	58	71	150	280	194	3	5	3	100
64	100	60	73	60	106	62	77	56	100	58	72	58	98	58	71	60	98	60	73	160	270	200	2	5	1	99
70	104	72	83	64	102	70	81	56	98	64	75	54	96	62	73	50	104	64	77	145	290	200	3	6	4	98
62	116	60	79	60	100	58	69	58	98	60	73	52	98	62	74	50	100	66	77	190	300	240	2	6	3	98
60	110	66	81	58	114	62	79	60	96	60	72	60	100	66	77	62	106	64	78	195	310	230	4	6	3	99
62	100	66	77	64	100	60	73	60	116	62	80	57	118	66	83	60	116	62	80	170	310	224	3	5	2	99
64	112	70	84	68	118	70	86	62	108	68	81	60	110	64	79	62	110	64	79	165	285	240	3	5	3	100
61	120	70	87	58	118	72	87	56	100	70	80	52	104	68	80	50	114	66	82	180	320	220	3	7	3	100
62	116	64	81	60	110	62	78	56	104	60	75	60	108	60	76	60	98	64	75	155	300	236	3	7	3	98
64	114	70	85	62	110	70	83	60	114	72	86	58	118	64	82	60	114	66	82	140	290	190	2	5	3	96
62	98	70	113	60	104	66	79	57	108	64	79	60	98	64	75	60	100	64	76	150	330	200	3	8	3	100
65	100	60	73	64	100	60	73	61	96	58	71	64	100	60	73	61	104	62	76	150	280	184	3	6	2	100
60	100	60	73	58	98	58	71	57	98	60	73	55	90	60	70	49	100	60	73	160	300	210	3	6	4	97
64	98	70	79	62	98	66	77	58	110	60	77	58	110	58	75	62	104	60	75	150	260	230	3	5	1	99
63	112	66	81	66	110	64	79	60	114	62	79	58	108	62	77	60	100	62	75	165	255	230	3	6	1	99
60	94	64	74	58	100	62	75	60	98	58	71	60	100	56	71	62	102	60	74	170	280	240	2	8	4	99
60	94	68	77	60	98	64	75	60	100	60	73	64	104	58	73	60	106	56	73	150	300	220	3	7	4	97
60	100	62	75	58	98	62	74	62	96	60	72	62	90	62	73	58	96	60	72	145	280	200	2	5	2	99
68	120	64	83	62	118	60	79	61	110	64	79	60	110	58	75	66	110	60	77	150	290	215	3	9	2	100
69	110	64	79	65	98	62	74	60	90	64	75	54	100	64	76	50	104	62	76	170	280	210	4	5	4	98
66	106	62	77	64	104	60	75	60	98	58	71	60	108	56	73	60	110	58	75	190	290	180	3	7	3	99
64	98	68	78	60	100	66	77	58	106	66	79	58	100	64	76	56	108	60	76	170	255	180	3	5	3	98
58	110	70	83	58	108	66	80	60	110	62	78	62	98	64	75	60	100	62	75	160	280	194	3	5	1	100
68	108	68	81	68	106	66	70	66	100	66	77	65	104	62	76	66	100	64	76	128	300	180	2	6	4	100
70	110	76	87	68	100	74	83	66	104	72	83	64	104	70	81	66	110	68	82	145	265	140	1	6	5	100
70	106	66	79	70	108	70	83	68	112	66	81	65	108	68	81	65	116	72	87	110	250	140	2	5	5	99
72	110	74	86	68	108	68	81	66	110	64	78	60	110	70	83	62	112	68	83	120	275	155	3	5	4	99
70	110	70	83	72	112	72	85	70	108	70	83	68	100	68	79	66	110	70	83	132	240	170	2	5	4	99
72	104	66	79	74	104	70	81	68	100	60	73	60	102	62	75	68	104	64	77	143	280	180	2	5	4	99
66	102	64	77	64	108	62	77	64	106	64	78	68	110	70	83	70	110	70	83	150	260	140	2	5	6	98
76	120	72	88	74	120	70	87	70	110	80	90	64	114	78	90	74	100	76	84	128	260	160	2	5	4	99
70	114	66	82	68	112	64	80	64	106	60	75	60	100	70	80	48	110	72	85	150	275	170	3	7	4	100
70	100	68	79	70	108	64	79	64	100	64	76	62	108	70	83	66	108	70	83	120	280	164	2	5	4	99
66	110	72	85	64	104	70	81	66	110	68	82	68	100	66	77	67	110	68	82	130	240	172	1	5	4	99
67	114	70	85	64	110	70	83	66	100	70	80	66	102	68	79	68	108	66	80	140	285	180	2	7	3	97
62	110	70	83	60	104	72	83	58	110	62	78	60	114	60	78	64	110	64	79	140	280	170	2	5	4	100
72	100	66	77	70	102	62	75	60	98	60	73	58	100	60	73	60	100	58	72	145	260	166	2	6	3	99
68	110	60	77	64	108	58	75	60	104	62	76	64	100	62	75	62	110	60	77	135	240	150	2	6	3	98
72	106	70	82	70	104	62	76	64	106	64	78	62	100	64	76	62	110	60	77	140	280	170	3	5	4	97
70	104	70	81	70	108	70	83	66	100	68	79	64	98	64	75	66	100	62	75	130	275	175	2	5	4	99
74	110	74	86	70	106	70	82	60	102	62	75	58	104	60	75	50	98	58	71	110	260	145	2	5	4	99
66	104	70	81	64	104	68	80	64	98	60	73	60	94	62	73	64	104	60	75	128	270	150	2	7	4	99
60	110	66	81	56	108	62	79	68	110	58	75	64	104	60	75	66	98	62	74	116	260	160	2	7	4	100
66	96	68	77	68	98	68	78	64	100	60	73	58	100	58	72	68	104	60	75	100	250	170	2	6	3	96
62	100	66	77	60	100	66	77	60	106	62	77	62	110	54	73	60	110	62	78	120	240	180	1	6	3	99
60	108	60	76	60	100	64	76	62	104	64	77	64	104	64	77	68	100	64	76	100	280	185	2	5	5	99
62	116	60	79	56	104	62	76	60	104	60	75	60	100	60	73	62	110	60	77	100	260	180	3	5	4	100
60	108	64	79	68	106	60	75	62	108	60	76	64	110	62	78	66	106	66	79	100	250	190	2	6	4	99
64	104	66	79	58	100	64	76	64	104	64	77	66	110	60	77	64	104	60	75	122	280	175	2	5	4	100
62	110	68	77	64	104	62	76	64	106	62	77	60	104	62	76	62	100	58	72	100	270	170	3	6	4	100
66	104	64	77	60	102	60	74	60	100	62	75	58	98	64	75	60	108	60	76	114	250	155	2	5	4	100
64	100	62	75	60	98	58	71	64	106	64	78	60	94	66	75	50	108	64	79	132	240	160	2	5	4	99
66	98	66	77	62	100	64	76	62	104	64	77	60	100	58	72	60	110	58	75	110	235	170	3	6	3	99

SIDE EFFECTS
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