"A RANDOMISED CLINICAL TRIAL TO COMPARE BETWEEN THE EFFECTIVENESS OF DEXMEDETOMIDINE AND FENTANYL AS ADJUVANTS IN SPINAL ANAESTHESIA"

By

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Under the guidance of

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I hereby declare that this dissertation entitled ***"A RANDOMISED CLINICAL TRIAL TO COMPARE BETWEEN THE EFFECTIVENESS OF DEXMEDETOMIDINE AND FENTANYL AS ADJUVANTS IN SPINAL ANAESTHESIA"*** *is a bonafide and genuine research work carried out by me under the guidance of* ***DR. D.G. TALIKOTI****, Professor and Head, Department of Anaesthesiology, Shri. B. M. Patil Medical College, Hospital and Research centre, Vijayapur.*

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LIST OF ABBREVIATIONS USED

α	:	Alpha
ASA	:	American society of Anesthesiologists
BP	:	Blood pressure
BT	:	Bleeding time
β	:	Beta
CNS	:	Central nervous system
CVS	:	Cardiovascular system
CSF	:	Cerebrospinal fluid
cm	:	Centimetre
cl	:	Clearance
COPD	:	Chroni obstructive pulmonary disease
CT	:	Clotting time
DBP	:	Diastolic blood pressure
ECG	:	Electrocardiography
G	:	Gauge
Hr/h/hr	:	Hour
Inj.	:	Injection
IV	:	Intravenous
Kg	:	Kilogram
KFT	:	Kidney function test
LVAS/VAS	:	Linear visual analogue scale
L/lit	:	litre
µ	:	mu
µg/mcg	:	Microgram

mg	:	Milligram
ml	:	Millilitre
mm	:	Millimetre
min	:	Minute
MAO	:	Monoamine oxidase
MAP	:	Mean arterial pressure
mmHg	:	Millilitre of mercury
PDPH	:	Postdural puncture headache
PR	:	Pulse rate
RR	:	Respiratory rate
SBP	:	Systolic blood pressure
SPO2	:	Peripheral oxygen saturation
Sec	:	Second
Sr.no.	:	Serial number
SD	:	Standard deviation
Vs	:	Versus
Yrs	:	Years

ABSTRACT

BACKGROUND AND OBJECTIVES

Subarachnoid block or spinal anesthesia has increasingly become the technique of choice for surgeries below the diaphragm including lower limb surgeries. Spinal anaesthesia with 0.5% Bupivacaine as a standard drug for infra-umbilical surgeries is still the most commonly used technique. However, insufficient duration of anesthesia and inadequate postoperative analgesia with local ananesthetics like 0.5% Bupivacaine solely is unable to provide an extended duration of anesthesia or postoperative analgesia. In order to maximise duration of anesthesia and postoperative analgesia, a number of adjuvant were added to local anaesthetics. With demonstration of μ opiod receptors in substantiagelatinosa of spinal cord, the deficiency of inadequate duration of anesthesia of local anaesthetics is overcome by addition of opiods like Fentanyl. Dexmedetomidine, a new highly selective alpha2–adrenergic agonist, a potent analgesic, free of some side effects of opiods, is under evaluation as a neuraxial adjuvant to intrathecal local anaesthesia as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects[7,8,9].

Considering the above facts this study was carried out to compare the two adjuvant agents, Dexmedetomidine (5ug) and Fentanyl (25ug) added to 15mg of 0.5% hyperbaric Bupivacaine introduced intrathecally for infraumbilical surgeries.

MATERIALS AND METHODS

90 patients belonging to ASA grade- I and grade-II of both the sexes in 3 groups (each group with 30 patients, n= 30, Group C – hyperbaric bupivacaine, Group D – hyperbaric bupivacaine with dexmedetomidine, Group F – hyperbaric bupivacaine with fentanyl) were randomly selected for the study. The time of onset of sensory and motor block, time to achieve maximum sensory & motor block,

maximum dermatomal levels achieved, time to two segment regression & regression to T12, total duration of block, haemodyamic changes, duration of analgesia and complications were compared among the three groups.

RESULTS

The mean time for onset of sensory and motor block was significantly shorter in Group D and Group F when compared to Group C but were comparable between each other. Mean time to achieve maximum sensory block in Group C (9.41 ± 0.56 min) was significantly longer ($p<0.001$) when compared to group D (7.33 ± 0.73 min) and group F (7.13 ± 0.61 min). Mean dermatomal level achieved in group C (T 6.8 ± 1.09) was statistically significant as compared to group D (T 5.96 ± 0.67) and group F (T 6.2 ± 0.76). Mean time to achieve maximum motor block in group C (8.6 ± 0.57 min) was significantly longer ($p<0.001$) when compared to group D (6.67 ± 0.63 min) and group F (6.41 ± 0.39 min). Mean time to achieve two segment regression of sensory level in group C (92.83 ± 8.37 min) was significantly shorter ($p<0.05$) when compared to group D (146.83 ± 9.14 min) and group F (122.16 ± 11.86 min). Mean time to achieve two segment regression of sensory level in group D was significantly longer than group F, which in turn was longer than group C. Mean time to achieve sensory regression to T12 level in group C (139.5 ± 13.60 min) was shorter as compared to group F (169.66 ± 13.76 min) and group D (2.8.116 ± 16.21 min) and these differences were found to be highly significant statistically ($p<0.001$).

CONCLUSION

From the present study it can be concluded that using Dexmedetomidine as an additive to spinal anaesthesia results in prolonged duration of block, with excellent quality of anaesthesia and prolonged duration of complete analgesia.

Keywords : Intrathecal, fentanyl, bupivacaine, visual analogue scale, dexmedetomidine, quality of anaesthesia, post operative analgesia.

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INTRODUCTION

The concept of pain was linked to the concept of original sin, and the ability to endure pain was regarded as a sign of character.

Subarachnoid block or spinal anesthesia has increasingly become the technique of choice for surgeries below the diaphragm including lower limb surgeries. Spinal anaesthesia is the fastest, predictable and reliable form of anaesthesia for infra-umbilical surgeries[(1)].

Spinal anesthesia is advantageous in that it uses a small dose of the anesthetic, is simple to perform, economical and offers a rapid onset of action, reliable surgical analgesia, less risk of pulmonary aspiration and excellent muscle relaxation. These advantages are sometimes offset by a relatively short duration of action and complaints of postoperative pain when it wears off.

Spanish discovery of the coca leaf in America paved a way for discovery and evolution of local anesthesia. The discovery of spinal anesthesia has been credited to J. Leonard Corning (1855-1923), a neurologist in New York. Lumbar puncture was standardized as a simple clinical procedure by Heinrich Iraneus Quincke (1842-1922) in Keil of Germany in 1891 and Essex Wynter (1862- 1945) in England in the same year.

The first planned spinal anesthesia for surgery in man was administered by August Bier (1 861-1 949) on 16 August 1898, in Kiel, when he injected 3 ml of 0.5% cocaine solution into a 34-year-old labourer. Later on a new era was marked with the introduction of lignocaine, in 1943 by Lofgren[(2)].

Spinal anesthesia has been in use for infra-umbilical surgeries for a long time. Local anaesthetics such as lignocaine and bupivacaine had been used for spinal anesthesia since many years. But as lignocaine is having more neurotoxic effects and

bupivacaine having cardio-toxic effects, local anaesthetics with fewer side effects like ropivacaine and levobupivacaine have been introduced for spinal anesthesia and the search for a perfect one is still going on.

Spinal anaesthesia with 0.5% Bupivacaine as a standard drug for infra-umbilical surgeries is still the most commonly used technique and so in our study 0.5% bupivacaine was used as a control group.

However, insufficient duration of anesthesia and inadequate postoperative analgesia with local anaesthetics like 0.5% Bupivacaine solely' 5 unable to provide an extended duration of anesthesia or postoperative analgesia. Visceral pain is an important component of many clinical pain states[(3)]. Deep pain associated with viscera is different from somatic cutaneous pain.

Moreover, surgeries involving the infra-umbilical region necessitates a good depth of regional anesthesia i.e. the ability to relieve visceral pain which is generally not obtund with use of intrathecal Bupivacaine alone.

This created the need to identify newer techniques and drug combinations which could prolong duration of local anaesthetics as well as provide sufficient analgesia in immediate postoperative period.

In order to maximise duration of anesthesia and postoperative analgesia, a number of adjuvant were added to local anaesthetic such as opioids (morphine, fentanyl), vasoconstrictors (adrenaline), ketamine, midazolam, clonidine etc. to name a few. It has been shown that there is favourable outcome regarding the speed of onset, improved quality of anaesthesia and duration of post operative analgesia on addition of these adjuvants.

Sedation, stable hemodynamics and an ability to provide smooth and prolonged postoperative analgesia are the main desirable qualities of an adjuvant in neuraxial anesthesia [4].

Experimental studies have shown that both opioids and alpha 2 adrenergic agonists administered intrathecally are able to relieve visceral pain[3]. With demonstration of μ opioids receptors in substantia gelatinosa of spinal cord, the deficiency of inadequate duration of anesthesia of local anaesthetics is overcome by addition of opioids like Morphine, Fentanyl, Buprenorphine, sufentanil etc.

Neuraxial administration of opioids along with local anaesthetics improves the quality of intraoperative analgesia and also provides postoperative pain relief for longer duration [5]. Despite their universal ability to alleviate pain, opioids have a number of unpleasant, even potentially dangerous side effects like nausea and vomiting, pruritus, urinary retention and respiratory depression[6]. This has prompted further research to develop non opioids analgesics with less worrisome side effects.

Dexmedetomidine, a new highly selective α2 - adrenergic agonist, a potent analgesic, free of some side effects of opioids, is under evaluation as a neuraxial adjuvant to intrathecal local anaesthesia as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects [7, 8, 9].

Intrathecal Dexmedetomidine potentiates the effect of intrathecal local anaesthetics. This makes alpha 2 agonists very effective adjuvants in regional anesthesia.

Considering the above facts our study was carried out to compare the two adjuvant agent, Dexmedetomidine (5μg) and Fentanyl (25μg) added to 15 mg of 0.5% hyperbaric Bupivacaine introduced intrathecally for infraumbilical surgeries. The

doses and concentrations of the drugs used are on the basis of various studies done earlier by various workers.

AIMS AND OBJECTIVES

After getting institutional ethical committee approval, the present study "**A randomised clinical trial to compare between the effectiveness of dexmedetomidine and fentanyl as adjuvants in spinal anaesthesia**" was conducted with the following aims and objectives :

Primary objectives:

To compare sensory and motor blockade characteristics with -

1) Onset of sensory block.
2) Onset of motor block.
3) Time to achieve maximum sensory block.
4) Time to achieve maximum motor block.
5) Maximum dermatomal level achieved.
6) Time of two segment regression.
7) Time of regression to T12.
8) Total duration of motor block.

Secondary objective:

1) To study and compare the hemodynamic changes between the 3 groups.
2) To study the incidence of side effects between the 3 groups.
3) To study and compare duration of analgesia and post operative analgesia required between the three groups.

REVIEW OF LITERATURE

K. S. Kuusniemi et al in 2000 [10] evaluated the effect of 25 µg of fentanyl added to bupivacaine on sensory and motor block. By using a double blinded study design, 80 men undergoing urologic surgery were randomized into the following four groups :

Group I = Bupivacaine 10 mg

Group II = Bupivacaine 10 mg + Fentanyl 25 µg

Group III = Bupivacaine 7.5 mg + Fentanyl 25 µg

Group IV = Bupivacaine 5 mg + Fentanyl 25 µg

The final volume of intrathecal injectate was adjusted to 2.5 ml with sterile distilled water.

Author found that in Group IV, in which the dose of bupivacaine was the smallest (5 mg), there was no motor block in any of the patients at the end of operation. In this group, there were also six patients (30%) who had no motor block after the injection; yet none of the patients needed supplementation of analgesia during the operation and the surgeons were satisfied with the intensity of the motor block.

There were statistically significant differences between groups in the motor block ($P < 0.001$). Group II resulted in the longest duration of the motor block ($P < 0.001$) and Group IV the shortest duration ($P < 0.001$). Between Groups I and III there was no statistically significant difference in the duration of the motor block.

The degree of motor block was more intense in Group II compared with Group I at the end of operation. The median of the upper limit of the sensory block was greater than T7 in all groups at the 30-min testing time, just before the operation

began. The mean duration of subjective block in Group I was 3 h 53 mm; in Group II, 4 h 48 mm; Group III, 3 h 46 mm; and Group IV, 2 h 16 mm.

The study concludes that the addition of fentanyl 25 µg to bupivacaine 5 mg resulted in short-lasting motor block but the same level of sensory analgesia as larger doses of bupivacaine (7.5-10 mg) with or without fentanyl. When fentanyl 25 µg was added to bupivacaine 10 mg it increased the duration and intensity of motor block.

A. YEGIN et al in 2005 [(11)] evaluated the effect of intrathecal fentanyl 25µg added to 18 mg hyperbaric ropivacaine on the characteristics of subarachnoid block and postoperative pain relief in patients undergoing TURP (Transurethral resection of prostate) surgery.

Thirty one patients classified as physical status I-II according to the American Society of Anaesthesiologists, undergoing TURP under spinal anesthesia were included in this study. This study was conducted in a randomized, double blind, controlled fashion. The patients were randomly assigned into two groups:

Group S (n=16) - 3 ml of 18 mg hyperbaric ropivacaine + 0.5ml saline (Total - 3.5 ml)

Group F (n=15) - 3ml of 18mg hyperbaric ropivacaine fentanyl + 0.5ml of 25µg fentanyl (Total - 3.5ml).

In both groups the onset and recovery times of the sensory block, degree and recovery times of the motor block and side effects were recorded and statistically compared.

There was no significant difference between the groups in achieving the highest level of sensory block, and in the times taken to reach the peak level. Regression to L1 was significantly prolonged in the fentanyl group compared with the saline group (P=0.004). Times to the first feeling of pain and the first analgesic

requirement were significantly prolonged in the fentanyl group compared with the saline group (P=0.011 and P=0.016, respectively). The frequency of pruritus was significantly higher in the fentanyl group compared with the saline group (P=0.022).

Thus study concluded that addition of fentanyl 25µg to hyperbaric ropivacaine 18mg for spinal anesthesia in patients undergoing TURP may significantly improve the quality and prolong the duration of analgesia, without causing a substantial increase in the frequency of major side - effects.

G. E. Kanazi et al in 2006 [9] studied the onset and duration of sensory and motor block, as well as the hemodynamic changes and level of sedation, following intrathecal bupivacaine supplemented with either dexmedetomidine or clonidine.

In a prospective, double - blind study, 60 patients undergoing transurethral resection of prostate or bladder tumour under spinal anesthesia were randomly allocated to one of three groups.

Group B - 12 mg of hyperbaric bupivacaine,

Group D - 12 mg of bupivacaine with 3µg of dexmedetomidine and

Group C - 12 mg of bupivacaine with 30 µg of clonidine.

Dexmedetomidine 100 µg/ml was diluted with preservative free normal saline to 10 µg/ml. Moreover, preservative free normal saline was added to the admixtures in groups B and C to achieve an equal volume of 1.9 ml.

The onset times to reach peak sensory and motor levels, and the sensory and motor regression times, were recorded. Hemodynamic changes and the level of sedation were also recorded.

Author found that patients in groups D and C had a significantly shorter onset time of motor block and significantly longer sensory and motor regression times than patients in group B.

The mean time of sensory regression to the Si segment was 303 ± 75 min in group D, 272 ± 38 mm in group C and 190 ± 48 mm in group B (B vs. D and B vs. C, P < 0.001). The regression of motor block to Bromage 0 was 250 ± 76 mm in group D, 216 ± 35 mm in group C and 163 ± 47 mm in group B (B vs. D and B vs. C, P <0.001).

The onset and regression times were not significantly different between groups D and C. The mean arterial pressure, heart rate and level of sedation were similar in the three groups intraoperatively and post - operatively.

The study concluded that the supplementation of bupivacaine spinal block with a low dose of intrathecal dexmedetomidine or clonidine produces a significantly shorter onset of motor block and a significantly longer sensory and motor block than bupivacaine alone. Dexmedetornidine 3 µg and clonidine 30 µg have an equipotent effect on the characteristics of the block without any significant hemodynamic instability or sedation.

Fauzia A. Khan, Gauhar A. Hamdani in 2006 [(1)] compared the characteristics of spinal block, its postoperative analgesic effects and side effects using intrathecal bupivacaine and its combination with fentanyl or buprenorphine in elderly patients undergoing urological surgery.

Sixty patients aged sixty and above scheduled for elective transurethral resection of prostate (TURP) randomly received either.

Group L -15mg hyperbaric bupivacaine 0.75% 2 ml (n = 20)

Group B- Buprenorphine 30 µg + 15mg hyperbaric bupivacaine 0.75% 2 ml (n = 20)

Group F - Fentanyl 10 µg + 15mg Hyperbaric bupivacaine 0.75% 2 ml (n = 20).

Characteristics of spinal block, haemodynamic stability, postoperative analgesia and incidence of adverse effects were compared. All patients were followed for twenty four hours.

Result found was that the patient's blood pressures remained within 20% of baseline values. The mean time for the sensory block to reach T10 dermatomal level was 3.2 ± 2 minute in fentanyl - bupivacaine group versus 4.3 ± 1 minute in buprenorphine - bupivacaine group and 4.5 ± 2 minute in bupivacaine alone group.

The duration of sensory block was significantly longer in buprenorphine bupivacaine group. Median block levels reached T8 in all groups. All patients required postoperative analgesia in group L and F except 6 in buprenorphine group.

Thus authors concluded that Buprenorphine 30 µg in combination with bupivacaine 0.75% 2 ml provided analgesia of comparable clinical onset and Longer duration but was associated with a clinically increased incidence of nausea and vomiting in elderly patients.

Iheb Labbene, K Lamine et al in 2007 [(12)] compared the efficiency of low dose vs. varying doses of hyperbaric bupivacaine in spinal anesthesia for endoscopic urological procedures.

Sixty consecutive patients were studied in a randomized prospective manner. They received either of 5 mg (Group I), 7.5 mg (Group II) or 10 mg (Group III) of hyperbaric bupivacaine 0.5% combined with 25 µg of fentanyl, through a 25 - gauge Whitacre spinal needle placed in the L3 - L4 interspace. Characteristics of sensory and motor block, dose of ephedrine required, secondary effects, the patients and the surgeons satisfaction were noted.

They found that maximum number of blocked segments was 14 ± 1 (Group I), 15 ± 2 (Group II) and 16 ± 2 (Group III). Time to T12 regression was significantly

shorter for Group I (53 ± 13 mm) than for Group II (69 ± 20 mm) or Group III (94 ± 14 mm). Bromage 3 block was not found in Group I compared to 4 patients in Group II and 15 patients in Group III.

The duration of motor block was shorter in Group I (51 ± 18 mm) than in Group II (86 ± 19 mm) and in Group III (138 ± 21 mm). Ephedrine was used for 16 patients in Group III (9.8 ± 12.2 mg), 5 patients in Group II (3.7 ± 7.8 mg) and 2 patients in Group I (0.5 ± 1 .5 mg). The difference is statistically significant between Group III and the other groups.

The results suggested that the use of a low dose of bupivacaine (5 mg) added to fentanyl (25 µg) for endoscopic urological surgery, resulted in short acting sensory block, without motor block and a lower incidence of cardiovascular side effects, as compared to either of 7.5 or 10 mg bupivacaine with 25 µg fentanyl.

Ishwar singh, Monika gupta et al in 2008 [13] studied fentanyl and sufentanhl in combination with bupivacaine and assessed their effect on duration of sensory block, correlating it with duration of postoperative pain relief.

Fifty ASA grade 1 or 2 patients aged 18-60 yrs scheduled for elective lower abdominal, lower limb and urological procedures were selected. These patients were randomly assigned using sealed envelope technique to two groups in a double blind manner.

Group S - 2.5 ml heavy bupivacaine + 0.2 ml sufentanil made up to 3ml with saline.

Group F - 2.5ml heavy bupivacaine + 0.5ml fentanyl.

They found that there was statistically significant difference in the time of onset of sensory block between Group S and Group F. Mean time to achieve peak sensory level in Group S was 6.6 mm and 8.48 mm in Group F. The difference was statistically significant.

The time to rescue analgesia in Group S was 378.6 ± 178.0 mm and in Group F was 331.0 ± 131.24 mm. The difference was not statistically significant in both the groups.

Hypotension and bradycardia in both groups were statistically insignificant with P value >0.05. Nausea and headache was significant in Group S, whereas none in group F. Therefore they recommend the use of fentanyl over sufentanil for intrathecal administration.

NK Girgin, A Gurbet et al in 2008 [(14)] investigated whether the addition of 25 µg intrathecal fentanyl to levobupivacaine spinal anaesthesia for outpatient inguinal herniorrhaphy allows a sub-anaesthetic levobupivacaine dose to be used.

A prospective, randomized, double-blind study was conducted. Patients accepted for the study were all American Society of Anaesthesiologists (ASA) physical status I - II adults undergoing inguinal hernia repair under spinal anaesthesia. Forty patients were assigned to receive either

Group LF - 5 mg levobupivacaine 0.5% with 25 µg fentanyl or

Group L - 7.5 mg levobupivacaine 0.5%.

They found that the highest median sensory blockade levels achieved were T7 (range T5 - T9) and T6 (range T4 - T9) in groups LF and L, respectively. There were no significant differences between the two groups in terms of the maximum motor blockade score that was achieved and the number of patients that were converted to general anaesthesia.

The time to reach two -segment regression, S2 regression, ambulation, urination and hospital discharge were all significantly shorter in group LF than group L, ($P < 0.05$ for all recovery parameters). There were no significant differences in the

number of episodes of hypotension, bradycardia or respiratory depression requiring treatment between the two groups.

The number of patients experiencing nausea/vomiting and headache was comparable in both groups. In addition, significantly fewer patients requested supplemental analgesic medication in the early post-operative period in group LF than in group L (10.5% versus 47.3%, respectively; $P < 0.05$).

In this study author concluded that, 25 µg intrathecal fentanyl added to low-dose (5 mg) levobupivacaine was shown to prolong the duration of sensory spinal block without increasing the incidence of opioid-related side-effects, except pruritus, or delaying hospital discharge in patients undergoing ambulatory inguinal herniorrhaphy.

In 2009, Hadil Magdi Abdel Hamid, M.D [15] studied effect of combined low-dose clonidine with fentanyl as an adjuvant to spinal bupivacaine 0.5% for anal surgery.

Sixty adult patients belonging to ASA grade I and II, scheduled for anal surgery under spinal anesthesia were randomly divided into 4 groups as follows:

Group CLG - Clonidine group, receive 30 clonidine + bupivacaine 0.5% (n=15)

Group FG -Fentanyl group, receive 25 pg fentanyl + bupivacaine 0.5% (n=15)

Group F/CLG -Fentanyl /clonidine group, receive 15 pg clonidine + 12.5 µg fentanyl + bupivacaine 0.5% (n15)

Group CG - Control group, received only bupivacaine 0.5% (n15).

The spinal anesthesia was performed in sitting position. All patients received 2 ml of the tested drugs. The patients were maintained in the sitting position for 10 mm.

Although the sensory block level was sufficient for surgery to all patients and satisfactory anesthesia were obtained in all patients, the addition of clonidine (15 µg) to fentanyl (12.5 µg) as adjuvant to bupivacaine 0.5%, prolonged the time to first analgesic request and decreased the postoperative pain with minimal risk of hypotension and sedation.

The cephaloid spread of sensory blocks were the same for all groups (mean level L5) ($P>0.05$) and adequate intraoperative anesthesia was achieved in all patients, as no patient require general anesthesia. The motor block was minimal for all patients and was no difference between groups in the extent of motor block 10mm after the spinal placement.

The duration of motor block to reach scale of (0) was comparable for all patients, with no significant difference between them ($p=0.261$). Postoperative pain relief was satisfactory in all patients. The mean time to first request of analgesics was shorter for the control group CG compared to all other groups ($p<0.001$) and also shorter for the FG and the CLG compared to the CL/F ($P<0.001$). There was no difference regarding the incidence of perioperative adverse effects ($p>0.05$).

Thus they concluded that the addition of low doses clonidine to fentanyl as adjuvant to spinal bupivacaine 0.5% significantly increased the duration of spinal analgesia with clinical insignificant influences on hemodynamic parameters and level of sedation.

M. M. Al-Mustafa, S. A. Abu-Halaweh et al in 2009 [8] carried out study to determine the effect of adding different doses of dexmedetomidine to bupivacaine for neuraxial anesthesia.

Sixty six patients were randomly assigned into 3 groups, each receiving spinal bupivacaine 12.5mg combined with normal saline (group N), dexmedetomidine 5 µg (group D5), or dexmedetomidine 10 µg (group D10).

The onset times to reach T10 sensory and Bromage 3 motor block, and the regression times to reach Si sensory level and Bromage 0 motor scale, were recorded.

They found that the mean time of sensory block to reach the T10 dermatome was 4.7 ± 2.0 mm in D10 group, 6.3 ± 2.7 mm in D5, and 9.5 ± 3.0 mm in group N. The mean time to reach Bromage 3 scale was 10.4 ± 3.4 mm in group D10, 13.0 ± 3.4 mm in D5, and 18.0 ± 3.3 mm group N.

The regression time to reach Si dermatome was 338.9 ± 44.8 mm in group D10, 277.1 ± 23.2 mm in D5, and 165.5 ± 32.9 mm in group N. The regression to Bromage 0 was 302.9 ± 36.7 mm in D10, 246.4 ± 25.7 mm in D5, and 140.1± 32.3 mm in group N. Onset and regression of sensory and motor block were highly significant (N versus D5, N versus D10, and D5 versus D10, $p<0.001$).

Thus study concluded that addition of dexmedetomidine precipitated the onset of sensory and motor block, and it prolonged the sensory and motor block significantly when used with bupivacaine in spinal anesthesia in a dose dependent manner.

S. Y. Kim, J. E. Cho et al in 2009 [16] studied the efficacy of intrathecal fentanyl and sufentanil with low-dose diluted bupivacaine for transurethral prostatectomy (TURP) in elderly patients.

Seventy patients undergoing TURP were randomly allocated into two groups.

Group F (n=35) - Fentanyl 25 µg + bupivacaine 0.5% (0.8 ml) + normal saline 0.3 ml

Group S (n35) - Sufentanil 5µg + bupivacaine 0.5% (0.8 ml) + normal saline 0.7 ml in total, bupivacaine 0.25% (1.6 ml) intrathecally.

Onset and duration of the sensory block, the degree of the motor block, side-effects, and the perioperative analgesic requirements were assessed.

Results found was that the median peak level of the sensory block was significantly higher in Group S than in Group F (P=0.049). Group S required fewer perioperative analgesics than Group F (P=0.008). The time to the first analgesic request was longer in Group S (P=0.025).

There were no differences between the groups for the onset and recovery time of the sensory block, degree of the motor block, quality of anaesthesia, or adverse effects.

Thus authors concluded that the low-dose diluted bupivacaine with fentanyl 25 µg or sufentanil 5 µg can provide adequate anaesthesia without hemodynamic instability for TURP in elderly patients. However, sufentanil was superior to fentanyl in the quality of the spinal block produced.

In 2009, K. Koltka, E. Uludag et al [(17)] studied a Comparison of bupivacaine fentanyl in spinal anaesthesia for lower abdominal surgery.

Fifty two male patients of ASA physical status 1 or 2, between 18 and 75 yrs of age and undergoing lower abdominal or urological surgery under spinal anaesthesia were recruited. The patients were randomised and allocated with a sealed envelope technique to receive either.

Group RF -2.6ml 0.75% Ropivacaine (7.5 mg/mi, 19.5mg) ÷ 0.4m1 of Fentanyl 50 µg/mI (3ml total) or

Group BF - 2.6 ml 0.5% Bupivacaine (5mg/ml, 13mg) + 0.4ml of Fentanyi 50 µg/ml (3ml total).

They found that the groups were comparable with respect to age height weight and ASA physical status. There was no significant difference in the type and duration of surgery.

The primary outcome, the duration of motor block, was significantly shorter (p=0.010) in the ropivacaine group, as was the duration of complete motor block and the number of patients with complete motor block (Bromage=3). The patients mobilised sooner in the ropivacaine group. Cephaloid spread of sensory block was higher with bupivacaine than ropivacaine. The duration of sensory block at the level of at least T10 did not significantly differ between groups.

No patient had pruritus, shivering, respiratory depression or nausea and vomiting. No patient had residual neurological deficit, postdural puncture headache or transient neurological symptoms at the postoperative follow-up.

In conclusion, they stated that plain ropivacaine 19.5 mg with fentanyl 20 µg provided effective spinal anaesthesia for lower abdominal surgery. In spite of significant difference in the upper level of sensory block, the quality of block was sufficient and similar to that from plain bupivacaine 13mg with fentanyl 20 µg. But the mean duration of motor block and time to patient mobilisation after ropivacaine spinal anaesthesia was shorter.

Therefore, intrathecal ropivacaine and fentanyl combinations can be recommended when these are important clinical aims. Combinations using

bupivacaine appear the method of choice for operations in which a complete motor block and a longer duration of block is necessary.

Subhi M.Al - Ghanem et al in 2009 [7] evaluated the onset and duration of sensory and motor block as well as operative analgesia and adverse effects of Dexmedetomidine or fentanyl given intrathecally with plain 0.5% bupivacaine for spinal anesthesia.

Seventy six patients classified as American Society of Anaesthesiologists (ASA) status I, II and III scheduled for vaginal hysterectomy, vaginal wall repair and tension free vaginal tape were prospectively studied. Patients were randomly allocated to receive intrathecally either

Group D (n = 38) - 10 mg isobaric Bupivacaine (2 ml) + 5µg Dexmedetomidine in 0.5 ml normal saline or

Group F (n = 38) - 10mg isobaric Bupivacaine (2 ml) + 25µg Fentanyl (0.5 ml).

The onset time to reach peak sensory and motor level, the regression time for sensory and motor block, hemodynamic changes, and side effects were recorded.

They found that, onset time of sensory block to reach T10 dermatome was 7.5 ± 7.4 mm for Group D and 7.4 ± 3.3 mm for Group F (p = 0.95). The time to reach the maximal sensory block was 19.34 ± 2.87 mm for group D and 18.39 ± 2.46 mm for Group F (p = 0.126).

The onset time of modified Bromage 3 motor block was also not different between group D and F; 14.4 ± 6.7 and 14.3 ± 5.7 mm respectively (p = 0.93). The regression time to reach modified Bromage 0 in Group D (240 ± 64 mm) was significantly longer than that for group F (155 ± 46 mm) (p<0.00l).

The time to reach Si segment was significantly longer in group D (274.8 ± 73.4 mm.) than in group F (179.5 ± 47.4 mm.) ($p< 0.001$). The peak sensory level was T6 (T4-T9) in group D and T6 (T3-T8) in group F, without significant difference between the group ($p = 0.88$).

The mean values of mean arterial blood pressure and heart rate were comparable among the 2 groups. The sedation score was between 0 and 1 in both groups. The overall side effects were significantly more in group F than in group D ($P < 0.002$).

Hypotension was mild to moderate in both groups except one patient in group F, who had a blood pressure less than 90 mmHg, and required 36 mg ephedrine to restore his blood pressure. Pruritus was absent in group D, but was present in 5 patients in group F, ($p = 0.169$).

Nausea and vomiting were more in group F, than group D, but it did not reach statistical difference, Five patients (three in group D, and two in group F), required intraoperative analgesia. Two patients in group F complained of postdural puncture headache which was treated by hydration and simple analgesia.

They concluded that in women undergoing vaginal reconstructive surgery under spinal analgesia, 10 mg plain bupivacaine supplemented with 5 µg dexmedetomidine produces prolonged motor and sensory block compared with 25 µg fentanyl.

Erkan Yavuz Akcaboya et al in 2010 [(18)] evaluated the clinical effectiveness and block quality of low dose levobupivacaine, and compared it with low dose bupivacaine when they are combined with fentanyl in transurethral resection of prostate surgery (TURP).

Forty nine ASA physical status 1 - 3 patients undergoing TURF surgery were enrolled in this prospective, randomized and double blind study. Patients in levobupivacaine group received 5 mg levobupivacaine + 25 µg fentanyl and bupivacaine group received 5 mg bupivacaine + 25 µg fentanyl. Demographic data, surgery times, hemodynamic parameters, block qualities, patient and surgeon satisfactions were recorded.

Results found that demographic data; surgery times, patient and surgeon satisfactions were similar in both groups. Hemodynamic parameters were comparable and stable during the procedure in both groups. Sensory block characteristics were comparable and clinically effective in both groups.

While 3 patients in bupivacaine group had Bromage score of 3 at the beginning of the surgery, no patient in levobupivacaine group had this score and this difference was significant (p =0.042). Bromage scores at the end of the surgery were comparable in both groups.

Thus authors concluded that for transurethral prostate surgery 5 mg levobupivacaine with 25 µg fentanyl can provide stable hemodynamic profile, patient and surgeon satisfaction and effective sensorial blockade with less motor blockade in spinal anaesthesia; so it could be used at low doses as a good alternative to bupivacaine.

In 2010, Ozgun Cuvas et al [19] conducted a study to compare the characteristics of spinal blocks produced by 0.5% levobupivacaine with and without fentanyl in transurethral resection and also to test the hypothesis that, fentanyl added to levobupivacaine, may be used as an alternative to pure levobupivacaine solution, in spinal anesthesia.

Forty males, aged >60 years, ASA I-III patients scheduled for elective transurethral resection were included in a prospective, randomized, double-blinded study. Following a spinal tap, intrathecal injection in.

Group L (n 20) - 2.5 ml of 0.5% levobupivacaine and

Group LF (n=20) - 2.2 ml of 0.5% levobupivacaine with fentanyl 15 µg (0.3 ml) was performed.

The characteristics of sensory and motor block, hemodynamic data, side effects, patients and surgeon satisfaction were recorded. Patients were observed until the level of sensory block was Si and the Bromage score was 0.

There were no significant differences between the two groups for patient demographic, intraoperative, hemodynamic parameters, side effects and satisfaction. The highest level of sensory block was T9 in the Group L, and T6 in the Group LF ($p = 0.001$). Duration of motor block was shorter in Group LF. Than in Group L (291.00 ± 81.08 mm in Group L; 213.75 ± 59.49 mm in Group LF) ($p = 0.001$).

They concluded that both regimes are effective, and the addition of fentanyl to levobupivacaine may offers the advantage of shorter duration of motor block and may be used as an alternative to pure levobupivacaine solution in spinal anesthesia, for transurethral resections.

In 2010, R. HAKAN ERBAY et al [(20)] compared effects of low-dose hyperbaric levobupivacaine and low-dose hyperbaric bupivacaine for transurethral procedures in spinal anaesthesia.

In this double-blind, randomized, controlled study, a total of 60 patients who were ASA I-III was randomized into two groups.

Group B - 7.5 mg hyperbaric bupivacaine + 25 µg fentanyl and

Group L - 7.5 mg hyperbaric levobupivacaine + 25 µg fentanyl

The onset time to T10 dermatome, times to maximum sensory and motor block levels, time to two-segment regression of sensory block, time to Bromage score zero, time to full recovery of sensory block, and hemodynamic values, as well as adverse effects, were recorded. The primary outcome was the time to complete regression of motor block.

Results found that the onset time of block to Tb, time to maximum sensory block, and time to two-segment regression were similar in both groups.

The time to maximum motor block was shorter in Group B (7 ± 3 mm) than in Group L (12 ± 5 mm), (P<0.001). The time to a Bromage score of zero (recovery of motor block) was shorter in Group L (105 ± 19 mm) than in Group B (113 ± 7 mm), (P=0.04).

The time to full recovery of sensory block was shorter in Group B (127 ± 14 mm) than in Group L (157 ± 34 mm), (P<0.001). The requirement for analgesia was earlier in Group B (305 ± 50 mm) than in Group L (389 ± 146 mm), (P=0.004).

Author concluded that, although both techniques provide adequate spinal block and have few similar side effects for transurethral surgery, the use of low-dose hyperbaric levobupivacaine plus fentanyl may be preferable to low-dose hyperbaric bupivacaine plus fentanyl because of the reduced motor block, shorter duration of motor block, longer duration of sensory block and longer time to the first requirement for analgesia.

In 2011, P. Motiani, S. Chaudhary et al [(21)] compared the efficacy and safety of intrathecal sufentanil or fentanyl as adjuvant to hyperbaric bupivacaine in patients undergoing major orthopaedic lower limb surgeries in terms of onset and duration of sensory block, motor block and postoperative pain relief.

Ninety patients were recruited in the prospective, randomized double blind study to receive either intrathecal

Group S -Sufentanil 5µg (0.5m1) + 15mg of 0.5% hyperbaric bupivacaine (3ml)

Group F - Fentanyl 25µg (0.5ml) + 15mg of 0.5% hyperbaric bupivacaine (3ml)

Group C -Normal saline (0.5ml) + 15mg of 0.5% hyperbaric bupivacaine (3ml)

A total volume of 3.5ml was injected intrathecally in all patients, irrespective of their height. Normal saline was used to dilute the study drug.

The demographic data, hemodynamic and respiratory parameters were comparable in the three groups. The median maximal block height (T6 dermatome level) achieved was comparable in all three groups. The time to reach maximal block height was significantly less in Group S (4.0 ± 1.5 mm) and Group F (4.73 ± 1.77 mm) as compared to Group C (7.26 ± 2.10 mm).

The time to two segment regression was significantly prolonged in Group S (150.2 ± 21.8 mm) and Group F (143.2 ± 17.3 mm) as compared to Group C (116.6 ± 13.7 mm).

The time to reach Bromage 1 was found to be comparable among the groups (9.6 ± 3.4, 9.3 ± 2.8 and 9.5 ± 4.2 mm in Groups S, F and C respectively) ($p>0.05$).Time to resolution to Bromage 6 was significantly prolonged in Group S (224.3 ± 24.3 mm) as compared to Group C (207.1 ± 22.2 mm) ($p=0.016$ between Groups S and C). It was prolonged though not significantly in Group F (211.5 ± 23.7 mm) ($p>0.05$ between Group F and C).

In all three groups sedation score never exceeded 2 in any patient. Minimum sedation score (0 ± 0) was achieved at 120 mins in Group S, at 105mins in Group F and at 75 mins in Group C implying prolonged sedation in Group S.

Maximum VAS scores were reached within 2 hours in Group C (2.9 ± 2.1), as compared to 6 hours in Group F (3.2 ± 1.7) and 8 hours in GroupS (2.6 ± 1.6). The duration of complete analgesia was significantly longer in Group S (312.3 ± 86.6 mm) and Group F (282.1 ± 59.7 mm) as compared to Group C (189.3 ± 29.9 mm).

Duration of effective analgesia was significantly prolonged in Group S (529.3 ± 96.6 mm) and Group F (485.1 ± 82.7 mm) as compared to Group C (256.3 ± 60.2 mm). The groups were comparable in terms of side effects such as nausea and vomiting, shivering, urinary retention and PDPH. The incidence of pruritus was significantly higher in group S as compared to group C.

This study concluded that intrathecal sufentanil (5µg) and fentanyl (25µg), as adjuvants leads to an earlier onset and prolonged duration of sensory block. The duration of effective analgesia with intrathecal sufentanil and fentanyl as adjuvants to hyperbaric bupivacaine is longer than that of bupivacaine alone.

In 2011, Mohammed Shawagfeh et al [(22)] assessed the usefulness and efficacy of low-dose Bupivacaine with Fentanyl spinal anesthesia for prevention of hypotension while maintaining good anaesthetic conditions.

This prospective study included 100 patients who underwent lower abdominal, anorectal, orthopaedic and obstetric surgery under spinal anesthesia technique. Patients were divided into two groups each with fifty patients.

Group (F) - 7.5-9 mg of 0.5% heavy bupivacaine + 25µg fentanyl.

Group (B) - 12.5-15mg of 0.5% heavy bupivacaine.

The study was randomized and double-blind regarding the anesthesia solution, with the subjects being assigned to a study group or a control group using a sealed envelope technique.

Results found were that the number of dermatomes blocked was relatively comparable in both groups as well as the median upper limit of the sensory block. Recovery of motor function took place significantly earlier in Group F compared with Group B (110.6 minute vs. 134.4 minute).

Time to reach peak sensory level was earlier in group F, however did not differ significantly. Although the two segment regression was slower in Group B compared with Group F, but it did not seemed to be significant. But time for sensory recovery was earlier in group F than group B, (174.3 minute vs. 191.2 minute).

No differences were found between the groups in the total analgesic consumption, or the number of patients who required postoperative analgesics in the recovery room. Lowest SBP (<30%) occurred in Group B (13 patients) and was significantly higher than those of Group F (3 patients), while incidence of bradycardia was comparable in both groups.

Total amount of the ephedrine used for treatment of hypotension was higher in Group B than Group F (97.5 mg vs. 20mg respectively). Other adverse effects seem to be comparable in both groups except for pruritus that is higher in group F.

Conclusion of this study was that a reduced dose of bupivacaine in combination with fentanyl provided reliable spinal anesthesia in adults for variable kinds of surgical procedures with few events of hypotension and little need for vasopressor support of blood pressure. It offers a reliable block, good post-operative analgesia and satisfactory for the patient and surgeon.

Hala MD, Mohamed MD et al in 2011 [23] studied the effect of intrathecal administration of dexmedetomidine on the duration of sensory and motor block and postoperative analgesic requirements produced by spinal bupivacaine.

Forty eight adult patients scheduled for anterior cruciate ligament reconstruction were randomized to one of three groups. Each patient was given 3.5 ml spinal injectate that consisted of 3 ml 0.5% hyperbaric bupivacaine and 0.5 ml containing either 10 µg dexmedetomidine (Group Dl), 15 µg dexmedetomidine (D2) or normal saline (Group B).

Heart rate, arterial blood pressure, sensory level, motor block, pain and level of sedation were assessed intraoperatively and upto 24 hours after spinal anesthesia. The incidence of adverse effects was recorded.

Study found that there was a dose dependant prolongation of the duration of sensory and motor block by the addition of intrathecal dexmedetomidine. Time to two segment regression, sensory level regression to SI and motor block regression to modified Bromage 0 were significantly prolonged in group D2 than in group Dl and group B and in group Dl than in group B.

Similarly, the duration of analgesia was significantly different among the groups. Group D2 had a significantly longer time to first analgesic requirement than both group B and group Dl and group Dl had a significantly longer time to first analgesic requirement than group B.

Doses of diclofenac taken over the 24-hour study duration were significantly lower in group D2 than in groups Dl and B, the difference between group DI and B was not statistically significant.

Dexmedetomidine significantly prolonged time to two segment regression, sensory regression to SI, regression of motor block to modified Bromage 0 and time

to first rescue analgesic. In addition, it significantly decreased postoperative pain scores.

The effects were greater in group D2 than in group Dl. In addition, group D2 patients had higher sedation scores and lower postoperative analgesic requirements than Group Dl or B. Hemodynamic stability was maintained in the three groups.

Author concluded that intrathecal dexmedetomidine in doses of 10 µg and 15 µg significantly prolong the anaesthetic and analgesic effects of spinal hyperbaric bupivacaine in a dose-dependent manner. A 15 µg dose may be of benefit for prolonged complex lower limb surgical procedures.

R. Gupta, J Bogra et al in 2011 [(24)] studied efficacy and safety of dexmedetomidine with isobaric ropivacaine for postoperative analgesia in patients undergoing lower limb surgeries.

The primary outcomes studied were time to regression of spinal blockade below level S2 and duration of pain relief. Postoperative cumulative analgesic consumption and maximum visual analog scale (VAS) pain score have been evaluated as secondary outcome.

Sixty patients were randomly allocated to receive intrathecally either Group R - 3m1 of 0.75% isobaric ropivacaine + 0.5m1 normal saline or Group D - 3ml of 0.75% isobaric ropivacaine + 5µg dexmedetomidine in 0.5m1 normal saline.

Author found that the mean time of sensory regression to S2 was 468.3 ± 36.78 mm in group D and 239.33 ± 16.8 mm in group R. Duration of analgesia (time to requirement of first rescue analgesia) was significantly prolonged in group D (478.4 ± 20.9 mm) as compared to group R (241.67 ± 21.67 min).The maximum visual analogue scale score for pain was less in group D (4.4 ± 1.4) as compared to group R(6.8 ±2.2).

Thus author concluded that the addition of dexmedetomidine to ropivacaine intrathecally produces a prolongation in the duration of the motor and sensory block and provides excellent quality of postoperative analgesia with minimal side effects.

Rajni Gupta et al in 2011 [25] carried out study to evaluate the onset and duration of sensory and motor block, hemodynamic effect, postoperative analgesia, and adverse effects of dexmedetomidine or fentanyl given intrathecally with hyperbaric 0.5% bupivacaine.

Sixty patients classified in ASA classes 1 and 2 scheduled for lower abdominal surgeries were studied. Patients were randomly allocated to

Group D (n30)- 12.5mg hyperbaric bupivacaine (2.5 ml, 0.5%) ÷ 5µg dexmedetomidine in 0.5 ml normal saline or

Group F (n=30) - 12.5mg hyperbaric bupivacaine (2.5 ml, 0.5%) + 25µg fentanyl (0.5 ml) intrathecal.

They found that there was no difference between groups D and F in the highest level of block achieved in the two groups (T5 and T6 respectively) or in the time to reach peak level.

Block regression was significantly slower with addition of intrathecal dexmedetomidine as compared with fentanyl, as both time to two segment regressions and time to S2 regression were significantly more with intrathecal dexmedetomidine.

There was no difference in the onset time to Bromage 3 motor block (11.6 ± 1.8 mm in group D and 11.2 ± 1.3 mm in group F) but the regression of motor block to Bromage 0 was significantly slower with addition of dexmedetomidine.

The mean time of sensory regression to S1 was 461 ± 23 mm in group D and 187 ± 21mm in group F ($P<0.001$). The regression time of motor block to reach

modified Bromage 0 was 421 ± 21 mm in group D and 149 ± 18 mm in group F (P<0.001).

The time to rescue analgesia was significantly longer in group D as compared to group F. The requirement of diclofenac in the first 24 hr was significantly lower in group D as compared to group F.

Although the patients in both groups remained hemodynamically stable intraoperatively, the sedation score was more in group D patients. The mean sedation score was 3.8 ± 0.5 in group D as compared to 2.2 ± 0.53 in group F, which was statistically significant (p<0.05).

There was no significant difference in complications, such as nausea, vomiting, shivering, itching, sedation, respiratory depression, and hypotension, in patients of either group. Intraoperative ephedrine requirement was more in group D (10 ± 4 mg) as compared to group F (6 ± 3 mg). No patient had residual neurological deficit, postdural puncture headache or transient neurological symptoms.

Thus they concluded that intrathecal dexmedetomidine is associated with prolonged motor and sensory block, hemodynamic stability, and reduced demand for rescue analgesia in 24hr as compared to fentanyl.

B. Kumar, A. Williams et al in 2011 [26] compared the safety and efficacy of anesthesia and analgesia of intrathecal bupivacaine-butorphanol mixture with intrathecal bupivacaine-fentanyl mixture.

In a prospective, randomized, double-blind study, eighty patients aged above l8yrs, of ASA physical status 1 or 2, undergoing lower limb orthopaedic surgeries were randomly allocated to two groups of 40 patients each.

Patient in group A and group B received intrathecal 2.5m1 of hyperbaric bupivacaine (0.5%), with 25pg of fentanyl and 25pg of butorphanol, respectively.

Results found were that the times required for onset of sensory and motor blockade were comparable among the two groups. Significantly slower block regression to S2 level was observed in the group receiving intrathecal butorphanol as compared to intrathecal fentanyl (P=0.0230).

The time of onset of maximum motor blockade (P=0.1288) and time to reach grade 1 motor blockade (P=0.1080) were similar among the two groups. Patients receiving butorphanol had lower LVAS pain scores at all observed times than patients who received fentanyl, although this difference in LVAS scores reached statistical significance only at l hr postoperative duration (P=0.0260).

A higher number of patients in the fentanyl group requested for rescue analgesia during the postoperative study period than the butorphanol group (9 versus 2; P0.0238). The average times to first request for rescue analgesia were 308 ± 14.9 mins and 365 ± 12.3 mins in group A and B respectively (P0.0254).

Thus author concluded that both 25pg fentanyl and 25pg butorphanol given intrathecally along with 12.5mg of hyperbaric bupivacaine provide effective anesthesia for lower limb surgeries. Intrathecal bupivacainebutorphanol mixture provides longer duration of sensory blockade and superior analgesia than intrathecal fentanyl-bupivacaine mixture.

D. Shukla, A.Verma et al in 2011 [27] in a prospective randomized double-blind study evaluated the onset and duration of sensory and motor block as well as perioperative analgesia and adverse effects of dexmedetomidine and magnesium sulfate given intrathecally with 0.5% hyperbaric bupivacaine for spinal anesthesia.

A total of 90 patients classified as American Society of Anaesthesiologists status I and II scheduled for lower abdominal and lower limb procedures were prospectively studied.

Patients were randomly allocated to receive intrathecally either

Group D - 15 mg hyperbaric bupivacaine + 0.1 ml (10 µg) dexmedetomidine (n=30)

Group M -15 mg hyperbaric bupivacaine + 0.1 ml (50 mg) magnesium sulphate (n30) or

Group C -15 mg hyperbaric bupivacaine + 0.1 ml saline (n=30) as control.

The onset time to reach peak sensory and motor level, the regression time for sensory and motor block, hemodynamic changes and side-effects were recorded.

The onset times to reach T10 dermatome and to reach peak sensory level as well as onset time to reach modified Bromage 3 motor block were significantly different in the three groups. The onset time to reach peak sensory and motor level was shorter in group D as compared with the control group C, and it was significantly prolonged in group M.

They also found that patients in group D had significant longer sensory and motor block times than patients in group M, which was greater than in the control group C.

They concluded that the onset of anesthesia was rapid and of prolonged duration in the dexmedetomidine group (D). However, in the magnesium sulfate group (M), although onset of block was delayed, the duration was significantly prolonged as compared with the control group (C), but to a lesser degree than in the dexmedetomidine group (D). The groups were similar with respect to hemodynamic variables and there were no significant side-effects in either of the groups.

Marzieh-Beigom Khezri et al in 2012 [28] carried out study to compare the analgesic efficacy and side effects of magnesium and fentanyl as an additive to intrathecal bupivacaine.

In a prospective, randomized controlled trial ninety adult patients scheduled for femur surgery under spinal anesthesia were randomly allocated to one of the following three groups to receive intrathecally either:

Group M - Bupivacaine 15 mg combined with 0.5 ml 10% $MgSO_4$

Group F -Bupivacaine 15 mg combined with 0.5 ml Fentanyl or

Group C - Bupivacaine 15 mg combined with 0.5 ml distilled water.

The time to first analgesic request, sensory and motor blockade onset time, duration of sensory and motor blockade, analgesic requirement in the first 12 hours after surgery, and The incidences of hypotension, bradycardia, hypoxemia and ephedrine were recorded.

Results found that Magnesium caused a significant delay in the onset of both sensory and motor blockade compared with the fentanyl (95% Cl 3 to 4; $p<0.001$) and control (95% Cl 3.5-5; $p < 0.001$) groups. The duration of spinal analgesia in group F (fentanyl) was significantly greater than in group C (control) (95% Cl 365-51 3; $p < 0.001$) and group M (magnesium) (95% Cl 385- 523; $p < 0.001$).

The total amount of methadone consumption over 12 hours was significantly lower in the magnesium and fentanyl groups than in the control group (5 mg vs. 5.666 ± 1.728 mg; $p = 0.04$).

Thus authors concluded that addition of intrathecal magnesium sulphate to spinal anesthesia induced by bupivacaine significantly prolonged the onset of both sensory and motor blockade compared with fentanyl. Although magnesium failed to prolong the time to first analgesic requirement as seen with fentanyl, it reduced the total consumption of opiolds in the first 12 hours postoperatively compared with the control group.

Ashraf A. Mohamed, MD et al in 2012 [29] studied comparison of the analgesic efficacy of intrathecally administered dexmedetomidine or dexmedetomidine combined with fentanyl in patients undergoing major abdominal cancer surgery.

In randomized, double-blind trial ninety patients were randomly assigned to receive intrathecally either

Control group - 10 mg bupivacaine 0.5% + l ml normal saline

Dexmedetomidine group - 10 mg bupivacaine 0.5% + 5 pg dexmedetomidine

Dexmedetomidine+ group - 10 mg bupivacaine 0.% + 5 µg dexmedetomidine and 25pg fentanyl (n = 30) each.

Assessment parameters included were hemodynamics, sedation score, pain severity, time of first analgesics request, total analgesic consumption, and side effects in the first 24 hours.

Result found was that the mean intraoperative heart rate was significantly reduced in the dexmedetomidine group ($P < 0.05$) and the dexmedetomidjne + group ($P < 0.05$) compared with the control group. Also, there was a significant reduction in mean intraoperative systolic and diastolic blood pressure in the dexmedetomidine group ($P < 0.05$) and the dexmedetomidine+ group ($P < 0.05$) compared with the control group, with no significant differences in postoperative hemodynamics or sedation scores among all the study groups.

The mean visual analog scale scores showed a significant reduction immediatandy and at 12 hours postoperatively in both the dexmedetomidine and dexmedetomidine+ groups compared to the control group.

The mean time of the first analgesic request was significantly prolonged in the dexmedetomidine group (3.30 ± 0.87 hours, $P < 0.01$) and the dexmedetomidine +

group (5.41 ± 1.23 hours, P <0.01) compared with the control group (0.23 ± 0.11 hours).

Moreover, postoperative tramadol consumption was significantly reduced in the dexmedetomidine (142.85 ± 13.04 mg, P < 0.01) and the dexmedetomidine + (131.25 ± 11.96 mg, P < 0.01) groups, compared with the control group (310.0 ± 12.08 mg). No significant serious adverse effects were recorded during the study.

Thus authors concluded that Dexmedetomidine 5 µg given intrathecally improves the quality and the duration of postoperative analgesia and also provides an analgesic sparing effect in patients undergoing major abdominal cancer surgery. Furthermore, the addition of intrathecal fentanyl 25 µg has no valuable clinical effect.

In 2012, Amit Jam, Kajal Jam and Neerja Bhardawaj [(30)] studied whether a combination of low-dose neostigmine intrathecally would enhance analgesia of a fixed dose of fentanyl intrathecally, in patients undergoing unilateral total knee replacement (TKR) surgery with spinal anesthesia.

Forty five patients scheduled for unilateral TKR were randomized to one of the three groups (n= 15) and prospectively studied using placebo controlled, double blinded design.

Group 1 - 15mg hyperbaric bupivacaine (3m1) + Normal saline (O.5ml)

Group 2 - 15mg hyperbaric bupivacaine (3m1) + fentanyl 20µg (O.4ml) ÷ normal saline (O.lml)

Group 3 - 15mg hyperbaric bupivacaine (3m1) + fentanyl 20µg (O.4m1) + neostimine 1 µg (O.lml).

Characteristics of sensory and motor block, heart rate, and blood pressure were recorded intraoperatively. Postoperatively, pain scores, postoperative nausea and vomiting scores, sedation scores, and postoperative analgesic dose were recorded.

They found that overall 24hr VAS score in group 3 was significantly less than in those who received fentanyl alone. The duration of complete and effective analgesia were longer for all patients in group 3 compared with group 2 (p<O.05) and group 1 (p<O.005) patients. The total number of epidural top ups (rescue analgesia) required was less in group 2 (p<O.05) and group 3 (p<O.005) patients, compared with control group. The incidence of nausea and vomiting was not increased in group 3 patients.

They concluded that the addition of lug neostigmine intrathecally increased the duration of analgesia and decreased the analgesic consumption in 24 hr in TKR. There was no increase in the incidence of adverse effects.

In 2012, Sangeeta Varun, MD et al[31] conducted a prospective, randomized, double blind study with an aim of comparing the effect of isobaric bupivacaine with fentanyl to isobaric ropivacaine with fentanyl with regards to sensory blockade, motor blockade and quality of analgesia in postoperative period.

After ethical committee approval and consent, 100 patients, aged 18 to 60 years, undergoing lower abdomen and lower limb surgery were included in the study. The patients were randomly divided into two groups:

Group I - 3 ml 0.5% isobaric bupivacaine + 20µg fentanyl.

Group II - 3 ml 0.5% isobaric ropivacaine + 20µg fentanyl.

The parameters observed included time of onset of sensory blockade, extent of sensory blockade, degree of motor blockade and duration of analgesia. The heart rate, blood pressure, oxygen saturation and respiratory rate were recorded.

They found that demographic parameters, duration of surgery and the types of surgery were comparable in the two groups. The time taken to achieve Tb, T8 and T6 level of sensory block was significantly more (p<0.O5) in Group II as compared to

Group I, but time to sensory block level was comparable (p<0.98I). Mean time taken to achieve maximum grade of motor blockade was lesser in Group I as compared to Group II (p<0 001).

The sensory block regression to S2 was faster in Group II as compared to Group I (p0.025). The motor recovery was comparable in the two groups (p=O.264). The duration of analgesia was prolonged in Group I as compared to Group II (p0.027).

The mean pulse rate was comparable in the two groups (p >0.05). The mean arterial blood pressure (MAP) was comparable (p>0.05) except between 10 mm to 30 mm intervals where MAP was relatively lower in group I (p<0.05). The episodes of hypotension was higher in Group I (p0.001).

They concluded that intrathecal administration of ropivacaine-fentanyl has faster onset and regression of sensory block, delayed onset but comparable regression of motor block and shorter duration of analgesia as compared to intrathecal bupivacaine-fentanyl.

R. JamlIya, V. Deshmukh et al in 2013 [(32)] conducted study to evaluate the onset and duration of sensory and motor block as well as operative analgesia and adverse effects of dexmedetomidine given intrathecally with hyperbaric 0.5% bupivacaine or hyperbaric 0.5% bupivacaine alone for spinal anaesthesia.

Sixty patients classified as American Society of Anaesthesiologists (ASA) status I, II and III scheduled for lower limb orthopaedic surgeries were prospectively studied. Patients were randomly allocated to receive intrathecally either

Group D (n = 30) - 15mg hyperbaric bupivacaine (0.5%, 3ml) + 5 µg dexmedetomidine in 0.5ml normal saline or

Group S (n = 30) - 15 mg hyperbaric bupivacaine (0.5%, 3m1) + 0.5m1normal saline.

The onset time to reach peak sensory and motor level, the regression time for sensory and motor block, hemodynamic changes, and side effects were recorded.

Patients in group D had significant longer sensory and motor block times than patients in group S. The mean time of sensory regression to SI was 306 ± 21.8 mm in group D and 192 ± 9.9mm in group S ($p < 0.05$).

The regression time of motor block to reach modified Bromage 0 was 236 ± 16.6 mm in group D and 162.5 ± 7.5 mm in group S ($P < 0.05$). The onset times to reach T10 dermatome as well as onset time to reach modified Bromage 3 motor block were slightly higher in group D.

They concluded that in patients undergoing lower limb orthopaedic surgeries surgery under spinal analgesia, I5 mg hyperbaric bupivacaine supplemented with 5 pg dexmedetomidine produces prolonged motor and sensory block compared with hyperbaric 0.5% bupivacaine alone.

Ji.Kim, N.Kim, H.Lee and H.KiI in 2013 [(33)] evaluated the adjuvant effects of intrathecal dexmedetomidine in elderly patients undergoing transurethral prostate surgery with low-dose bupivacaine spinal anesthesia.

Fifty-four patients undergoing transurethral resection of prostate surgery were randomized into two groups receiving either

Group D - 3µg dexmedetomidine (0.3m1) + 6 mg of 0.5% hyperbaric bupivacaine (n=27) or

Group S - normal saline (0.3ml) + 6 mg of 0.5% hyperbaric bupivacaine (n=27). Total volume = 1.5 ml

The characteristics of the spinal block and postoperative analgesic effects were evaluated. The peak block level was similar for the two groups. However, the dexmedetomidine group demonstrated a faster onset time to the peak block and longer duration of spinal block than the saline group ($p<0.01$).

The motor block scales at the time of peak sensory block and regression of 2-sensory dermatomes were higher in the dexmedetomidine group than in the saline group ($p<0.001$). There was less analgesic request and the time to the first analgesic request wasionger in the dexmedetomidine group than in the saline group (each 487, 345 mm, $p<0.05$).

Thus author study showed that 3 pg of dexmedetomidine added to 6 mg of bupivacaine produced a fast onset and long duration of sensory block as well as a prolonged postoperative analgesia compared to bupivacaine alone.

Although, the dexmedetomidine group showed higher motor block scales at the time of 2-sensory dermatomal regression as well as at the time of peak sensory block, none of the patients reported discomfort in the lower extremities at the time of discharge.

B.Maharani, M. Prakash et al in 2013 [(34)] compared the onset and duration of sensory and motor block, perioperative analgesia, side effect profile of dexmedetomidifle and buprenorphine when used as adjuvant to bupivacaine in spinal anaesthesia for surgeries below the level of umbilicus.

Sixty patients of ASA I and II scheduled for lower abdominal and lower limb surgeries were randomly allocated in to two groups and received the following drugs

Group A - 15 mg of 0.5% hyperbaric bupivacaine + 10 µg of dexmedetomidine

Group B - 15 mg of 0.5% hyperbaric bupivacaine + 60 µg of buprenorphine.

Sensory and motor blockade characteristics (onset time, time to reach maximum level and regression), time for rescue analgesia and side effects were recorded.

They found that addition of dexmedetomidine as adjuvant to bupivacaine had significantly shortened the onset of sensory blockade (100.50 ± 31.74 mm and 122.13 ± 36.25 mm, $P<0.05$), prolonged the duration of motor and sensory block ($P<0.001$, $P<0.001$ respectively) and had postponed the time for first analgesic request (295.83 ± 93.21 mm and 238.27 ± 110.36 mm, $P<0.05$) without any side effects when compared to buprenorphine ($P<0.05$, $P<0.001$).

Nausea, vomiting and respiratory depression was significantly present only in group B receiving buprenorphine ($P< 0.05$). It had also produced bradycardia, pruritus and shivering which are not significant. Both the group patients were arousable throughout the surgery.

The incidence of residual neurological deficit, postdural puncture headache or transient neurological symptoms during the postoperative follow up was nil in both groups.

Author concluded that 10 µg of dexmedetomidine seems to be a better alternative to 60 µg of buprenorphine when added as adjuvant to bupivacaine in spinal block for lower abdominal and lower limb surgeries below the level of umbilicus.

PHARMACOLOGY

PHARMACOLOGY OF BUPIVACAINE: [35-38]

Bupivacaine is a widely used amide local anesthetic agent and its structure is similar to that of Ropivacaine except that the butyl group is attached to the nitrogen atom of the piperidine ring. First synthesized by Ekenstan A.F and his colleagues in 1957 and used clinically by Telivuo in 1963.

Bupivacaine is a potent agent capable of producing prolonged anesthesia. Its long duration of action plus its tendency to provide more sensory than motor block has made it a popular drug for providing prolonged analgesia during labor or the postoperative period. By taking advantage of indwelling catheters and continuous infusions, Bupivacaine can be used to provide several days of effective analgesia.

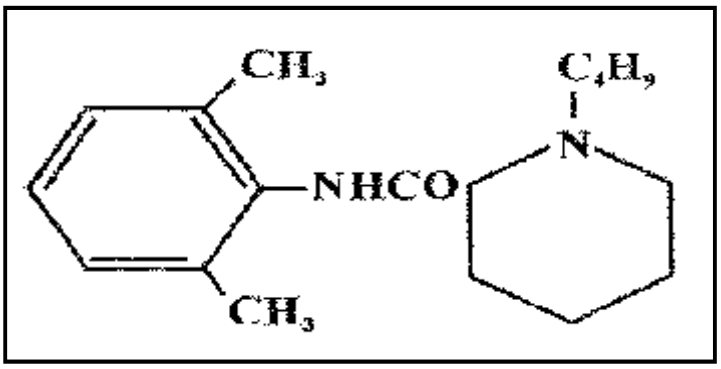


Figure 2: Structure of Bupivacaine

Physiochemical properties:

- Molecular formula : $C_{18}H_{28}N_2O$
- Molecular weight : 288.43 g/mol
- Solubility in water : 25 mg/ml
- pH of saturated solution : 5.2
- pKa : 8.1
- Specific gravity : 1.021 at 37^0C

Mechanism of action: [39]

Mechanism of action of Bupivacaine is similar to that of any other local anesthetic agent. The primary action of local anesthetics is on the cell membrane axon, on which it produces electrical stabilization. Bupivacaine prevents the generation and the conduction of the nerve impulse. Bupivacaine blocks conduction by decreasing or preventing the large transient increase in permeability of excitable membranes to sodium that normally is produced by a slight depolarization of the membrane. This action of Bupivacaine is due to its direct interaction with the voltage gated sodium channels. As the anesthetic action progressively develops in a nerve, the threshold for electrical excitability gradually decreases, the rate of rise of the action potential declines, impulse conduction slows, and the safety factor for conduction decreases, these factors decrease the probability of propagation of the action potential and nerve conduction fails.

The mechanism by which local anesthetics block sodium conductance is as follows:

1) Local anesthetics in the cationic form act on the receptors within the sodium channels on cell membrane and block it. The local anesthetics can reach the sodium channel either via the lipophilic pathway directly across the lipid membrane, or via the axoplasmic opening. This mechanism accounts for 90% of the nerve blocking effects of amide local anaesthetics.
2) The second mechanism of action is by membrane expansion. This is a non-specific drug receptor interaction.

Dosage depends on

Area to be anesthetized, number of nerve segments to be blocked, individual tolerance, technique of local anesthesia, vascularity of area. Bupivacaine is available in the following concentrations:

- 0.25%, 0.5%and 1%
- 0.25% and 0.5% solution in isotonic saline.
- 0.5% solution in 8% dextrose.
- Dosage is 2mg/kg limited to 150 mg in four hours.
- The intrathecal minimum local analgesic dose of Bupivacaine is 2.37 mg.[40]

Pharmacokinetics

The concentration of Bupivacaine in blood is determined by the amount injected, the rate of absorption from the site of injection, the rate of tissue distribution and the rate of biotransformation and excretion of Bupivacaine.

Absorption

The site of injection, dose and addition of a vasoconstrictor determine the systemic absorption of Bupivacaine. The maximum blood level of Bupivacaine is related to the total dose of drug administered from any particular site. Absorption is faster in areas of high vascularity.

Distribution

The two-compartment model can describe this. The rapid distribution phase α is believed to be related to uptake by rapid equilibrating tissue i.e., tissues that have high vascular perfusion. The slow distribution phase β is mainly a function of distribution to slowly equilibrating tissue, biotransformation and excretion of the compound. More highly perfused organs show higher concentrations of the drug.

Bupivacaine is rapidly excreted by lung tissue. Though skeletal muscle does not show any particular affinity for Bupivacaine it is the largest reservoir of the drug.

Actions

Central Nervous System

Bupivacaine readily crosses the blood brain barrier causing CNS depression following higher doses. The initial symptoms involve feeling of lightheadedness and dizziness followed by visual and auditory disturbances. Disorientation and occasional feeling of lightheadedness may occur. Objective signs are usually excitatory in nature, which includes shivering, muscular twitches and tremors, initially involving muscles of the face (perioral numbness) and part of extremities. At still higher doses cardiovascular or respiratory arrest may occur. Acidosis increases the risk of CNS toxicity from Bupivacaine, since an elevation of PaCO2 enhances cerebral blood flow, so that more of the anesthetic agent is delivered rapidly to the brain.

Autonomic nervous system

Bupivacaine does not inhibit the noradrenaline uptake and hence has no sympathetic potentiating effect. Myelinated preganglionic B fibers have a faster conduction time and are more sensitive to action of Bupivacaine. When used for conduction blockade, all local anesthetics particularly Bupivacaine produces higher incidence of conduction blockade in sensory than that of motor fibers.

Cardiovascular System

The primary cardiac electrophysiological effect of a local anesthetic agent is a decrease in the maximum rate of depolarization in Purkinje fibers and ventricular muscle. This action by Bupivacaine is far greater compared to Lignocaine. Also, the rate of recovery of block is slower with Bupivacaine.

Therefore Bupivacaine is highly arrythmogenic. Bupivacaine reduces the cardiac contractility. This is by blocking the calcium transport. Low concentration of Bupivacaine produces vasoconstriction whereas high doses cause vasoconstriction.

Respiratory System

Respiratory depression may be caused if excessive plasma level is reached which in turn results in depression of medullary respiratory center. Respiratory depression may be also caused by paralysis of respiratory muscles of diaphragm as may occur in high spinal or total spinal anesthesia.

Biotransformation and Excretion

Bupivacaine undergoes enzymatic degradation primarily in the liver. The excretion occurs primarily via the kidney. Renal perfusion and factors affecting urinary pH affect urinary excretion. Less than 5% of Bupivacaine is excreted via the kidney unchanged through urine. The major portion of injected agent appears in urine in the form of 2, 6 pipecolyoxylidine (ppx) which is a ndealkylated metabolite of Bupivacaine. Renal clearance of the drug is related inversely to its protein binding capacity and pH of urine.

Adverse effects are encountered in clinical practice mostly due to overdose, inadvertent intravascular injection or slow metabolic degradation.

Uses of Bupivacaine

Bupivacaine is used for

1) Local infiltration.
2) Regional anaesthesia like spinal, caudal, epidural, peripheral nerve block.
3) Sympathetic block

Contraindications

- Known hypersensitivity to Bupivacaine.
- Obstetrical paracervical blockade, its use in pregnancy causes foetal bradycardia

Drug interactions

- Administration of local anaesthetic solution containing epinephrine to patients receiving monoamine oxidase inhibitor or tricyclic antidepressant may produce severe prolonged hypertension.

Adverse Effects

CNS : nervousness, dizziness, blurring of vision or tremors, drowsiness, convulsions and respiratory arrest.

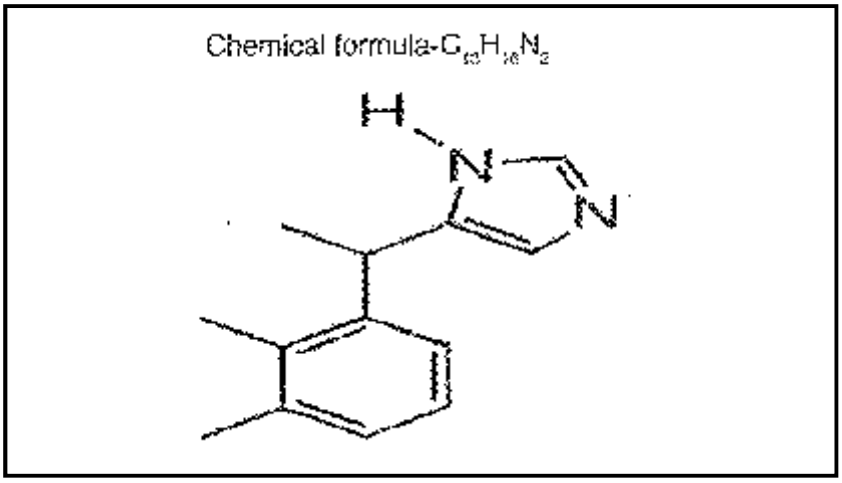
CVS : myocardial depression, hypotension, arrhythtnia, ventricular type conduction defect, SA node depression and cardiac arrest.

Allergic reactions: urticaria, bronchospasm, hypotension.

PHARMACOLOGY OF DEXMEDETOMIDINE: [41, 53]

Dexmedetomidine, a highly selective and specific alpha 2 adrenergic agonist and was first synthesized in late 1980's. Dexmedetomidine is pharmacologically active S - enantiomer of medetomidine and is dextro isomer. Dexmedetomidine became α_2 agonist of choice, due to its greatest $\alpha_2 : \alpha_1$ affinity (8 times greater than clonidine).

Chemical structure



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

Mechanism of action: [42, 47]

Alpha 2 receptors are pre and post synaptic receptors found within central and peripheral nervous system. In CNS, the specific sites are locus coeruleus of upper brain stem and substantia gelatinosa in spinal cord. α2A receptors located in locus cerulus are responsible for sedation, anxiolysis and sympatholysis mediated by G- protein inhibition of L type calcium channels in post synaptic receptors. Dexmedetomidine appears to inhibit ion conductance through L- or P - type calcium channels and to facilitate conductance through voltage gated calcium activated potassium channels. It is reversible by α2- adrenergic antagonists (e.g. atipamezole). Effects are noncortical and sub cortical.

Dexmedetomidine produces analgesic effect by action on α2 receptor within locus coeruleus and spinal cord. Stimulation of α2 adrenergic receptors at this site reduces central sympathetic output, resulting in increased firing of inhibitory neurons. The presence of dexmedetomidine at α2 adrenergic receptors in the dorsal horn of the

‘spinal cord modulates release of substance P to produce analgesic effects. Both α2B and α2C receptors are mostly post- synaptic.

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

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

PHARMACOLOGICAL EFFECTS:

Dexmedetomidine is both potent and safe.

A. Cardiovascular system: (4852) It decreases heart rate, systemic vascular resistance and indirectly decreased myocardial contractility, cardiac output and systemic blood pressure. However, the hemodynamic effects of a bolus of dexmedetomidine are biphasic in a dose dependent manner. The initial hypertensive response is due to peripheral post- synaptic α2B stimulation with vasoconstriction and can be avoided by elimination or slow administration of the bolus dose.

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

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

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

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

E. Respiratory system: [46, 47] Dexmedetomidine produces sedation retaining the ventilatory response to increasing CO2. It enhances analgesia without causing further respiratory depression.

Pharmacokinetics [54]

Following intravenous administration, it exhibits following pharmacokinetic characteristics: rapid distribution phase with distribution half life (t ½α) of about 6 minutes; and a terminal elimination half life (t ½) approximately 2 hours. It exhibits linear pharmacokinetics in the dosage range of 0.2 to 0.7 mcg/kg/hr when administered by IV infusion for up to 24 hours.

Distribution

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

Metabolism

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

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

Elimination

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

Factors affecting dexmedetomidine pharmacokinetics

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

Clinical efficacy

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

The use of dexmedetomidine as adjuvant in regional anesthesia is still not validated. But researchers have found that 3 µg dexmedetomidine and 30 µg clonidine are equipotent intrathecally [(9)]. The addition of 5 µg of dexmedetomidine prolonged the postoperative analgesic effect of ropivacaine by 8 hours [(24)].

Safety and tolerability:

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

Counter measures for adverse effects:

- Hypotension treated by decreasing or stopping infusion of drug, increases the rate of IV fluid administration, elevation of lower extremities, and use of pressor agents.
- Bradycardia treated by injection atropine.
- Reduced lacrimation treated by lubrication of patients eye to prevent corneal dryness.
- Transient hypertension treated by decreasing the dose infusion rate.
- Nausea and vomiting can be treated with antiemetic.
- Significant cardiovascular dysfunction treated by resuscitative measures.
- Parental drug products inspected visually for particulate matter and discoloration prior administration.

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

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

Dosage and administration:

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

Recommended dosage regimen for dexmedetomidine:

Adjunct to general anesthesia: for adult patients

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

Adjunct to regional anesthesia:

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

PHARMACOLOGY OF FENTANYL: [55]

Synthesized in the 1960, Fentanyl Citrate is a phenylpiperidine opioid agonist. As an analgesic, Fentanyl is 75-1 25 times more potent than morphine.

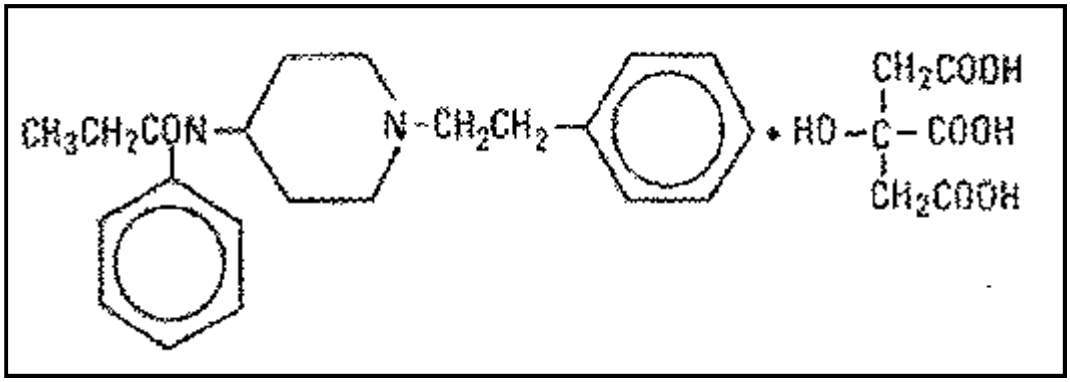


Figure 3: Chemical Structure of Fentanyl

Physicochemical properties

- Molecular formula : $C_{22}H_8N_2O$
- Molecular weight : 336.471 g/mol
- Melting point : 87.5°C
- Water solubility : 200 mg/l
- Half-life $t_{½}$: 3-12 hours

Pharmacokinetics [56]

- Pk : 8.4
- Protein binding : 84%
- Vd (l/kg) : 4
- Cl (ml/kg/mm) : 13
- $t_{½}$ (mm) : 96

Routes of Administration

Oral as syrup or lozenges, intravenous route, epidural route, intrathecal route. After IV administration, onset of action is within 1-2 mm and duration of action is 60 minutes. After epidural route onset is immediate and duration is 3-4 hours. In intrathecal administration, onset is 3-5 mm and duration is 3-4 hours.

Mechanisms of Action

Primarily a μ receptor agonist with an analgesic potency greater than Morphine, Pethidine and Alfentanyl. Analgesia is produced due to its action which is exerted directly on the spinal cord neurons in Rexed's laminae 1 - 2 and 5 of the dorsal horn - rich in opioid binding sites. Inhibition of transmission of A- delta and C pain fibres input occurs. It also binds to a lesser degree to kappa receptor.

PHARMACOLOGICAL ACTION

Cardiovascular System:

Due to stimulation of central nucleus, there is a decrease in heart rate, which is dependent on dose and speed of injection. There is fall in blood pressure which is primarily due to a reduction in systemic vascular resistance through centrally mediated reduction in systemic tone are often associated with bradycardia. It also

slows A.V conduction, prolongs RR interval, AV refractory period and duration of Purkinje fiber action potential.

Respiratory System:

Fentanyl produces dose dependent depression of breathing. Resting minute voIume tidal volume and respiratory rate is decreased. The ventilatory response to hypoxia and hypercarbia is blunted.

Rigidity:

Seen frequently during IV induction of anaesthesia with large doses. No such reaction is seen after intrathecal administration.

Central Nervous System:

It produces no change or modest reduction in cerebral blood flow and cerebral metabolism and oxygen consumption.

GIT:

Intestinal motility is decreased and constipation can be a problem. It can increase the tone of sphincter of Oddi and can produce increased pressure in the biliary ducts.

Therapeutic Efficacy:

Fentanyl is both potent and safe. Therapeutic index of 323 is much greater than that of Morphine 69 and Pethidin 4.8.

Indications

- Postoperative pain relief.
- Induction of general anesthesia in cardiovascular procedures.
- Prevention of surgical pain.
- Labor analgesia.
- Sedative for patients on mechanical ventilator.

Relative Contrairidications

- Patients receiving MAO inhibitors within 14 days.
- COPD.
- Neuromuscular disorder like myasthenia gravis (with decreased respiratory drive).

Intrathecal actions

Intrathecal administration of Fentanyl produces selective spinal analgesia by acting on opiold receptors at substantia gelatinosa of dorsal horn of spinal cord.

The major advantage of "selective ' blockade of pain by Fentanyl lies in the absence of sympathetic blockade and postural hypotension potentially allowing early ambulation of the patient and avoidance of cardiovascular collapse or convulsions, which are major complications of spinal anesthetic blockade. [57]

- Intrathecal dose 10-25 micrograms
- Duration 2-6 hours

Fentanyl is 100 times more potent in terms of dose than Morphine when administered LV but is only 4 times more potent when administered intrathecally. This 25 times decrease in the dose potency of Fentanyl relative to Morphine is explained by greater exposure of spinal cord to Morphine than with Fentanyl. It is a less hydrophilic opioid and has little rostral spread & cause less respiratory depression when compared to Morphine, which has great rostral spread.

Fentanyl by virtue of high volume of distribution in the spinal cord epidural space results in very low integral exposure within the spinal cord. Addition of vasoconstrictors would be modestly beneficial to spinal cord exposure because most of the dose of Fentanyl is lost into the epidural space[57].

Side Effects of Intrathecal Fentanyl: [58]

1) Pruritus
2) Nausea and Vomiting
3) Urinary retention
4) Respiratory depression
5) Mental status changes
6) CNS excitation
7) Neonatal morbidity
8) Sexual dysfunction
9) Ocular dysfunction
10) Cardiac dysarrhythmia
11) Neurotoxicity

1. **Pruritus** May be generalized but more likely over face, neck and thorax. Mechanism of action is by the cephalad migration of the drug in the CSF and subsequent interaction with the trigeminal nucleus located in the medulla. The "itch reflex" may be initiated by opioid interaction in substantia gelatinosa through indirect action on the trigeminal nucleus.
2. **Nausea and Vomiting** Incidence of 30%, more frequent in women

Mechanism:

- Opioid receptors located at area postrema are activated by cephalad spread of drug.
- Sensitization of vestibular system to motion.
- Decreased gastric emptying time also play a role.

3. **Urinary Retention** Incidence is 0-80%, common in young males. Related to dose of opioid administered. Interaction with opioid receptor located in sacral spinal cord, which promotes inhibition of sacral parasympathetic nerves causing detrusor muscle relaxation and increased bladder capacity leading to urinary retention.

4. **Respiratory Depression** Early respiratory depression occurs within 2 hours of injection, which is very rare following intrathecal fentanyl. Delayed respiratory depression, which occurs 2 hours after administration has not been described with fentanyl single dose. However it is dependent on the dose and concomitant use of sedatives.

Counter measures for adverse effects:

- Pruritus, nausea and urinary retention can be treated with antihistaminics, antiemetics and catheterization respectively.
- Respiratory depression by Naloxone and mechanical ventilation.
- Bradycardia: Injection. Atropine or Glycopyrrolate.

MATERIAL AND METHOD

The present study of comparison of intrathecal Dexmedetomidine (5 µg) and Fentanyl (25 µg) as an adjuvantto 0.5% (15 mg) hyperbaric Bupivacaine in infra-umbilical surgeries was carried out in a tertiary care centre in the Department of Anaesthesiology, Shri B M Patil Medical College, BLDE University.

ETHICS COMMITTEE PERMISSION

The study was initiated only after obtaining permission from the Institutional Ethics Committee from December 2014 to August 2016.

STUDY DESIGN

This was a prospective, randomized clinical study.

Inclusion criteria

- ASA grade I or II of either sex.
- Age between 18-60 years.
- Height between 150-1 70 cm.
- Patient undergoing elective infra-umbilical surgeries.
- Patient willing to undergo surgery under regional anesthesia

Exclusion criteria

- ASA grade III or IV
- Patients not willing for the procedure.
- Contraindication to spinal / epidural anaesthesia, e.g. bleeding diathesis, local infection and patients on anticoagulants.
- Height<l50cm.
- Patient with spinal deformities.
- History of hypersensitivity to any oploid or local anaesthetic agent.

- History of neurological diseases / deformities.
- Patient on α2 antagonist therapy.
- History of cardiovascular diseases like Hypertension, Arrhythmias, lschemic heart disease.
- Liver, Respiratory, Kidney, Endocrine diseases.
- Pregnant patients.

METHODOLOGY

The study was conducted in 90 adult patients belonging to ASA Grade I and II of either sex undergoing elective infra-umbilical surgeries.

PATIENT PREPARATION

Patients posted for elective infra-umbilical surgery were included in the study and informed consent was taken. To allow for sufficient time for informed consent, the patients were provided with written information at the outpatient preoperative evaluation clinic a few days before the actual operation. Patients were also explained about Visual Analogue Scale (VAS) and were taught how to express the degree of pain on the scale.

Pre-anesthetic assessment was done in participated subjects. Investigations like hemogram, complete blood count, blood group, cross match, blood sugar, blood urea, urine analysis, BT, CT were advised. Electrocardiogram, chest X-ray and other investigations like LFT, KFT, and coagulation profile were done in all patients above 45 years or as and when required according to history, clinical examination in younger patients too.

All patients were explained about the procedure. Preparation of patients included over-night fasting for 8-l0hr. Vitals was noted in pre-anaesthetic room. No

premedication was given to any patient. On operation table, baseline monitoring devices ECG, SpO2, non-invasive blood pressure were attached to the patient.

Pulse rate, systolic blood pressure, diastolic blood pressure, respiratory rate, oxygen saturation and VAS were noted before giving subarachnoid block. A wide bore 18-20 G intravenous canula was inserted into a peripheral vein of an arm, and patient preloaded with 10ml/kg of Ringer Lactate solution.

Patients were randomly allocated to 3 groups of 30 each.

Group C : 15mg hyperbaric Bupivacaine (0.5%, 3ml) + 0.5m1 of Normal saline

Group D : 15mg hyperbaric Bupivacaine (0.5%, 3ml) + 5µg Dexmedetomidine in 0.5m1 of normal saline

Group F : 15mg hyperbaric Bupivacaine (0.5%, 3m1) + 25µg Fentanyl.

Dexmedetomidine 100 pg/mI was diluted with preservative-free normal saline to 10µg/ml. 0.5ml of dexmedetomidine (10µg/ml), fentanyl (50µg/m)) and preservative normal saline was added to 3m1 of 0.5% hyperbaric bupivacaine in a 5rn1 syringe. The total volume injected was 3.5 ml in each group.

MONITORING

Baseline pulse, blood pressure and respiratory rate were recorded. Surgery was performed under spinal anesthesia. lntraoperative monitoring consisted of pulse rate, BP, ECG, RR and SpO2. The readings of pulse rate, SBP, DBP, SpO2 and RR were taken at 2 mm intervals for first 10 minutes, then every 5 minutes interval till 30 minutes, then at 15 minutes interval till 60 minutes, then every hour till 4 hour and then 2 hourly up to 8hr. Fluid was maintained with Ringer's lactate intra-operatively.

PROCEDURE OF THE BLOCK

Patients were placed in left lateral position on the operation table and with strict aseptic precaution; midline approach subarachnoid block was achieved in L3-L4

space with 25G disposable Quincke's spinal needle with cutting bevel. Drug was injected after free flow and clear aspiration of CSF over 10-15 seconds.

Patients were immediately placed in the supine position slowly and given oxygen 4lit/min by nasal oxygen. The onset of sensory analgesia was tested by pinprick.

The time of drug injection was noted and recorded as 0.

Following parameters were observed and recorded:

1) Time of onset of sensory block.
2) Time of onset of motor blockade.
3) Time to achieve maximum sensory level.
4) Time to achieve maximum motor blockade.
5) Maximum dermatomal level achieved
6) Grade of motor blockade
7) Duration of surgery
8) Time of two segment sensory regression. -
9) Time to regression to T12'
10) Total duration f complete motor blockade.
11) Total duration of complete analgesia.
12) Time of rescue analgesia.
13) Quality of anesthesia, quality of analgesia and amount of analgesic required postoperatively
14) Sedation score
15) Hemodynamic changes
16) Side effects and complications

The time of start of monitoring was taken from the time the drug was injected into the intrathecal space. (T=0).

1. **Time of onset of sensory block:** It was defined as time interval between the completions of intrathecal injection of the study drug to the onset of complete loss of sensation to pinprick at the level of Lumbar dermatome 1 by using non-traumatic pin-prick method tested immediately after making the patient supine.
2. **Time of onset of motor block:** The time for onset of motor block was assessed subjectively by the patient from the time of injection of the drug in subarachnoid space till the onset of feeling of heaviness in legs.
3. **Time to achieve maximum sensory level:** The duration from intrathecal injection of study drug and time to maximum cephalic sensory level achieved was noted in minutes. It was tested by pinprick with sterile blunt 23G hypodermic needle. Patients were tested every 2 mm for 10 mm, every 5 mm for 30 mm or till start of surgery, whichever was earlier.
4. **Time to achieve maximum motor blockade:** Maximum block was considered as the time taken from completion of intrathecal injection to the inability of the patient to move legs or feet (Grade 3 block) (ANNEXURE).
5. **Maximum dermatomal level achieved:** It was defined as the highest dermatomal level of sensory blockade achieved.
6. **Grade of motor blockade:** Grade of motor blockade was assessed by Modified Bromage Scale (ANNEXURE).
7. **Duration of surgery:** Duration of surgery was taken as time from surgical incision to skin closure.

8. **Time of two segment sensory regression:** It was defined as the time taken for the dermatomal level to regress from the highest levels to two segments below.
9. **Time to regression to T12:** It was defined as the time taken for the sensory level to regress from the highest dermatomal level to T12.
10. **Total duration of complete motor blockade:** It was time taken from injection of study drug to regression of motor block to Bromage grade 0 and noted in minutes.
11. **Total duration of complete analgesia.** Total defined as time from intrathecal injection to VAS score greater administrations of the local anaesthetic intrathecally to the onset of the tolerable pain (VAS≥0) at rest.
12. **Time of rescue analgesia:** It was defined as time from intrathecal injection to VAS score greater than or equal to 4 at rest requiring supplementary (rescue) analgesia in the form of mi. diclofenac sodium intramuscular in the dosage of 1.5 mg/kg.
13. **Quality of anesthesia, quality of analgesia and amount of analgesic required postoperatively:** VAS scores were used to assess quality of anesthesia during surgery, while quality of analgesia and amount of analgesic required postoperatively. Visual Analogue Scale (VAS) score (ANNEXURE) was used intraoperative and post-operatively at 0, 60, 120, 180, 240, 360, 480 minute, 12 and 24 hour. When score found more than 4, Injection Diclofenac was given intramuscularly as a rescue analgesic in the dosage of 1.5 mg/kg.

Severity of pain was measured using 10 cm Visual Analogue Scale (VAS). VAS was assessed on a 10 cm (100mm) pain scale on which 0 end indicates no pain, and 10 cm indicates worst possible pain. Patients were asked to point out on the scale, the intensity of pain.

First rescue analgesic was given with Inj. Diclofenac sodium 75 mg intramuscularly when patient showed VAS score was 4 or more after which pafient received analgesic whenever VAS score was 4 or more till 24 hour and after that patients were excluded from the study. Total amount of analgesic required postoperatively till 24hour was recorded.

14. **Sedation score:** Level of sedation was assessed by Ramsay sedation score, and was noted at 0mm as baseline then at 15 mm, 30mm, 60mm, then every 1 hourly till 4hour, then every 2 hourly till 8hour. Sedation was studied as a central effect of drug and sedation was graded by Ramsay sedation scale. (ANNEXURE)

15. **Hemodynamic stability:** Pulse rate, blood, pressure, respiratory rate and oxygen saturation were monitored continuously every 2 min for 10 min, every 15 min for 60 mm, every 30mm till 120mm, every 1 hour till 4hour and every 2hour till 8 hour. Patients were visited at 12 and 24 hours to note about the incidence of side effects and complications.

A fall of systolic blood pressure of less than 80 mmHg or more than 20% of baseline was considered as hypotension and treated with rapid infusion of intravenous fluid ringer lactate 250 ml and 6 mg intravenous inj. Ephedrine if there was no response to intravenous fluid administration.

Heart rate of less than 50 beats per minute was considered as bradycardia and treated with inj. Atropine sulphate 0.6 mg intravenously.

Respiratory depression was defined as fall in respiratory rate <10 breaths/mm or of fall in peripheral oxygen saturation <90% with oxygen supplementation of 4 lit/min by nasal oxygen and was treated by encouraging to take voluntary deep breathing and providing 100% O2 supplementation.

Intravenous fluids were administered in the form of Ringer Lactate solution and DNS in calculated doses depending on patient's body weight and further adjusted as per blood loss during surgery. Colloid and blood was administered as per the loss and requirement.

16. Side effects and Complications: Intraoperative side effects like nausea and vomiting, shivering, bradycardia, hypotension, respiratory depression and dryness of mouth requiring active treatment were noted.

All patients were observed in post anaesthesia recovery room and then in ward. Patients were observed for postoperative complications like nausea, vomiting, shivering, urinary retention and pruritus at 12 and 24 hours.

Nausea and vomiting was treated with Injection Ondansetron 4mg IV. Pruritus was treated with antihistaminic like injection Pheniramine maleate (Avil) and urinary retention, by catheterizing the patient.

Statistical analysis:

Parametric and non-parametric data were collected and were entered in master chart in Microsoft Excel worksheet 2007. All Continuous variables (demographic and hemodynamic parameters) were presented as Mean ± SD. Categorical variables (gender, ASA status, sensory and motor block characteristics, analgesia, side effects) were expressed in actual numbers and percentages. Demographic parameters and sensory and motor block chacteristics between three groups were compared by

performing one way analysis of variance (ANOVA). Post hoc multiple comparisons were performed by bonferroni test.

Variation in haemodynamic parameters at different time point were compared by Repeated measure ANOVA. Changes in haemodynamic parameters at different time point between 3 groups were compared by performing oneway ANOVA. Post operative complications were compared between 3 groups by computing chi square test. All the tests were 2 sided. Statistical software STATA version 10.0 and SPSS version 16.0 were used for statistical analysis. The results were tested at 5% level of significance. Microsoft Word and Excel have been used to generate graphs, table's etc. $p<0.05$ was considered as level of statistical significance.

To calculate the sample size, a power analysis of a = 5% and 3 = 80% showed that 25 patients per study groups were needed to detect an increase of 36% difference between the median duration of spinal sensory block between the groups using Fisher's test reffering to study conducted by Rajni gupta et al.[25] Minimum sample size required in each group*as n25, hence 30 patients were randomly selected for each of the three groups. The total sample size was taken as 90.

OBSERVATION AND RESULTS

Table no: 1

Comparison of Demographic characteristics including Age, Height and Weight

	Group C	Group D	Group F	p – value
Age (years)	**41.93 ± 9.02**	**39.83 ± 10.40**	**39.5 ± 8.25**	**0.5779, NS**
Height (cm)	**160.13 ± 4.48**	**159.1 ± 3.48**	**158.4 ± 4.21**	**0.2602, NS**
Weight (kg)	**55.9 ± 7.31**	**51.56 ±4.94**	**53.36 ± 6.65**	**0.4250, NS**

p – value is significant if < 0.05 and highly significant if < 0.001.

The patients in the age range of 18-60 yrs were included in the study. The distribution of patients according to age was found to be statistically insignificant (p-value >0.05) and comparable amongst the three groups.

The patients having height >150 cm were included in the study. The distribution of patients according to height was found to be statistically insignificant (p-value >0.05) and comparable amongst the three groups.

The distribution of patients according to the weight was also found to be statistically insignificant (p-value >0.05) and comparable between the three groups.

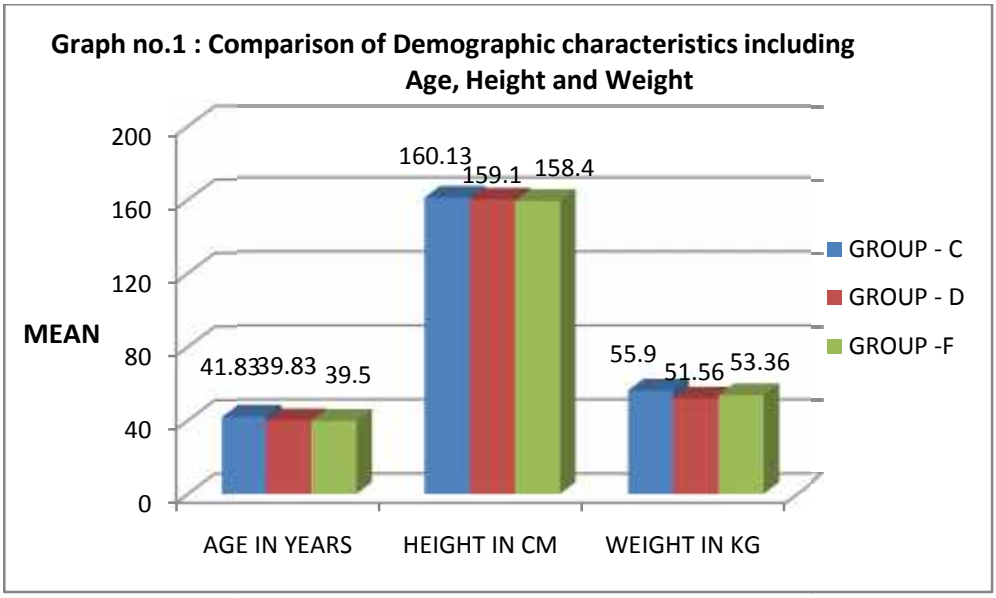


Table no: 2

Comparison of Demographic Characteristics including Gender

	Group C	Group D	Group F	p-value
Male	**17**	**16**	**18**	**1.00, NS**
Female	**13**	**14**	**12**	
Total	**30**	**30**	**30**	

p – value is significant if <0.05 and highly significant if <0.001.

The distribution of patients according to Gender was found to be statistically insignificant amongst the three groups. Sex ratio of 1.30:1 (male: female) in group C, 1.14:1 in group D and 1.5:1 in group F was found to be comparable between all three groups. (p>0.05)

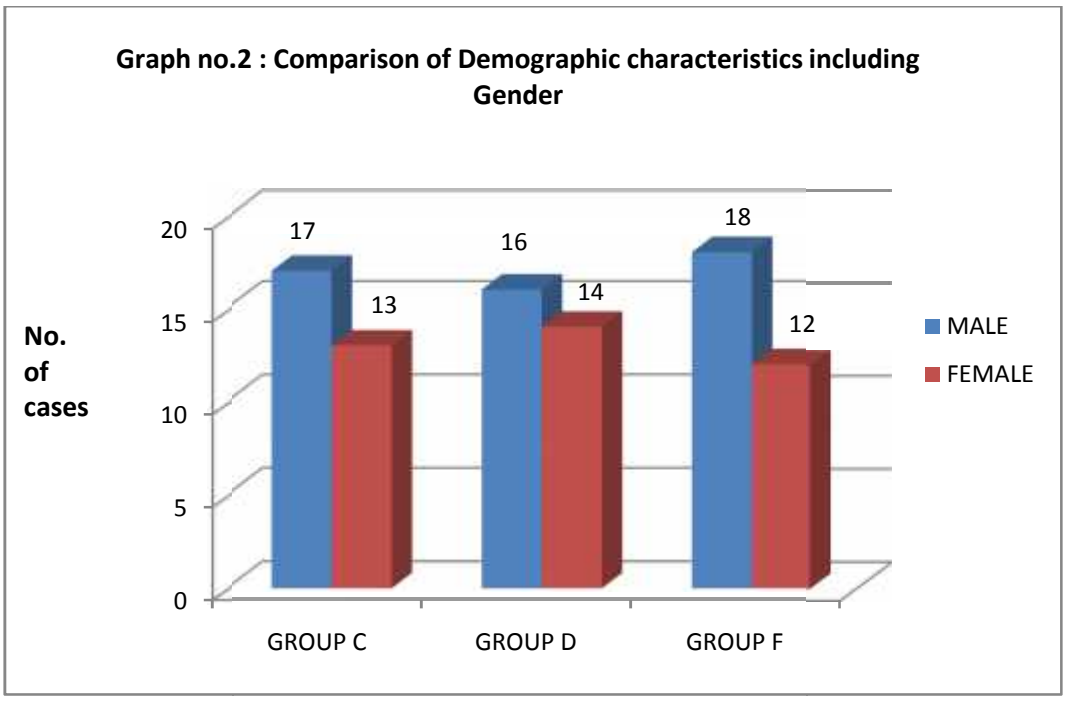


Table no: 3

Distribution of patients according to ASA grade

ASA grade	Group C	Group D	Group F
1	19 (63.3%)	15 (50%)	15 (15%)
2	11 (36.7%)	15 (50%)	15 (15%)
Total	30 (100%)	30 (100%)	30 (100%)

Though randomly allocated, the distribution of patients according to ASA grading was comparable between all the three groups.

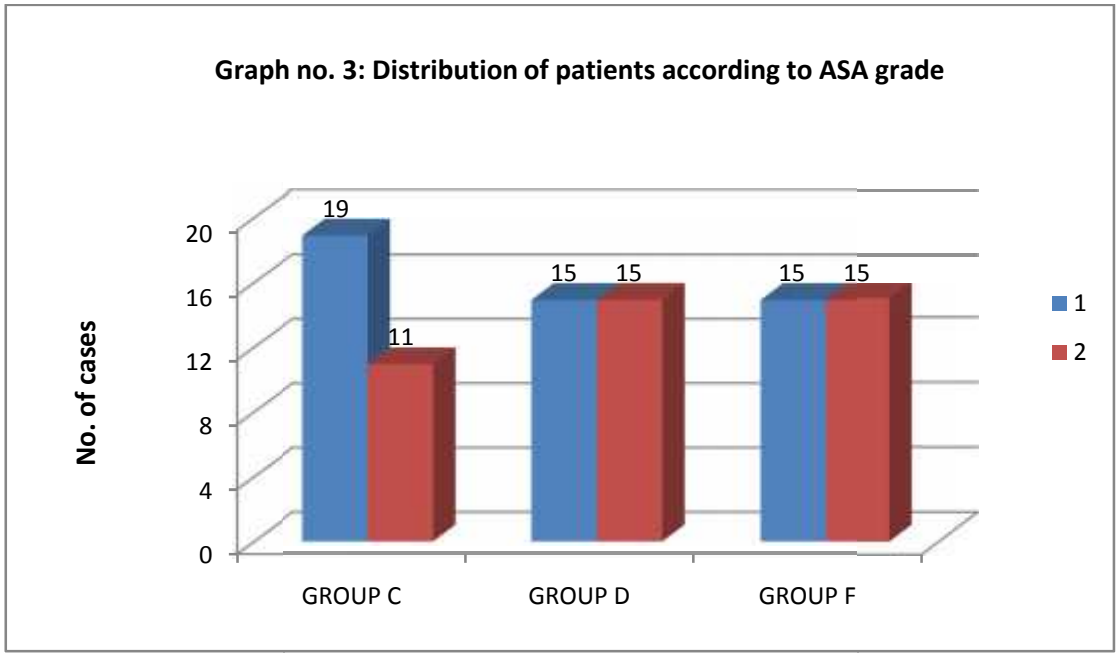


Table no: 4

Showing distribution of patients according to Type of surgery

Type of surgery	Group C	Group D	Group F
Eversion of sac	3 (10%)	4 (13.3%)	4 (13.3%)
Meshplasty	7 (23.3%)	6 (20%)	6 (20%)
Femur plating	1 (3.3%)	1 (3.3%)	1 (3.3%)
Femur nailing	4 (13.3%)	3 (10%)	3 (10%)
Tibia plating	2 (6.7%)	2 (6.7%)	1 (3.3%)
Tibia nailing	3 (10%)	4 (13.3%)	5 (16.7%)
Ovarian cyst excision	2 (6.7%)	4 (13.3%)	3 (10%)
Vaginal hysterectomy	8 (26.7%)	6 (20%)	7 (23.3%)
Total	**30 (100%)**	**30 (100%)**	**30 (100%)**

Though randomly allocated, distribution of patients according to the type of surgery undergone by them was comparable amongst the three groups. Surgeries of inguinal hernia repair, orthopaedic surgeries and vaginal hysterectomy were the most common surgeries undertaken.

Graph no. 4 : Distribution of patients according to Type of surgery

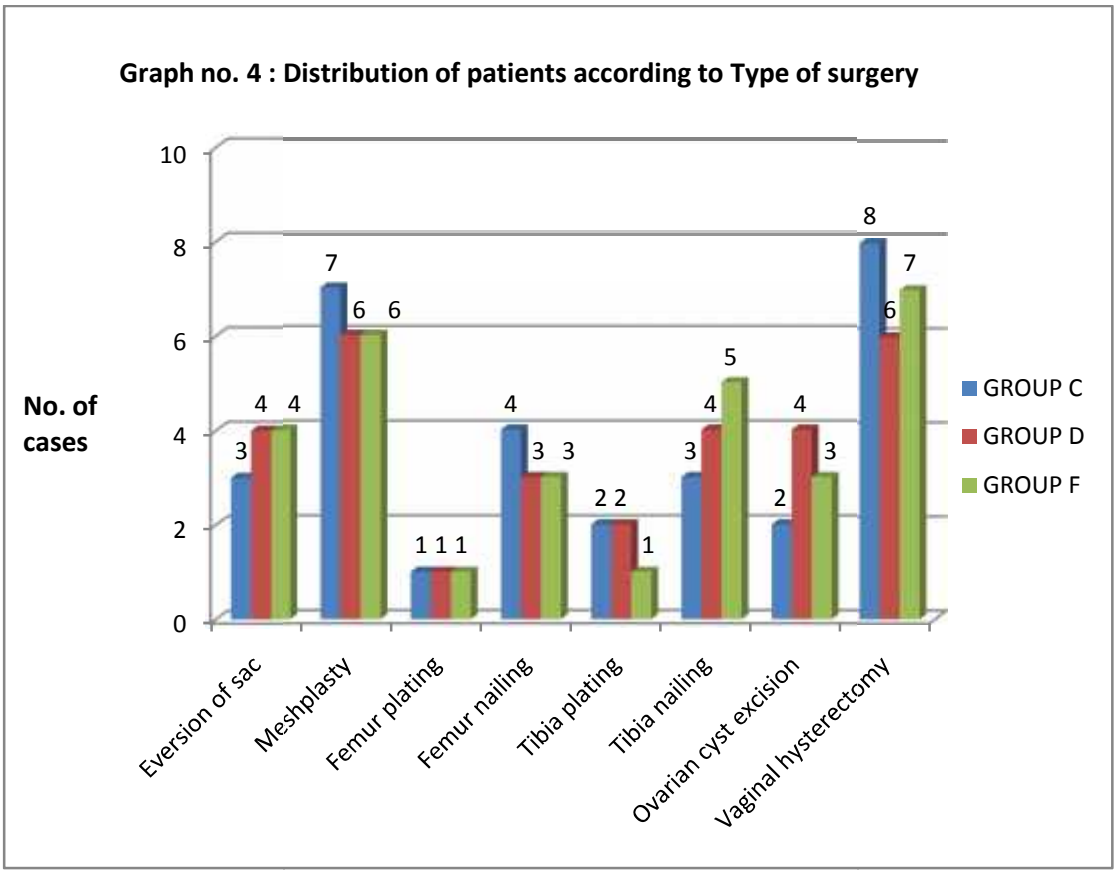


Table no: 5

Comparison of time to onset of sensory analgesia

Time (sec)	Group C	Group D	Group F
91-120	0 (0%)	11 (36.7%)	15 (50%)
121-150	19 (63.3%)	19 (63.3%)	15 (50%)
151-180	11 (36.7%)	0 (0%)	0 (0%)
Total	**30 (100%)**	**30 (100%)**	**30 (100%)**
MEAN ± SD	151.66 ± 15.33 sec	128.66 ± 11.36 sec	125.66 ± 10.06 sec
One way ANOVA	F = 39.12 , p<0.001, HS		
Multiple comparison	**Group C vs Group D**	**Group C vs Group F**	**Group D vs Group F**
p-value	<0.001, HS	<0.001, HS	1.000, NS

p – value is significant if <0.05 and highly significant if <0.001.

The onset of sensory analgesia was assessed and confirmed by complete loss of sensation to pinprick at the Lumbar dermatomal level 1 by using non-traumatic pin-prick method tested immediately after making the patient supine and thereafter at 30 sec intervals from the time of intrathecal drug injection (t=0).

Maximum number of patients in all three groups i.e. 19 (63.3%) in group C, 30 (100%) in both group D and F had onset of sensory analgesia within 150 seconds. However, 100% patients in group C depicted an onset within 180 seconds.

Mean time for the onset of sensory block was significantly longer (p<0.001) in group C (151.66 ± 15.33 sec) when compared to group D (128.66 ± 11.36 sec) and group F (125.66 ± 10.06 sec). Group D and group F were comparable with respect to the onset of sensory block (p=1.000).

Graph no. 5 : Comparison of time to onset of sensory analgesia

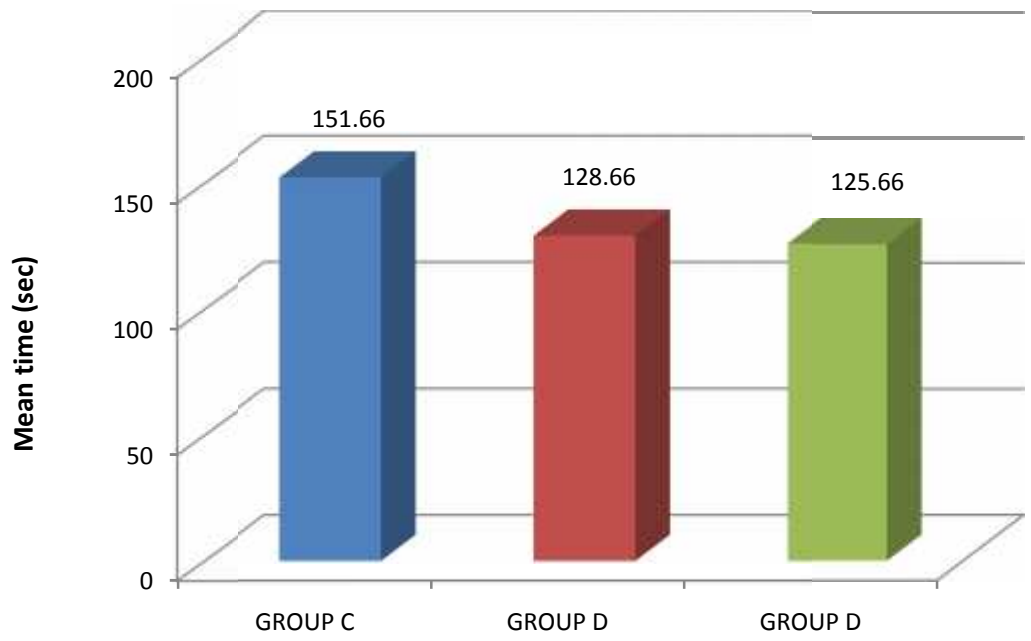


Table no: 6

Comparison of time to achieve maximum level of sensory block :

Time (min)	**Group C**	**Group D**	**Group F**
6-7	0 (0%)	7 (23.3%)	9 (30%)
7-8	0 (0%)	14 (46.7%)	15 (50%)
8-9	3 (10%)	7 (23.3%)	6 (20%)
9-10	18 (60%)	2 (6.7%)	0 (0%)
10-11	9 (30%)	0 (0%)	0 (0%)
Total	**30 (100%)**	**30 (100%)**	**30 (100%)**
MEAN ± SD	9.41 ± 0.56 min	7.33 ± 0.73 min	7.13 ± 0.61 min
One way ANOVA	F =116.98, p<0.001, HS		
Multiple comparison	**Group C vs Group D**	**Group C vs Group F**	**Group D vs Group F**
p-value	<0.001, HS	<0.001, HS	0.689, NS

p-value is significant if <0.05 and highly significant if < 0.001.

28 (93.3%) patients in group D and 30 (100%) patients in group F achieved the maximum sensory block level within 9 minutes, while only 3 (10%) patients in group C could achieve this in 9 minutes. Maximum number of patients in group C recquired more time than group D and group F to achieve highest level of sensory block.

Mean time to achieve maximum sensory block in group C (9.41 ± 0.56 min) was significantly longer (p<0.001) when compared to group D (7.33 ± 0.73 min) and group F (7.13 ± 0.61 min). However, the differences between the group D and group F were comparable and statistically insignificant (p>0.05).

Graph no. 6 Comparison of time to achieve maximum level of sensory block

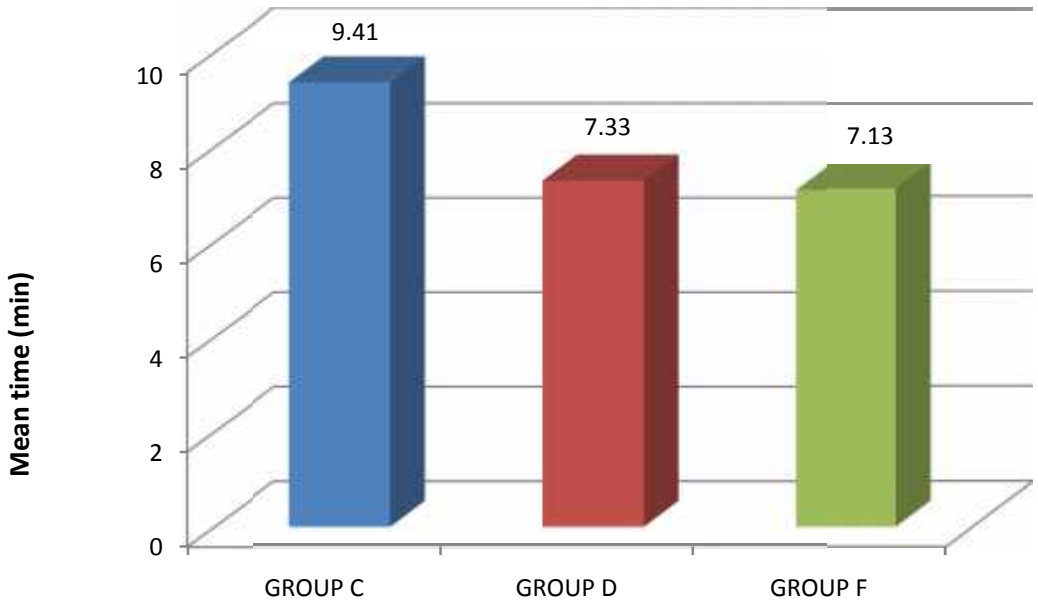


Table no: 7

Comparison of highest dermatomal level achieved

Sensory level	**Group C**	**Group D**	**Group F**
T5	0 (0%)	5 (16.7%)	2 (6.7%)
T6	18 (60%)	23 (76.7%)	24 (80%)
T7	2 (6.7%)	0 (0%)	0 (0%)
T8	9 (26.7%)	2 (6.7%)	4 (13.3%)
T10	1 (3.3%)	0 (0%)	0 (0%)
TOTAL	**30 (100%)**	**30 (100%)**	**30 (100%)**
MEAN ± SD	6.8 ± 1.09	5.96 ± 0.67	6.2 ± 0.76
One way ANOVA	F = 7.47 p= 0.0010, HS		
Multiple comparison	**Group C vs Group D**	**Group C vs Group F**	**Group D vs Group F**
p-value	0.001, HS	0.025, S	0.891, NS

p-value is significant if <0.05 and highly significant if < 0.001.

The highest dermatomal level achieved was T5-T6 in maximum number of patients in group D and F i.e. 28 and 26 respectively. While highest sensory level achieved in group B was T6-T7 in 20 patients.

Mean dermatomal level achieved in group C (T 6.8 ± 1.09) was statistically significant as compared to group D (T 5.96 ± 0.67) and group F (T 6.2 ± 0.76). However, the differences between the group D and group F were comparable and statistically insignificant (p>0.05).

Graph no. 7 : Comparison of highest dermatomal level achieved

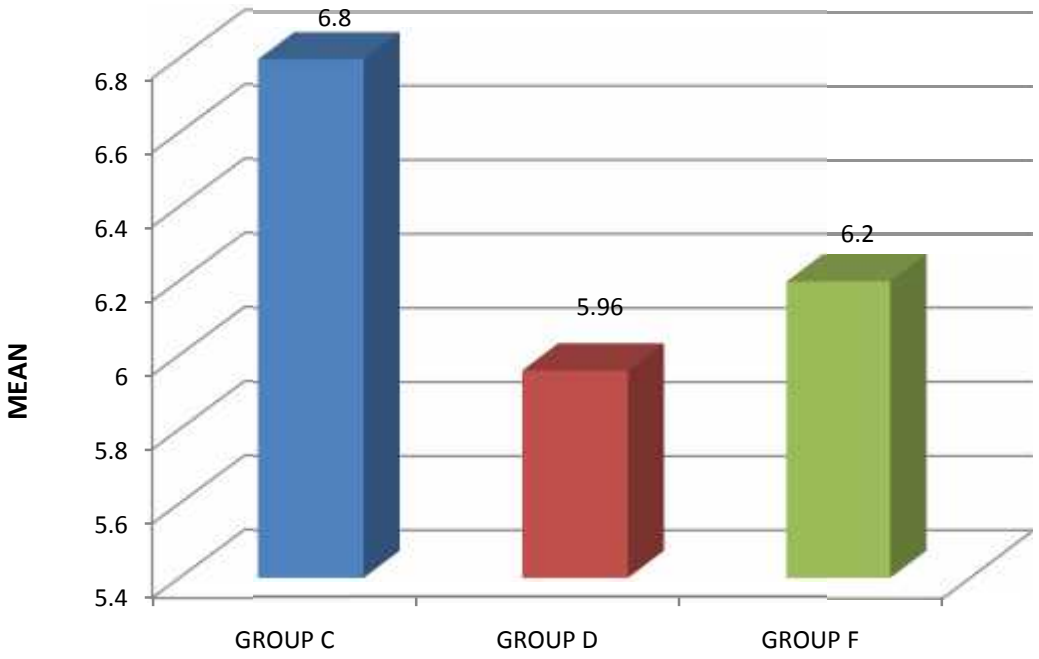


Table no: 8

Comparison of time to onset of motor blockade

Time (sec)	Group C	Group D	Group F
90-120	0 (0%)	5 (16.7%)	1 (3.3%)
121-150	2 (6.7%)	20 (66.7%)	27 (90%)
151-180	21 (76.7%)	5 (16.7%)	2 (6.7%)
181-210	7 (23.3%)	0 (0%)	0 (0%)
TOTAL	**30 (100%)**	**30 (100%)**	**30 (100%)**
MEAN ± SD	178.0 ± 16.48 sec	140.0 ± 13.89 sec	138.33 ± 9.12 sec
One way ANOVA	F = 82.65 p<0.001, HS		
Multiple comparison	**Group C vs Group D**	**Group C vs Group F**	**Group D vs Group F**
p-value	<0.001, HS	<0.001, HS	1.000, NS

p-value is significant if <0.05 and highly significant if < 0.001.

The onset of motor blockade was assessed subjectively when the patient had a feeling of heaviness in his/her lower limbs from the time of injection of the drug into the intrathecal space.

25 (83.3%) patients in group D and 28 (93.3%) patients in group F had onset of motor analgesia within 150 seconds, while only 2 (6.7%) patients in group C had an onset within 150 seconds. Remaining 28 (93.3%) patients in group C recquired more than 150 seconds.

Mean time for the onset of motor block was significantly longer (p<0.001) in group C (178.0 ± 16.48 sec) when compared to group D (140.0 ± 13.89 sec) and group F (138.33 ± 9.12 sec). Group D and group F were comparable with respect to the onset of motor block (p=1.000).

Graph no. 8 : Comparison of time to onset of motor block

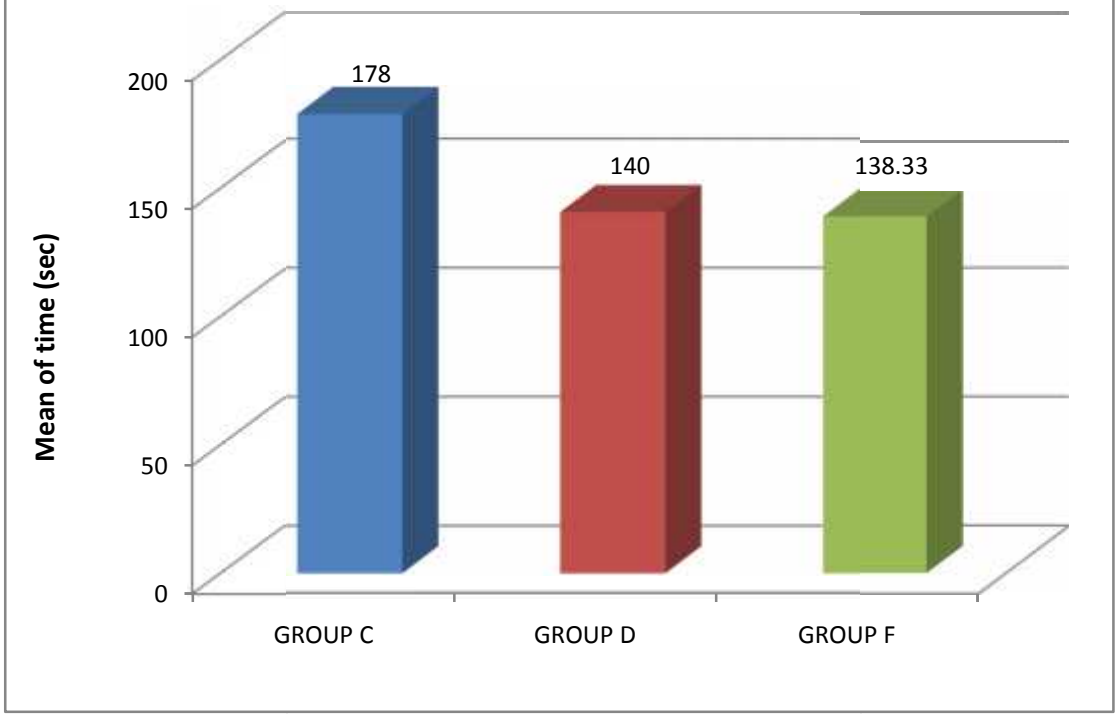


Table no: 9

Comparison of time to achieve complete motor blockade

Time (min)	Group C	Group D	Group F
5-6	0 (0%)	10 (33.3%)	12 (40%)
6-7	1 (3.3%)	16 (53.3%)	18 (60%)
7-8	8 (26.7%)	4 (13.3%)	0 (0%)
8-9	18 (60%)	0 (0%)	0 (0%)
9-10	3 (10%)	0 (0%)	0 (0%)
TOTAL	**30 (100%)**	**30 (100%)**	**30 (100%)**
MEAN ± SD	8.6 ± 0.57 min	6.67 ± 0.63 min	6.41 ± 0.39 min
One way ANOVA	F = 143.84 p<0.001, HS		
Multiple comparison	**Group C vs Group D**	**Group C vs Group F**	**Group D vs Group F**
p-value	<0.001, HS	<0.001, HS	0.239, NS

p-value is significant if <0.05 and highly significant if < 0.001.

All the patients in the three groups achieved grade 3 motor blockade. 26 (86.7%) patients in group D and 30 (100%) in group F achieved the maximum motor block level within 7 minutes, while only 1 (3.3%) patients in group C could achieve this in 7 minutes. Maximum number of patients in group C i.e.27 (90%) achieved the maximum motor block level within 9 minutes.

Mean time to achieve maximum motor block in group C (8.6 ± 0.57 min) was significantly longer (p<0.001) when compared to group D (6.67 ± 0.63 min) and group F (6.41 ± 0.39 min). However, the difference between the group D and group F were comparable and statistically insignificant (p>0.05).

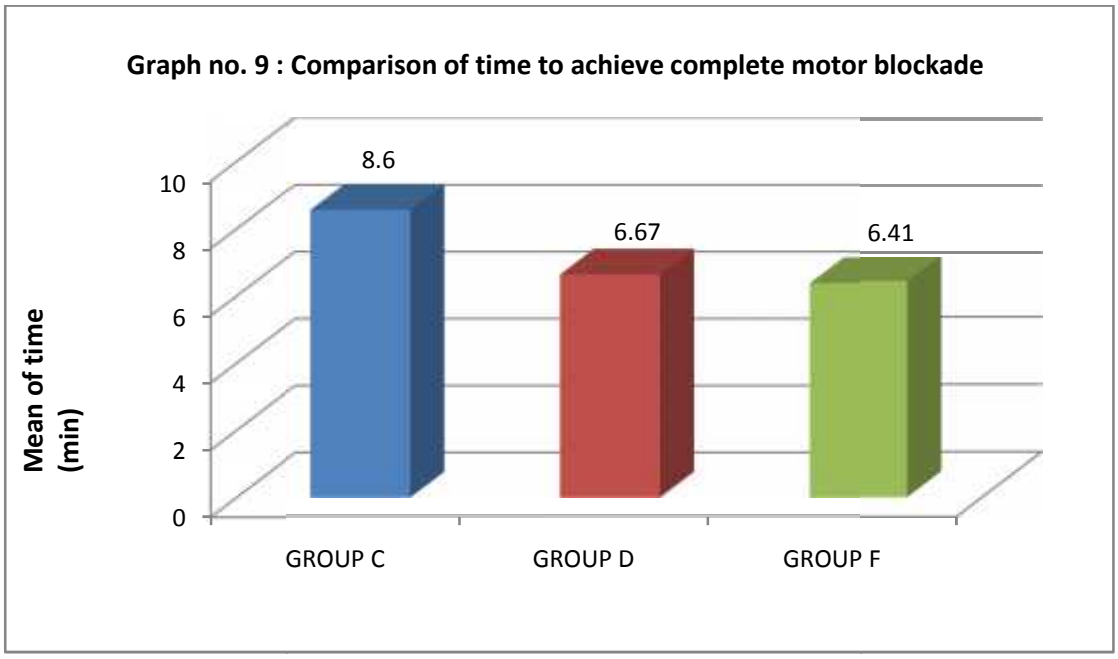

Graph no. 9 : Comparison of time to achieve complete motor blockade
Mean of time (min)
10
8
6
4
2
0
8.6
6.67
6.41
GROUP C
GROUP D
GROUP F

Table no: 10

Showing distribution of patients according to duration of surgery

Duration (min)	**Group C**	**Group D**	**Group F**
60-90	11 (36.7%)	6 (20%)	11 (36.7%)
91-120	18 (60%)	23 (76.7%)	18 (80%)
121-150	1 (3.3%)	1 (3.3%)	1 (3.3%)
TOTAL	**30 (100%)**	**30 (100%)**	**30 (100%)**
MEAN ± SD	100.66 ± 12.84 min	107.33 ± 11.42 min	101 ± 13.73 min
One way ANOVA	F = 2.62 p=0.0783, NS		

p-value is significant if <0.05 and highly significant if < 0.001.

Total duration of surgery was taken as time from surgical incision to skin closure. Mean duration of surgery in group C was seen to be 100.66 ± 11.42 min and in group F was seen as 101 ± 13.73 min. Mean duration of surgery in all the three groups were comparable and statistically insignificant as p-value > 0.05.

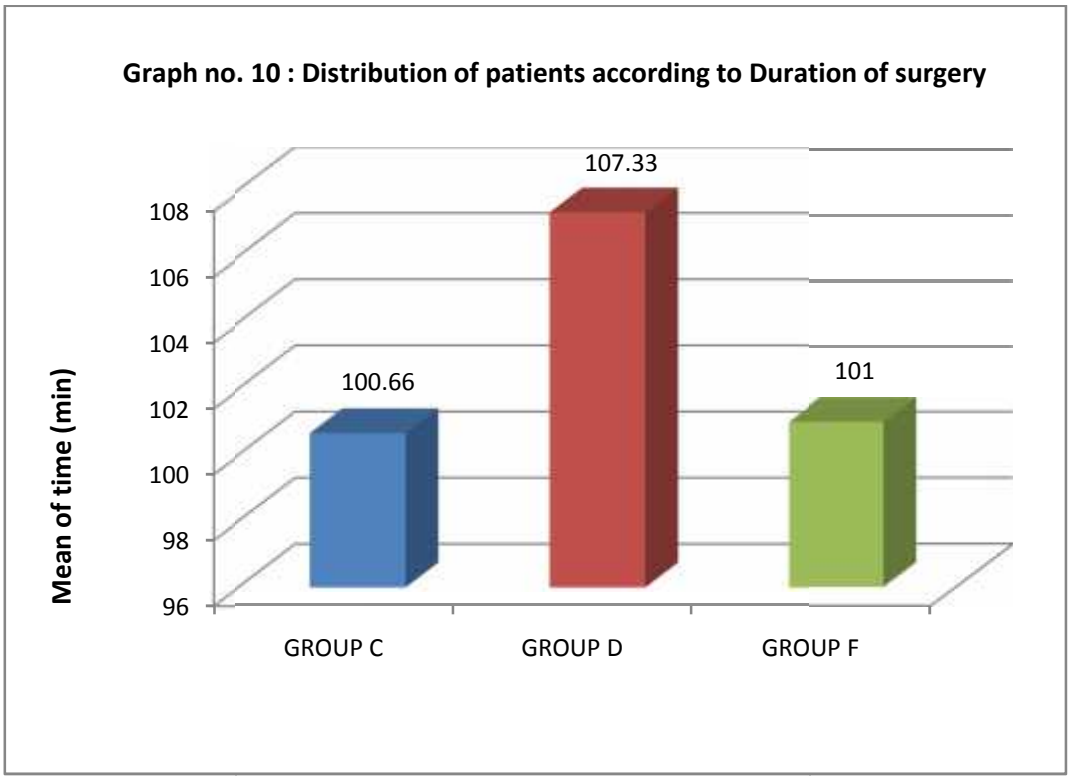


Table no: 11

Comparison of time for two segment regression of sensory block

Time (min)	Group C	Group D	Group F
75-90	16 (53.3%)	0 (0%)	0 (0%)
91-105	12 (40%)	0 (0%)	2 (6.7%)
106-120	2 (6.7%)	0 (0%)	16 (53.3%)
121-135	0 (0%)	5 (16.7%)	9 (30%)
136-150	0 (0%)	18 (60%)	3 (10%)
151-180	0 (0%)	7 (23.3%)	0 (0%)
TOTAL	**30 (100%)**	**30 (100%)**	**30 (100%)**
MEAN ± SD	92.83 ± 8.37 min	146.83 ± 9.14 min	122.16 ± 11.86 min
One way ANOVA	F = 223.29 p<0.001, HS		
Multiple comparison	**Group C vs Group D**	**Group C vs Group F**	**Group D vs Group F**
p-value	<0.001, HS	<0.001, HS	<0.001, HS

p-value is significant if <0.05 and highly significant if < 0.001.

In 28 (93.3%) patients of group C, 27 (90%) patients of group F and 23 (76.7%) patients of group D the dermatomal level showed two segment regression within 105 min, 135 min, and 150 minutes respectively.

Mean time to achieve two segment regression of sensory level in group C (92.83 ± 8.37 min) was significantly shorter ($p<0.05$) when compared to group D (146.83 ± 9.14 min) and group F (122.16 ± 11.86 min). Mean time to achieve two segment regression of sensory level in group D was significantly longer than group F, which in turn was longer than group C.

Graph no. 11 : Comparison of time for two segment regression of sensory block

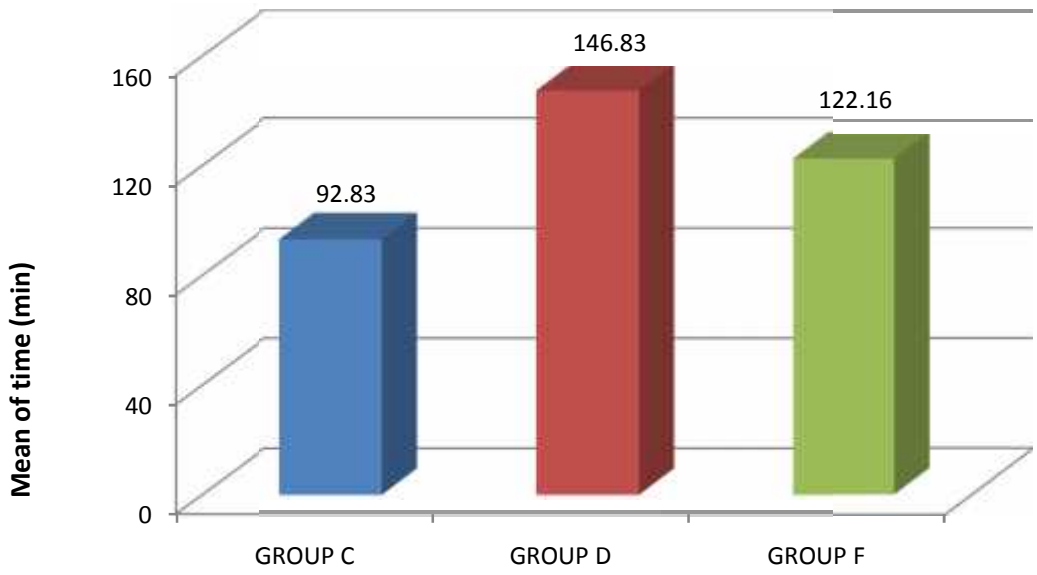


Table no: 12

Comparison of time of regression to T12

Time (min)	Group C	Group D	Group F
90-120	4 (13.3%)	0 (0%)	0 (0%)
121-150	24 (80%)	0 (0%)	6 (20%)
151-180	2 (6.7%)	3 (10%)	19 (63.3%)
181-210	0 (0%)	17 (56.7%)	5 (16.7%)
211-240	0 (0%)	10 (33.3%)	0 (0%)
TOTAL	**30 (100%)**	**30 (100%)**	**30 (100%)**
MEAN ± SD	139.5 ± 13.60 min	208.116 ± 16.21 min	169.66 ± 13.76 min
One way ANOVA	F = 167.23 p<0.001, HS		
Multiple comparison	**Group C vs Group D**	**Group C vs Group F**	**Group D vs Group F**
p-value	<0.001, HS	<0.001, HS	<0.001, HS

p-value is significant if <0.05 and highly significant if < 0.001.

It was defined as the time taken for the sensory level to regress from the highest levels to dermatome level T12. In 30 (100%) patients of group C, 3 (10%) patients of group D and 25 (83.3%) patients of group F, the sensory level showed regression to T12 within 180 minutes. However, 27 (90%) patients of group D and 5 (16.7%) patients of group F showed sensory regression to T12 after 180 minutes.

Mean time to achieve sensory regression to T12 level in group C (139.5 ± 13.60 min) was shorter as compared to group F (169.66 ± 13.76 min) and group D (208.116 ± 16.21 min) and these differences were found to be highly significant statistically (p<0.001). The difference in the results of group D and group F was statistically significant with group D having longer duration of sensory block.

Thus, Dexmedetomidine (Group D) has longer duration of sensory block than Bupivacaine (Group C) and Fentanyl (Group F).

Graph no. 12 : Comparison of time of regression to T12

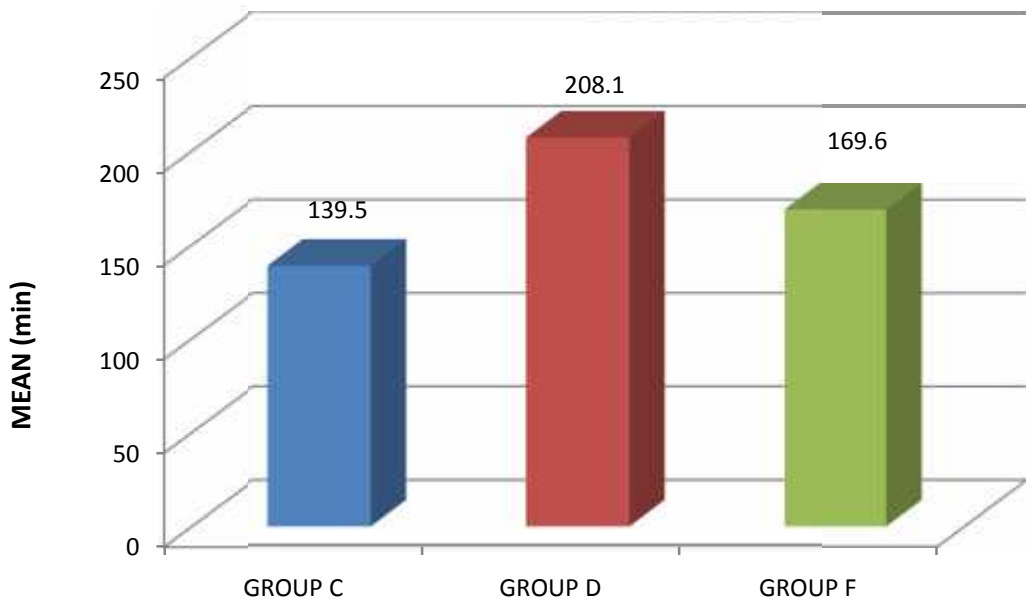


Table no: 13

Comparison of total duration of complete motor blockade

Time (min)	Group C	Group D	Group F
150-180	18 (60%)	0 (0%)	2 (6.7%)
181-210	12 (40%)	0 (0%)	16 (53.3%)
211-240	0 (0%)	6 (20%)	12 (40%)
241-270	0 (0%)	15 (50%)	0 (0%)
271-300	0 (0%)	9 (30%)	0 (0%)
TOTAL	**30 (100%)**	**30 (100%)**	**30 (100%)**
MEAN ± SD	179.16 ± 14.62 min	265.66 ± 19.24 min	209.66 ± 14.73 min
One way ANOVA	F = 216.18 p<0.001, HS		
Multiple comparison	**Group C vs Group D**	**Group C vs Group F**	**Group D vs Group F**
p-value	<0.001, HS	<0.001, HS	<0.001, HS

p-value is significant if <0.05 and highly significant if < 0.001.

It was time taken from injection of study drug to regression of motor block to Bromage grade 0 and noted in minutes.

Mean duration of complete motor block in group C was 179.16 ± 14.62 min, in group D was 265.66 ± 19.24 min and in group F was 209.66 ± 14.73 min.

The differences for mean duration of complete motor block between the three groups were found to be statistically highly significant (p<0.001). The group D showed longer duration of complete motor block than group C and group F, while duration of complete motor block in group F was longer than group C, both of which was found to be statistically highly significant (p<0.001).

Thus, Dexmedetomidine (Group D) has longer duration of complete motor block than Bupivacaine (Group C) and Fentanyl (Group F).

Graph no. 13 : Comparison of total duration of motor blockade

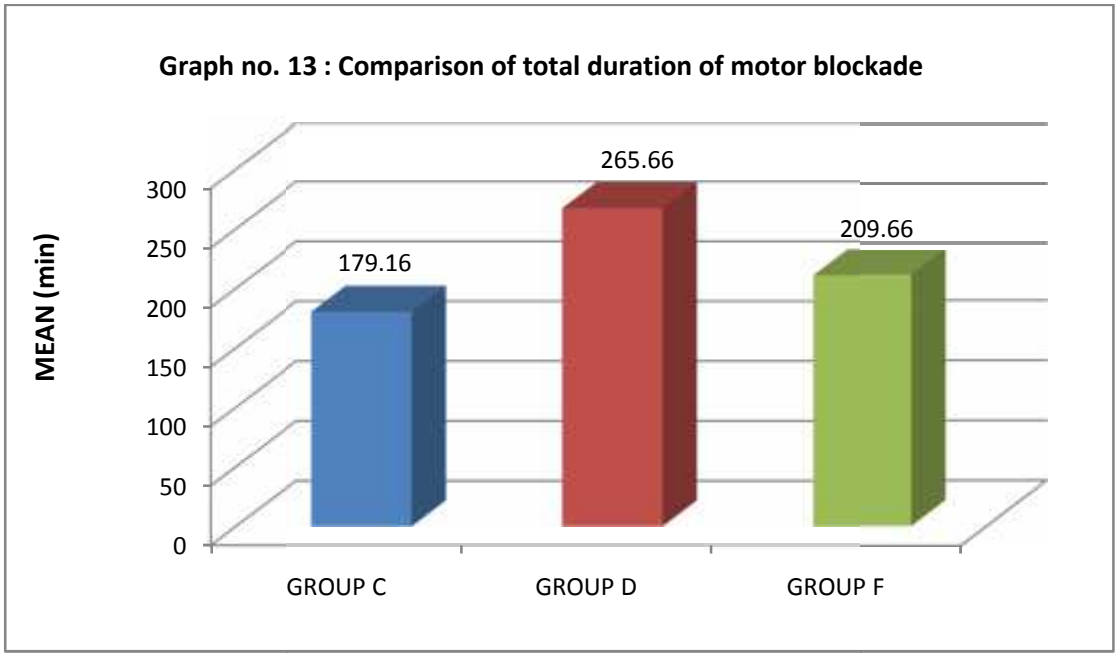


Table no: 14

Comparison of duration of complete analgesia

Time (min)	Group C	Group D	Group F
120-150	1 (3.3%)	0 (0%)	0 (0%)
151-180	12 (40%)	0 (0%)	0 (0%)
181-210	17 (56.7%)	0 (0%)	5 (16.7%)
211-240	0 (0%)	0 (0%)	17 (56.7%)
241-270	0 (0%)	6 (20%)	8 (26.7%)
271-300	0 (0%)	11 (36.7%)	0 (0%)
301-330	0 (0%)	11 (36.7%)	0 (0%)
331-360	0 (0%)	2 (6.7%)	0 (0%)
TOTAL	**30 (100%)**	**30 (100%)**	**30 (100%)**
MEAN ± SD	187.5 ± 15.07 min	301 ± 25.77 min	234 ± 16.31 min
One way ANOVA	F = 253.06 p<0.001, HS		
Multiple comparison	**Group C vs Group D**	**Group C vs Group F**	**Group D vs Group F**
p-value	<0.001, HS	<0.001, HS	<0.001, HS

p-value is significant if <0.05 and highly significant if < 0.001.

Total duration of complete analgesia was taken as the time between the administration of the local anaesthetic intrathecally to the onset of the tolerable pain (VAS ≥ 0) at rest.

The mean duration of complete analgesia in the group C was 187.5 ± 15.07 min, in the group F was 234 ± 16.31 min and in the group D was 301 ± 25.77 min.

The differences for mean duration of complete analgesia between the three groups were found to be statistically highly significant (p<0.001). The group D showed longer duration of complete analgesia than group C and group F, while duration of analgesia in group F was longer than group C, both of which was found to be statistically highly significant (p<0.001).

Thus, Dexmedetomidine (Group D) has longer duration of complete analgesia than Bupivacaine (Group C) and Fentanyl (Group F).

Graph no. 14 : Comparison of duration of complete analgesia

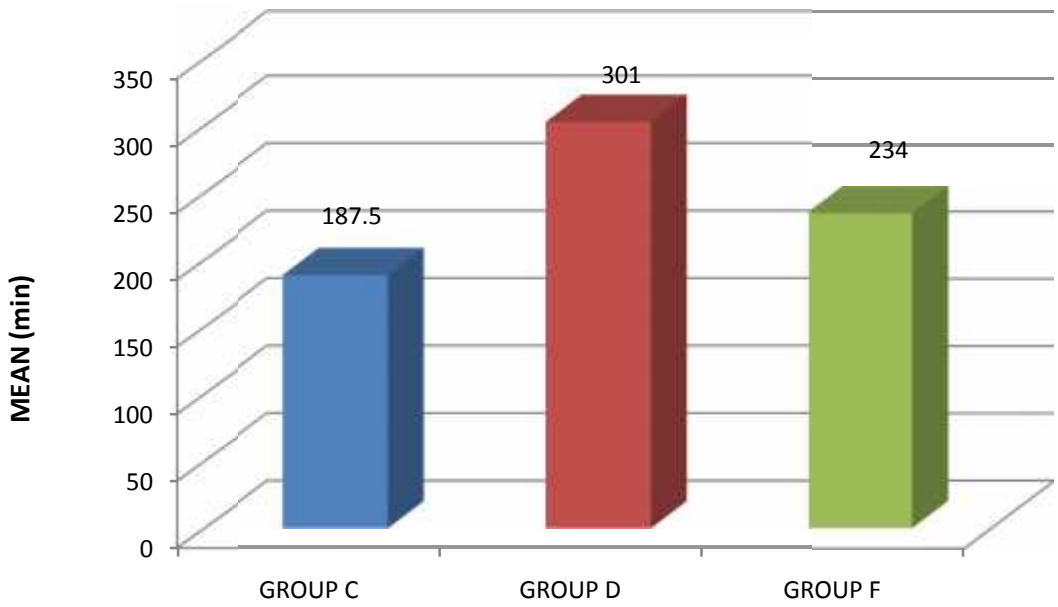


Table no: 15
Comparison of time of rescue analgesia

Time (min)	Group C	Group D	Group F
181-210	9 (30%)	0 (0%)	0 (0%)
211-240	15 (50%)	0 (0%)	1 (3.3%)
241-270	6 (20%)	0 (0%)	10 (33.3%)
271-300	0 (0%)	4 (13.3%)	15 (50%)
301-330	0 (0%)	5 (16.7)	4 (13.3%)
331-360	0 (0%)	10 (33.3%)	0 (0%)
361-390	0 (0%)	8 (26.7%)	0 (0%)
391-420	0 (0%)	3 (10%)	0 (0%)
TOTAL	**30 (100%)**	**30 (100%)**	**30 (100%)**
MEAN ± SD	228.16 ± 17.54 min	358 ± 32.63 min	284.33 ± 20.45 min
One way ANOVA	F = 213.04 p<0.001, HS		
Multiple comparison	**Group C vs Group D**	**Group C vs Group F**	**Group D vs Group F**
p-value	<0.001, HS	<0.001, HS	<0.001, HS

p-value is significant if <0.05 and highly significant if < 0.001.

Time of rescue analgesia was time from intrathecal injection to VAS score greater than or equal to 4 at rest recquiring supplementary (rescue) analgesia in the form of Inj. Diclofenac sodium intramuscular in the dosage of 1.5 mg/kg.

The mean time of rescue analgesia in the group C was 228.16 ± 17.54 min, in the group F was 284.33 ± 20.45 min and in the group D was 358 ± 32.63 min.

The differences for mean time of rescue analgesia between the three groups were found to be statistically highly significant (p<0.001). The group D showed longer duration of time of rescue analgesia than group C and group F, while time of rescue analgesia in group F was longer than group C, both of which was found to be statistically highly significant (p<0.001).

Thus, Dexmedetomidine (Group D) has longer duration of time of rescue analgesia than Bupivacaine (Group C) and Fentanyl (Group F).

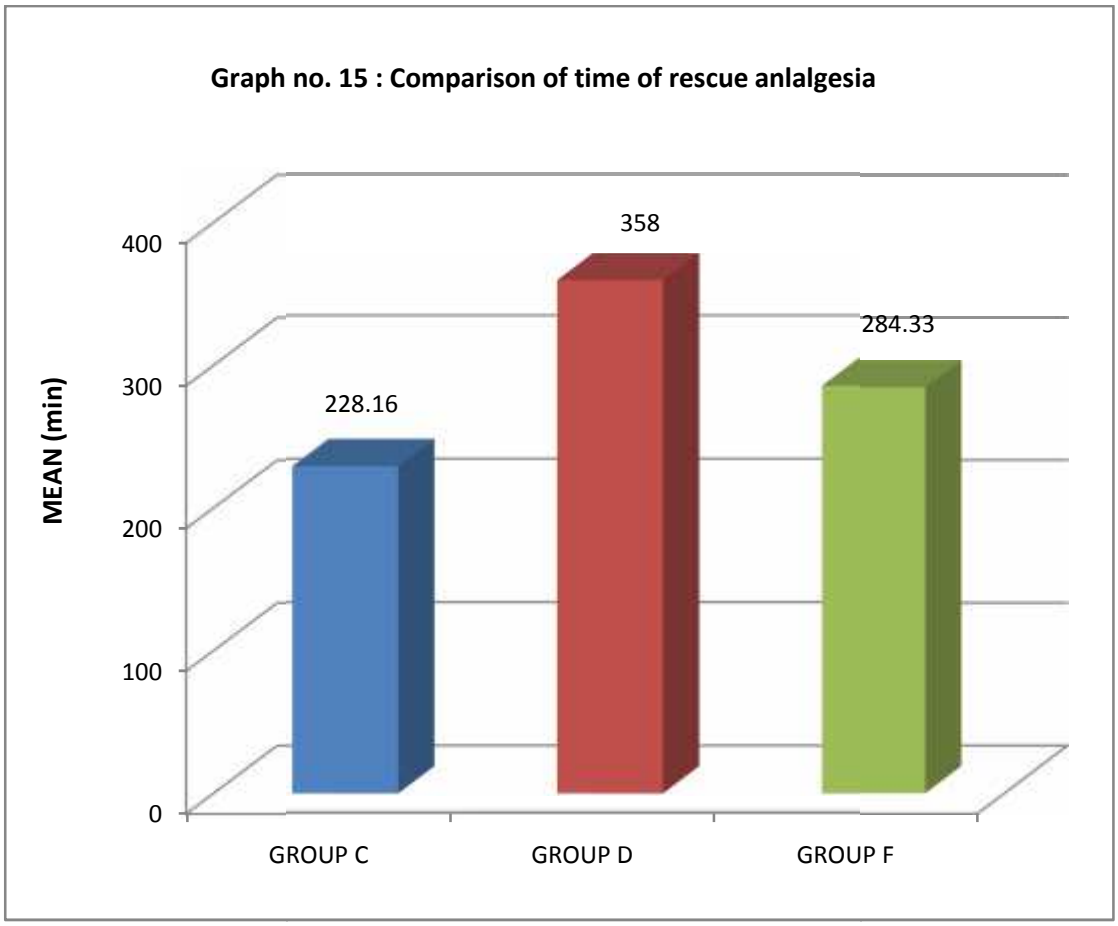

Graph no. 15 : Comparison of time of rescue anlalgesia
MEAN (min)
400
300
200
100
0
228.16
358
284.33
GROUP C
GROUP D
GROUP F

Table no: 16

Comparison of total amount of analgesia recquired postoperatively

	Group C	**Group D**	**Group F**
MEAN ± SD	212.5 ± 28.42 mg	160 ± 38.05 mg	187.5 ± 38.14 mg
One way ANOVA	F = 16.72 p<0.0001, HS		
Multiple comparison	**Group C vs Group D**	**Group C vs Group F**	**Group D vs Group F**
p-value	<0.001, HS	0.022, S	0.010, S

p-value is significant if <0.05 and highly significant if < 0.001.

VAS scores were used to assess the amount of analgesic recquired postoperatively. Visual Analogue Scale (VAS) score was used intraoperatively and post-operatively at 0, 60,120, 180, 240, 360, 480 minute, 12 and 24 hour. When score found more than 4, Injection Diclofenac was given intramuscularly as a rescue analgesic in the dosage of 1.5mg/kg.

The mean amount of analgesic recquired postoperatively in the group C was 212.5 ± 28.42 mg, in the group F was 187.5 ± 38.14 mg and in the group D was 160 ± 38.05 mg.

The difference for mean amount of analgesic recquired postoperatively between the three groups were found to be statistically significant. The group D recquired lesser amount of drug for analgesia than group C and group F, while amount of analgesia recquired in Group F was less than group C, both of which was found to be statistically significant.

Thus, Dexmedetomidine (Group D) recquired lesser amount of analgesic drug as compared to Bupivacaine (Group C) and Fentanyl (Group F).

Graph no. 16 : Comparison of total amount of analgesia recquired postopertively

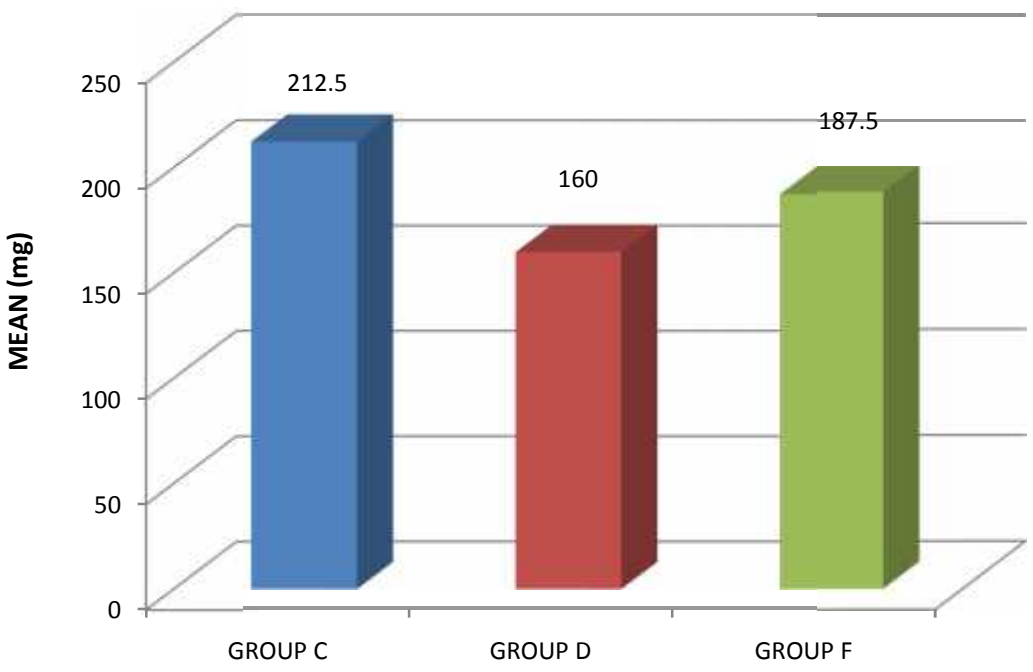


Table no: 17

Comparison of mean pain scores at various time intervals

Time (min)	Group C	Group D	Group F	p-value
0	1.53 ± 1.96	1.46 ± 2.12	1.5 ± 2.17	
60	0	0	0	0.9924, NS
120	0	0	0	0.9924, NS
180	1 ± 1.20	0	0	0.1780, NS
240	1.6 ± 2.09	0	1.16 ± 1.08	0.0504, NS
360	0	2.56 ± 2.04	0	0.0001, HS
480	1.93 ± 0.25	0	0	0.00006, HS
12 hr	2.36 ± 0.49	1.56 ± 0.50	2.13 ± 0.34	0.3824, NS
24 hr	2.23 ± 0.43	1.66 ± 0.48	1.76 ± 0.50	0.6146, NS

p-value is significant if <0.05 and highly significant if < 0.001.

VAS was assessed on a 10cm scale with 0 cm showing no pain and 10 cm = worst pain. Mean VAS score in between the three groups was comparable preoperatively and till the 120 minutes after the injection of the spinal drug.

At 180 and 240 min increasing VAS was seen in group C when compared with the other two groups D and F, but it was statistically insignificant ($p>0.05$). However, at 480 min VAS score in group C was raised at statistically significant level as compared to group D and F. This increase in VAS can be attributed to the lesser duration of analgesia of bupivacaine alone showing higher pain scores at 180, 240 and 480 min intervals.

At 360 min VAS score in group D was more as compared to both groups C and F, which was found to be statistically significant. At 12 and 24 hour postoperatively, VAS score among three groups was found to be comparable. The quality of analgesia was assessed subjectively by the VAS and the comparable mean VAS shows good quality of analgesia in between the three groups.

Graph no. 17 : Comparison of mean pain scores at various time intervals

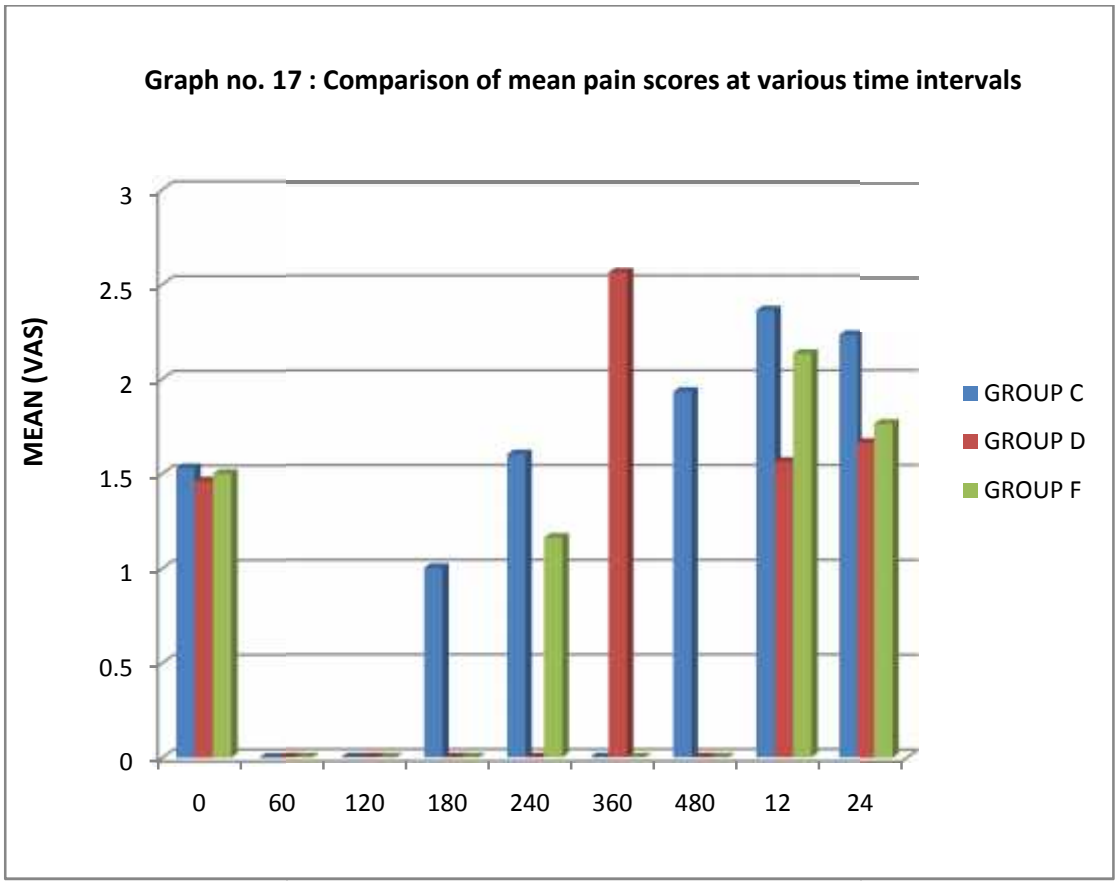


Table no: 18

Comparison of Sedation score using Ramsay Sedation Scale

Time (min)	Group C	Group D	Group F	p-value
0	2	2	2	
15	2	2.03 ± 0.28	2	0.3721, NS
30	2	2.66 ± 0.47	2.16 ± 0.37	<0.0001, HS
60	2.3 ± 0.46	3.16 ± 0.53	2.36 ± 0.49	<0.0001, HS
120	2.5 ± 0.50	3.1 ± 0.66	2.4 ± 0.49	<0.0001, HS
180	2	2.53 ± 0.50	2.46 ± 0.50	<0.0001, HS
240	2	2.46 ± 0.50	2.26 ± 0.44	0.0001, HS
360	2	2.2 ± 0.40	2	0.0012, HS
480	2	2	2	-

p-value is significant if <0.05 and highly significant if < 0.001.

The mean sedation scores were found to be comparable and statistically insignificant ($p>0.05$) preoperatively and at 15 mins among the three groups. But it was found that sedation score was more in group D as compared to both groups C and F at 30, 60, 120, 240 and 360 mins intervals, which was found to be statistically significant ($p<0.001$).

Maximum number of patients in the three groups exhibited a score of two or more at all the time intervals. Intraoperative sedation in any form was avoided to minimize the interference during assessment of the blockade characteristics.

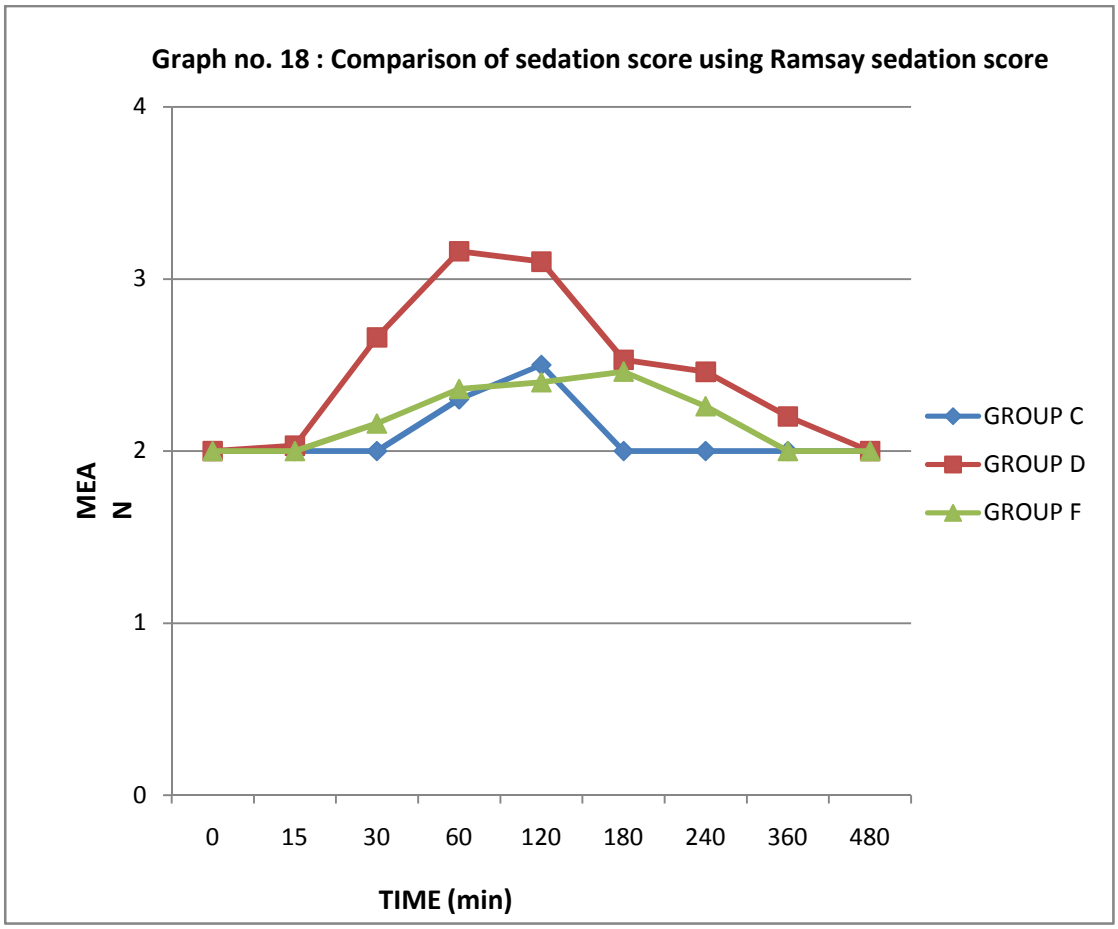

Graph no. 18 : Comparison of sedation score using Ramsay sedation score
MEAN
4
3
2
1
0
0
15
30
60
120
180
240
360
480
TIME (min)
GROUP C
GROUP D
GROUP F

Table no: 19

Comparison of preoperative baseline parameters

Parameter	Group C	Group D	Group F	p-value
PR (beats/min)	82.6 ± 6.06	82.6 ± 6.12	83.4 ± 7.31	0.8608, NS
SBP (mmHg)	122.6 ± 9.44	120.6 ± 6.91	123 ± 8.76	0.5143, NS
DBP (mmHg)	76.6 ± 4.79	78.66 ± 4.34	77.67 ± 5.04	0.2676, NS
MAP (mmHg)	92 ± 4.98	92.56 ± 4.36	92.76 ± 5.49	0.8293, NS
RR (breaths/min)	16.26 ± 1.79	17.13 ± 1.35	17.13 ± 1.71	0.0659, NS
SPO2 (%)	99.3 ± 0.46	99.43 ± 0.50	99.23 ± 0.50	0.7492, NS
VAS	1.73 ± 2.14	1.7 ± 2.24	1.56 ± 2.28	0.9541, NS

p-value is significant if <0.05 and highly significant if < 0.001.

Preoperative baseline parameters like mean baseline pulse rate (PR), mean systolic blood pressure (SBP), mean diastolic blood pressure (DBP), mean arterial pressure (MAP), mean Respiratory rate (RR), peripheral oxygen saturation (SPO2) and visual analogue score (VAS) were comparable and statistically insignificant (p>0.05) between all the three groups.

Graph no. 19 : Comparison of preoperative baseline parameters

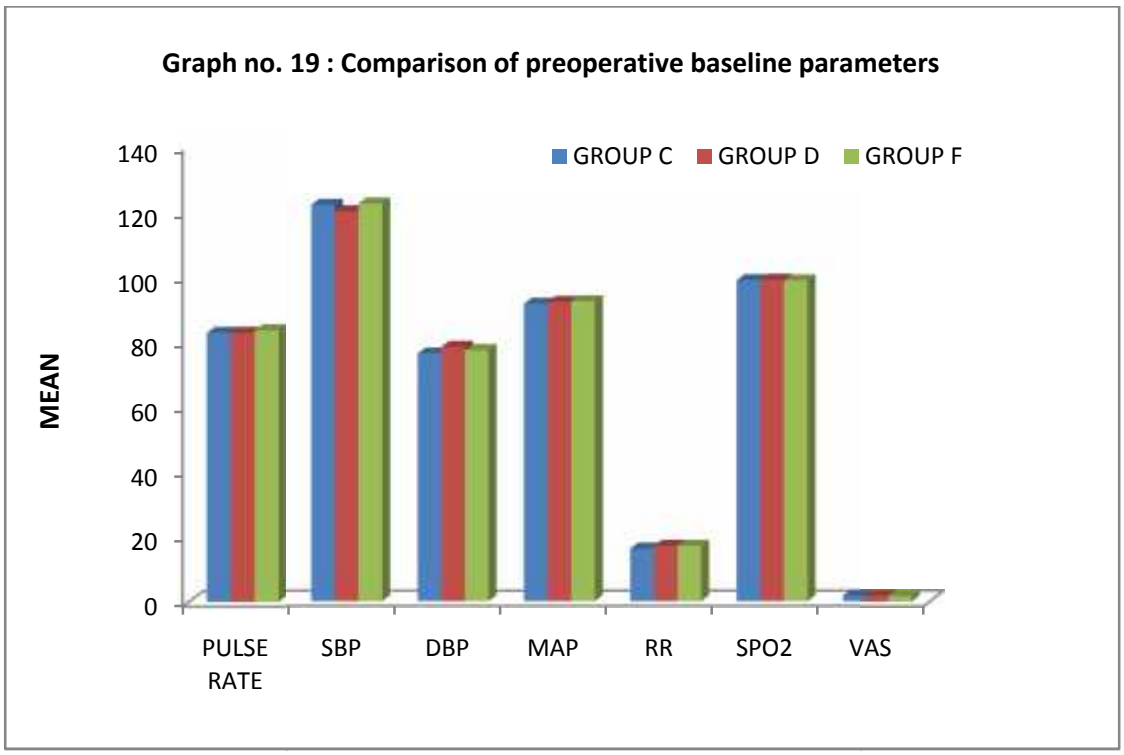


Table no: 20

Comparison of Mean Pulse Rate (beats/min) at various time intervals

Time (min)	Group C	Group D	Group F	p-value
0	82.6 ± 6.06	82.6 ± 6.12	83.4 ± 7.31	
2	81.86 ± 6.32	81.93 ± 6.79	82.53 ± 7.29	0.5406, NS
4	79.8 ± 6.46	80.53 ± 6.21	79.8 ± 7.22	0.3016, NS
6	77.46 ± 6.66	79.2 ± 7.21	77.86 ± 7.04	0.0869, NS
8	75.86 ± 6.88	77.06 ± 6.82	76.46 ± 7.56	0.1827, NS
10	73.86 ± 7.48	75 ± 6.94	74.8 ± 7.90	0.3371, NS
15	71.8 ± 8.15	73.2 ± 6.69	72.73 ± 8.24	0.2550, NS
20	70.33 ± 7.24	71.06 ± 7.29	70.86 ± 7.92	0.8973, NS
25	70.66 ± 5.64	69.8 ± 7.72	70.33 ± 7.39	0.7556, NS
30	71.06 ± 5.50	69.4 ± 5.75	71.06 ± 5.37	0.3468, NS
60	71.33 ± 5.83	70.2 ± 5.04	72.26 ± 6.09	0.4653, NS
90	71.8 ± 5.86	71.53 ± 5.60	73.46 ± 6.27	0.4982, NS
120	73.2 ± 5.86	72.53 ± 5.82	75 ± 6.14	0.3580, NS
180	75.53 ± 4.32	75.26 ± 4.94	76.53 ± 5.40	0.7027, NS
240	76.8 ± 4.77	75.6 ± 4.79	78.33 ± 5.04	0.1063, NS
360	77.93 ± 4.85	76.13 ± 4.78	78.86 ± 5.50	0.0868, NS
480	78.8 ± 4.38	77.26 ± 4.13	79.53 ± 5.52	0.1205, NS

p-value is significant if <0.05 and highly significant if < 0.001.

Preoperatively the mean baseline pulse rate in group C (82.6 ± 6.06 beats/min), group D (82.6 ± 6.12 beats/min) and in group F (83.4 ± 7.31 beats/min) was found to be statistically comparable (p>0.05).

Mean pulse rate changes at all time intervals was found to be statistically insignificant and comparable (p>0.05) in between the 3 groups.

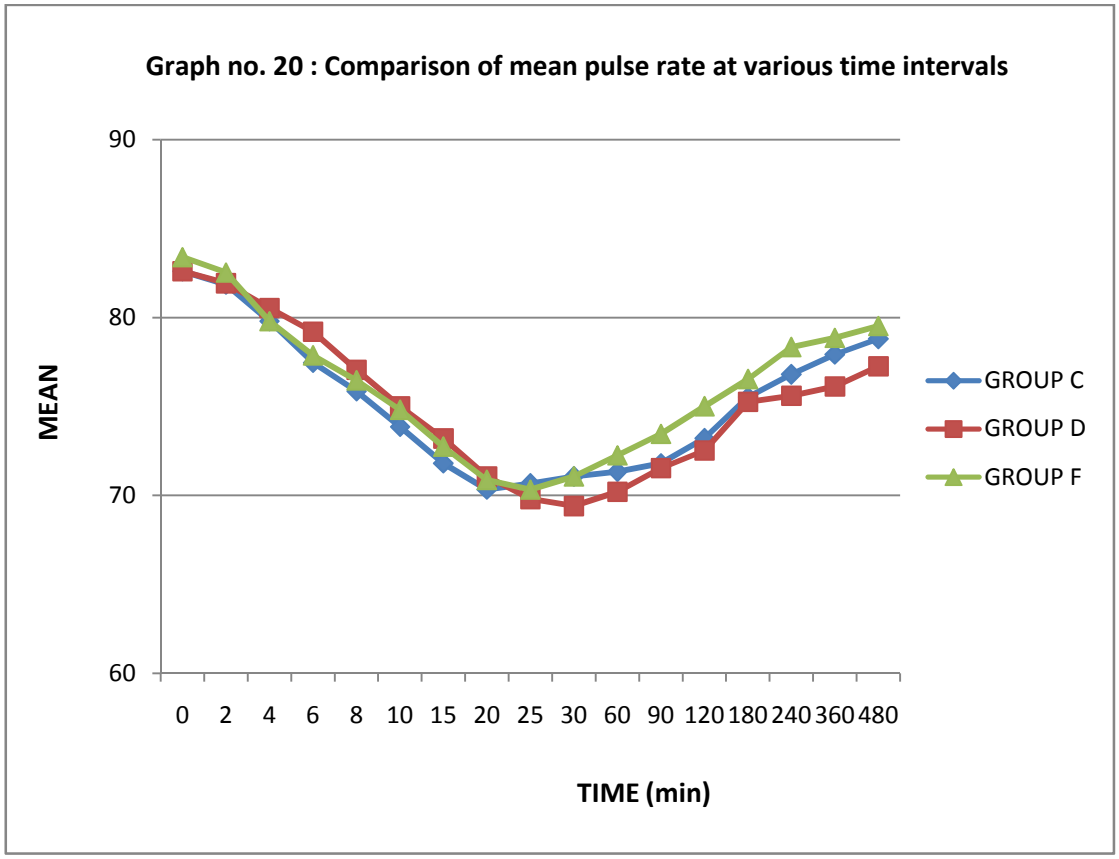

Graph no. 20 : Comparison of mean pulse rate at various time intervals
90
80
70
60
MEAN
0 2 4 6 8 10 15 20 25 30 60 90 120 180 240 360 480
TIME (min)
GROUP C
GROUP D
GROUP F

Table no: 21

Comparison of Mean Systolic Blood Pressure (SBP) at various time intervals

Time (min)	Group C	Group D	Group F	p-value
0	122.66 ± 9.44	120.66 ± 6.91	123.0 ± 8.76	
2	120.8 ± 8.33	120.33 ± 6.86	121.13 ± 8.02	0.1543, NS
4	118.26 ± 7.87	116.53 ± 6.57	118.2 ± 8.02	0.6284, NS
6	116.06 ± 8.55	113.26 ± 6.65	115.26 ± 8.04	0.0728, NS
8	114.2 ± 8.77	111.73 ± 7.67	113.73 ± 8.98	0.2804, NS
10	112.26 ± 9.10	109.46 ± 7.42	112.2 ± 9.01	0.2422, NS
15	109.93 ± 10.20	106.53 ± 7.91	109.53 ± 10.42	0.2677, NS
20	107.6 ± 9.10	103.66 ± 9.27	107 ± 10.20	0.1655, NS
25	105.6 ± 11.35	102.33 ± 6.88	105 ± 9.55	0.2730, NS
30	104.66 ± 8.93	101.53 ± 6.20	103.66 ± 7.82	0.1603, NS
60	103.6 ± 5.83	102.6 ± 4.76	105.13 ± 5.55	0.6814, NS
90	104.6 ± 5.63	104.13 ± 5.60	106.86 ± 5.42	0.5244, NS
120	106.13 ± 6.43	106.06 ± 5.59	108.93 ± 5.24	0.3909, NS
180	110.66 ± 6.43	110 ± 5.27	112.93 ± 5.08	0.4828, NS
240	117.8 ± 14.49	113.86 ± 4.36	117.06 ± 5.11	0.5158, NS
360	116.93 ± 6.25	115.06 ± 4.83	118.53 ± 5.17	0.4434, NS
480	119 ± 6.92	116.46 ± 5.62	118.53 ± 6.86	0.7121, NS

p-value is significant if <0.05 and highly significant if < 0.001.

Preoperatively the mean systolic blood pressure (SBP) between the group C (122.66 ± 9.44 mmHg), group D (120.66 ± 6.91) and group F (123.0 ± 8.76 mmHg) was found to be statistically comparable (p>0.05).

Mean systolic blood pressure (SBP) changes at all time intervals was found to be statistically insignificant and comparable (p>0.05) in between the 3 groups.

Graph no. 21 : Comparison of mean Systolic blood pressure (SBP) at various time intervals

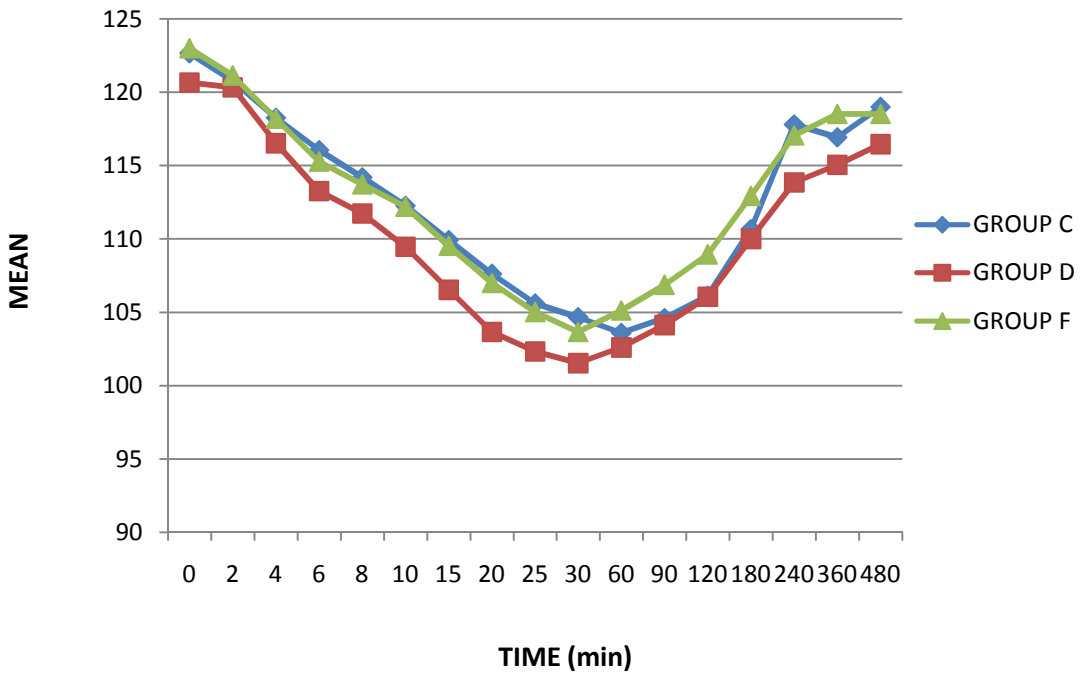


Table no: 22

Comparison of mean diastolic blood pressure (DBP) at various time intervals

Time (min)	Group C	Group D	Group F	p-value
0	76.66 ± 4.79	78.66 ± 4.34	77.66 ± 5.04	
2	75 ± 4.29	77.6 ± 4.53	76 ± 4.54	0.3199, NS
4	73 ± 3.95	75 ± 4.22	73.33 ± 4.14	0.2494, NS
6	71.4 ± 4.55	72.26 ± 4.35	71.6 ± 4.21	0.1708, NS
8	69.06 ± 4.89	70.2 ± 4.18	69.6 ± 4.21	0.4277, NS
10	66.86 ± 4.74	69.4 ± 4.55	67.6 ± 4.85	0.5403, NS
15	64.6 ± 4.78	66.66 ± 3.57	66 ± 4.63	0.8776, NS
20	63.46 ± 5.48	64.26 ± 4.29	63.8 ± 4.24	0.5103, NS
25	61.2 ± 4.65	64.13 ± 2.96	62.53 ± 4.89	0.6175, NS
30	61.26 ± 4.56	64 ± 3.89	62.4 ± 3.90	0.7858, NS
60	62.33 ± 4.98	65.8 ± 4.11	65.2 ± 4.15	0.4208, NS
90	64.46 ± 5.42	67.6 ± 4.40	66.8 ± 4.08	0.6735, NS
120	66.13 ± 4.86	68.53 ± 4.19	68 ± 3.82	0.8573, NS
180	69.13 ± 4.12	71.13 ± 4.05	70.2 ± 3.07	0.9943, NS
240	72.33 ± 3.06	72.93 ± 4.16	74.4 ± 3.76	0.1335, NS
360	73.66 ± 3.56	74.8 ± 3.98	75.46 ± 3.96	0.4407, NS
480	76.26 ± 3.70	76.2 ± 4.04	76.13 ± 4.13	0.3153, NS

p-value is significant if <0.05 and highly significant if < 0.001.

Preoperatively the mean diastolic blood pressure (DBP) between the group C (76.66 ± 4.79 mmHg), group D (78.66 ± 4.34 mmHg) and group F (77.66 ± 5.04 mmHg) was found to be statistically comparable ($p>0.05$).

Mean diastolic blood pressure (DBP) changes at all time intervals was found to be statistically insignificant and comparable ($p>0.05$) in between the 3 groups.

Graph no. 22 : Comparison of mean Diastolic blood pressure (DBP) at various time intervals

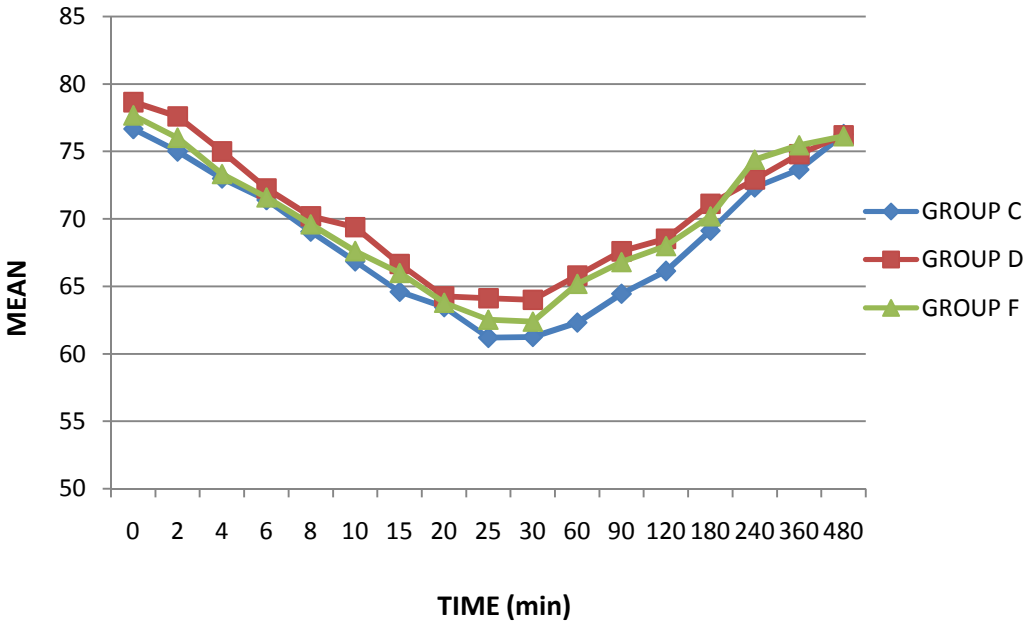


Table no: 23

Comparison of mean of Mean Arterial Pressure (MAP) at various time intervals

Time (min)	Group C	Group D	Group F	p-value
0	92 ± 4.98	92.56 ± 4.56	92.76 ± 5.49	
2	90.2 ± 4.35	91.66 ± 4.56	91 ± 4.84	0.0535, NS
4	88.1 ± 3.88	89.13 ± 4.36	88.3 ± 4.53	0.0705, NS
6	86.3 ± 4.42	85.9 ± 4.39	86.2 ± 4.70	0.1602, NS
8	84.1 ± 4.58	83.96 ± 4.64	84.33 ± 5.08	0.4957, NS
10	82.06 ± 4.80	82.76 ± 4.88	82.4 ± 5.41	0.7090, NS
15	79.76 ± 5.17	79.93 ± 4.50	80.43 ± 5.69	0.8925, NS
20	77.9 ± 4.81	77.43 ± 5.41	78.26 ± 5.23	0.5812, NS
25	76 ± 5.47	76.76 ± 3.37	76.8 ± 5.33	0.9713, NS
30	75.73 ± 4.32	76.43 ± 3.33	76.2 ± 4.02	0.8998, NS
60	76.1 ± 3.88	78.03 ± 3.86	78.56 ± 3.49	0.4262, NS
90	77.9 ± 4.48	79.8 ± 4.17	80.16 ± 3.49	0.5685, NS
120	79.5 ± 4.53	81.03 ± 4.10	81.56 ± 3.70	0.6819, NS
180	83 ± 3.97	84.03 ± 3.84	84.43 ± 3.14	0.8658, NS
240	86 ± 3.06	86.5 ± 3.94	88.53 ± 3.77	0.1785, NS
360	88.33 ± 3.32	88.13 ± 3.50	89.8 ± 3.99	0.4141, NS
480	90.46 ± 4.11	89.56 ± 4.02	90.2 ± 4.36	0.4588, NS

p-value is significant if <0.05 and highly significant if < 0.001.

Preoperatively the mean of mean arterial pressure (MAP) between the group C (92 ± 4.98 mmHg), group D (92.56 ± 4.56 mmHg) and group F (92.76 ± 5.49 mmHg) was found to be statistically comparable ($p>0.05$)

The mean of mean arterial pressure of all the patients at all time intervals was found to be comparable and statistically insignificant ($p>0.05$).

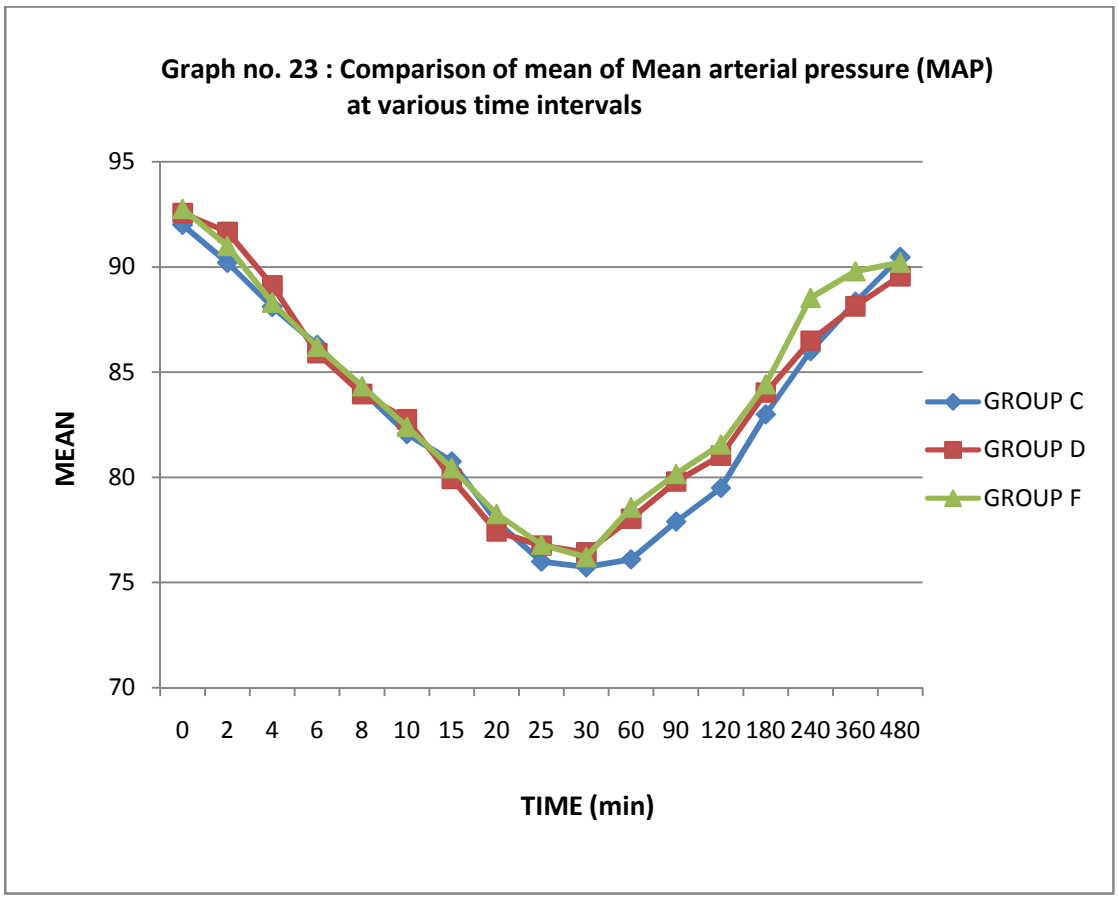

Graph no. 23 : Comparison of mean of Mean arterial pressure (MAP) at various time intervals
95
90
85
80
75
70
MEAN
0 2 4 6 8 10 15 20 25 30 60 90 120 180 240 360 480
TIME (min)
GROUP C
GROUP D
GROUP F

Table no: 24

Comparison of mean respiratory rate (breaths/min) at various time intervals

Time (min)	Group C	Group D	Group F	p-value
0	16.33 ± 1.89	17.13 ± 1.35	17.13 ± 1.71	
2	16.2 ± 1.76	17.0 ± 1.36	16.8 ± 1.44	0.8950, NS
4	16.0 ± 1.81	16.8 ± 1.34	16.73 ± 1.33	0.7949, NS
6	15.93 ± 1.70	17.13 ± 1.35	16.46 ± 1.35	0.9523, NS
8	15.8 ± 1.51	16.86 ± 1.35	16.4 ± 1.32	0.8784, NS
10	15.53 ± 1.71	16.2 ± 1.42	16.0 ± 1.28	0.9122, NS
15	15.06 ± 1.72	15.6 ± 1.22	15.46 ± 1.38	0.6949, NS
20	14.66 ± 1.76	15.33 ± .96	14.93 ± 1.26	0.6506, NS
25	14.26 ± 1.79	14.73 ± 1.33	14.73 ± 1.33	0.4994, NS
30	14.2 ± 1.68	14.46 ± 1.25	14.4 ± 1.32	0.3920, NS
60	13.93 ± 1.52	13.43 ± 1.04	13.26 ± 1.11	0.5403, NS
90	14.13 ± 1.65	12.86 ± 1.00	13.06 ± 1.14	0.2333, NS
120	14.53 ± 1.65	12.66 ± 0.96	13.0 ± 1.01	0.1004, NS
180	14.8 ± 0.99	13.13 ± 1.13	13.13 ± 1.00	0.2604, NS
240	15.0 ± 1.36	14.2 ± 0.80	14.2 ± 1.09	0.3935, NS
360	15.06 ± 1.36	14.33 ± 1.18	14.6 ± 0.93	0.1105, NS
480	15.06 ± 1.25	15.2 ± 1.12	14.93 ± 1.01	0.1816, NS

p-value is significant if <0.05 and highly significant if < 0.001.

Preoperatively the mean Respiratory rate (RR) between the group C (16.33 ± 1.89 breaths/min), group D (17.13 ± 1.35 breaths/min) and group F (17.13 ± 1.71 breaths/min) was found to be statistically comparable (p>0.05).

Mean Respiratory rate (breaths/min) changes at all time intervals was found to be statistically insignificant and comparable (p>0.05) in between the 3 groups.

Graph no. 24 : Comparison of mean respiratory rate at various time intervals

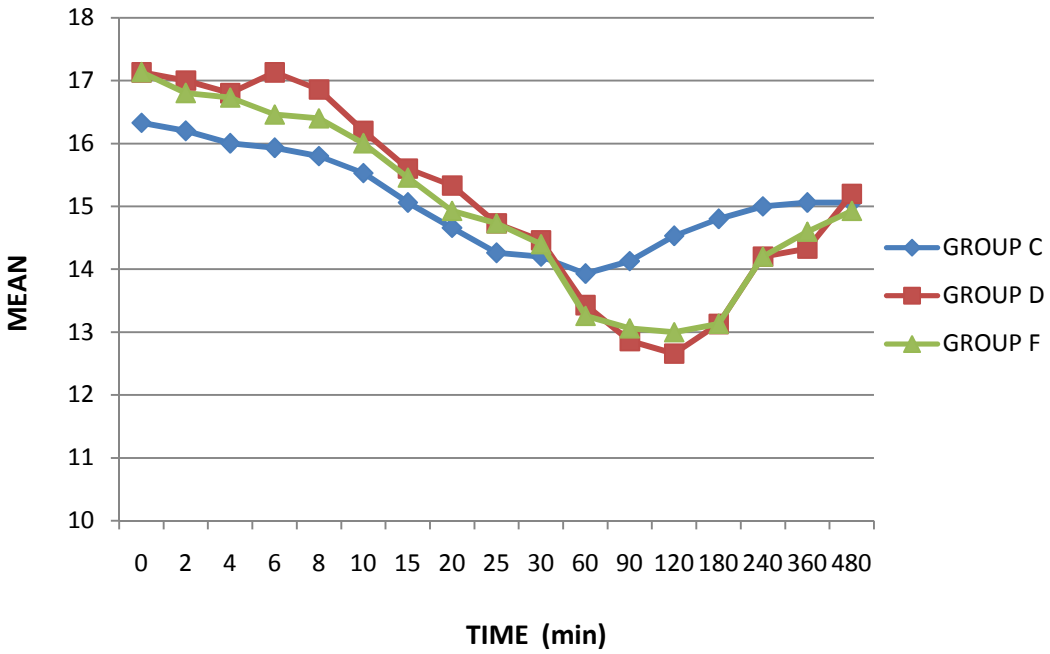


Table no: 25

Comparison of overall incidence of side effects and complications

Complication	Group C	Group D	Group F	p-value
Bradycardia	2 (6.7%)	1 (3.3%)	2 (6.7%)	0.809, NS
Hypotension	4 (13.3%)	2 (6.7%)	3 (10%)	0.690, NS
Nausea and vomiting	3 (10%)	1 (3.3%)	2 (6.7%)	0.585, NS
Shivering	3 (10%)	1 (3.3%)	3 (10%)	0.538, NS
Pruritus	0 (0%)	0 (0%)	3 (10%)	0.104, NS
Respiratory depression	0 (0%)	0 (0%)	0 (0%)	-
Retention of urine	0 (0%)	0 (0%)	0 (0%)	-

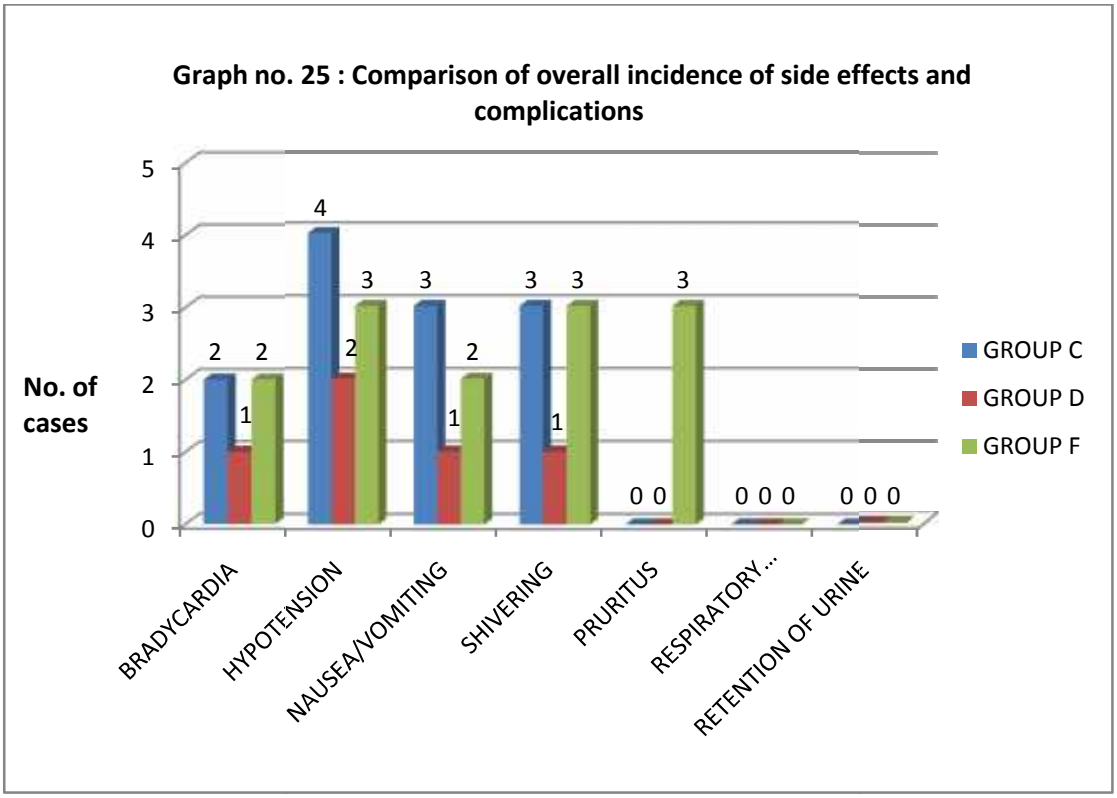
p-value is significant if <0.05 and highly significant if < 0.001.

The incidence of bradycardia was senn in 2 (6.7%) patients in group C and F, and 1 (3.3%) patient in group D. The incidence of hypotension was seen in 4 (13.3%) patients in the bupivacaine group, 3 (10%) patients in the fentanyl group and 2 (6.7%) patients in the dexmedetomidine group. But the differences seen were statistically insignificant.

The incidence of nausea and vomiting was seen in 3 (10%) patients in group C, 2 (6.7%) patient in group F and 1 (3.3%) patient in group D, which was comparable and statistically insignificant (p>0.05). 3 patients each in group C and group F had shivering, while only 1 patient in the group D showed shivering. Pruritus was seen in 3 patients only in group F.

We did not observe respiratory depression (RR < 10 breaths/min) and retention of urine in any of the patients in the three groups. No other side effects like headache, back pain, residual neurologic deficit or transient neurological symptoms were observed in our study.

Graph no. 25 : Comparison of overall incidence of side effects and complications



DISCUSSION

With the advancement in the field of regional anaesthesia and better availability of drugs, spinal anaesthesia has increasingly become the technique of choice and reliable form of anaesthesia for infra-umbilcial surgeries.

There are many choices of drugs to produce spinal anaesthesia. These are procaine, mepivacaine, tetracaine, lidocaine, bupivacaine, levobupivacaine and ropivacaine. These drugs provide spinal anaesthesia of varying duration. Out of these bupivacaine is given routinely for infra-umbilical and lower limb surgeries. It provides with sensory and motor blockade for patient's well being and surgeons work.

It also provides some pain relief in initial postoperative period. But the duration of analgesia is not lengthy enough to relieve pain for extended period in postoperative setting after wearing off of the local anaesthetic effect. It has thus been suggested that anaesthetic technique be designed in such a way, that it will provide residual analgesia in the immediate postoperative period.

Inadequate block intraoperatively as well as inadequate pain relief in postoperative period increases morbidity by causing,

- Sympathetic stimulation thereby leading to increase in heart rate, blood pressure and oxygen consumption.
- Stress response leading to depressed immune function.

Adequate pain relief decreases fear, anxiety, reduces morbidity and thus must be included in anaesthesia planning before induction of anaesthesia. The quality of the spinal anaesthesia has been reported to be improved by the addition of opiods (such as morphine, fentanyl, sufentanil) and other drugs (such as dexmedetomidine, clonidine, magnesium sulphate, neostigmine, ketamine and midazolam) but no drug to inhibit nociception is without associated adverse effects[27] .

Numerous studies since the first clinical use of intrathecal morphine in 1979 have confirmed the efficacy of spinally administered opioids for postoperative pain relief. However, opioids do not remain localized to the site of intrathecal injection after spinal injection, they undergo redistribution by rostral spread, which explains occurrence of nausea, vomiting and respiratory depression.

Fentanyl is a lipophilic µ- receptor agonist opioid. Intrathecal fentanyl prolongs the duration of spinal anaesthesia produced by bupivacaine and lignocaine and this effect has been shown in obstetric and non-obstetric patients undergoing various surgeries[10,59]. The prolongation of the duration of spinal analgesia produced by intrathecal fentanyl is not dose related. In non-obstetric patient studies it was demonstrated that a dose of 25 µg fentanyl for supplementation of spinal anaesthesia produces excellent quality of perioperative analgesia[61,62,63] . Based on previous studies , fentanyl in a dose of 25 µg was used for supplementation of spinal bupivacaine in the present study.

Dexmedetomidine is a highly selective α-2 adrenoreceptor agonist approved as intravenous sedative and adjuvant to anaesthesia. Dexmedetomidine when used intravenously during anaesthesia reduces opiods and inhalational anaesthetic recquirements[64,65] . It is under evaluation as a neuraxial adjuvant as it provides stable haemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects[7,8,9] .

Intrathecal α -2 receptor agonists have been found to have antinociceptive action for both somatic and visceral pain[7] . Compared with clonidine , an α-2 adrenoreceptor agonist, the affinity of dexmedetomidine to α-2 receptors has been reported to be 10 times more than clonidine[66] . Moreover, Kalso et al[67] and Post et al[66] reported a 1:10 dose ratio between intrathecal dexmedetomidine and clonidine in animals.

Al-Ghanem et al[7] assumed that 3-5 µg dexmedetomidine would be equipotent to 30-45 µg clonidine when used for supplementation of spinal bupivacaine. Based on the previous studies and findings, dexmedetomidine in a dose of 5 µg was used for supplementation of spinal bupivacaine in our present study.

After the institutional ethical committee clearance we conducted a prospective, randomized clinical study in the Department of Anaesthesiology, Shri B M Patil Medical College, BLDE University during the period from December 2014 to August 2016, with the aim to study and compare the influence of Fentanyl (25 µg) and Dexmedetomidine (µg) when either drug is injected intrathecally as an adjuvant with hyperbaric Bupivacaine 0.5% (15mg) for spinal anaesthesia.

Ninety patient of ASA physical status I or II undergoing elective infraumbilical surgeries were randomly assigned to receive either

Group C : 15 mg hyperbaric Bupivacaine (0.5%, 3ml) + 0.5ml Normal saline

Group D : 15mg hyperbaric Bupivacaine (0.5%, 3ml) + 5 µg Dexmedetomidine in 0.5ml of normal saine

Group F : 15 mg hyperbaric Bupivacaine (0.5%, 3ml) + 25 µg Fentanyl (0.5ml)

Thorough pre-anaesthetic evaluation was done with minimum necessary investigations for all patients. After clinical evaluation, the procedure to be undertaken was explained in details with the advantages and the risk of possible complications of the procedure and a written informed consent was obtained from each patient and baseline vital parameters were noted in the pre-anaesthetic room.

In the operation theatre, all the necessary equipments and drugs needed for administration of general anaesthesia and for emergency resuscitation were kept ready.

A wide bore 18-20 gauge intravenous line was secured. On operation table, baseline monitoring devices ECG, SpO2, NIBP were attached to patient.

Pulse rate, systolic blood pressure, diastolic blood pressure, respiratory rate, oxygen saturation and VAS were noted before giving subarachnoid block. All patients were preloaded with ringer's lactate solution 10 ml/kg before initiation of subarachnoid block.

With operation table in neutral position, and under all aseptic precautions, lumbar puncture was done in L3-L4 space with 25 G disposable Quincke's spinal needle. Patients were immediately placed in the supine position slowly and given oxygen 4lit/min by nasal oxygen. The onset of sensory analgesia was tested by pinprick.
The time of drug injection was noted and recorded as 0 (t=0).

Following parameters were observed and recorded:

Demographic data: (Refer table no:1,2 and Graph no:1,2)

The patients in the age range of 18 -60 years were included in the study. The mean age in group C was 41.83 ± 9.02 years, in group D was 39.83 ± 10.40 years and in group F was 39.5 ± 8.25 years..

Patients having height > 150cm were included in the study. The mean height in group C was 160.13 ±4.48cm, in group D was 159.1 ± 3.48cm and that of in group F was 158.4 ± 4.21cm.

The mean weight in group C was 55.9 ± 7.31 kg, in group D was 51.56 ± 4.94 kg and in group F it was 53.36 ± 6.65 kg. Thus distribution of patients according to age, height and weight was comparable and statistically insignificant (p>0.05).

Studies conducted by Rajni Gupta et al[25] , Al-Ghanem et al[7] , J.Bogra et al[24] , Hala Eid et al [23] , Kanazi et al [9] , and P Motiani et al [21] showed that all patients were

comparable with respect to age, height and weight in their studies. Thus our study results correlate with above studies.

The distribution of patients according to gender was found to be statistically insignificant amongst the three groups. Sex ratio of 1.30:1 (male:female) in group C,1.14:1 in group D and 1.5:1 in group F was found to be comparable between all three groups ($p>0.05$).

Studies conducted by Rajni Gupta et al [25] , J Bogra et al[24] , Kanazi et al[9] showed that all patients were comparable with respect to gender distribution and sex ratio in their studies. Our study results correlate with above studies.

Distribution of patients according to ASA grading : (Refer Table no: 3 and Graph no: 3)

The distribution of patients according to ASA grading was comparable and statistically insignificant.

Studies conducted by Rajni Gupta et al[25] , Al- Ghanem et al[7] , Kanazi et al[9] showed that all patients were comparable with respect to distribution according to ASA grading in their studies . The above study results are corroborative with our studies.

Type of surgery : (Refer Table no: 4 and Graph no:4)

Though randomly allocated, distribution of patients according to the type of surgery undergone by them was comparable amongst the groups. Surgeries of inguinal hernia repair, orthopaedic surgeries and vaginal hysterectomy were the most common surgeries undertaken.

Studies conducted by Rajni Gupta et al[25] , Al-Ghanem et al[7] , R. Jamliya et al[32] showed that all patients were comparable with respect to distribution of patients according to type of surgery in their studies and our study results correlate with them.

Time of onset of sensory analgesia: (Refer Table no: 5 and Graph no: 5)

The onset of sensory block was observed by assessing the time interval from the injection of the study drug in the subarachnoid space to the complete loss of sensation to pin-prick at the level of L1 dermatome. Sensory block in the present study was tested using the loss of sensation to pin prick as used by others[25] .

The subjective sensation of tingling and warmth in the lower limbs was seen within one minute in all the patients included in the present study. Mean time for the onset of sensory block was significantly longer ($p<0.001$) in group C (151.66 ± 15.33 sec) when compared to group D (128.66 ± 11.36 sec) and group F (125.66 ± 10.06 sec). Group D and group F were comparable with respect to the onset of sensory block ($p=1.000$), while both had onset of sensory block earlier than control group C.

J.Bogra et al[24] , showed comparable onset of sensory block as assessed by loss of pinprick sensation between dexmedetomidine 5 µg added to 3ml of 0.75% isobaric ropivacaine (4.8 ± 1.2 min) and plain ropivacaine (4.7 ± 1.1 min) in patiens operated for lower limb surgeries. Regarding the onset time, our findings do not correlate with that of others. However , a faster onset in our study could be attributed to the use of hyperbaric bupivacaine as compared to isobaric ropivacaine in their study.

Time to achieve maximum level of sensory block : (Refer Table no: 6 and Graph no: 6)

The time to maximum sensory block was considered as the time from the injection of the drug in the subrachnoid space to the time when the maximum level of sensory block was reached.

28 (93.3%) patients in group D and 30 (100%) patients in group F achieved the maximum sensory block level within 9 minutes, while only 3(10%), patients in group

C could achieve this in 9 minutes. Maximum number of patients in group C recquired more time than group D and group F to achieve highest level of sensory block.

Mean time to reach maximum sensory block in group C (9.41 ± 0.56 min) was significantly longer ($p<0.001$) when compared to group D (7.33 ± 0.73 min) and group F (7.13 0.61 min). However, the differences between the group D and group F were comparable and statistically insignificant ($p>0.05$).

Rajni Gupta et al [25] in their study stated that time to achieve complete sensory blockade in the group receiving dexmedetomidine 5 µg was 12.3 ± 1.8 min and in the group receiving fentanyl 25 µg was 12.1 ± 1.7 min and this difference was found to be statistically insignificant. Thus our study results are comparable to it.

Maximum dermatomal level achieved : (Refer Table no: 7 and Graph no: 7)

In the present study highest dermatomal level achieved was T5-T6 in maximum number of patients in group D and F i.e. 28 and 26 respectively. While highest dermatomal level achieved in group C was T6-T7 in 20 patients.

Mean dermatomal level achieved in group C (6.8 ± 1.09) was statistically significant as compared to group D (5.96 ± 0.67) and group F (6.2 ±0.76). however the differences between the group D and group F were comparable and statistically insignificant ($p>0.05$).

The highest cephalad spread of the sensory block was found to be similar between the dexmedetomidine and fentanyl in varying concentrations but equipotent doses and the values were found to be statistically insignificant in the studies done by Rajni Gupta et al [25] and Al-Ghanem et al[7]. The highest cephalad spread of the sensory block in varying concentrations but equipotent doses was found to be similar for dexmedetomidine (T6) in the studies done by J. Bogra et al[24] , R. Jamliya et al[32]

and similar for fentanyl (T6) in the studies done by Amit Jain et al [30] , Binay Kumar et al[26].

Thus our result was in accordance with the findings of the above mentioned studies which states the similar maximum sensory dermatomal level achieved by dexmedetomidine and fentanyl in equipotent doses.

Time of onset of motor blockade : (Refer Table no: 8 and Graph no: 8)

The onset of motor blockade was assessed subjectively when the patient had a feeling of heaviness in his/her lower limbs from the time of injection of the drug into the intrathecal space.

25 (83.3%) patients in groups D and 28 (93.3%) patients in group F had onset of motor analgesia within 150 seconds, while only 2 (6.7%) patients in group C had an onset within 150 seconds. Remaining 28 (93.3%) patients in group C recquired more than 150 seconds.

Mean time for the onset of motor block was significantly longer ($p<0.001$) in group C (178.0 ± 16.48 sec) when compared to group D (140.0 ± 13.89 sec) and group F (138.33 ± 9.12 sec). Group D and group F were comparable with respect to the onset of motor block ($p=1.000$).

Onset characteristics of motor block induced by fentanyl with bupivcaine have not been clearly mentioned by most of the authors. However, onset of motor blockade in group F was not comparable to that reported by Fauzia Khan et al[1] due to lower dose of fentanyl (10 µg) used intrathecally as compared to 25 µg used in our study. Kanazi et al[9] mentioned a faster onset of motor block with the addition of dexmedetomidine with bupivacaine compared to bupivacaine alone.

Time to achieve complete motor blockade: (Refer Table no: 9 and Graph no: 9)

All the patients in the three groups achieved grade 3 motor blockade. 26 (86.7%) patients in group D and 30 (100%) in group F achieved the maximum motor block level within 7 minutes, while only 1 (3.3%) patients in group C could achieve this in 7 minutes. Maximum number of patients in group C i.e. 27 (90%) achieved the maximum motor block level within 9 minutes.

Mean time to achieve maximum motor block in Group C (8.6 ± 0.57 min) was significantly longer ($p<0.001$) when compared to group D (6.67 ±0.63 min) and group F (6.41 ± 0.39 min). However, the differences between the group D and group F were comparable and statistically insignificant ($p<0.05$).

Rajni Gupta et al [25] in their study stated that time to achieve complete motor blockade in the group receiving dexmedetomidine 5 µg was 11.6 ± 1.8 min and in the group receiving fentanyl 25 µg was 11.2 ± 1.3 min and this difference was found to be statistically insignificant. B. Maharani et al[34] in their study stated that addition of dexmeditomidine 10µg to 15 mg of 0.5% hyperbaric bupivacaine had similar time to achieve complete motor block (3.56 ± 1.13 min) as compared to buprenorphine.

In our study we noted that time to achieve complete motor block was faster compared to above studies. The reason for the observed differences between our results and those seen in the other studies mentioned above is not apparent but it could be attributed to the methodological differences such as a difference in the drug dosage, volume of total drug, baricity or subjective difference in interpretation of results.

Total duration of surgery: (Refer Table no: 10 and Graph no: 10)

Total duration of surgery was taken as time from surgical incision to skin closure. Mean duration of surgery in group C was seen to be 100.66 ± 12.84 min, in group D was seen to be 107.33 ± 11.42 min and in group F was seen as 101 ± 13.73

min. Mean time of duration of surgery in all the three groups was comparable and statistically insignificant as p value > 0.05.

Studies conducted by Rajni Gupta et al[25] , Al- Ghanem et al[7], J. Bogra et al [24] showed that all patients were comparable with respect to mean duration of surgery in their studies. Thus our results correlate with above studies.

Time for two segment regression of sensory block : (Refer Table no: 11 and Graph no: 11)

It was defined as the time taken for the dermatomal level to regress from the highest levels to two segments below.

In 28 (93.3%) patients of group C, 27 (90%) patients of group F and 23 (76.7%) patients of group D the dermatomal level showed two segment regression within 105 min, 135 min and 150 minutes respectively.

Mean time to achieve two segment regression of sensory level in group C (92.83 ± 8.37 min) was significantly shorter ($p<0.05$) when compared to group D (146.83 ± 9.14 min) and group F (122.16 ± 11.86 min). Mean time to achieve two segment regression of sensory level in group D was significantly longer than group F, which in turn was longer than group C.

Rajni Gupta et al[25] in their study comparing dexmedetomidine 5µg and fentanyl 25µg stated that the difference was significant ($p<0.05$) between the dexmedetomidine (120 ± 22.2 min) and fentanyl (76 ± 20.3 min) groups for two segment regression. Hala et al [23] showed significantly longer duration for two segment regression with dexmedetomidine 15 µg (200.6 ± 0.9 min), dexmedetomidine 10µg (103 ± 28.7 min) and bupivacaine 15 mg (76.9 ± 26.8 min) in their study.

Our study results correlate with above studies and shows that dexmedetomidine significantly prolongs the time for two segment regression as compared to fentanyl and

bupivacaine, while fentanyl significantly prolongs two segment regression time as compared to bupivacaine.

Time of regression to T12 : (Refer Table no: 12 and Graph no: 12)

It was defined as the time taken for the sensory level to regress from the highest levels of dermatome level T12. In 30 (100%) patients of group C, 3 (10%) patients of group D and 25 (83.3%) of group F, the sensory level showed regression to T12 within 180 minutes. However, 27 (90%) patients of group D and 5 (16.7%) patients of group F showed sensory regression to T12 after 180 minutes.

Mean time to achieve sensory regression to T12 level in group C (139.5 ± 13.60 min) was shorter as compared to group F (169.66 ± 13.76 min) and group D (208.116 ± 16.21 min) and these differences were found to be highly significant statistically ($p<0.001$). The difference in the results of group D and group F was statistically significant with group D having longer duration of sensory block.

Iheb Labbene et al[(12)] in their study of comparison between different doses of hyperbaric bupivacaine (5, 7.5 or 10 mg) with 25 µg of Fentanyl reported that time to T12 regression was prolonged in dose dependent manner. Time to regression to T12 in patients induced with fentanyl has not been mentioned by most of the authors. However, our study shows more prolonged time to regression to T12 in fentanyl group as compared to above stuies. This might be attributed to higher dosage of Bupivacaine used in our study.

Thus in our study we found that dexmedetomidine (Group D) has significantly longer duration of sensory block than Bupivacaine (Group C) and fentanyl (Group F). However , fentanyl has longer duration of sensory block than bupivacaine (Group C).

Total duration of motor blockade : (Refer Table no: 13 and Graph no: 13)

It was time taken from injection of study drug intrathecally to regression of motor block to Bromage grade 0 and noted in minutes. Mean duration of complete motor block in group C was 179.16 ± 14.62 min, in group D was 265.66 ± 19.24 min and in group F was 209.66 ± 14.73 min.

The differences for mean duration of complete motor block between the three groups were found to be statistically highly significant ($p<0.001$). The group D showed longer duration of complete motor block than group C and group F, while duration of complete motor block in group F was longer than group C, both of which was found to be statistically highly significant ($p<0.001$).

Thus, Dexmedetomidine (Group D) has longer duration of complete motor block than Bupivacaine (Group C) and Fentanyl (Group F).

Rajni Gupta et al[25] stated that duration of complete motor block was significantly longer in the dexmedetomidine group (421 ± 21 min) than fentanyl group (149.3 ± 18.2 min) in their study. Al-Ghanem et al[7] in their study stated that duration of complete motor block was significantly prolonged in the dexmedetomidine group (240 ± 64 min) than fentanyl group (155 ± 46 min).

Results of above all studies corroborate with our study as it shows that duration of complete motor block was significantly prolonged in the dexmedetomidine group than fentanyl and bupivacaine group. While at the same time, duration of motor block in fentanyl was significantly prolonged than bupivacaine group.

Total duration of complete analgesia : (Refer Table no: 14 and Graph no: 14)

Total duration of complete analgesia was taken as the time between the administrations of the local anaesthetic intrathecally to the onset of the tolerable pain (VAS ≥ 0) at rest.

The mean duration of analgesia in Group C was 187.5 ± 15.07 min, in the group F was 234 ± 16.31 min and in the group D was 301 ± 25.77 min.

The differences for mean duration of analgesia between the three groups were found to be statistically highly significant ($p<0.001$). The group D showed longer duration of analgesia than group C and group F, while duration of analgesia in group F was longer than group C, both of which was found to be statistically highly significant ($p<0.001$).

Dexmedetomine by acting on α2 adrenoreceptors in substantia gelatinosa of spinal cord and by blocking C and Aδ fibres, increasing the potassium conductance had intensified conduction block of local anaesthetics. It may have an additive or synergistic effect with local anaesthetic in increasing the time of two segment regression and total duration of complete analagesia.

Both the capacity of spinal opiates to reduce the release of excitatory neurotransmitter from C fibres and to decrease the excitability of dorsal horn neuron is believed to account for the powerful and selective effect of opiates on spinal nociceptive processing.

Yegin et al [(11)] in the study reported that the time to first feeling of pain i.e. duration of analgesia was 150 ± 33 min in fentanyl group as compared to 120 ± 32 min in ropivacaine group which was statistically significant. Amit jain et al [30)] in their study in patients undergone total knee replacement surgery found that duration of complete analgesia was 187.1 ± 27.3 min in fentanyl group as compared to 130 ± 16.2 min in

bupivacaine group which was statistically significant. P. Motiani et al [21] stated that duration of analgesia was significantly prolonged in fentanyl (282.1 ± 59.7 min) as compared to bupivacaine group (189.3 ± 29.9 min).

Though there are studies in literature on beneficial effects of addition of intrathecal dexmedeomidine to hyperbaric bupivacaine on prolonged postoperative analgesia, but its influence on the duration of complete analgesia has not been commented in most of studies.

Thus in our study we found that Dexmedetomidine (Group D) has significantly longer duration of analgesia than Fentanyl (Group F) and Bupivacaine (Group C).

Time of rescue analgesia: (Refer Table no: 15 and Graph no: 15)

Time of rescue analgesia was time from intrathecal injection to VAS score greater than or equal to 4 at rest recquiring supplementary (rescue) analgesia in the form of inj. Diclofenac sodium intramuscular in the dosage of 1.5mg/kg.

The mean time of rescue analgesia in the group C was 228.16 ± 17.54 min, in the group F was 284 ± 20.45 min and in the group D was 358 ± 32.63 min.

The differences for mean time of rescue analgesia between the three groups were found to be statistically highly significant ($p<0.01$). The Group D showed longer duration of time of rescue analgesia than Group C and Group F, while time of rescue analgesia in Group F was longer than Group C, both of which was found to be statistically highly significant ($p<0.001$).

Yegin et al [11] in their study reported that the time to first rescue analgesia was 210 ± 31 min in fentanyl group compared to 180 ± 26 min in ropivacaine group ($p<0.05$). Amit Jain et al [30] in their study in patients undergone total knee replacement surgery found that duration of effective analgesia i.e. time of rescue analgesia was

significantly prolonged in fentanyl group (210.7 ± 32.5 min) as compared to bupivacaine group (141.4 ± 21.4 min).

P. Motiani et al [21] stated that duration of effective analgesia i.e. time of rescue analgesia was 485.1 ± 82.7 min in fentanyl group as compared to 256.3 ±60.2 min in bupivacaine group which as statistically significant. Ishwar singh et al [13] in their study stated that time of rescue analgesia in fentanyl was found to be 331 ± 131.2 min with bupivacaine. Rajni Gupta et al [25] in their study stated that time of rescue analgesia was significantly prolonged in dexmedetomidine (251.7 ± 30.6 min) as compared to fentanyl (168.9 ±15.9 min).

B. Maharani et al[34] in their study stated that time of rescue analgesia in dexmedetomidine (295.83 ± 93.21 min) was significantly prolonged as compared to buprenorphine. J. Bogra et al[24] in their study reported that time of rescue analgesia was 478.4 ± 20.9 min in dexmedetomidine as compared to ropivacaine (241.7 ± 21.7 min) which was statistically significant. Ashraf et al [29] in their study on patients operated for major abdominal surgeries found that dexmedetomidine significantly prolongs duration of time of first rescue analgesic.

Results of above all studies were found statistically significant. Thus above study results corroborate with the results of our studies, showing that dexmedetomdine has significantly longer duration of time of rescue analgesia than fentanyl and bupivacaine with prolonged analgesia. While at the same time fentanyl has significantly longer duration of time of resuce analgesia than bupivacaine.

Comparison of total amount of analgesia recquired postoperatively : (Refer Table no: 16 and Graph no: 16)

VAS scores were used to assess the amount of analgesic recquired postoperatively. Visual Analogue Scale (VAS) score was used intraoperatively and not post-operatively at 0, 60, 120, 180, 240,360,480 minute,12 and 24 hour. When score found more than 4, Injection Diclofenac was given intramuscularly as a rescue analgesic in the dosage of 1.5 mg/kg.

The mean amount of analgesic recquired postoperatively in the group C was 212.5 ± 28.42 mg, in the group F was 187.5 ± 38.14 mg and in the group D was 160 ± 38.05 mg.

The differences for mean amount of analgesic recquired postoperatively between the three groups were found to be statistically significant. The group D recquired lesser amount of drug of analgesia than group C and group F, while amount of analgesia recquired in Group F was less than group C, both of which was found to be statistically significant.

Study conducted by Rajni Gupta et al[25] stated that the total analgesic dose of diclofenac recquired in 24 hours was significantly lower in dexmedetomidine (80 ± 67 mg) as compared to fentanyl (180 ± 70 mg) in their study.Thus our study correlates with the above study showing that postoperative analgesic recquirement was lower in dexmedetomidine as compared to fentanyl and bupivacaine with prolonged analgesia.

Study conducted by Amit Jain et al[30] showed that the total number of rescue analgesic doses recquired over 24 hours postoperatively in fentanyl (9.4 ± 1.3) was significantly lower than 0.5% bupivacaine (10.8 ± 1.1).Thus above studies are corroborative with our study showing that the fentanyl recquired less amount of analgesic drug postoperatively as rescue analgesia as compared to hyperbaric bupivacaine.

Quality of anethesia and analgesia : (Refer Table no: 17 and Graph no: 17)

Quality of anesthesia and analgesia was assessed subjectively by VAS score which is a 10 cm scale with 0cm showing no pain and 10cm= worst pain. Mean VAS score in between the three groups was comparable preoperatively and till the 120 minutes after the injection of the spinal drug. Hence, the quality of anaesthesia was comparable in all the three groups even if the duration of analgesia is less with bupivacaine.

At 180 and 240 min increasing VAS score was seen in group C when compared with the other two groups D and F, but it was statistically insignificant ($p>0.05$). However, at 480 min, VAS score in group C was raised at statistically significant level as compared to group D and F. This increase in VAS can be attributed to the lesser duration of analgesia of bupivacaine alone showing higher pain scores at 180,240 and 480 min intervals.

At 360 min VAS score in group D was more as compared to both groups C and F, which was found to be statistically significant. At 12 and 24 hour postoperatively, VAS score among three groups was found to be comparable. The comparable mean VAS score shows good quality of analgesia in between the three groups. Overall, 24 hour VAS score was less in dexmedetomidine with prolonged postoperative analgesia as compared to fentanyl and bupivacaine.

Ashraff et al[29] in their study found that the VAS score showed significant reduction over 24 hours in dexmedetomidine as compared to 0.5% bupivacaine. Above finding correlates with our study showing that overall VAS score was significantly reduced in dexmedetomidine as compared to bupivacaine with improved quality of analgesia. Amit Jain et al[30] in their study showed that overall 24 hour VAS score was

significantly lower in fentanyl (4.3 ± 0.7) as compared to hyperbaric bupivacaine (4.9 ± 0.6). Thus our study findings correlate with the result of above studies.

Sedation score : (Refer Table no: 18 and Graph no: 18)

This was judged subjectively to assess the degree of sedation produced in the patient and evaluated preoperatively and intra-operatively at regular intervals of 0,15, 30, 60, 180,240, 360 and 480 min according to Ramsay Sedation scale.

The mean sedation scores were found to be comparable and statistically insignificant ($p>0.05$) preoperatively and at 15 mins among the three groups. But it was found that sedation score was more in group D as compared to both groups C and F at 30, 60, 120, 240, 360 mins intervals, which was found to be statistically significant ($p<0.001$).

Maximum number of patients in the three groups exhibited a score of two or more at all the time intervals. Intraoperative sedation in any form was avoided to minimize the interference during assessment of the blockade characteristics.

Rajni Gupta et al [25] in their study reported that the mean sedation score was more in dexmedetomidine (3.8 ± 0.5) as compared to 2.2 ± 0.53 in fentanyl, which was statistically significant. Thus our study results correlate with the above study findings.

Monitoring of vitals :

Vital parameters (like pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, respiratory rate and SpO2) of the patient were monitored every 2 min intervals for first 10 minutes, then every 5 minutes interval till 30 minutes, every 15 minutes interval till 60 minutes, every 30 min till 120 min, every hour till 4 hour and then 2 hourly up to 8 hr.

Preoperative baseline parameters : (Refer Table no: 19 and Graph no: 19)

Preoperative baseline parameters like mean baseline pulse rate (PR), mean systolic blood pressure (SBP), mean diastolic blood pressure (DBP), mean arterial pressure (MAP), mean respiratory rate (RR), peripheral oxygen saturation (SpO2) and visual analogue scale (VAS) were comparable and statistically insignificant ($p>0.05$) between all the three groups.

Haemodynamic parameters : (Refer Table no: 20-23 and Graph no: 20-23)

Preoperatively the mean baseline pulse rate in Group C (82.6 ± 6.06 beats/min), in group D (82.6 ± 6.12 beats/min) and in group F (83.4 ± 7.31 beats/min) was found to be statistically comparable ($p>0.05$). Mean pulse rate changes at all time intervals was found to be statistically insignificant and comparable ($p>0.05$) in between the 3 groups.

The mean systolic blood pressure (SBP) between the group C (122.66 ± 9.44 mmHg), group D (120.66 ± 6.91 mmHg) and group F (123.0 ± 8.76 mmHg) and mean diastolic blood pressure (DBP) between the group C (76.66 ± 4.79 mmHg), group D (78.66 ± 4.34 mmHg) and group F (77.66 ± 5.04 mmHg) was found to be statistically insignificant and comparable ($p>0.05$).

The mean of mean arterial pressure (MAP) preoperatively between the group C (92 ± 4.98 mmHg), group D (92.56 ± 4.56 mmHg) and group F (92.76 ± 5.49 mmHg) was found to be statistically comparable ($p>0.05$). The mean systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean of mean arterial pressure (MAP) of all the patients at all time intervals was found to be comparable and statistically insignificant ($p>0.05$)

Kanazi et al[9] in their study of comparison between dexmedetomidine,clonidine and hyperbaric bupivacaine stated that the mean values of MAP and HR were comparable between the three groups throughout the intraoperative and postoperative

period. Al-Ghanem et al [7] in their study of dexmedetomidine and fentanyl added to isobaric bupivacaine showed that the mean values of MAP and HR were comparable between the two groups throughout the study duration. Thus our study results correlate with results of studies conducted by above authors.

Respiratory rate : (Refer Table no: 24 and Graph no: 24)

Opioids are known to depress all phases of respiration by their action on the opioid receptors in the ventral medualla, irrespective of route of administration, but one of the serious side effects is respiratory depression reported after both intrathecal and epidural injections. But it is not necessary to nurse these patients in an ICU, and simple bedside assessment of level of consciousness and respiratory rate is adequate. Guidelines have been issued by European Society of Regional Anaesthesia, that irrespective of age all patients who receive spinal opioids can be nursed in regular wards.[77] .

Intrathecal narcotics, along with enhancing the sensory blockade, provide prolonged postoperative analgesia. But it is associated with increased risk of nausea, vomiting, itching and respiratory depression. Fentanyl is a μ opioid receptor agonist which can be administered safely in subarachnoid space. It is highly lipophilic which prevents its rostral spread. But systemic absorption of the drug could contribute to the lower respiratory rates by direct depressant action on μ receptors in brainstem.

Pre- operatively in our study the mean respiratory rate between the Group C (16.33 ± 1.89 breaths/min), group D (17.13 ± 1.35 breaths/min) and group F (17.13 ± 1.71 breaths/min) was found to be statistically comparable ($p>0.05$). Mean respiratory rate (breaths/min) changes at all time intervals was found to be statistically insignificant and comparable ($p>0.05$) in between the 3 groups.

We did not observe respiratory depression in our study as fentanyl is a highly lipid soluble opioid known to penetrate and egress rapidly from the CSF and this leaves only small quantities of free drug in the CSF for redistribution to higher centres and are therefore less prone to cause delayed respiratory depression. Dexmedetomidine has not been reported to produce any respiratory depression in different studies conducted by various authors.

Side effects and complications : (Refer Table no: 25 and Graph no: 25)

Bradycardia :

Heart rate less than 50 beats/min was considered as bradycardia and treated with inj. Atropine sulphate 0.6mg intravenously.

The incidence of bradycardia was seen in 2 patients each in Group C & Group F and in 1 patient in Group D. It was treated with inj. Atropine sulphate 0.6mg intravenously.

Rajni Gupta et al [(25)] in their study stated that 1 patient in dexmedetomidine group and no patient in fentanyl group as an additive to hyperbaric bupivacaine had bradycardia which was comparable and statistically insignificant. Thus the incidence of bradycardia in our study with dexmedetomidine and fentanyl were consistent with above author's studies.

Hypotension :

A fall of systolic blood pressure of less than 80mmHg or more than 20% of baseline was considered as hypotension and treated with rapid infusion of intravenous fluid ringer lactate 250 ml and 6 mg intravenous inj. Ephedrine if there was no response to intravenous fluid administration.

The incidence of hypotension was seen in 4 patients in the bupivacaine group, 3 patients in the fentanyl group and 2 patients in the dexmedetomidine group. But the

differences were comparable and statistically insignificant. This was treated with rapid infusion of intravenous fluid ringer lactate 250 ml and 6 mg intravenous inj. Ephedrine.

Rajni Gupta et al [25] in their study stated that 3 patients in dexmedetomidine and 2 patients in fentanyl group as an additive to hyperbaric bupivacaine had hypotension which was comparable and statistically insignificant. Thus the incidence of hypotension in our study with dexmedetomdine and fentanyl were consistent with above author's study.

Nausea and vomiting :

The incidence of nausea and vomiting was seen in 3 patients in group C, 2 patients in group F and 1 patient in group D, which was comparable and statistically insignificant ($p>0.05$). It was treated with Inj. Ondansetron 4 mg i.v.

After spinal injection, opioids undergo redistribution by rostral spread leading to direct stimulation of chemoreceptor trigger zone in the floor of fourth ventricle thereby causing nausea and vomiting [78] . Though the incidence of nausea and vomiting is common with opioids, studies have shown decreased incidence of it with intrathecal opioids [77] .

Rajni Gupta et al[25] in their study stated that 1 patient in dexmedetomidine and 2 patients in fentanyl group as an additive to hyperbaric bupivacaine had nausea and only 1 patient in fentanyl group had vomiting which was comparable and statistically insignificant. Thus the incidence of nausea and vomiting in our study with dexmedetomidine and fentanyl correlate with above studies.

Shivering :

Though neuraxial opioids are said to decrease shivering, we observed 3 patients each in group C and group F had shivering, while only 1 patient in the group D showed

shivering intraoperatively which was comparable and statistically insignificant ($p>0.05$).

Pruritus:

Pruritus was seen in 3 patients only in group F, while no patients in group D and C had pruritus. Pruritus was treated with anthihistaminic like injection Pheniramine maleate (Avil). The likely cause of pruritus with spinal opioids is cephalad migration of opioids in CSF, and subsequent interaction of opioid receptor in trigeminal nucleus. Opioid released histamine from mast cells can be another reason of pruritus[79] .

Rajni Gupta et al [25] in their study stated that 1 patient in fentanyl group and none of the patients in dexmedetomidine group as an additive to hyperbaric bupivacaine had pruritus which was statistically insignificant. Thus the incidence of pruritus in our study with dexmedetomidine and fentanyl were consistent with above authors study.

Retention of urine and respiratory depression :

We did not observe respiratory depression (RR <10 breaths/min) or fall in peripheral oxygen saturation below 90% or retention of urine in any of the patients in the three groups.

Other side effects :

No other side effects like headache, back pain, residual neurologic deficit or transient neurological symptoms were observed in our study.

SUMMARY

The present study of comparison of intrathecal Dexmedetomidine (5 µg) and Fentanyl (25 µg) as an adjuvant to 0.5% (15 mg) hyperbaric Bupivacaine in infra-umbilical surgeries was carried out in Shri B M Patil Medical College, BLDE University, during the period of December 2014 to August 2015, after obtaining permission from the institutional Ehical Committee.

It was a prospective, randomized clinical study. The aim of the research was to compare the block characteristics of Dexmedetomidine and Fentanyl when added as an adjuvant to bupivacaine. The study included total 90 patients belonging to ASA grade 1 and 2 in the age group of 18-60 years with height more than 150 cm posted for elective infra-umbilical surgeries.

A detailed history and pre-anaesthetic examination was done. Necessary investigations were done. The detailed prodedure to be undertaken was explained to the patient. Written informed consent was taken. Patients were randomly allocated to 3 groups of 30 each, receiving

Group C : 15 mg hyperbaric Bupivacaine (0.5%, 3ml) + 0.5ml of normal saline

Group D : 15 mg hyperbaric Bupivacaine (0.5%,3ml) + 5 µg Dexmedetomidine in 0.5ml of Normal saline

Group F : 15 mg hyperbaric Bupivacaine (0.5%,3ml) + 25 µg Fentanyl (0.5ml) intrathecally.

Under all aseptic precautions, lumbar puncture was carried out in left lateral position in L_{3-4} interspace with 25 G Quincke's lumbar puncture needle. After free flow and aspiration of CSF, the proposed drug was injected slowly over 10-15 sec. Patients turned supine slowly.

Vital parameters, blockade characteristics, VAS, sedation, intraoperative complications and adverse reactions of drugs were noted. The demographic data such as age, sex, height and weight being comparable had no influence on outcome of the study. There was no significant difference in the type and duration of surgery.

Mean time for the onset of sensory block(time taken to reach the L1 dermatome from the injection of the drug in the subarachnoid space) was found to be significantly longer ($p<0.001$) in group C (151.66 ± 15.33 sec) when compared to Group D (128.66 ± 11.36 sec) and group F (125.66 ± 10.06 sec). Group D and Group F were comparable with respect to the onset of sensory block ($p = 1.000$), while both had onset of sensory block earlier than control group C.

In our study mean time to achieve maximum sensory block in Group C (9.41 ± 0.56 min) was significantly longer ($p<0.001$) when compared to group D (7.33 ± 0.73 min) and group F (7.13 ± 0.61 min). However, the differences between the group D and group F were comparable and statistically insignificant ($p>0.05$). Mean dermatomal level achieved in group C (T 6.8 ± 1.09) was statistically significant as compared to group D (T 5.96 ± 0.67) and group F (T 6.2 ± 0.76). however, the differences between the group D and group F were comparable and statistically insignificant ($p>0.05$).

Mean time for the onset of motor block was significantly longer ($p<0.001$) in group C (178.0 ± 16.48 sec) when compared to group D (140.0 ± 13.89 sec) and group F (138.33 ± 9.12 sec). Group D and group F were comparable with respect to the onset of motor block ($p= 1.000$), while both having faster onset as compared to bupivacaine.

Mean time to achieve maximum motor block in group C (8.6 ± 0.57 min) was significantly longer ($p<0.001$) when compared to group D (6.67 ± 0.63 min) and group F (6.41 ± 0.39 min). However, the difference between the group D and group F were

comparable and statistically insignificant ($p>0.05$), while both recquiring less time to achieve maximum motor block.

Mean time to achieve two segment regression of sensory level in group C (92.83 ± 8.37 min) was significantly shorter ($p<0.05$) when compared to group D (146.83 ± 9.14 min) and group F (122.16 ± 11.86 min). Mean time to achieve two segment regression of sensory level in group D was significantly longer than group F, which in turn was longer than group C.

Mean time to achieve sensory regression to T12 level in group C (139.5 ± 13.60 min) was shorter as compared to group F (169.66 ± 13.76 min) and group D (2.8.116 ± 16.21 min) and these differences were found to be highly significant statistically ($p<0.001$). the difference in the results of group D and group F was statistically significant with group D having longer duration of sensory block.

Mean time of total duration of complete motor block in group C was 179.16 ± 14.62 min, in group D was 265.66 ± 19.24 min and in group F was 209.66 ± 14.73 min. The group C achieved complete motor recovery in a shorter time compared to both group D and group F, and this difference was found to be highly significant statistically ($p<0.001$). However, Group D showed prolonged duration of motor blockade than both group F and group C, while group F showed earlier complete motor recovery than group D and both were found to be statistically significant ($p<0.001$).

The mean duration of complete analgesia in the group C was 187.5 ± 15.07 min, in the group F was 234 ± 16.31 min and in the group D was 301 ± 25.77 min. The differences for mean duration of complete analgesia between the three groups were found to be statistically highly significant ($p<0.001$). The group D showed longer duration of analgesia than group C and group F, while duration of analgesia in group F was longer than group C.

The mean time of rescue analgesia in the group C was 228.16 ± 17.54 min, in the group F was 284.33 ± 20.45 min and in the group D was 358 ± 32.63 min. The differences between the three groups were found to be statistically highly significant ($p<0.001$). The group D showed longer duration of time of rescue analgesia than group C and group F, while time of rescue analgesia in group F was longer than group C, both of which was found to be statistically highly significant ($p<0.001$).

The mean amount of analgesic recquired postoperatively in the group C was 212.5 ± 28.42 mg, in the group F was 187.5 ± 38.14 mg and in the group D was 160 ± 38.05 mg. The differences between the three groups were found to be statistically significant. The group D recquired lesser amount of drug for analgesia than group C and group F, while amount of analgesia recquired in group F was lesser than group C.

Mean VAS score in between the three groups was comparable preoperatively and till the 120 minutes after the injection of the spinal drug. Hence the quality of anaesthesia was comparable in all the three groups even if the duration of analgesia is less with bupivacaine. Overall 24 hour VAS score was less in dexmedetomidine with prolonged postoperative analgesia as compared to fentanyl and bupivacaine.

The mean sedation scores were found to be comparable and statistically insignificant ($p>0.05$) preoperatively and at 15 mins among the three groups. But it was found that sedation score was more in group D as compared to both groups C and F at 30, 60,120,240 and 360 mins intervals, which was found to be statistically significant ($p<0.001$).

Mean pulse rate changes at all time intervals was found to be statistically insignificant and comparable ($p>0.05$) in between the 3 groups. The mean systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean of mean arterial

pressure (MAP) of all the patients at all time intervals was found to be comparable and statistically insignificant ($p>0.05$).

Respiratory rates were clinically comparable at all time intervals in the three groups and none of the patients showed respiratory depression. Peripheral oxygen saturation remained in between 99-100% in all patients of both the groups during intraoperative and postoperative period with oxygen supplementation by nasal prongs.

In our study incidence of bradycardia was seen in 2 patients each in group C and F, while only 1 patient in group D. It was treated with Inj. Atropine sulphate 0.6 mg intravenously. Hypotension was seen in 4 patients in the bupivacaine group, 3 patients in the fentanyl group and 2 patients in the dexmedetomidine group. But the differences seen were comparable and statistically insignificant. This was treated with rapid infusion of intravenous fluid ringer lactate 250 ml and 6 mg intravenous inj. Ephedrine.

The incidence of nausea and vomiting was seen in 3 patients in group C, 2 patients in group F and 1 patient in group D. Though neuraxial opioids are said to decrease shivering, we observed 3 patients each in group C and group F had shivering, while only 1 patient in group D showed shivering intraoperatively which was comparable and statistically insignificant. Pruritus was seen in 3 patients only in group F, while no patients in group D and C had pruritus. Pruritus was treated with antihistaminic like injection Pheniramine maleate (Avil).

We did not observe respiratory depression (RR<10 breaths/min) or fall in peripheral oxygen saturation below 90% and retention of urine in any of the patients in the three groups. No other side effects like headache, back pain, residual neurologic deficit or transient neurological symptoms were observed in our study.

CONCLUSIONS

After the clinical comparative study of intrathecal Dexmedetomidine (5 µg) and Fentanyl (25 µg) as an adjuvant to 0.5% (15 mg) hyperbaric Bupivacaine in infraumbilical surgeries following conclusions were drawn:

- Both Dexmedetomidine and Fentanyl had comparably faster onset of sensory and motor blockade as compared to 0.5% Bupivacaine.
- Dexmedetomidine significantly prolonged the duration of sensory and motor block with excellent quality of anaesthesia as compared to fentanyl and bupivacaine.
- Dexmedetomidine as an adjuvant significantly prolonged the duration of complete analgesia and time of rescue analgesia as compared to fentanyl and bupivacaine.
- Amount of postoperative analgesic recquirement was less in dexmedetomidine as compared to fentanyl and bupivacaine leading to improved quality of analgesia.
- Haemodynamic alterations in the three groups were found to be minimal. No unexpected adverse events were registered. Adverse effects that occurred in the three groups were statistically insignificant.

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ANNEXURES

ETHICAL CLEARANCE CERTIFICATE

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

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 22-1-2014 *at* 3.30pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title "A randomised clinical trial to compare between the effectiveness of Dexmedetomidine & fentanyl as adjuvants in spinal Anaesthesia"

Name of P.G. student Dr Tom George
Dept of Anaesthesiology.

Name of Guide/Co-investigator Dr S.G. Talikoti Prof & HOD
Dept of Anaesthesiology

for
DR.TEJASWINI VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDE(U)'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

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

CONSENT FORM

CONFIDENTIALITY:

I understand that medical information produced by this study will become a part of this hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code key connecting name to numbers will be kept in a separate secure location.

If the data is used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photographs and videotapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time. **Dr. Tom George** is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me.

And that a copy of this consent form will be given to me to keep for careful reading.

REFUSAL OR WITHDRAWL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that **Dr. Tom George** will terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist, if this is appropriate.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have explained to _____ the purpose of this research, the procedure required and the possible risks and benefits, to the best of my ability in patient's own language.

Date : Dr. D G Talikoti (Guide) Dr. Tom George (Investigator)

STUDY SUBJECT CONSENT STATEMENT:

I confirm that **Dr. Tom George** has explained to me the purpose of this research, the study procedure that I will undergo and possible discomforts and benefits that I may experience, in my own language.

I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give my consent to participate as a subject in this research project.

_____ _____

(Participant) (Date)

_____ _____

(Witness to above signature) (Date)

CASE STUDY PROFORMA

A RANDOMISED CLINICAL TRIAL TO COMPARE BETWEEN THE EFFECTIVENESS OF DEXMEDETOMIDINE AND FENTANYL AS ADJUVANTS IN SPINAL ANAESTHESIA.

Case no. Date :

Name of patient: Age :

Sex: M / F Weight: Height: Reg. no.:

Diagnosis:

Name of surgery:

Preoperative assessment:

History:

G/E: PR: /min BP : / mmHg

RR: /min

S/E : CVS: PS :

CNS: P/A :

Investigation:

HB: gm% Blood group:

Urine Albumin/sugar: BSL:

KFT : LFT:

ECG : BT:

CXR : CT:

Patient to receive intrathecally either of the three:

Group C : Inj. Bupivacaine 15mg (0.5%, 3ml) + Normal Saline (0.5m1)

Group D : Inj. Bupivacaine 15mg (0.5%, 3m1) + Inj. Dexmedetomidine 5µg (Diluted in Normal Saline 0.5m1)

Group F : Inj. Bupivacaine 15mg (0.5%, 3m1) + Inj. Fentanyl 25µg (0.5m1) Time of subarachnoid block

Blockade characteristics:

1) Onset of sensory analgesia:
2) Onset of motor blockade:
3) Time of maximum sensory level:
4) Time of maximum motor blockade:
5) Maximum dermatomal level achieved:
6) Degree of motor blockade:

Morning of vital and block parameters

Time of drug injection	Pulse rate (/min)	Blood pressure (mmHg)	Resp. rate (/min)	SpO2 (%)	Sensory level	Grade of motor block	VAS (cm)	Sedation score	Intra op supplementation	Complication
0 min										
2 min										
4 min										
6 min										
8 min										
10 min										
15 min										
20 min										
25 min										
30 min										
45 min										
60 min										
90 min										
120 min										
150 min										
180 min										
210 min										
240 min										
360 min										
480 min										

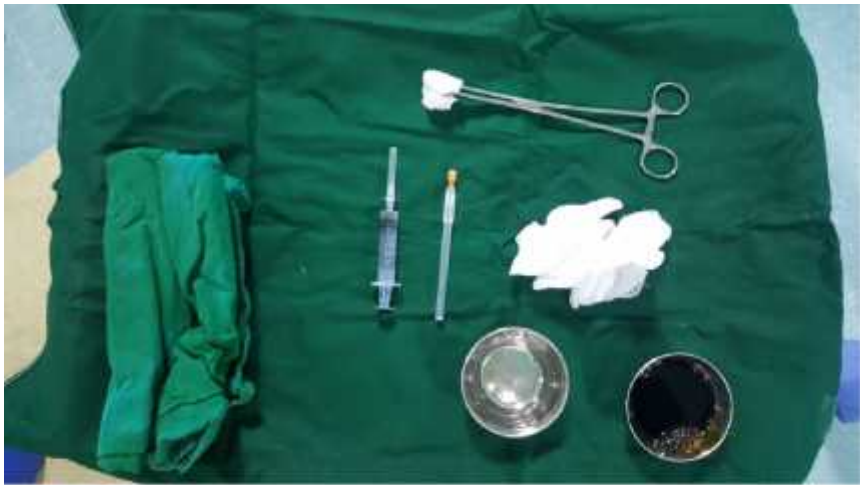
Total IV fluid given intraoperatively:

1) Duration of surgery:
2) Time of two segment regression:
3) Time to regression to T12:
4) Total duration of motor blockade:
5) Duration of complete analgesia
6) Time of rescue analgesia:

Intra operative / Post operative complication and treatment:

- Bradycardia:
- Hypotension:
- Nausea:
- Vomiting:
- Shivering:
- Pruritus:
- Respiratory depression:
- Urinary retention:

PHOTOGRAPHS

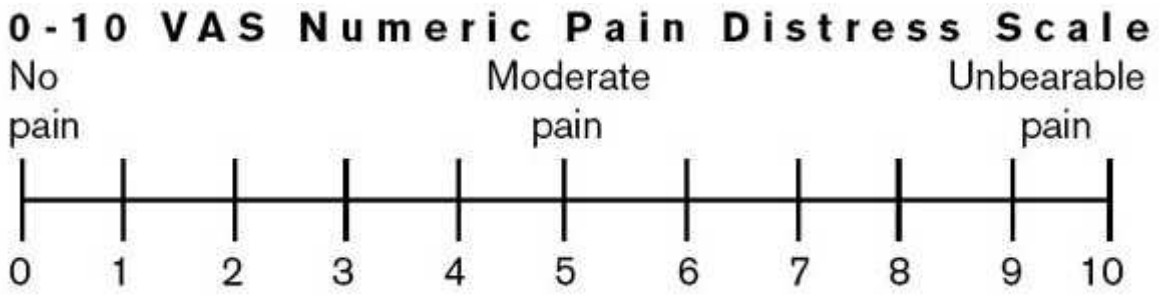


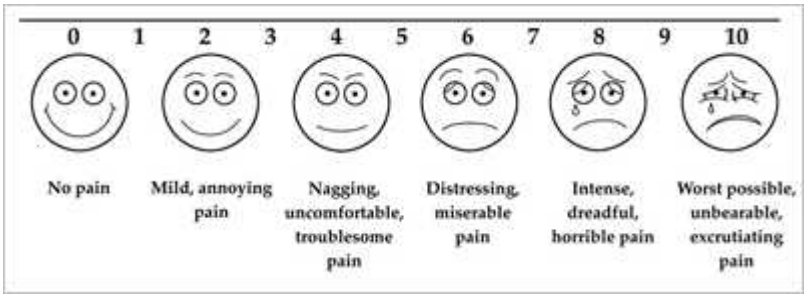
SCORE AND SCALE

MODIFIED BROMAGE SCALE [80]

Grade	Criteria	Degree of block
0	Free movements of leg and feet	Nil (0%)
1	Knee flexion decreased but with full flexion of feet and ankles	Partial (33%)
2	Unable to flex knees, flexion of ankle and feet present	Partial (33%)
3	Unable to flex knee or ankle, or move toes	Complete paralysis (100%)

VISUAL ANLOGUE SCALE (VAS) [81]





Ramsay sedation score [32, 82]

Score	Criteria
I	Patient is anxious, agitated and restless or both
II	Patient is co-operative, oriented and tranquil
III	Patients respond to verbal commands only
IV	Patient exhibits brisk response to glabellar tap or loud auditory stimulus
V	Patient exhibits sluggish response to glabellar tap or loud auditory stimulus
VI	Patient exhibits no response

MASTERSHEET - GROUP D (BUPIVACAINE - DEXMEDETOMIDINE)

Sr.No.	Age (yrs)	Gender	Height (cm)	Weight (kg)	ASA	Type of surgery	Preoperative monitoring PR	BP	MAP	RR	Spo2 (%)	VAS	Time of onset of sensory analgesia (sec)	Time of onset of motor blockade (sec)	Time of highest sensory level (mins)	Time of maximum motor block (mins)	Highest sensory level	Grade of motor block
1	30	Male	162	62	2	Tibia nailing	92	130/90	103	16	100	4	120	150	8	6	T6	3
2	21	Male	160	48	2	Femur nailing	84	130/80	97	14	100	5	140	160	7	6	T6	3
3	22	Male	165	55	2	Tibia plating	90	120/80	93	16	99	5	120	140	6	6	T6	3
4	24	Male	160	45	2	Tibia plating	82	120/80	93	14	100	5	130	150	7	6.5	T6	3
5	50	Male	158	45	2	Tibia nailing	74	110/70	83	18	99	6	140	160	8	7	T8	3
6	35	Female	156	51	2	Femur nailing	94	120/80	93	16	99	4	150	150	7	6.5	T6	3
7	40	Female	164	52	2	Femur plating	84	120/80	93	18	100	4	110	140	6.5	6	T5	3
8	25	Male	158	56	2	Tibia nailing	92	130/80	97	16	100	5	130	140	8	7	T6	3
9	39	Female	156	52	2	Tibia nailing	90	120/80	93	20	100	5	150	160	8	7	T5	3
10	42	Female	160	58	2	Femur nailing	86	110/80	90	18	100	4	130	130	7	8	T6	3
11	21	Male	160	46	1	Meshplasty	78	120/80	93	16	100	0	110	120	6.5	6.5	T6	3
12	52	Male	158	52	1	Meshplasty	86	130/80	97	18	100	0	140	140	9	8	T6	3
13	55	Male	166	56	1	Meshplasty	82	120/80	93	16	100	0	120	120	6.5	6	T6	3
14	28	Male	160	58	1	Eversion of sac	84	120/80	93	18	99	0	130	140	9	8	T6	3
15	30	Male	162	52	1	Meshplasty	76	130/80	97	18	99	0	140	160	8	7	T6	3
16	35	Male	158	55	1	Meshplasty	80	120/80	93	18	100	0	120	150	7.5	7	T5	3
17	42	Male	156	54	1	Eversion of sac	76	120/80	93	16	100	0	130	160	8	7.5	T5	3
18	46	Male	166	52	1	Eversion of sac	88	130/80	97	18	100	0	140	150	8	7	T6	3
19	48	Male	160	48	1	Eversion of sac	76	120/80	93	18	99	0	120	150	7.5	7	T5	3
20	37	Male	164	62	1	Meshplasty	86	130/80	97	18	99	0	140	140	7	6	T6	3
21	52	Female	154	46	2	Vaginal hysterectomy	76	120/80	93	18	99	0	130	120	6.5	6	T6	3
22	42	Female	156	50	2	Ovarian cyst excision	80	110/80	90	18	99	2	130	110	7.5	6.5	T6	3
23	45	Female	156	45	2	Vaginal hysterectomy	82	120/70	87	16	99	0	110	120	6.5	6	T6	3
24	40	Female	152	48	1	Vaginal hysterectomy	86	120/80	93	18	99	0	130	130	7.5	7	T6	3
25	46	Female	158	52	2	Vaginal hysterectomy	72	110/70	83	18	100	0	120	140	7	6	T8	3
26	48	Female	160	56	2	Ovarian cyst excision	88	130/80	97	18	100	2	120	130	7.5	6.5	T6	3
27	50	Female	158	52	1	Ovarian cyst excision	86	120/80	93	16	100	0	130	140	6.5	6	T6	3
28	52	Female	156	48	1	Vaginal hysterectomy	78	110/80	90	16	100	0	130	130	7	6.5	T6	3
29	47	Female	158	46	1	Ovarian cyst excision	72	110/70	83	18	100	0	110	130	7	7	T6	3
30	51	Female	156	45	1	Vaginal hysterectomy	78	120/70	87	18	99	0	140	140	7.5	6.5	T6	3

Intraoperative and postoperative monitoring – Pulse rate / min (mins)

Sr.No.	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480
1	92	94	90	94	88	86	86	84	80	82	78	76	74	72	76	78	82	80	84	86
2	84	84	88	86	80	78	76	72	74	70	68	66	70	74	72	76	74	72	72	78
3	90	88	86	86	88	86	84	80	78	76	78	80	82	80	80	84	86	82	84	82
4	82	82	80	84	78	76	74	72	68	66	64	68	66	70	72	74	72	70	72	76
5	74	74	76	72	70	70	68	66	62	60	64	66	68	68	72	70	70	72	74	76
6	94	96	92	90	88	86	84	82	86	80	76	78	80	82	80	84	82	86	82	84
7	84	82	82	80	76	74	68	66	76	78	82	80	84	86	82	80	76	78	74	74
8	92	96	94	92	90	86	84	82	80	78	76	74	78	80	82	84	80	84	82	86
9	90	88	86	84	82	84	82	82	80	76	74	72	70	70	74	72	72	76	74	78
10	86	86	84	82	80	78	76	78	74	74	72	70	70	72	74	76	76	78	80	78
11	78	76	74	76	72	68	64	58	48	66	76	78	76	74	74	76	78	76	76	74
12	86	84	80	80	78	76	74	72	70	70	72	68	66	64	68	68	70	70	72	74
13	82	82	80	84	80	78	78	74	72	70	70	72	74	72	76	76	78	76	80	78
14	84	84	82	80	78	76	72	70	68	66	68	68	70	66	70	72	70	74	76	74
15	76	76	74	70	68	66	64	60	62	66	68	72	74	76	76	78	80	78	76	74
16	80	80	76	78	74	72	70	68	66	64	64	66	68	70	70	72	70	74	76	76
17	76	70	68	64	62	60	62	66	64	64	66	58	70	72	74	76	74	78	74	78
18	88	86	86	84	84	80	78	76	74	72	72	70	70	72	74	76	72	76	78	78
19	76	76	78	74	72	68	70	66	64	62	66	68	68	70	72	74	76	72	70	74
20	86	84	80	82	80	78	74	76	72	70	68	66	70	72	74	76	72	72	74	76
21	76	76	74	70	72	68	68	66	62	64	68	68	70	72	68	70	70	74	74	76
22	80	78	78	74	76	76	74	72	70	66	68	70	72	72	74	76	76	74	76	76
23	82	82	80	78	76	72	74	68	66	68	70	68	70	72	74	76	74	72	74	78
24	86	84	80	80	78	76	72	70	70	68	68	66	62	64	68	70	70	74	72	76
25	72	70	70	68	66	64	62	58	64	66	60	60	62	62	64	64	66	68	68	70
26	88	86	86	84	80	80	78	76	78	76	74	78	82	86	82	84	88	86	90	88
27	86	86	84	82	82	80	76	78	74	70	72	72	76	76	78	80	80	82	78	80
28	78	78	76	72	74	70	70	68	66	62	60	64	66	68	70	72	74	70	76	74
29	72	72	76	74	70	70	68	64	62	66	68	64	66	68	70	70	72	72	70	70
30	78	78	76	72	70	68	66	52	64	66	68	70	72	74	76	74	72	72	76	76

Intraoperative and postoperative monitoring – Systolic Blood pressure in mmHg (mins)

Sr.No.	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480
1	130	130	126	122	120	118	114	112	110	108	112	110	114	116	114	118	120	122	120	130
2	130	126	122	120	120	118	116	112	110	108	106	110	114	116	116	120	120	126	122	128
3	120	120	112	110	110	104	100	98	96	94	98	100	104	106	108	110	112	110	120	120
4	120	122	118	116	114	112	110	108	104	100	96	102	104	106	108	110	120	118	120	110
5	110	110	108	106	102	100	98	94	90	92	96	100	102	102	104	100	102	108	110	120
6	120	120	118	116	112	108	104	102	100	106	104	108	110	112	114	116	112	118	120	110
7	120	116	112	102	96	92	88	80	96	102	104	108	110	106	108	112	114	110	104	110
8	130	128	126	122	122	118	114	112	110	108	106	108	110	112	116	118	120	116	118	120
9	120	120	116	114	112	114	110	108	102	98	94	98	100	102	104	100	106	110	112	116
10	110	108	106	102	100	98	94	96	96	98	102	100	102	104	110	106	108	110	120	120
11	120	130	116	114	110	108	104	100	98	96	102	106	108	110	112	114	116	114	110	110
12	130	130	126	122	124	120	118	116	112	108	106	108	104	102	108	110	112	116	118	120
13	120	120	114	114	112	108	106	108	104	102	100	98	102	106	108	110	110	114	110	110
14	120	120	116	112	110	110	108	104	100	102	104	106	108	110	112	114	116	112	110	114
15	130	130	126	122	122	118	116	114	112	110	106	104	104	108	106	110	112	116	120	120
16	120	120	116	114	112	110	106	104	102	108	110	112	116	118	120	120	116	118	116	120
17	120	120	118	110	112	112	110	108	106	106	104	102	100	100	104	106	110	112	114	116
18	130	126	122	122	120	116	114	112	110	108	104	102	100	104	108	110	110	114	116	116
19	120	118	114	112	110	108	96	80	96	98	102	100	102	106	108	110	112	116	118	120
20	130	130	128	124	122	120	116	114	112	110	106	104	106	110	110	112	116	114	118	120
21	120	120	118	112	114	110	110	108	106	102	100	98	94	96	100	106	108	110	114	116
22	110	110	108	104	102	100	96	92	90	96	98	104	108	104	102	106	108	110	112	108
23	120	120	116	112	110	108	106	100	98	96	98	100	104	108	110	112	114	118	120	120
24	120	120	116	114	112	112	110	110	106	104	100	98	94	96	100	104	108	110	112	114
25	110	110	106	105	102	100	100	98	98	94	90	94	96	98	100	106	104	108	110	110
26	130	128	126	122	122	120	118	114	112	110	110	106	104	108	106	110	112	116	118	120
27	120	118	116	112	112	110	108	104	102	100	98	100	104	106	108	110	112	114	114	118
28	110	110	108	104	102	100	98	96	92	90	94	98	100	104	106	106	108	110	110	108
29	110	110	106	104	100	102	98	98	94	90	90	94	96	98	100	102	104	108	106	110
30	120	120	116	112	114	110	110	108	106	102	100	100	104	108	110	112	114	118	120	120

Intraoperative and postoperative monitoring – Diastolic Blood pressure in mmHg (mins)

Sr.No.	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480	0	2	4	6	8
1	90	90	88	84	80	76	72	70	70	68	66	68	72	70	74	78	82	84	80	80	103	103	101	97	93
2	80	78	76	70	72	74	68	66	68	64	70	68	72	74	80	82	80	84	84	72	97	94	91	87	88
3	80	80	72	68	66	64	62	60	62	64	60	60	64	66	70	72	70	70	70	80	93	93	95	82	81
4	80	84	78	78	76	74	72	70	68	66	68	70	74	70	74	78	80	76	80	70	93	97	91	90	89
5	70	70	68	68	66	64	66	62	62	64	66	68	70	68	66	68	68	70	70	80	83	83	81	81	78
6	80	78	76	74	72	68	64	62	64	66	68	70	70	68	72	74	70	74	80	70	93	92	90	88	85
7	80	76	70	66	62	60	58	56	62	66	68	68	66	70	72	70	70	70	72	70	93	89	84	78	73
8	80	78	76	74	70	72	68	66	62	68	64	70	70	74	74	72	76	78	80	82	97	95	93	90	87
9	80	80	76	74	72	76	70	72	68	66	64	66	68	68	70	70	66	68	70	72	93	93	89	87	85
10	80	78	78	74	72	70	66	62	68	70	68	66	70	70	72	68	70	70	70	80	90	88	87	83	81
11	80	80	76	72	68	66	66	64	62	66	68	70	70	70	72	74	72	76	76	80	93	93	89	86	82
12	80	80	76	74	72	70	68	66	64	62	66	70	66	68	68	70	70	74	76	78	97	97	93	90	89
13	80	78	76	76	70	74	66	66	64	64	60	64	66	68	68	70	72	70	74	70	93	92	89	89	84
14	80	78	76	72	70	68	68	66	62	66	68	66	70	72	70	68	72	74	78	76	93	92	89	85	83
15	80	80	78	76	74	70	68	66	66	64	66	62	60	64	66	64	68	70	74	76	97	97	94	91	90
16	80	80	76	74	70	70	68	66	68	70	72	74	76	78	80	76	78	76	76	80	93	93	89	87	84
17	80	80	78	74	72	76	74	70	68	66	64	62	64	66	68	70	70	70	72	74	93	93	91	86	85
18	80	80	76	74	70	68	68	66	62	60	58	60	64	62	66	68	70	72	74	78	97	95	91	90	87
19	80	80	78	76	76	72	62	54	66	68	68	66	68	68	70	70	74	72	76	80	93	93	90	88	87
20	80	76	74	72	70	70	68	66	64	60	62	66	68	68	70	72	70	74	78	80	97	94	92	89	87
21	80	74	76	72	70	70	66	64	64	60	60	66	68	64	70	68	72	70	74	76	93	89	90	85	85
22	80	78	76	74	70	70	68	66	64	68	70	70	72	74	76	72	78	70	70	74	90	89	87	84	81
23	70	70	68	66	64	66	62	62	60	58	60	66	68	70	70	66	68	70	74	76	87	87	84	81	79
24	80	80	78	76	72	70	68	64	60	58	60	56	58	58	62	68	66	70	68	72	93	93	91	89	85
25	70	70	68	64	64	62	60	58	64	66	62	66	68	66	70	72	68	66	70	68	83	83	81	78	77
26	80	78	74	72	76	74	70	68	66	62	60	58	56	60	64	66	68	70	72	76	97	95	91	89	91
27	80	78	76	72	70	74	68	66	64	66	68	66	70	72	76	78	76	76	80	80	93	91	89	85	84
28	80	78	76	72	72	70	68	66	64	62	66	68	70	72	74	70	72	76	74	78	90	89	87	83	82
29	70	70	68	66	62	64	66	62	60	58	62	64	66	68	66	70	72	74	76	78	83	83	81	79	75
30	70	68	68	64	66	60	62	56	58	54	52	60	64	68	70	70	72	74	76	80	87	85	84	80	82

Intraoperative and postoperative monitoring: Mean blood pressure in mmHg (mins)															Intraoperative and postoperative monitoring: Respiratory rate / min (mins)																				Intraoperative and postoperative monitoring: Oxygen saturation (%) (mins)																				Intraoperative and postoperative monitoring: Visual Analouge Scale (mins)							(hr)		Intraoperative and postoperative monitoring: Sedation score (mins)									Intraoperative supplementation	Intraoperative or postoperative complication	Total duration of surgery (mins)	Time of two segment regression (mins)	Time to regression to T12 (mins)	Total duration of motor block (mins)	Duration of analgesia (mins)	Time of rescue analgesia (mins)	Total amount of analgesia required postoperatively (mg)
10	15	20	25	30	45	60	90	120	150	180	210	240	360	480	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480	0	60	120	180	240	360	480	12	24	0	15	30	60	120	180	240	360	480									
90	86	84	83	81	81	82	86	85	87	91	94	96	93	97	16	14	16	16	16	16	16	16	14	14	14	14	14	14	12	12	12	14	12	12	100	99	99	99	98	98	98	98	99	99	99	99	100	99	98	99	99	99	99	99	4	0	0	0	0	5	0	1	2	2	2	2	3	3	3	3	2	2	NIL	NIL	110	140	220	280	280	360	150
89	84	81	82	79	82	82	86	88	92	94	93	98	96	90	14	14	14	14	14	14	14	14	12	12	12	13	12	12	12	12	14	14	14	14	100	100	100	100	99	99	99	99	99	99	100	99	99	99	99	99	99	100	99	99	4	0	0	0	0	5	0	1	2	2	2	2	3	3	2	2	2	2	NIL	NIL	120	150	210	270	300	360	150
77	75	73	73	74	73	73	77	79	83	85	84	83	87	93	16	16	16	16	16	16	16	16	14	14	14	14	12	12	12	12	14	14	14	14	99	99	99	99	99	99	98	98	98	98	98	99	99	99	99	99	99	98	98	98	5	0	0	0	0	0	0	2	2	2	2	2	4	4	2	2	2	2	NIL	NIL	100	135	190	250	250	300	150
87	85	83	80	77	77	81	84	82	85	89	93	90	93	83	14	14	14	14	14	14	14	14	12	12	12	12	12	14	14	14	14	12	12	14	100	100	99	99	98	98	98	98	98	98	99	98	99	99	99	99	99	98	99	99	5	0	0	0	0	0	0	2	2	2	2	3	3	3	3	3	2	2	NIL	NIL	90	145	200	240	260	300	150
76	77	73	71	73	76	79	81	79	79	79	79	83	83	93	18	18	18	18	18	18	18	16	16	16	16	14	14	12	12	12	14	14	14	14	99	99	99	99	98	98	98	98	98	98	98	99	99	98	99	99	99	99	99	99	4	0	0	0	0	0	0	1	2	2	2	2	2	3	2	2	2	2	NIL	NIL	110	130	170	240	270	330	150
81	77	75	76	79	80	83	83	83	86	88	84	89	93	83	16	16	16	16	16	16	16	14	14	14	14	12	12	12	14	14	14	14	16	16	99	99	99	99	99	98	98	98	98	99	99	99	99	98	98	98	99	99	99	99	4	0	0	0	0	2	0	1	2	2	2	3	3	3	3	2	2	2	NIL	NIL	120	140	180	270	300	390	150
71	68	64	73	78	80	81	81	82	84	84	85	83	83	83	18	18	18	18	18	18	16	16	16	16	14	14	12	12	12	12	14	14	14	16	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	4	0	0	0	0	2	0	1	1	2	2	3	3	2	2	3	2	2	inj.Ephedrine	Hypotension	130	150	240	300	320	420	75
87	83	81	78	81	78	83	83	87	88	87	91	90	93	95	16	16	16	16	16	14	14	14	14	14	12	12	12	12	12	14	14	14	12	16	100	100	100	99	99	99	98	98	99	99	99	99	99	99	99	99	99	99	99	99	5	0	0	0	0	5	0	2	1	2	2	3	3	3	3	2	2	2	NIL	NIL	120	160	230	270	280	360	150
89	83	84	79	77	74	77	79	79	81	80	79	82	84	87	20	18	20	20	18	18	18	16	16	14	14	14	12	12	12	14	14	14	14	16	100	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	5	0	0	0	0	5	0	2	2	2	2	2	4	4	3	2	2	2	NIL	NIL	90	160	220	250	290	360	150
79	75	73	77	79	79	77	81	81	85	81	83	83	87	93	18	18	18	18	18	18	16	16	16	16	16	14	14	14	12	12	12	14	14	16	100	100	99	99	99	99	99	98	98	98	99	99	99	99	99	99	99	99	99	99	4	0	0	0	0	0	0	2	2	2	2	3	3	3	2	2	3	2	NIL	NIL	100	150	200	230	270	330	225
80	79	76	74	76	79	82	83	83	85	87	87	89	87	90	16	16	16	16	16	14	14	14	14	14	14	12	12	12	12	14	14	14	14	16	100	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	0	2	0	1	2	2	2	2	3	3	3	3	3	2	Inj. Atropine	Bradycardia	110	150	225	300	330	390	150
87	85	83	80	77	79	83	79	79	81	83	84	88	90	92	18	18	18	18	18	16	16	16	16	14	14	14	12	12	12	12	12	14	14	16	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	0	5	0	1	2	2	2	3	3	3	3	2	3	2	NIL	NIL	90	140	200	270	300	360	150
85	79	80	77	77	73	75	75	81	81	83	85	85	86	83	16	16	16	16	16	16	14	14	14	14	14	12	12	12	12	12	14	14	14	16	100	100	100	99	99	99	99	99	99	99	98	98	98	99	99	99	99	99	99	99	0	0	0	0	0	3	0	2	1	2	2	2	4	4	2	3	2	2	NIL	NIL	100	150	210	280	320	380	150
82	81	79	75	78	80	79	83	85	84	83	87	87	89	89	18	18	18	18	18	16	16	16	16	14	14	14	12	12	14	14	14	14	16	16	99	99	99	99	99	99	99	99	98	98	98	99	99	99	99	99	99	99	99	99	0	0	0	0	0	3	0	2	1	2	2	3	3	2	3	3	2	2	NIL	NIL	90	140	200	260	310	370	225
86	84	82	81	79	79	76	75	79	79	79	83	85	89	91	18	18	16	18	18	18	16	16	16	16	14	14	14	14	12	12	14	14	14	16	99	99	99	99	99	99	99	98	98	98	99	99	99	99	99	98	99	99	99	99	0	0	0	0	0	5	0	1	2	2	2	3	3	3	2	2	2	2	NIL	NIL	90	135	210	270	300	360	150
83	81	79	79	83	85	87	89	91	93	91	91	90	89	93	18	18	18	18	18	18	16	16	16	16	14	14	14	12	12	14	14	16	16	14	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	98	99	99	99	99	0	0	0	0	0	3	0	1	2	2	2	3	3	3	2	2	2	2	NIL	Shivering	110	160	230	300	340	380	150
88	66	83	81	79	77	75	76	77	80	82	83	84	86	88	16	16	16	16	16	16	14	14	14	14	12	12	12	12	14	14	14	14	14	16	100	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	98	98	99	0	0	0	0	0	5	0	2	2	2	2	3	4	3	3	3	2	2	NIL	NIL	100	145	210	290	320	360	150
84	83	81	78	76	73	74	76	76	80	82	83	86	88	91	18	18	18	18	18	16	16	16	16	16	14	14	14	12	12	12	12	14	14	16	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	98	98	99	99	99	0	0	0	0	0	0	0	2	1	2	2	3	3	4	3	3	3	2	NIL	NIL	90	140	190	250	270	300	225
84	73	63	76	78	79	77	79	81	83	83	87	87	90	93	18	18	16	18	15	16	16	16	14	14	14	14	12	12	12	14	14	14	16	16	99	99	99	99	99	99	98	98	98	98	99	99	99	99	99	99	99	99	99	99	0	0	0	0	0	0	0	2	1	2	2	3	3	4	3	3	3	2	Inj. Ephedrine	Hypotension	110	130	200	240	290	330	150
87	84	82	80	77	77	79	81	82	83	85	85	87	91	93	18	18	18	18	18	16	16	16	14	14	12	12	12	14	14	15	16	14	14	16	99	99	99	99	98	98	98	98	98	98	99	99	99	99	99	99	98	98	99	99	0	0	0	0	0	0	0	1	2	2	2	2	3	3	2	2	2	2	NIL	NIL	110	145	220	260	300	330	225
83	81	79	78	74	73	77	77	75	80	81	84	83	87	89	18	18	18	18	18	16	16	16	16	14	14	14	12	12	14	14	14	16	14	14	99	99	99	99	99	98	98	98	98	98	98	98	99	99	99	99	99	99	99	99	0	0	0	0	0	5	0	2	2	2	2	3	4	3	2	2	2	2	NIL	NIL	120	155	210	270	310	360	150
80	77	75	73	77	79	81	84	84	85	83	88	83	84	85	18	18	18	18	18	16	16	16	14	14	14	14	12	12	12	12	14	14	16	14	99	99	99	99	98	98	98	98	98	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	0	2	0	2	2	2	2	3	3	4	2	3	2	2	NIL	NIL	110	150	200	280	360	390	150
80	77	75	73	71	73	77	80	83	83	81	83	86	89	91	16	16	16	16	14	14	14	14	12	12	12	12	14	14	14	12	14	16	14	16	99	99	99	99	99	99	98	98	98	98	99	99	99	99	99	99	99	99	99	99	0	0	0	0	0	5	0	2	1	2	2	3	3	3	3	3	2	2	NIL	NIL	120	160	220	270	320	360	150
84	82	79	75	73	73	70	70	71	75	80	80	83	83	86	18	18	16	18	16	16	16	16	16	16	14	14	14	12	12	12	12	14	14	14	99	99	99	99	99	98	98	98	98	98	98	98	99	99	99	99	99	99	99	99	0	0	0	0	0	3	0	2	1	2	2	3	3	4	3	3	2	2	NIL	NIL	100	150	210	280	330	380	150
75	73	71	75	75	71	75	77	78	80	83	80	80	83	82	18	18	18	18	18	16	16	16	14	14	14	12	12	12	14	14	14	16	16	16	100	100	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	0	0	0	2	2	2	2	3	4	2	2	3	2	2	Inj. Ondansetron	Nausea	110	145	180	240	280	300	225
89	86	83	81	78	77	74	72	76	78	81	83	85	87	91	18	18	16	18	18	18	16	16	16	16	16	14	14	14	14	14	14	14	16	16	100	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	0	2	0	1	2	2	5	3	2	4	2	3	3	2	NIL	NIL	110	160	230	260	310	400	75
86	81	79	77	77	78	77	81	83	87	89	88	89	91	93	16	16	16	16	16	14	14	14	14	14	14	14	14	12	12	14	14	14	14	14	100	100	99	99	99	99	99	99	99	99	98	99	99	99	99	99	99	99	99	99	0	0	0	0	0	0	0	1	1	2	2	3	4	2	3	2	2	2	NIL	NIL	120	150	200	240	270	330	225
80	73	76	73	71	75	78	80	83	85	82	84	87	86	88	16	16	16	16	16	16	14	14	14	14	14	14	14	14	12	12	14	14	14	14	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	0	5	0	1	2	2	2	3	3	2	3	2	2	2	NIL	NIL	110	160	210	270	300	360	150
77	77	74	71	69	71	74	76	78	77	81	83	85	86	89	18	18	18	18	18	18	16	16	16	16	16	14	14	14	11	14	14	14	16	16	100	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	0	2	0	2	1	2	2	2	3	3	3	2	2	2	NIL	NIL	110	145	210	280	330	410	150
77	78	73	74	70	68	73	77	81	83	84	86	89	91	93	18	18	16	18	18	18	18	16	16	16	16	16	14	14	11	14	14	14	14	16	99	99	99	99	99	99	99	98	98	98	99	99	99	99	98	98	99	99	99	99	0	0	0	0	0	3	0	2	2	2	2	2	3	3	2	2	2	2	NIL	NIL	120	135	220	260	320	380	150

MASTERSHEET - GROUP C (BUPIVACAINE)

Sr.No.	Age (yrs)	Gender	Height (cm)	Weight (kg)	ASA	Type of surgery	Preoperative monitoring PR	BP	MAP	RR	Spo2 (%)	VAS	Time of onset of sensory analgesia (sec)	Time of onset of motor blockade (sec)	Time of highest sensory level (mins)	Time of maximum motor block (mins)	Highest sensory level	Grade of motor block
1	26	Male	160	62	2	Tibia nailing	90	130/80	97	16	100	4	150	160	9	7	T8	3
2	32	Female	158	58	2	Femur nailing	92	120/80	93	18	100	5	140	170	9.5	8.5	T6	3
3	50	Male	152	56	2	Tibia plating	86	120/80	93	18	99	5	150	180	10	9	T8	3
4	45	Female	166	65	2	Tibia nailing	80	120/70	87	16	99	6	140	170	10	9.5	T6	3
5	37	Male	168	68	2	Femur nailing	86	110/80	90	20	99	4	180	160	9.5	9	T6	3
6	48	Male	160	64	2	Femur plating	88	110/70	83	18	99	3	150	180	10.5	9	T6	3
7	29	Male	158	60	2	Tibia nailing	92	120/80	93	14	100	5	180	210	10	8.5	T8	3
8	36	Male	158	58	2	Tibia plating	84	130/80	97	16	99	4	130	180	9	8	T6	3
9	42	Female	156	56	2	Femur nailing	76	140/80	100	16	99	3	150	180	9	9	T7	3
10	27	Male	162	68	2	Femur nailing	72	130/70	90	14	99	4	150	190	9.5	8.5	T6	3
11	34	Male	166	64	1	Meshplasty	80	120/80	93	18	99	5	130	170	8.5	8	T6	3
12	46	Male	160	62	1	Meshplasty	84	130/80	97	20	100	0	130	150	9	8.5	T8	3
13	53	Male	158	55	1	Meshplasty	78	110/80	90	18	100	0	150	170	10	9	T8	3
14	47	Male	164	52	1	Meshplasty	94	110/70	83	14	100	0	160	180	9.5	9	T6	3
15	38	Male	162	58	1	Meshplasty	70	120/70	87	16	99	0	170	200	10.5	9.5	T7	3
16	26	Male	170	66	1	Meshplasty	88	120/80	93	16	99	0	140	180	9	8.5	T6	3
17	30	Male	168	62	1	Meshplasty	82	130/80	97	14	100	0	130	160	9.5	9	T8	3
18	39	Male	160	57	1	Eversion of sac	76	140/80	100	16	99	0	160	190	9.5	9	T8	3
19	41	Male	158	54	1	Eversion of sac	86	130/70	90	14	99	0	160	180	9	8	T10	3
20	55	Male	160	52	1	Eversion of sac	84	120/70	87	18	99	0	170	210	10	9	T6	3
21	48	Female	156	48	1	Vaginal hysterectomy	86	120/80	93	18	99	0	180	210	10	9.5	T8	3
22	52	Female	160	55	2	Vaginal hysterectomy	80	110/80	90	16	99	0	150	170	8.5	8	T6	3
23	56	Female	158	51	2	Vaginal hysterectomy	88	130/80	97	14	100	0	160	180	9	8.5	T6	3
24	36	Female	154	45	2	Vaginal hysterectomy	78	120/80	93	16	99	0	160	180	8.5	8	T6	3
25	40	Female	152	42	1	Vaginal hysterectomy	84	140/80	100	16	99	0	140	160	9	8	T6	3
26	44	Female	158	46	2	Vaginal hysterectomy	82	130/80	97	16	100	1	150	180	9.5	8.5	T6	3
27	52	Female	162	49	1	Vaginal hysterectomy	76	120/70	87	14	99	0	170	200	10	9	T8	3
28	49	Female	156	44	1	Ovarian cyst excision	74	110/80	90	14	99	1	150	180	9	8	T6	3
29	51	Female	160	52	2	Ovarian cyst excision	84	130/70	90	16	99	2	140	160	9.5	9	T6	3
30	46	Female	164	48	1	Vaginal hysterectomy	78	110/70	83	18	99	0	130	150	9	8	T6	3

Intraoperative and postoperative monitoring — Pulse rate / min (mins)

Sr.No.	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480
1	90	86	84	80	82	76	78	74	74	76	72	74	72	76	80	78	80	84	86	82
2	92	92	90	88	86	84	86	82	80	78	80	76	76	74	78	82	86	84	86	82
3	86	84	86	82	84	80	78	76	78	74	76	72	70	68	66	68	72	74	76	80
4	80	80	76	78	72	74	70	68	66	64	62	60	64	66	62	66	68	70	74	76
5	86	82	80	78	74	70	72	76	74	70	76	74	76	76	78	80	82	80	84	82
6	88	86	86	82	84	84	80	76	74	76	76	78	80	84	86	82	84	84	86	86
7	92	92	90	88	84	86	82	80	80	78	80	76	74	72	76	78	80	80	82	84
8	84	80	76	74	72	76	70	72	74	72	70	66	68	68	70	72	76	74	72	76
9	76	76	72	70	68	66	62	64	66	68	64	64	68	70	72	74	70	72	76	74
10	72	74	70	66	62	58	56	48	74	80	84	82	84	86	82	76	74	72	76	74
11	80	76	78	72	74	70	66	64	66	68	68	70	72	74	76	76	74	72	78	76
12	84	80	78	74	76	72	76	74	70	68	70	72	74	76	72	76	74	76	76	80
13	78	78	76	72	74	70	66	68	64	62	60	64	66	64	68	70	72	74	76	74
14	94	98	96	92	90	86	84	82	80	78	80	84	86	83	86	84	84	86	88	90
15	70	68	66	62	60	54	48	66	74	76	74	78	76	72	74	76	78	76	74	76
16	88	86	82	84	80	78	74	72	70	72	76	74	74	75	78	76	80	76	74	76
17	82	86	84	80	78	74	76	72	74	72	70	66	68	70	72	76	74	72	76	78
18	76	76	72	74	70	68	66	62	60	64	66	68	66	70	68	72	74	76	74	76
19	86	84	82	80	76	74	72	70	68	66	64	68	70	72	76	74	72	76	78	76
20	84	82	82	80	78	76	72	74	74	76	74	76	78	80	80	82	84	86	84	84
21	86	88	84	82	82	82	80	78	74	76	72	70	74	76	78	72	74	76	80	84
22	80	78	74	76	72	78	76	78	74	76	72	74	76	72	70	76	78	72	74	78
23	88	88	84	86	82	80	78	74	72	76	74	76	72	76	78	80	78	84	82	86
24	78	76	74	72	70	68	64	66	62	60	66	64	68	70	72	76	74	72	70	74
25	84	84	82	80	80	78	76	74	72	70	74	76	72	78	76	78	80	82	80	78
26	82	80	78	74	76	72	70	66	62	64	66	68	66	70	72	74	76	74	78	80
27	76	78	74	72	70	68	66	62	64	66	68	70	68	70	72	76	74	76	72	78
28	74	76	78	72	70	68	66	62	64	66	68	70	70	68	66	70	72	74	76	72
29	84	86	82	80	78	76	72	74	70	72	70	68	66	70	72	76	74	76	78	76
30	78	76	78	74	72	70	72	68	66	68	64	62	60	64	66	70	72	74	72	76

Intraoperative and postoperative monitoring — Systolic Blood pressure in mmHg (mins)

Sr.No.	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480
1	130	126	122	124	122	120	120	116	118	114	112	110	108	106	112	116	114	118	120	122
2	120	118	114	112	110	112	108	106	102	100	98	94	96	100	104	108	106	110	112	116
3	120	120	116	118	114	112	110	108	106	104	102	100	98	94	96	100	100	104	106	106
4	120	120	118	114	112	110	110	110	108	106	104	102	106	110	112	114	118	120	124	120
5	110	110	108	104	102	100	96	92	80	96	98	100	104	102	106	108	106	110	112	116
6	110	110	106	104	96	90	80	94	98	98	96	100	102	104	106	100	102	104	108	110
7	120	120	116	114	112	110	110	106	104	100	102	106	108	110	112	114	110	114	116	120
8	130	126	124	122	118	114	116	112	110	110	108	104	106	110	112	116	118	120	120	124
9	140	136	132	134	130	130	128	124	126	122	120	116	114	116	118	120	122	126	124	126
10	130	130	126	122	120	120	118	116	114	110	108	108	110	114	118	120	118	166	120	126
11	120	116	114	112	110	110	106	106	102	100	96	98	100	104	108	110	112	166	120	120
12	130	126	124	120	122	118	116	112	116	114	112	110	110	106	108	110	112	116	118	120
13	110	110	112	108	104	104	100	92	86	80	102	100	100	104	108	110	108	110	108	112
14	110	110	108	104	106	102	98	94	80	96	106	108	110	114	112	110	108	106	110	110
15	120	118	116	112	110	108	106	102	106	106	102	98	104	102	106	104	108	110	114	116
16	120	116	114	112	114	110	108	104	100	98	94	96	100	104	106	102	108	110	114	110
17	130	128	124	126	122	120	120	116	114	112	110	108	104	100	106	110	112	114	118	120
18	140	136	134	130	130	128	124	122	124	120	118	114	110	114	116	118	120	122	126	130
19	130	126	124	122	120	118	114	114	112	110	108	104	110	112	116	118	120	122	126	130
20	120	120	118	116	114	112	110	108	104	102	100	98	94	90	96	100	104	108	110	112
21	120	118	116	112	114	110	108	104	102	98	96	98	100	104	106	104	108	110	112	116
22	110	110	108	104	102	100	98	96	98	100	102	106	108	110	112	116	120	116	118	120
23	130	128	126	122	122	120	120	118	114	112	110	108	106	110	112	116	118	120	122	126
24	120	118	116	114	112	110	108	106	102	100	98	96	94	98	100	102	106	108	110	114
25	140	138	134	130	128	124	122	120	118	116	114	112	116	116	120	120	122	126	128	130
26	130	126	124	122	120	120	118	114	116	112	110	108	104	102	100	106	108	110	112	116
27	120	118	116	114	112	114	110	108	106	104	102	106	110	112	114	116	120	122	126	130
28	110	110	108	104	102	100	98	96	92	96	98	100	102	106	108	110	112	116	120	110
29	130	126	122	124	122	120	118	114	112	110	108	104	106	110	112	116	118	120	122	126
30	110	110	108	106	104	102	100	98	98	94	90	96	98	100	102	106	108	110	112	116

Intraoperative and postoperative monitoring — Diastolic Blood pressure in mmHg (mins)

Sr.No.	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480
1	80	78	76	72	70	66	64	66	68	62	62	60	58	62	64	66	70	70	72	76
2	80	80	76	74	72	70	68	66	62	60	56	58	60	64	66	68	66	70	72	76
3	80	80	76	78	76	74	72	68	66	64	66	64	66	62	66	68	70	72	74	72
4	70	74	68	66	66	62	64	60	58	56	54	56	58	64	66	68	70	72	74	76
5	80	78	74	76	74	68	64	66	60	66	64	68	70	68	66	70	72	76	74	76
6	70	70	68	66	60	58	56	60	62	64	66	68	70	72	70	72	74	74	76	80
7	80	76	78	74	70	72	70	68	66	68	62	60	64	66	68	64	70	74	76	70
8	80	78	76	72	70	68	66	64	66	62	60	58	66	68	70	72	74	72	76	78
9	80	78	74	76	72	70	68	66	62	64	60	64	68	68	70	70	68	70	72	76
10	70	66	68	64	60	62	56	58	52	54	56	60	62	64	66	70	68	70	72	76
11	80	76	74	76	72	68	64	62	60	58	56	58	62	66	68	70	70	70	68	70
12	80	78	76	72	74	70	68	64	66	62	60	60	58	64	68	70	68	72	76	80
13	80	76	74	76	74	72	70	54	54	50	62	68	66	64	64	66	70	70	72	76
14	70	68	66	64	62	60	60	56	52	66	72	74	78	80	76	72	68	70	72	70
15	70	68	66	64	62	58	56	58	60	62	58	56	64	66	64	68	70	70	72	76
16	80	76	78	74	72	70	68	66	64	60	56	58	60	62	64	62	66	70	72	70
17	80	78	76	78	72	72	70	68	66	68	64	62	64	60	66	68	70	74	76	80
18	80	78	76	72	70	68	66	68	64	60	56	58	60	64	66	70	74	72	76	80
19	70	70	68	66	62	60	58	56	54	56	60	62	66	64	68	70	70	72	74	80
20	70	74	70	68	66	62	60	56	58	56	58	56	52	56	58	60	64	66	68	70
21	80	78	76	74	72	70	70	68	66	64	66	68	70	72	75	78	76	78	80	80
22	80	78	76	72	74	70	68	64	62	68	70	72	76	78	76	78	80	76	64	80
23	80	76	74	76	72	70	66	68	64	62	60	56	60	64	66	68	70	70	74	76
24	80	76	74	72	74	72	70	68	64	66	62	64	62	66	64	66	70	72	70	72
25	80	80	76	74	70	68	66	62	56	58	60	62	66	64	66	70	72	76	78	80
26	80	78	76	74	72	70	66	68	64	62	70	68	66	64	60	62	66	68	70	74
27	70	70	68	66	62	64	60	56	58	56	58	60	62	66	68	70	70	74	76	78
28	80	78	76	74	72	70	66	78	64	66	64	68	70	72	76	76	78	80	80	80
29	70	68	66	64	62	60	58	56	54	56	58	60	64	66	68	70	72	74	76	80
30	70	68	70	68	66	62	60	66	64	62	60	64	66	68	70	72	76	76	78	80

Intraoperative — Mean

Sr.No.	0	2	4	6	8	10	15	20	25
1	97	94	91	89	87	84	83	83	85
2	93	93	89	87	85	84	81	79	75
3	93	93	89	91	89	87	85	81	79
4	87	89	85	82	81	78	79	77	75
5	90	89	85	85	83	79	75	75	67
6	83	83	81	79	72	69	64	71	74
7	93	91	91	87	84	85	83	81	79
8	97	94	92	89	86	83	83	80	81
9	100	97	93	95	91	90	88	85	83
10	90	87	87	83	80	81	77	77	73
11	93	89	87	88	85	82	78	77	74
12	97	94	92	88	90	86	84	80	83
13	90	87	87	87	84	83	80	67	65
14	83	82	80	77	76	74	72	69	61
15	87	85	83	80	78	75	73	73	75
16	93	89	90	87	86	83	81	79	7
17	97	95	92	94	89	88	87	84	8
18	100	97	95	91	90	88	85	86	8
19	90	89	87	85	81	79	77	75	7
20	87	89	86	84	82	79	77	73	7
21	93	91	89	87	86	83	83	80	7
22	90	89	87	83	83	80	78	75	7
23	97	93	91	91	89	87	84	85	8
24	93	90	88	86	87	85	83	81	7
25	100	99	95	93	89	87	85	81	7
26	97	94	92	90	88	87	83	83	8
27	87	86	84	82	79	81	77	73	7
28	90	89	87	84	82	80	77	75	7
29	90	87	85	84	82	80	78	75	7
30	83	82	83	81	79	75	73	77	7

nd postoperative monitoring											Intraoperative and postoperative monitoring																				Intraoperative and postoperative monitoring																				Intraoperative and postoperative monitoring									Intraoperative and postoperative monitoring									Intraoperative supplementation	Intraoperative or postoperative complication	Total duration of surgery (mins)	Time of two segment regression (mins)	Time to regression to T12 (mins)	Total duration of motor block (mins)	Duration of analgesia (mins)	Time of rescue analgesia (mins)	Total amount of analgesia required postoperatively (mg)
lood pressure in mmHg (mins)											Respiratory rate / min (mins)																				Oxygen saturation (%) (mins)																				Visual Analouge Scale (mins)							(hr)		Sedation score (mins)																	
30	45	60	90	120	150	180	210	240	360	480	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480	0	60	120	180	240	360	480	12	24	0	15	30	60	120	180	240	360	480									
79	79	77	75	77	80	83	85	86	88	91	16	16	16	16	16	14	14	14	14	14	16	16	14	14	14	14	16	14	14	14	100	100	100	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	100	99	4	0	0	2	0	0	2	3	2	2	2	2	2	2	2	2	2	2	Nil	Nil	100	90	130	160	170	210	225
73	70	70	72	76	79	81	79	83	85	89	18	18	18	18	16	16	16	16	16	16	14	14	14	14	14	14	14	16	16	16	100	100	100	100	100	99	99	99	99	98	98	98	98	99	99	99	99	99	99	99	4	0	0	0	3	0	2	2	2	2	2	2	2	2	2	2	2	2	Nil	Nil	90	100	150	190	200	250	225
77	78	76	77	73	76	79	80	83	85	83	18	18	18	18	18	18	18	16	16	16	16	16	16	16	16	16	14	16	16	16	99	99	99	99	99	99	98	98	98	98	99	99	99	99	99	99	99	99	99	99	5	0	0	2	0	0	2	3	2	2	2	2	3	3	2	2	2	2	Nil	Nil	120	90	135	170	170	210	225
73	71	71	74	79	81	83	86	88	91	91	16	16	16	16	16	16	16	16	14	14	14	14	14	14	14	14	14	16	16	16	99	99	99	99	99	99	98	98	99	99	99	99	99	99	99	98	98	98	99	99	4	0	0	2	0	0	2	2	2	2	2	2	2	2	2	2	2	2	Nil	Nil	100	80	130	165	180	210	225
76	75	79	81	79	79	83	83	87	87	89	20	20	20	20	20	20	18	18	18	18	16	16	16	16	16	16	16	16	16	18	99	99	99	99	99	99	99	99	98	98	98	99	99	99	99	99	99	99	99	99	4	0	0	0	0	0	2	2	3	2	2	2	2	3	2	2	2	2	Inj. Ephedrine	Hypotension	110	95	140	180	190	230	225
75	76	79	81	83	82	81	83	84	87	90	18	18	18	18	18	18	18	16	16	16	16	14	14	14	14	14	14	16	16	16	99	99	99	99	98	98	98	99	99	99	99	99	99	99	99	99	99	99	99	99	4	0	0	0	5	0	2	3	2	2	2	2	2	2	2	2	2	2	Inj. Ephedrine	Hypotension	80	90	150	190	200	240	150
79	75	75	79	81	83	81	83	87	89	87	14	14	14	14	14	14	14	14	12	12	12	12	12	12	12	14	14	14	14	14	100	100	100	99	99	99	99	99	99	99	99	99	99	98	99	99	99	99	99	99	4	0	0	0	3	0	1	3	2	2	2	2	3	2	2	2	2	2	Nil	Nil	90	100	140	200	190	250	225
78	76	73	79	82	84	87	89	88	91	93	16	16	16	16	16	16	16	16	14	14	14	14	14	14	14	14	16	16	16	16	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	98	99	99	4	0	0	2	0	0	2	2	2	2	2	2	2	3	2	2	2	2	Nil	Nil	100	85	130	165	180	230	225
83	80	81	83	84	86	87	86	89	89	93	16	16	16	16	16	16	14	14	14	14	14	16	16	16	16	14	14	14	16	16	99	99	99	99	98	98	98	99	99	99	99	99	99	99	99	99	99	99	99	99	3	0	0	0	0	0	2	2	2	2	2	2	2	2	2	2	2	2	Inj. Ondansetron	Nausea	90	90	140	180	200	230	225
73	73	76	78	81	83	87	85	85	88	93	14	14	14	14	14	14	14	12	12	12	12	12	12	14	14	14	14	12	14	14	99	99	99	99	99	99	98	98	98	98	99	99	99	99	99	99	99	99	99	99	4	0	0	0	5	0	2	2	3	2	2	2	3	3	2	2	2	2	Inj. Atropine	Bradycardia	110	100	150	200	210	240	150
72	69	71	75	79	81	83	84	85	85	87	18	18	18	18	18	18	18	18	16	16	16	16	18	18	16	16	16	16	16	16	99	99	99	99	99	98	98	98	99	99	99	99	98	98	99	99	99	99	99	99	4	0	0	0	5	0	2	3	3	2	2	2	3	2	2	2	2	2	Nil	Nil	80	90	140	190	200	240	225
79	77	77	75	78	81	83	83	87	90	93	20	20	20	18	18	18	18	18	18	16	16	16	16	18	18	16	16	18	18	16	100	100	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	2	0	0	2	2	3	2	2	2	2	3	2	2	2	2	Nil	Nil	90	100	160	160	180	220	225
60	75	79	77	77	79	81	83	83	84	88	18	18	18	18	16	16	16	16	16	16	16	16	16	16	14	14	14	14	16	16	100	100	100	99	99	99	98	98	98	99	99	99	99	99	99	99	99	99	99	99	0	0	0	2	0	0	2	2	2	2	2	2	2	3	2	2	2	2	Inj. Ephedrine	Hypotension	100	90	130	170	180	210	225
76	83	85	89	91	88	85	81	82	85	83	14	14	14	14	14	14	14	14	12	12	12	12	12	14	14	14	14	14	12	14	100	100	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	3	0	2	2	2	2	2	2	3	3	2	2	2	2	Inj. Ephedrine	Hypotension	110	95	150	200	200	260	225
77	73	70	77	78	78	80	83	83	86	89	16	16	16	16	16	16	14	14	14	14	14	14	14	14	16	16	16	14	14	16	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	3	0	2	2	3	2	2	2	2	2	2	2	2	2	Inj. Atropine	Bradycardia	100	110	165	190	200	250	150
73	69	71	73	76	78	75	80	83	86	83	16	16	14	16	14	16	14	14	14	16	16	14	14	14	14	16	16	14	16	14	99	99	99	99	99	99	98	98	98	98	99	99	99	99	99	99	99	99	99	99	0	0	0	0	0	0	1	3	2	2	2	2	2	2	2	2	2	2	Nil	Nil	90	100	150	180	190	220	225
33	79	77	77	73	79	82	84	87	90	93	14	14	14	14	14	14	14	14	12	12	12	12	12	12	14	14	14	14	14	14	100	99	99	100	100	99	99	98	98	99	99	99	99	99	99	99	99	99	99	99	0	0	0	3	0	0	2	2	2	2	2	2	3	3	2	2	2	2	Nil	Nil	90	95	120	160	170	210	225
30	77	77	77	81	83	86	89	89	93	97	16	16	14	14	16	16	14	14	14	14	12	12	14	14	14	14	14	14	14	14	99	99	99	99	99	99	98	98	98	98	98	99	99	99	99	99	99	99	99	99	0	0	0	3	0	0	2	3	2	2	2	2	2	3	2	2	2	2	Nil	Shivering	80	85	120	165	165	210	225
74	76	76	81	80	84	86	87	89	91	97	14	14	14	14	14	14	14	12	12	12	12	12	12	12	14	14	14	14	14	14	99	99	99	99	99	98	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	3	0	0	2	3	3	2	2	2	2	3	2	2	2	2	Nil	Nil	90	100	100	150	150	190	225
71	72	70	66	67	71	73	72	80	82	84	18	18	18	16	16	16	16	16	16	16	16	16	14	14	16	16	16	16	16	16	99	99	99	99	98	98	98	98	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	5	0	2	2	3	2	2	2	2	2	2	2	2	2	Nil	Nil	100	90	140	195	195	240	150
75	76	78	80	83	86	87	87	89	91	92	18	18	16	16	16	14	16	16	16	16	16	14	14	14	16	16	16	16	16	16	99	99	99	99	99	99	99	99	98	98	99	99	99	99	99	99	99	99	99	99	0	0	0	0	3	0	2	2	2	2	2	2	3	2	2	2	2	2	Inj. Ondansetron	Nausea	90	100	150	170	200	250	225
79	81	83	87	89	88	91	93	89	89	93	16	16	16	14	16	14	14	14	14	14	14	14	14	16	16	16	16	16	16	16	99	99	99	99	98	98	98	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	0	0	2	2	2	2	2	2	2	3	2	2	2	2	Nil	Nil	110	90	140	180	190	220	225
79	77	73	75	79	81	84	86	87	90	93	14	14	14	14	14	14	12	12	12	12	12	12	12	12	14	14	14	14	14	14	100	99	99	99	98	98	98	98	98	98	98	99	99	99	99	99	99	99	99	99	0	0	0	0	3	0	2	3	2	2	2	2	2	3	2	2	2	2	Nil	Shivering	110	100	150	200	210	255	150
77	74	75	73	77	76	78	82	84	83	86	16	16	16	16	16	16	14	14	14	14	14	14	16	16	16	14	14	16	16	14	99	99	99	99	99	99	99	99	98	98	98	98	98	99	99	99	99	99	99	99	0	0	0	0	5	0	2	3	2	2	2	2	3	3	2	2	2	2	Nil	Nil	100	90	140	190	210	240	225
77	78	79	83	81	84	87	89	93	95	97	16	16	16	16	16	14	14	14	14	14	14	14	16	16	14	14	14	16	16	16	99	99	99	99	99	99	98	98	98	98	98	99	99	99	99	99	99	99	99	99	0	0	0	2	0	0	2	2	2	2	2	2	2	2	2	2	2	2	Nil	Nil	120	80	130	160	180	220	225
79	83	81	79	77	73	77	80	82	84	88	16	16	16	16	16	16	16	14	14	14	14	14	14	14	16	16	16	16	14	14	100	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	2	0	0	2	2	2	2	2	2	2	3	2	2	2	2	Nil	Shivering	110	110	150	195	180	210	225
72	73	75	78	81	83	85	87	90	93	95	14	14	14	14	14	14	14	12	12	12	12	12	12	14	14	14	14	12	12	12	99	99	99	99	99	99	98	98	98	98	98	98	98	99	99	99	99	99	99	99	0	0	0	3	0	0	2	2	2	2	2	2	3	2	2	2	2	2	Inj. Ondansetron	Nausea	100	80	120	170	165	210	225
76	75	79	81	83	87	87	89	82	93	90	14	14	14	14	14	12	12	12	12	12	12	12	12	12	12	14	14	14	14	14	99	99	99	99	98	98	98	98	98	98	98	99	99	99	99	99	99	99	99	99	0	0	0	2	0	0	2	3	2	2	2	2	2	3	2	2	2	2	Nil	Nil	120	75	135	180	180	220	225
74	75	75	78	81	83	85	87	89	91	95	16	16	16	16	16	16	14	14	14	14	14	14	14	16	16	16	16	16	14	14	99	99	99	99	99	98	98	98	98	98	98	98	99	99	99	99	99	99	99	99	2	0	0	0	5	0	2	2	2	2	2	2	2	2	2	2	2	2	Nil	Nil	130	90	150	190	200	240	225
73	70	75	77	79	81	83	87	87	89	92	18	16	16	18	16	16	16	16	16	14	14	14	16	16	16	16	16	16	16	16	99	99	99	99	99	99	99	98	98	98	98	99	99	99	99	99	99	99	99	99	0	0	0	0	0	0	2	2	2	2	2	2	2	2	2	2	2	2	Nil	Nil	110	95	150	180	190	230	225

MASTERSHEET - GROUP F (BUPIVACAINE - FENTANYL)

Sr.No.	Age (yrs)	Gender	Height (cm)	Weight (kg)	ASA	Type of surgery	Preoperative monitoring PR	BP	MAP	RR	Spo2 (%)	VAS	Time of onset of sensory analgesia (sec)	Time of onset of motor blockade (sec)	Time of highest sensory level (mins)	Time of maximum motor block (mins)	Highest sensory level	Grade of motor block
1	42	Male	162	56	2	Tibia nailing	86	120/80	93	16	99	5	130	130	7	6	T6	3
2	45	Male	158	52	2	Femur nailing	82	120/80	93	18	99	4	120	140	7.5	6.5	T6	3
3	40	Male	156	48	2	Tibia nailing	78	130/80	97	18	100	6	120	130	6.5	6	T6	3
4	32	Male	152	50	2	Tibia nailing	76	120/80	93	20	99	5	110	120	8	6.5	T5	3
5	26	Female	158	48	2	Femur nailing	88	130/80	97	18	100	4	130	150	7.5	6	T6	3
6	42	Male	160	62	2	Femur plating	90	130/80	97	20	99	5	110	130	6.5	6	T6	3
7	22	Male	162	55	2	Femur nailing	96	120/70	87	20	99	5	140	130	6.5	6.5	T5	3
8	26	Male	160	58	2	Tibia plating	90	120/80	93	18	100	4	130	140	7	6	T6	3
9	46	Male	156	45	2	Tibia nailing	80	110/80	90	16	99	4	120	130	6.5	6.5	T6	3
10	35	Female	154	44	2	Tibia nailing	86	120/80	93	16	99	5	130	140	7	6	T6	3
11	38	Male	158	52	1	Meshplasty	82	130/80	97	16	99	0	120	130	7.5	7	T6	3
12	50	Male	160	46	1	Meshplasty	76	110/70	83	18	99	0	130	140	6.5	6.5	T8	3
13	42	Male	166	62	1	Meshplasty	96	120/70	87	16	99	0	120	130	7	6	T6	3
14	25	Male	156	54	1	Meshplasty	70	110/70	83	18	100	0	140	150	8	7	T8	3
15	30	Male	154	66	1	Meshplasty	90	130/90	103	16	99	0	130	140	7	6.5	T6	3
16	46	Male	164	62	1	Meshplasty	68	130/80	97	16	100	0	150	160	8.5	7	T6	3
17	35	Male	168	60	1	Eversion of sac	88	120/80	93	18	99	0	120	130	6.5	6	T6	3
18	32	Male	164	68	1	Eversion of sac	90	130/80	97	16	99	0	130	140	7.5	7	T8	3
19	44	Male	158	60	1	Eversion of sac	86	120/70	87	14	99	0	120	140	7	6	T6	3
20	36	Male	156	58	1	Eversion of sac	80	110/70	83	18	100	0	140	150	8	6	T6	3
21	45	Female	154	50	2	Vaginal hysterectomy	74	110/80	90	16	100	0	120	140	7	6.5	T6	3
22	50	Female	156	48	2	Vaginal hysterectomy	86	130/80	97	18	99	0	110	130	7.5	7	T6	3
23	36	Female	152	45	1	Ovarian cyst excision	78	140/80	100	14	99	0	130	160	8	7	T6	3
24	47	Female	160	54	2	Vaginal hysterectomy	84	130/80	97	18	99	0	140	140	7	6	T6	3
25	38	Female	162	51	1	Ovarian cyst excision	86	120/80	93	16	99	0	130	140	7	6.5	T6	3
26	40	Female	156	47	1	Ovarian cyst excision	74	110/70	83	14	100	0	120	140	6.5	6.5	T6	3
27	49	Female	164	55	2	Vaginal hysterectomy	80	130/70	90	20	98	0	120	140	6	6	T8	3
28	52	Female	158	52	2	Vaginal hysterectomy	94	140/80	100	18	99	0	130	140	7	6.5	T6	3
29	48	Female	152	45	1	Vaginal hysterectomy	90	130/80	97	18	99	0	120	130	6.5	6.5	T6	3
30	46	Female	156	48	1	Vaginal hysterectomy	78	120/80	93	16	99	0	110	140	8	7	T6	3

Intraoperative and postoperative monitoring — Pulse rate / min (mins)

Sr.No.	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480
1	86	88	84	80	78	78	76	72	70	72	72	76	74	72	74	74	76	80	76	78
2	82	80	76	74	72	70	70	72	72	74	76	72	76	74	78	76	76	80	76	74
3	78	78	76	76	72	74	70	68	64	62	66	66	68	70	72	72	74	72	76	76
4	76	76	74	70	70	66	68	64	62	60	64	66	68	70	70	72	70	74	72	76
5	88	88	84	82	80	80	78	74	72	70	76	74	74	76	76	74	78	80	84	86
6	90	90	86	88	84	84	82	80	78	74	72	76	76	74	74	76	78	76	80	84
7	96	96	94	90	88	84	86	82	80	78	80	84	82	86	86	84	84	82	88	86
8	90	90	88	84	86	84	84	82	82	80	78	76	78	80	84	82	86	88	90	86
9	80	80	76	76	72	74	74	72	70	66	68	64	64	66	68	70	70	74	72	76
10	86	86	84	80	82	84	78	76	74	72	70	74	76	78	76	76	78	78	80	86
11	82	82	80	76	74	70	72	72	76	74	74	78	78	74	72	76	76	78	76	76
12	76	74	74	70	68	66	64	64	62	68	66	66	64	68	70	70	72	74	74	76
13	96	94	90	88	84	86	82	78	76	76	78	80	84	86	84	88	86	86	84	90
14	70	68	64	66	62	60	58	54	48	66	72	76	74	76	78	74	76	72	74	70
15	90	88	86	82	84	84	82	80	82	80	78	80	82	84	86	86	88	84	84	82
16	68	68	66	64	60	56	52	48	66	68	70	74	76	78	70	76	74	74	76	76
17	88	88	86	82	84	82	78	76	74	74	76	78	80	84	86	84	82	86	88	86
18	90	90	86	84	80	78	76	72	70	74	76	74	78	76	76	80	84	86	82	86
19	86	84	80	76	78	74	70	72	74	76	72	70	74	74	76	78	76	80	82	80
20	80	80	76	76	72	74	72	70	68	66	62	64	66	70	72	74	76	74	76	76
21	74	72	70	66	68	64	60	62	64	66	68	64	62	64	66	68	70	70	68	74
22	86	84	82	88	86	82	80	76	78	74	72	70	74	72	76	74	76	78	76	72
23	78	78	74	76	72	70	68	66	62	64	62	66	68	70	72	76	74	74	78	76
24	84	84	82	80	78	76	76	78	74	76	74	74	76	78	76	76	80	80	80	82
25	86	84	80	82	78	76	74	70	72	74	76	78	80	84	80	78	82	76	80	84
26	74	76	72	70	66	68	62	64	66	68	64	62	64	68	66	70	72	74	70	74
27	80	76	78	74	72	70	66	68	62	64	66	66	68	70	72	70	74	76	78	76
28	94	90	88	84	86	82	80	78	76	74	76	78	82	84	86	88	82	84	86	86
29	90	88	86	82	84	80	78	74	72	76	76	78	72	74	78	80	82	86	84	84
30	78	76	72	70	74	68	66	62	64	66	62	64	66	70	70	74	72	74	76	72

Intraoperative and postoperative monitoring — Systolic Blood pressure in mmHg (mins)

Sr.No.	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480
1	120	120	114	112	110	110	112	106	102	102	100	106	108	108	110	112	114	120	120	110
2	120	120	116	114	112	112	110	108	106	102	102	104	106	108	106	110	110	114	116	120
3	130	126	122	124	126	122	120	118	116	112	110	108	106	104	108	110	112	116	118	120
4	120	116	112	110	110	108	98	80	92	96	102	100	104	108	110	112	116	114	118	118
5	130	128	126	122	124	122	120	119	116	112	112	110	108	110	112	116	118	120	120	130
6	130	126	120	118	114	112	110	110	106	104	106	110	110	116	114	118	118	120	120	124
7	120	120	116	112	110	110	106	98	82	92	100	102	100	104	106	108	110	112	114	118
8	120	116	114	112	112	110	106	104	102	100	100	102	106	110	110	112	116	118	118	120
9	110	110	110	106	104	102	100	96	98	92	96	98	100	102	106	108	106	108	110	106
10	120	116	112	112	110	110	112	108	104	102	100	102	106	108	110	114	116	120	120	110
11	130	130	126	122	122	120	120	118	116	114	112	110	112	110	116	118	120	124	120	120
12	110	110	110	106	104	102	100	100	98	96	92	98	100	104	106	106	108	110	110	110
13	120	120	118	114	114	112	110	110	106	104	100	104	106	108	106	110	110	112	116	110
14	110	108	104	102	100	100	98	94	90	92	96	98	100	104	102	106	108	110	110	100
15	130	130	126	122	120	118	116	112	110	108	106	108	110	114	116	118	120	122	126	120
16	130	126	124	122	120	118	116	114	112	110	106	108	110	112	116	120	124	126	122	124
17	120	116	114	112	110	110	108	104	100	98	94	96	100	104	108	110	112	116	120	120
18	130	126	126	124	122	120	118	114	116	114	110	110	106	110	114	116	118	120	122	120
19	120	120	118	114	112	114	110	106	104	102	108	104	100	106	110	110	114	116	118	120
20	110	110	106	102	98	94	90	92	96	98	100	102	106	108	110	114	116	112	110	120
21	110	110	106	104	102	100	96	94	92	94	98	102	106	104	108	108	110	112	114	118
22	130	126	122	122	120	120	118	116	114	112	110	112	108	106	108	110	112	116	118	120
23	140	136	134	130	128	126	124	122	120	118	116	116	122	124	126	124	122	128	130	126
24	130	130	126	122	122	124	120	118	114	112	114	110	112	106	108	110	114	116	120	120
25	120	118	114	106	100	94	80	96	98	100	100	102	106	108	110	112	116	120	122	126
26	110	110	110	106	104	100	100	96	94	92	96	100	104	106	108	110	114	110	112	110
27	130	130	126	122	124	120	120	118	114	112	110	112	114	116	118	120	120	122	126	122
28	140	136	134	130	128	122	118	116	112	110	110	114	116	120	122	126	126	124	128	130
29	130	126	126	122	120	120	118	116	114	110	108	110	114	116	112	110	116	118	120	124
30	120	118	114	112	110	114	112	108	106	100	98	96	100	104	108	110	112	116	118	120

Intraoperative and postoperative monitoring — Diastolic Blood pressure in mmHg (mins)

Sr.No.	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480
1	80	78	76	74	70	74	72	68	66	64	66	68	64	68	70	72	75	80	80	80
2	80	80	76	76	74	70	70	70	68	66	64	62	64	66	68	70	70	72	76	80
3	80	78	76	78	76	72	68	66	64	66	62	64	62	68	70	70	63	72	74	76
4	80	78	76	72	70	68	64	56	58	66	64	68	70	68	70	72	72	74	70	78
5	80	80	76	72	70	68	66	68	64	62	64	68	70	70	68	72	71	80	80	80
6	80	76	74	76	70	68	66	64	68	66	68	70	70	72	74	76	80	80	76	76
7	70	70	68	64	66	62	66	60	54	58	64	66	68	70	72	68	65	68	68	68
8	80	78	76	74	70	70	68	66	64	66	64	68	70	68	70	68	70	72	74	80
9	80	80	76	74	74	72	70	68	66	64	60	66	68	70	72	74	70	72	76	70
10	80	78	74	70	70	68	66	64	66	64	62	66	68	70	70	72	75	80	80	80
11	80	78	76	74	76	72	70	68	68	66	64	66	60	60	66	68	70	72	76	80
12	70	70	68	66	64	62	60	60	56	58	60	64	66	64	66	62	61	68	70	70
13	70	68	66	64	62	60	60	58	56	54	56	58	60	64	62	66	63	70	72	70
14	70	68	66	66	64	60	58	56	54	58	56	60	60	62	64	68	70	70	70	70
15	90	86	80	76	78	76	74	70	68	70	74	76	72	76	78	76	80	80	82	80
16	80	78	76	74	70	66	64	60	58	56	58	60	64	66	68	70	74	76	74	76
17	80	78	76	74	70	68	68	66	62	64	62	66	68	70	74	72	76	78	82	80
18	80	80	76	74	72	76	70	68	66	64	60	62	66	68	70	72	76	74	80	76
19	70	68	68	66	62	60	60	56	54	58	60	62	64	66	68	70	72	74	70	74
20	70	70	68	66	64	60	60	64	66	64	68	70	72	68	70	68	72	74	70	70
21	80	78	74	72	70	70	68	64	66	68	70	70	74	70	76	74	72	76	78	78
22	80	78	74	70	70	68	72	66	64	62	66	60	62	60	64	56	70	72	76	80
23	80	78	76	72	70	68	66	62	60	58	62	66	68	70	72	74	76	78	80	76
24	80	76	74	76	72	70	72	66	64	62	60	58	64	66	68	70	72	70	76	80
25	80	78	74	70	68	64	60	64	66	62	68	66	64	70	70	68	70	74	76	78
26	70	68	64	66	62	62	58	60	56	58	62	64	70	68	72	70	66	70	74	70
27	70	72	68	66	68	62	60	58	56	58	60	64	66	68	66	68	70	74	76	74
28	80	78	74	76	72	74	70	68	66	62	60	64	66	68	70	72	70	78	76	80
29	80	76	78	76	74	70	68	66	64	66	70	72	76	78	70	68	76	78	80	74
30	80	78	76	74	70	68	66	64	68	62	66	62	68	68	70	70	74	76	72	80

Intraoperative and — Mean blood

Sr.No.	0	2	4	6	8	10	15	20	25	30
1	93	92	89	87	83	86	85	81	78	77
2	93	93	89	89	87	84	83	83	81	79
3	97	94	91	93	93	89	85	83	81	81
4	93	91	88	85	83	81	75	64	69	76
5	97	96	93	89	88	86	84	85	81	79
6	97	93	89	90	85	83	81	79	81	79
7	87	87	84	80	81	78	79	73	63	69
8	93	91	89	87	84	83	81	79	77	77
9	90	90	87	85	84	82	80	77	77	73
10	93	91	87	84	83	82	81	79	79	77
11	97	95	93	90	91	88	87	85	84	82
12	83	83	82	79	77	75	73	73	70	71
13	87	85	83	81	79	77	77	75	73	71
14	83	81	79	78	76	73	71	69	66	67
15	103	##	95	91	92	90	88	84	82	83
16	97	94	92	90	87	83	81	78	76	74
17	93	91	89	87	83	82	81	79	75	75
18	97	95	93	91	89	91	86	83	83	81
19	87	85	85	82	79	78	77	73	71	73
20	83	83	81	78	75	71	70	73	76	75
21	90	89	85	83	81	80	77	74	75	77
22	97	94	90	87	87	85	87	83	81	79
23	100	97	95	91	89	87	85	82	80	78
24	97	94	91	91	89	88	88	83	81	79
25	93	91	87	82	79	74	67	75	77	75
26	83	82	79	79	76	75	72	72	69	69
27	90	91	87	85	87	81	80	78	75	76
28	100	97	94	94	91	90	86	84	81	78
29	97	93	94	91	89	87	85	83	81	81
30	93	91	89	87	83	83	81	79	81	75

postoperative monitoring										Intraoperative and postoperative monitoring																				Intraoperative and postoperative monitoring																				Intraoperative and postoperative monitoring									Intraoperative and postoperative monitoring									Intraoperative supplementation	Intraoperative or postoperative complication	Total duration of surgery (mins)	Time of two segment regression (mins)	Time to regression to T12 (mins)	Total duration of motor block (mins)	Duration of analgesia (mins)	Time of rescue analgesia (mins)	Total amount of analgesia required postoperatively (mg)
pressure in mmHg (mins)										Respiratory rate / min (mins)																				Oxygen saturation (%) (mins)																				Visual Analouge Scale (mins)							(hr)		Sedation score (mins)																	
45	60	90	120	150	180	210	240	360	480	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480	0	2	4	6	8	10	15	20	25	30	45	60	90	120	150	180	210	240	360	480	0	60	120	180	240	360	480	12	24	0	15	30	60	120	180	240	360	480									
77	81	79	81	83	85	89	93	93	90	16	16	16	14	16	14	14	14	14	12	12	12	12	12	12	12	12	12	14	14	99	99	99	99	99	98	98	98	98	98	99	99	99	99	99	99	99	99	99	99	5	0	0	0	2	0	0	2	2	2	2	2	2	3	2	2	2	2	Nil	Nil	90	120	170	210	230	300	225
77	76	78	80	81	83	83	86	89	93	18	16	16	16	16	16	16	16	16	14	14	14	12	12	12	14	14	14	14	16	99	99	99	99	99	99	99	99	99	98	98	98	98	99	99	99	99	99	99	99	4	0	0	0	0	0	0	2	3	2	2	2	3	2	3	3	2	2	Nil	Nil	100	135	180	200	250	310	225
78	79	77	80	83	83	83	87	89	91	18	16	18	18	18	16	16	16	16	16	16	14	14	14	14	12	12	14	14	16	100	100	100	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	5	0	0	0	0	0	0	2	1	2	2	3	2	2	3	2	2	2	Inj. Avil	Pruritus	110	135	190	220	260	310	150
77	79	81	81	83	85	87	87	86	91	20	18	18	18	18	18	16	16	14	14	12	12	12	12	14	14	14	14	16	16	93	99	99	99	99	99	99	99	98	98	99	99	99	99	99	98	98	98	99	99	5	0	0	0	1	0	0	2	1	2	2	2	2	3	2	2	2	2	Inj. Ephedrine	Hypotension	90	130	170	210	240	290	150
80	82	83	83	83	87	89	93	93	97	18	18	18	16	16	16	16	16	16	16	16	14	14	14	14	12	12	14	14	14	100	100	100	100	100	100	##	99	99	99	99	99	99	99	99	99	99	99	99	99	4	0	0	0	2	0	0	3	2	2	2	2	3	2	2	3	2	2	Nil	Nil	120	110	160	190	210	260	225
81	83	83	87	87	90	93	93	91	92	20	18	18	18	20	18	18	16	16	16	16	14	14	14	14	14	16	16	16	16	99	99	99	99	99	98	98	98	98	98	99	99	99	99	99	99	99	99	99	99	4	0	0	0	1	0	0	2	2	2	2	2	2	3	3	2	2	2	Nil	Nil	90	120	180	210	230	280	225
76	78	79	81	83	81	81	83	83	85	20	18	18	18	16	18	18	16	16	16	16	14	14	12	14	14	16	16	16	16	99	99	99	98	98	98	98	98	98	99	99	98	99	99	99	99	99	99	99	99	5	0	0	0	0	0	0	2	2	2	2	2	2	2	2	2	2	2	Inj. Ephedrine	Hypotension	110	140	190	220	250	300	150
76	79	82	82	83	83	85	87	89	93	18	16	18	18	16	16	16	16	16	14	14	14	12	12	12	12	12	14	14	14	100	100	99	99	98	98	98	98	99	99	99	99	99	99	99	99	99	99	99	99	4	0	0	0	1	0	0	2	1	2	2	2	3	3	2	2	2	2	Nil	Nil	80	130	190	230	240	290	225
72	77	79	81	83	85	82	84	87	82	16	16	16	16	16	16	14	14	14	14	14	12	12	12	12	12	14	14	14	14	99	99	99	99	99	99	99	99	99	98	98	98	98	98	99	99	99	98	99	99	4	0	0	0	0	0	0	2	1	2	2	2	2	3	3	3	2	2	Nil	Nil	90	140	180	210	260	310	150
75	73	81	83	83	86	89	93	93	90	16	16	16	16	16	14	14	14	14	14	12	12	12	12	12	14	14	14	14	14	99	99	99	99	99	99	99	99	99	99	99	99	99	99	98	98	98	99	99	99	5	0	0	0	1	0	0	5	2	2	2	2	3	2	2	2	2	2	Nil	Shivering	100	120	180	220	240	280	225
80	81	77	77	83	85	87	89	91	93	16	16	16	16	16	14	14	14	14	14	12	12	12	12	12	12	14	14	14	16	99	99	99	99	99	99	99	99	99	98	98	98	99	99	99	99	99	99	99	99	0	0	0	0	0	0	0	2	2	2	2	2	3	2	2	2	2	2	Nil	Nil	90	140	170	230	250	300	150
71	75	77	77	79	77	79	82	83	83	18	18	18	16	16	16	16	16	16	16	16	14	14	12	12	14	14	14	16	16	99	99	99	99	99	99	99	99	99	99	98	98	98	99	99	99	99	99	99	99	0	0	0	0	2	0	0	2	2	2	2	3	3	3	3	3	2	2	Inj. Ondansetron	Nausea	100	120	150	200	220	260	225
71	73	75	79	77	81	82	84	87	83	16	16	16	16	16	16	14	14	14	14	14	14	12	12	12	12	14	14	14	14	99	99	99	99	99	99	99	99	99	98	98	98	99	99	99	99	99	99	99	99	0	0	0	0	1	0	0	2	2	2	2	2	2	2	2	2	2	2	Nil	Nil	90	135	170	210	240	290	225
69	73	73	75	77	81	83	83	83	80	18	18	18	18	16	16	16	14	14	14	14	14	14	14	14	14	14	14	14	14	100	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	1	0	0	2	1	2	2	2	3	2	3	2	2	2	Inj. Atropine	Bradycardia	100	120	150	200	230	270	150
85	87	85	89	91	90	93	94	97	93	16	18	16	16	16	16	14	14	14	14	14	12	12	14	12	12	12	14	14	14	99	99	99	99	98	98	98	98	98	98	99	99	99	99	99	99	99	99	99	99	0	0	0	0	3	0	0	2	2	2	2	2	2	3	3	3	2	2	Nil	Nil	90	135	160	220	210	250	225
74	76	79	81	84	87	91	93	90	92	16	16	16	16	16	16	14	14	14	14	14	14	12	12	14	12	12	14	14	14	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	5	0	0	2	2	2	2	2	3	2	2	2	2	2	Inj. Atropine	Bradycardia	80	110	160	180	200	240	225
73	76	79	81	85	85	88	91	95	93	18	18	18	18	18	18	18	16	16	16	14	14	14	14	14	14	16	16	16	16	99	99	99	99	99	99	99	99	99	99	99	99	98	98	99	99	99	99	99	99	0	0	0	0	1	0	0	2	2	2	2	3	2	3	2	2	2	2	Nil	Nil	110	135	190	210	230	270	150
77	78	79	82	85	87	90	89	94	91	16	16	16	16	16	16	14	14	14	14	14	14	12	14	14	12	12	14	14	14	99	99	99	99	99	99	99	98	98	98	98	98	99	99	99	99	99	99	99	99	0	0	0	0	0	0	0	3	2	2	2	2	2	2	3	3	2	2	Nil	Shivering	80	120	180	230	260	300	150
76	76	76	79	82	83	86	88	86	89	14	14	14	14	14	14	14	14	12	12	12	12	14	12	12	12	14	14	14	14	99	99	99	99	99	98	98	98	98	98	99	99	99	99	99	99	99	99	99	99	0	0	0	0	0	0	0	2	1	2	2	2	3	2	2	2	2	2	Nil	Nil	90	110	170	220	250	290	225
79	81	83	81	83	83	87	87	83	87	18	18	16	18	18	16	16	16	16	14	12	12	14	14	14	14	14	14	14	16	100	100	99	99	99	98	98	98	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	2	0	0	2	1	2	2	2	3	3	2	2	2	2	Inj. Avil	Pruritus	100	100	150	190	230	250	150
79	81	85	81	87	85	85	88	90	91	16	16	16	16	16	16	14	14	14	14	12	12	12	12	14	14	14	14	14	14	100	100	99	99	99	98	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	1	0	0	2	2	2	2	3	2	2	3	2	2	2	Nil	Nil	110	110	170	200	240	300	150
81	77	77	75	79	81	84	87	90	93	16	16	16	16	16	16	16	14	14	14	14	12	12	14	14	14	14	14	14	14	99	99	99	99	99	98	98	98	98	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	1	0	0	2	2	2	2	2	2	3	2	3	2	2	Inj. Ondansetron	Nausea	120	120	160	220	230	270	150
80	83	86	88	90	91	91	95	97	93	18	18	18	16	16	16	16	16	16	14	14	14	14	14	14	14	16	16	16	16	100	100	100	100	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	1	0	0	2	2	2	2	3	2	2	3	2	2	2	Nil	Nil	100	130	180	230	240	300	225
78	75	80	79	81	83	86	85	91	93	14	14	14	14	14	14	14	12	12	12	12	12	12	12	14	14	14	14	14	14	99	99	99	99	99	99	98	98	98	98	98	99	99	99	99	99	99	99	99	99	0	0	0	0	1	0	0	2	2	2	2	2	2	2	2	2	2	2	Nil	Nil	110	110	150	190	220	270	150
79	78	78	83	83	83	85	89	91	94	18	18	18	18	18	18	16	16	16	16	14	14	14	14	14	14	14	14	16	16	99	99	99	99	99	99	99	99	98	98	98	98	98	99	99	99	99	99	99	99	0	0	0	0	0	0	0	3	1	2	2	2	3	2	3	2	2	2	Inj. Ephedrine	Hypotension	100	120	170	220	250	300	225
73	76	81	81	84	83	83	83	87	83	16	16	16	16	16	16	16	16	14	14	14	14	14	14	12	12	12	12	14	14	99	99	99	99	99	99	99	98	98	98	98	98	99	99	99	99	99	99	99	99	0	0	0	0	2	0	0	2	2	2	2	2	2	2	3	2	2	2	Nil	Nil	110	100	150	200	220	270	150
77	80	82	84	83	85	87	90	93	90	14	14	14	14	14	14	14	12	12	12	12	12	12	12	12	12	12	12	14	14	99	99	99	99	99	98	98	98	98	98	98	99	99	99	99	99	99	99	99	99	0	0	0	0	2	0	0	2	2	2	2	2	2	2	3	2	2	2	Inj. Avil	Pruritus	120	110	160	210	210	270	225
77	81	83	85	87	90	89	93	93	97	20	20	18	18	16	18	18	16	16	16	16	16	16	14	14	14	16	16	16	16	98	98	98	98	98	98	98	98	98	99	99	98	98	98	98	98	98	98	98	98	0	0	0	0	1	0	0	2	2	2	2	2	2	3	3	2	2	2	Nil	Nil	140	120	170	200	230	300	225
83	85	89	91	84	82	89	91	93	91	18	18	18	16	18	16	16	16	16	16	14	14	14	14	14	14	14	14	14	16	99	99	99	99	99	99	99	99	98	99	99	99	99	99	99	99	99	99	99	99	0	0	0	0	2	0	0	2	2	2	2	2	2	3	2	2	2	2	Nil	Nil	110	110	150	180	210	280	150
77	73	79	80	83	83	87	89	87	93	18	18	18	18	18	16	16	16	16	16	14	14	14	14	14	14	14	16	16	16	99	99	99	99	99	99	98	98	98	98	99	99	99	99	99	99	99	99	99	99	0	0	0	0	1	0	0	2	2	2	2	2	2	2	2	3	2	2	Nil	Shivering	100	130	190	230	240	320	150