"COMPARISON OF FRACTIONATED DOSE VERSUS BOLUS DOSE INJECTION OF HEAVY BUPIVACAINE WITH FENTANYL IN SPINAL ANAESTHESIA FOR PATIENTS UNDERGOING ELECTIVE CAESAREAN SECTION: ONE YEAR RANDOMIZED CLINICAL TRIAL"

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LIST OF ABBREVIATIONS USED

ASA	-	American Society of Anaesthesiologists
BP	-	Blood pressure
bpm	-	Beats per minute
C	-	Cervical
cAMP	-	Cyclic adenosine monophosphate
CO	-	Cardiac output
CO2	-	Carbon dioxide
cc	-	Cubic centimeter
cm	-	centimeter
CSF	-	Cerebrospinal fluid
DBP	-	Diastolic blood pressure
dl	-	deciliter
ECG	-	Electrocardiography
FRC	-	Functional residual volume
G	-	Gauge
HCO_3	-	Bicarbonate
HR	-	Heart rate
HCL	-	Hydrochloric Acid
ICP	-	Increased intracranial pressure
IV	-	Intravenous
kg	-	Kilogram
L	-	Lumbar
LA	-	Local anaesthetic

LSCS	-	Lower segment caesarean section
Lt	-	litre
m	-	Meters
MAC	-	Minimum alveolar concentration
MAP	-	Mean arterial pressure
MCV	-	Mean corpuscular volume
MCHC	-	Mean corpuscular hemoglobin concentration
mEq	-	Milliequivalents
mg	-	Milligram
Mins	-	Minutes
ml	-	Millilitre
mmol	-	Millimole
MV	-	Minute ventilation
NIBP	-	Non invasive blood pressure
Na^+	-	Sodium ion
O_2	-	Oxygen
$PaCO_2$	-	Partial pressure of carbon dioxide
PaO_2	-	Partial pressure of oxygen
pka	-	negative log of the acid dissociation constant
pH	-	measure of the hydrogen ion concentration of a solution
PIH	-	Pregnancy induced hypertension
S	-	Sacral
SA	-	Spinal anaesthesia
SAB	-	Subarachnoid block
SBP	-	Systolic blood pressure

SD	-	Standard deviation
sec	-	Second
SpO_2	-	Peripheral saturation of oxygen
T	-	Thoracic
TV	-	Tidal volume
VAS	-	Visual analogue scale
VC	-	Vital capacity
µg	-	Microgram

ABSTRACT

Background and aim:

Maternal hypotension is the common complication encountered after subarachnoid block (SAB). This needs attention and treatment for the better maternal and foetal outcome. Administration of SAB with a bolus dose of local anaesthetic produce faster onset and precipitate maternal hypotension. Injecting a fractionated dose provides dense block and haemodynamic stability. Aim of this study was to compare fractionated and bolus dose of SAB in terms of haemodynamic stability and analgesia period.

Methodology:

Eighty parturients undergoing caesarean delivery under SAB were included in the study. They were divided into Group B or F according to computer randomization. Group B parturients received bolus dose SAB with 2ml of 0.5% hyperbaric bupivacaine and 10µg of fentanyl. Group F parturients received fractionated dose of 2ml of 0.5% hyperbaric bupivacaine and 10µg of fentanyl. In which, from the total dose two-third was given initially. After 90 sec remaining one-third of the dose was injected. Haemodynamic parameters and analgesia period were analyzed using Student's unpaired *t*-test.

Results:

The haemodynamic parameters were better in group F than group B. The number of patients required vasopressor in group F were six and group B were seventeen. There was a prolonged analgesia period in group F than group B (214.40 + 15.48 and195.95 + 8.98 min respectively).

Conclusion:

The parturients in fractionated dose group were haemodynamically better with longer analgesia period than bolus dose group. It is a newer technique to prevent maternal hypotension after SAB.

Keywords: fractionated dose, hypotension, caesarean section

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INTRODUCTION

The subarachnoid block (SAB) is the preferred anaesthetic technique used in pregnant women undergoing lower segment caesarean section (LSCS). It is the most used method because of its rapid onset and postoperative analgesia. Complications related to general anaesthesia and vulnerability of the foetus to drugs are avoided. Hypotension is the most common problem associated with spinal anaesthesia. Pregnant women have profound hypotension with spinal anaesthesia because of anatomical and hormonal changes in pregnancy. Incidence of hypotension among pregnant women is 92% - 94% without any preventive measures.[1] Maternal hypotension compromises uteroplacental blood flow leading various complications in the foetus.[2,3]

In spinal anaesthesia (SA), administration of hyperbaric bupivacaine in bolus dose cause high sympathetic block and produce profound hypotension. Whereas administration of hyperbaric bupivacaine in fractionated dose, in which from the total dose two- third is injected initially. After 90sec remaining one- third of the drug is injected. This provide dense block with better haemodynamic stability.[4]

Many studies have been conducted to administer adjuvant in subarachnoid space along with local anaesthetic agents. The aim of administering adjuvant in the intrathecal space is to decrease the volume of local anaesthetic agents and decrease the complication caused by a large volume of local anaesthetic drug.[5] Adding adjuvant like fentanyl to the local anaesthetic agent in spinal anaesthesia provides prolonged analgesia and early recovery from motor block.[6,7]

In LSCS, adding opioid like fentanyl to intrathecal injection reduces the volume of hyperbaric bupivacaine and improves the intensity and quality of spinal anaesthesia.[8] Administration of opioid into cerebrospinal fluid provides prolong analgesia without compromising the quality and effectiveness of the block.[9]

Recently many studies have been done on intrathecal hyperbaric bupivacaine and fentanyl in LSCS to improve postoperative analgesia. Comparison of fractionated and bolus dose injection of hyperbaric bupivacaine in SAB for patients undergoing elective LSCS has been less evaluated. The fractionated dose of hyperbaric bupivacaine with fentanyl in SAB for haemodynamic stability and prolonged analgesia has not been evaluated. Hence this study was intended to compare haemodynamic changes and postoperative analgesia of fractionated dose versus bolus dose with hyperbaric bupivacaine and fentanyl in SAB for patients undergoing elective LSCS.

OBJECTIVES

Primary objective-

To compare haemodynamic parameter like heart rate (HR), blood pressure (BP) and mean arterial pressure (MAP) of fractionated dose and single bolus dose of bupivacaine with fentanyl in SAB for parturients undergoing caesarean section delivery.

Secondary objective-

To study the onset and regression of motor and sensory block, duration of analgesia and Apgar score of the new born.

REVIEW OF LITERATURE

James Leonard Corning in 1885 accidentally injected cocaine in the spinal nerve of a dog. Later in 1898, planned spinal anaesthesia was given by Bier. He administered cocaine intrathecally for local anaesthesia. From then on various drugs and techniques were invented to provide local anaesthesia. The subarachnoid block is the commonly followed anaesthetic method in pregnant women undergoing LSCS. The main advantages of the subarachnoid block are rapid onset of action, less systemic toxicity of local anaesthesia and maternal comfort. The Disadvantage is hypotension which is profound in pregnant women. Various medical treatment and techniques were tried to prevent this hypotension. Adding opioids decreases the dose of local anaesthetic drugs thereby decrease the extent of sensory block, hypotension and increase the analgesia period. First publication of adding opioid to local anaesthetic drugs was done in 1901.

Badheka J.P et al[10] in 2017 conducted a study on "Comparison of fractionated dose versus bolus dose injection in spinal anaesthesia for patients undergoing elective caesarean section: A randomized, double-blind study."

The study was performed in 60 parturients undergoing elective C-section delivery. Patients were separated into two groups. B Group parturients were administrated spinal anaesthesia with single bolus injection of 0.5% bupivacaine and F Group parturients received fractionated dose of 0.5% bupivacaine in which from the total calculated local anaesthetic dose two-third of the drug was injected initially. After 90 sec remaining one- third of the drug was injected. The time of onset and

regression of the motor and sensory block, intraoperative haemodynamic parameters and analgesia period were compared between the groups.

The sensory and motor block onset was comparable between the groups. The sensory and motor block duration of regression was more in F Group with 161 ± 29min and 236 ± 42min respectively whereas B Group had 145 ± 25min and 204 ± 42min which was significant with $P < 0.05$. Patients were haemodynamically better in F Group as compared to B Group. The number of parturients required vasopressor in F Group were five (16.66%) and fourteen (46.66%) in B Group [$P = 0.013$]. F Group showed prolonged duration of analgesia as compared to B Group [$P < 0.001$].

They concluded that the use of fractionated dose in spinal anaesthesia produce more haemodynamic stability with less use of a vasopressor and increased analgesia period for parturients undergoing elective LSCS.

Another study was conducted by Monika Gandhi et al[11] in August 2019 Comparing fractionated and single dose of the local anaesthetic in elective caesarean section delivery. 200 pregnant women were divided into Group F and Group B. Group F pregnant women received fractionated dose of hyperbaric bupivacaine 0.5% and Group B received bolus dose of spinal anaesthesia. The sensory and motor block-onset, duration and regression were assessed. The analgesia period was also noted.

The sensory and motor block onset was much earlier in Group F (71.53 $\pm$ 5.66sec) and (88.95$\pm$4.516 sec) respectively when compared to Group B (88.95$\pm$4.51sec) and (116.20$\pm$2.554 sec) respectively which was statistically significant. The sensory and motor block regression in Group F was (170.53$\pm$5.902) and (152.34$\pm$4.64) min respectively whereas Group B had (152.34$\pm$4.67) and

(134.25±8.70) min respectively. The duration of analgesia was increased in Group F compared to Group B. The first supplement analgesia in Group F was 3.17 ± 0.377 hours and in Group B was 2.61 ± 0.53 hours which was statistically significant with P < 0.05. The study also concluded that Group F patients were haemodynamically more stable with only 15 of them requiring vasopressor intraoperatively while 39 women in Group B needed vasopressor.

Nugroho AM et al[12] in February 2019 conducted "A Comparative Study of Fractionated Versus Single Dose Injection for Spinal Anesthesia during Cesarean Section in Patients with Pregnancy-Induced Hypertension."

The study included 42 pregnant women with hypertension associated with pregnancy undergoing emergency or semi-emergency caesarean section under spinal anaesthesia with heavy 0.5% bupivacaine and fentanyl. They were divided into fractionated dose (FD) and single dose (SD) groups, 21 patients in each. Fractionated dose (FD) group received 1.5 ml total dose of bupivacaine and fentanyl initially followed by 1ml after 90 seconds. Single dose (SD) group received 2.5ml in a single injection. MAP, usage of ephedrine and the sensory block level were compared between the groups.

There was no significant statistical difference in MAP between the groups [P >0.05]. But FD group had higher MAP during the first 3 min than SD group. There is no notable statistical difference in the level of sensory block among the two groups. The dose of ephedrine needed in the group FD was 10mg whereas SD group needed 15mg which was not statistically significant [P = 0.30].

A study was done by Deepak K et al[13] in 2019 on "comparison of bolus dose versus fractionated dose of injection bupivacaine heavy (0.5%) in spinal anaesthesia for patients undergoing emergency caesarean section."

A total of 60 pregnant women undergoing LSCS were included in the prospective study and they were divided into B Group and F Group randomly. The B Group patients received single-dose of bupivacaine while F Group patients received fractionated-dose of bupivacaine. They assessed the onset of sensory and motor block, duration of analgesia and intraoperative haemodynamics.

The onset of sensory block in Group B was 1.4 ± 0.509 min and in Group F was 1.29 ± 0.5 min which was not significant statistically [P=0.076]. The motor block onset in B Group and F Group was 5.767 ± 1.13 min and 4.666 ± 1.074 min which was significant with P value of 0.000031. Group F patients were haemodynamically more stable than Group B. The number of patients required vasopressor in F Group were four (13.33%) and in B Group were thirteen (43.33%). The analgesia period was more in F Group than B Group [P <0.001].

They concluded that pregnant women who received spinal anaesthesia in fractionated dose were haemodynamically more stable and had increased duration of analgesia than the patients received bolus dose.

RamasaliManjula V et al[14] in 2018 conducted a "Comparative Study of Bolus versus Fractionated Dose Injection in Spinal Anaesthesia for Pregnant Women undergoing elective Caesarean Section."

The study was done on sixty pregnant women undergoing elective C-section delivery. They were separated into two groups. Group A was administered with bolus-dose of 0.5% bupivacaine (H) in intrathecal space. Group B was administerd with fractionated-dose of 0.5% bupivacaine (H) in intrathecal space. In fractionated dose, one-third of the total calculated local anaesthetic dose was injected first. After 60 seconds the remaining dose was injected.

They assessed intraoperative MAP, HR and duration of analgesia. The time of motor and sensory block- onset and regression were also noted. The MAP and HR were on higher trend in Group B. Group A patients required more vasopressor than Group B (5.50±3.79 vs. 2.40±3.1). The analgesia period was increased in Group B than Group A (188.97±18.80 vs. 154±22.56 min). The onset and two segment regression were significantly delayed in Group B as compared to Group A with $P<0.05$.

Thus they concluded that pregnant women received spinal anaesthesia in fractionated dose were haemodynamically more stable with longer duration of analgesia.

Lakshmi Sowmya .N et al[15] in January 2020 conducted a study on "Comparison of Fractionated versus Bolus Dose Injection of Drug in Spinal Anaesthesia for Lower Limb Surgeries."

The study was done on 60 patients of age 15-80 years and divided them into two groups. B Group patients received 3ml of bolus-dose of bupivacaine. F Group patients received 3ml of bupivacaine in divided-dose. They assessed sensory and

motor block- onset and duration. The number of episodes of hypotension, low HR and analgesia period were also assessed.

The sensory block onset in Group B and Group F was 4.90 ±0.80 and 4.90 ±0.76 min respectively with no notable difference. The motor block onset was 7.17±0.95 min and 6.93 ±0.87 min in Group B and Group F respectively [P=0.324]. The sensory block duration was 125.77± 15.54 min and 147.77± 14.38 min in Group B and Group F respectively which was significant. The duration of motor block was 107.5± 13.24 min in Group B and 118.5± 13.11 min in Group F. Group F had increased duration of analgesia than Group B (180.80 ±17.16 vs. 154.07±15.78 min). The episodes of bradycardia and hypotension were more in Group B than Group F. They conclude that the divided dose of bupivacaine administration in spinal anaesthesia had more haemodynamic stability with longer duration of analgesia.

A study was conducted by Roopesh Kumar et al[16] in 2016 on "Effect of Intrathecal Fentanyl with Bupivacaine on Maternal Haemodynamics and Fetal Outcome during Cesarean Section: A Comparative Study with Two Different Doses."

The study included 120 pregnant women of ASA I and ASA II undergoing LSCS. They were separated into three groups. The B Group received 10 mg of bupivacaine 0.5%. Group BF1 received 10mg of bupivacaine 0.5% with 0.25ml of fentanyl (12.5 µg). Group BF2 received 10mg of bupivacaine 0.5% with 0.5ml of fentanyl (25 µg). Intraoperative haemodynamic parameter like MAP, HR, number of patients required vasopressor, side effects and neonatal outcome were assessed.

Intraoperative discomfort was noted in four patients (10%) in Group B whereas none of the patients complained of pain in fentanyl groups. About nineteen

(47.50%), eleven (27.50%), eight (20%) patients in Group BF2, Group B F1, Group B respectively required vasopressors. Five patients in Group B (12.5%), three patients in Group BF1 (7.5%) and one patient in Group BF2 (2.5%) had nausea (P< 0.05). No significant statistical difference was noted in neonatal outcome.

They concluded that 25µg of fentanyl caused more hypotension than 12.5µg when added with bupivacaine. The neonatal outcome was the same in all the groups. Adverse effects were less in all of them.

Sowmya N et al[17] in 2016 compared "Intrathecal Fentanyl in Different Doses (10µg, 15µg) with Hyperbaric Bupivacaine (10mg) for Caesarean Section."

Parturients of ASA I and ASAII were included in the study. 10mg of bupivacaine with 10µg of fentanyl was administered to Group A. 10mg of bupivacaine with 15 µg of fentanyl was administered to Group B. The sensory and motor blockade- onset, duration, two segment regression and need of rescue analgesia were assessed.

The haemodynamic parameters in A Group were in the higher trend than in B Group with P <0.001. The sensory block onset was 2.1$\pm$0.3 min in Group A whereas Group B had 1.5$\pm$0.1 min which was significant statistically (P<0.001). The motor block onset in Group A and Group B were 4.1$\pm$0.4 and 3.1$\pm$0.1 min respectively. Two segment regressions were statistically significant in Group A and Group B (148.1$\pm$4.3 vs. 165.8$\pm$3.7 min). Postoperative analgesia was increased in Group B with 169.6$\pm$3.7 min whereas Group A had 157.7$\pm$3.6 min.

Another study was conducted by C C Chu et al[18] in 1995 on "The Effect of Intrathecal Bupivacaine with Combined Fentanyl in Cesarean Section."

Seventy parturients undergoing LSCS were involved in the study. They were separated into five groups. Each group received different dose of fentanyl with bupivacaine. Group I (0µg), Group II (7.5 µg), Group III (10µg), Group IV (12.5µg) and Group V (15µg) of fentanyl were given. Haemodynamics, analgesia and side effects were noted in all the groups.

Group IV and V had increased duration of complete analgesia (201.3±16.4 vs. 210.3±18.6 min). 12.5µg of fentanyl group had increased duration of effective analgesia (293±22.4 min). The side effects like shivering and pruritus were less in Group IV and V when compared to other groups.

They concluded that clinical effects were observed when the dose of fentanyl was increased to 12.5µg or 15µg. 12.5µg fentanyl with bupivacaine had longer analgesia with lesser side effects.

Moran DH et al[1] in 1991 done a study on "Phenylephrine in the Prevention of Hypotension Following Spinal Anesthesia for Cesarean Delivery."

The study included 60 parturients undergoing LSCS done under spinal anaesthesia. They were divided into Group 1 and Group 2. Group 1 patients received ephedrine when systolic blood pressure (SBP) was 5mmHg low from the baseline. Phenylephrine was administered to Group 2 when SBP was low as per above mentioned criteria. Once the baby was delivered maternal venous blood, umbilical artery and vein samples were collected to analyze blood gases.

The pH of umbilical artery was 7.28 ±0.01 and 7.32 ±0.01 in Group 1 and 2 respectively. The pCO_2 in Group 1 and 2 were 56.6±1.4 and 52.1±1.3 mmHg respectively. Base defect in Group 1 was 2.2±0.04 mEq whereas in Group 2 was

0.38±0.35 mEq. There was no statistical difference in blood gas between the groups. Thus they concluded that phenylephrine could also be used to treat maternal hypotension.

A study was conducted by MandalM et al[19] in 2016 on "Comparison of crystalloid and colloid preload on maternal hemodynamics in elective caesarean section under spinal anaesthesia."

Eighty pregnant women were selected to participate in the study. They were split up into Group 1 and Group 2. Group 1 patients received Ringer lactate and Group 2 patients received 6% hydroxylethyl starch before undergoing the anaesthetic procedure. SBP, MAP and Apgar scores were assessed between the groups.

Group 2 had high SBP than Group 1. At 2, 4, 6, 8, 12, 16, 18 min significant differences were found between the groups with P=0.000. MAP was on higher trend in Group 2 than Group 1. Incidence of hypotension was 60% in Group 1 and 30% in Group 2 (P=0.011). The one minute Apgar score in Group 1 was 6.47±0.84 and 6.77±0.83 in Group 2. They concluded that maternal hypotension was prevented when patients were preloaded with 6% hydroxyethyl starch than with Ringer lactate.

"A randomized trial comparing prophylactic phenylephrine and ephedrine infusion during spinal anesthesia for emergency cesarean delivery in cases of acute foetal compromise" was conducted by K Jain et al[20] in 2016.

Ninety pregnant women with intraoperative foetal compromise were separated into two groups. They received 30µg/min of phenylephrine and 2.5 mg/min of ephedrine as a prophylactic infusion dose. The target SBP was to maintain between

90% and 110% from baseline. Foetal acidosis was identified by analyzing cord blood gases. Apgar score and foetal outcome were also compared.

Fourteen neonates in Group E and nine in Group PE were in acidosis (pH <7.2) which was not statistically significant (P=0.22). Base deficit > 12 mmol had a low one minute Apgar score. This was seen among six neonates in Group E and three in Group PE. Neonates with low Apgar scores needed resuscitation and intubation for a short period. They concluded that foetal outcome was the same with phenylephrine and ephedrine when administered to treat maternal hypotension after spinal anaesthesia.

BASIC SCIENCES

SUBARACHNOID BLOCK

The subarachnoid block (SAB) is a regional anaesthesia involving injection of local anaesthetics into subarachnoid space. It acts on spinal nerve roots & dorsal ganglion to produce sympathetic block, sensory analgesia and motor block.

Indication:

- Surgery involving the lower half of the body
    - Lower abdomen
    - Lower extremity
    - Perineum
- Caesarean section
- Procedures below the diaphragm- diagnostic and therapeutic

Contraindication:

- Absolute
    - Lack of consent /patient refusal
    - Increase intracranial pressure
    - Coagulopathy
    - Severe hypovolemia
    - Sepsis
    - Severe Aortic stenosis or Mitral stenosis

- Relative
    - Severe spinal deformity
    - Pre-existing neurological deficits
    - Demyelinating lesions
    - Uncooperative patient
    - Skin infection at the injection site

ANATOMY

To perform subarachnoid block, knowledge about anatomy of spinal canal, vertebral column and spinal nerve are essential.

Vertebral column[21]

It gives protection and structural support to the spinal cord.

There are

- Cervical vertebra- 7
- Thoracic vertebra- 12
- Sacral- 5 and coccyges- 4 (which are fused)

Parts of the vertebra (fig. 1)

- Body- anterior
- Two pedicles- project posteriorly
- Two lamellae- connect the pedicles
- Lamella- gives rise to the transverse process laterally and spinous process posteriorly

Pedicles of vertebra are notched. The opposite notches fuse to form foramen. Spinal nerve comes out through this foramen. At the lamellar junction, articular processes (superior and inferior) arise.

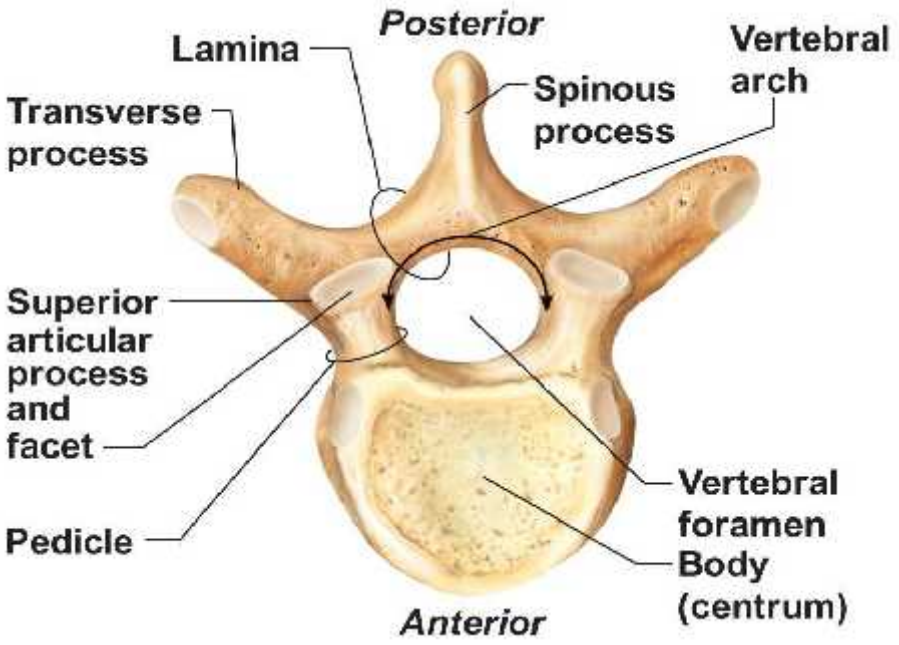


Figure 1Parts of vertebra

Ligaments

Ligaments give support to the body of vertebra. They are

Supraspinous ligament- It is a Strong, thick and fibrous band extending from cervical (7^{th}) to sacrum. It continues as ligament nuchae from C7. It attaches to the occipital protuberance.

Interspinous ligament - Thin, fibrous structure extending from the apex & lower spine (upper surface) toward the root and inferior surface of the next higher vertebrae.

Ligamentumflavum- They extend in vertical direction from the anterior surface of upper lamina to the inferior surface and inferiorly to antero-superior surface of lower lamina. While exiting the intervertebral foramen, the ligament divides into right and left halves and they fuse in the midline.

Curvatures of the spine (fig. 2)

- Cervical curve - Convex (anterior)
- Thoracic curve - Convex (posterior)
- Lumbar curve - Convex (anterior)
- Sacrococcygeal – Convex (posterior)

Figure 2Curvature of spine

Meninges[22,23]

Meninges of spinal canal comprise of 3 membranes which are in sequence with the meninges of cranium (fig. 3). They are

- Pia mater
- Arachnoid mater
- Dura mater

Subarachnoid space

The space between the arachnoid and pia mater is called subarachnoid space. It consists of CSF. It communicates with the space around the blood vessels of pia mater which is known as Virchow Robin Space. This space consists of blood vessels, nerve roots and CSF.

Subdural space

It is a space between arachnoid mater and dura mater. They are separated from each other by thin serous fluid. The traumatic brain injury commonly presents as subdural haematoma.

Epidural space

It is a space between the dura mater and the periostium lining the vertebral canal. It stretches from foramen magnum to sacrococcygeal ligament (sacral-hiatus). This space consists of fat, loose areolar tissue, spinal arteries and Batson's plexus and nerve roots. The epidural block is the common anaesthesia technique used for surgeries involving lower half of the body.

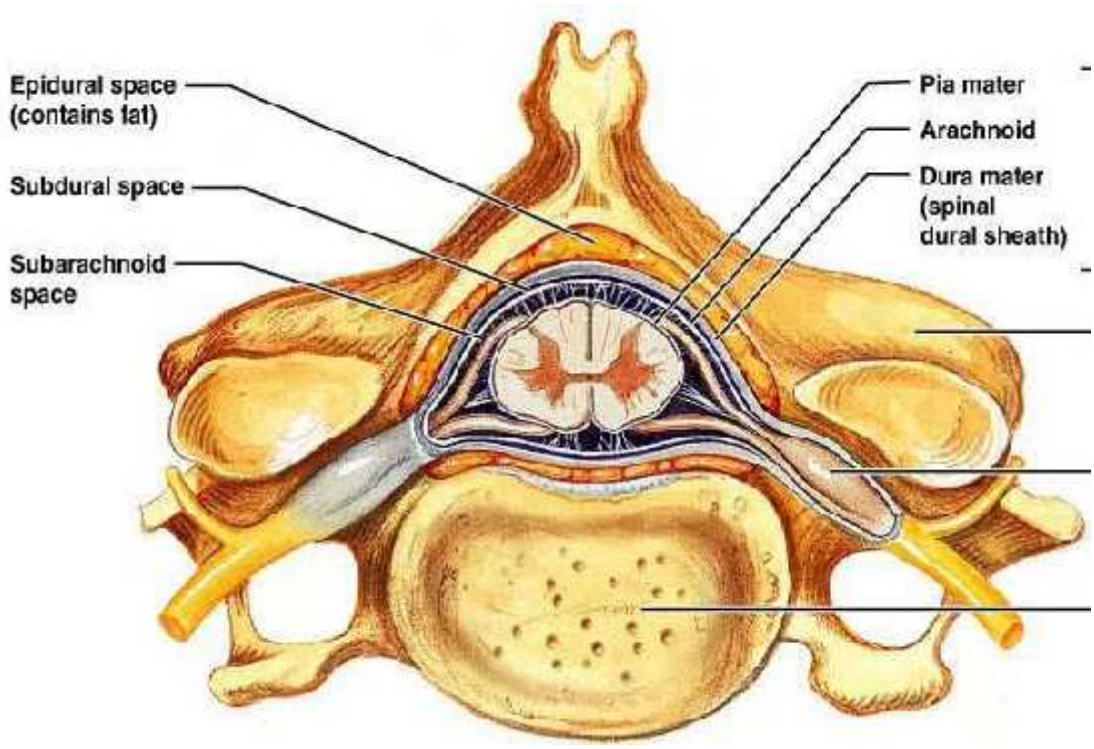


Figure 3Meninges of spinal cord

Cerebrospinal fluid (CSF)[24]

CSF is a thin clear fluid covering brain and subarachnoid space. It is formed either by secretion or ultra filtration from the choroid plexus. It flows from lateral ventricle to 3rd ventricle and it enters foramen of Monro to 4th ventricle. Through foramen of luschka and megendie, it reaches subarachnoid space. The total CSF volume in adult is about 150 ml. In which 25ml is present in ventricle and 125ml in subarachnoid space. Around 400- 600ml is produced per day. In the end it gets absorbed into arachnoid villi.

Composition of CSF

- Specific gravity- 1.003-1.009
- pH- 7.27 - 7.37
- pCO_2- 48 mm Hg
- Na- 135-145mEq/L
- Cl- 15-20mEq/L
- HCO_3- 23mEq/L
- Proteins – 23-38mg/dl
- Sugar- 50-80mg/dl

Spinal cord

Spinal cord is a thin, long structure consisting of nervous tissue. It extends from the medulla oblongata (in the brain stem) to the lumbar vertebral column. They are divided into gray and white matter. In children, spinal cord terminates at L3 vertebra (lower border). In adult, it terminates between L1 and L2 vertebra. There are thirty one pairs of spinal nerve. After L1 vertebra, the spinal cord terminates as fibrous extension known as filumterminale.

Spinal nerves

There are 8 cervical (C) nerves, thoracic (T) - 12, lumbar (L) - 5, sacral (S) - 5, and coccygeal- 1. Each is formed by the combination of anterior & posterior spinal root. Each pair of spinal nerve passes through a pair of intervertebral foramina.

Each pair of spinal nerve divides into anterior and posterior root (anterior forms- motor root, posterior forms- sensory root).

Structures pierced during subarachnoid block (fig. 4)

- Skin
- Subcutaneous tissue
- Supraspinous ligament
- Interspinous ligament
- Ligamentumflavum
- Dura mater

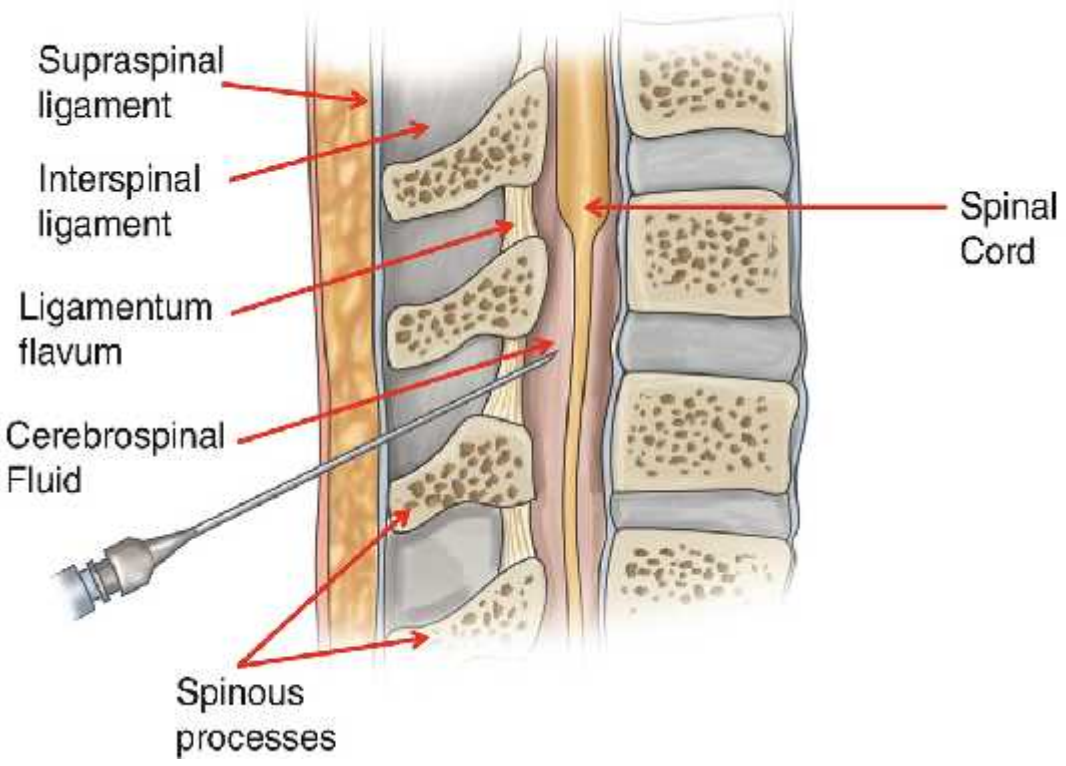


Figure 4Structures pierced during subarachnoid block

PHYSIOLOGICAL CHANGES DURING SUBARACHNOID BLOCK

Cardiovascular effects:[25]

Clinically, the most important effect of the sympathetic block during SA is on the cardiovascular system. Neuraxial block produces hypotension along with decreases in heart rate. An extensive sympathetic block at cephalad dermatome produces these effects. Vasomotor tone determined by T5 to L1 sympathetic fibers, innervating smooth muscles of blood vessels. Blocking of these nerves cause venous vasodilatation and accumulation of blood in lower extremities and viscera. They decrease preload and cardiac output (CO). Arterial vasodilatation decreases the systemic vascular resistance which can be compensated by vasoconstriction of arteries above the level of blockade. In a high sympathetic level of block, this compensatory mechanism is lost. The cardiac accelerator fibers arising at T1 to T4 are also blocked in the high sympathetic block which leads to decreased cardiac contractility.

Pulmonary effects:

Pulmonary function is minimally altered because the diaphragm is innervated from C3 to C5. Tidal volume (TV) is unchanged even with the high thoracic level of sympathetic block. A minimal decrease in vital capacity (VC) is due to paralysis of abdominal muscles which is necessary for forced exhalation.

Gastrointestinal effects:

Vagal tone (parasympathetic) predominance results in the small contracted intestine with increased peristalsis and provides magnificent operative field for some

laparoscopic procedures when neuraxial block is used as an adjunct to general anaesthesia. Hepatic blood flow is reduced with a decrease in mean arterial pressure.

Renal effects:

Blood flow to the renal system is maintained by autoregulation and there is reduced effect on kidney due to neuraxial block. Both parasympathetic and sympathetic innervations of urinary bladder are blocked in spinal anaesthesia. Loss of autonomic control of urinary bladder results in retention of urine.

PHYSIOLOGICAL CHANGES DURING PREGNANCY

During pregnancy period, there are major changes in the systemic organ of the parturient.These changes are mainly due to hormone produced by placenta and corpus luteum. The mechanical effects of the growing uterus and compression of surrounding structures play an important role in the 2^{nd} and 3^{rd} trimesters of pregnancy.

Cardiovascular system changes:[26]

During pregnancy, oxygen consumption increases. To meet the metabolic demands of the growing foetus the maternal cardiovascular system changes. Cardiovascular changes start from 4^{th} week of gestation and these occur to increases oxygen transport to the placenta.These changes are caused by raised levels of circulating oestrogen and progesterone, which cause vasodilatation leading to 20% decrease in peripheral vascular resistance. Systemic vascular resistance also decreases due to reduce response to angiotensin and other pressor agents, which causes an increase in CO by 30%-50%. Stroke volume increases by 20%-50% with mild increase in heart rate.Myocardial thickness as well as the volume of chambers

increases resulting in left heart enlargement. Flow murmurs are common due to increased plasma volume and CO. Additional increase in CO occurs during labour and also in the immediate postpartum period because of added blood volume from the contracted uterus.

Supine hypotensive syndrome- occurs during lying in supine position. Growing uterus compresses the vessels like inferior venacava which decrease the preload resulting in low CO and blood pressure. It is seen during the second trimester as gravid uterus increase in size and more prominent during 36 – 38 week of gestation. It is not seen when pregnant women lie in the left lateral position. It can be prevented by displacing uterus to left by placing a wedge under the right side of the hip and left lateral tilt of the table (fig. 5).

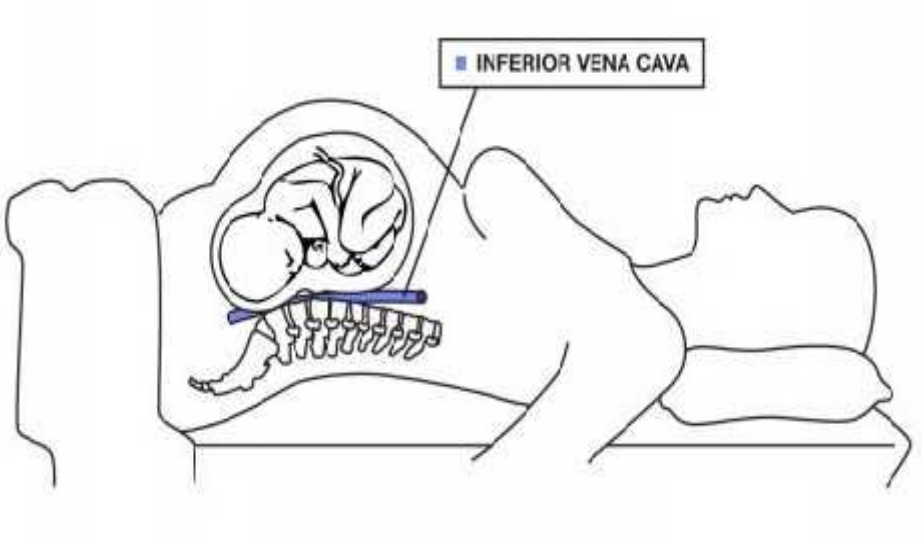


Figure 5Compression of inferior vena cava by gravid uterus

Respiratory system changes:

Hormonal changes, increased extracellular volume and vascular engorgement cause oedema of the upper airway. The diaphragm is displaced upwards as the uterus increases in size. This is accompanied by increase in the anteroposterior and transverse diameter of the rib cage so that total lung capacity decreases slightly. Minute ventilation (MV) increases by rise in tidal volume and minimal increase in respiratory rate (1-2 breaths/min). Stimulation of respiratory centre and sensitization of chemoreceptor to carbon dioxide (CO_2) are caused by progesterone. Due to rise in MV, $PaCO_2$ falls to 30-32 mmHg in the 1^{st} trimester and remains in the same range throughout the pregnancy. Increase in alveolar ventilation cause increase in PO_2 in the initial period of gestation. After the mid gestational period, PO_2 decreases in supine position due to fall in functional residual volume (FRC) below closing capacity. Oxygen delivery to foetus increases by the rightward shift of maternal oxygen dissociation curve. Haemoglobin of foetus has a high affinity to oxygen with P50 of 18mmHg.

Minimum alveolar concentration (MAC) value of volatile anaesthetic agents decreases to 30%.Mallampati classification changes during pregnancy. Intubation is difficult due to oedema of the upper airway, obesity and enlarged breast. Short handled laryngoscope, smaller size endotracheal tube and ramp position might be helpful for difficult intubation. Rapid desaturation despite of adequate preoxygenation is common due to decreased FRC and increase oxygen consumption.

Haematological changes:[27]

Plasma volume increases slowly throughout pregnancy. Increase in plasma volume is more than the increase in RBC so there is decrease in haematocrit, haemoglobin and red blood cell. There is no change in MCV and MCHC value despite of haemodilution. All clotting factors except II, V, XI, and XIII increase. Increased fibrinogen and decreased fibrinolytic activity make pregnancy a hypercoagulable state. Thromboembolism is common during pregnancy and postpartum period. The leucocyte count increases throughout the pregnancy to around 15000 /mm^3.

In severe preeclampsia patient, there is a high chance for haematoma formation while placing the epidural catheter as there is an exponential decrease in platelet count. Assessment of both platelet count and function are necessary.

Gastrointestinal system changes:

Motility of oesophagus is majorly affected in the gastrointestinal system in pregnancy. The abdominal portion of oesophagus is displaced into thorax and progesterone cause relaxation of lower oesophagus sphincter. These anatomical and hormonal changes decrease the tone of the lower oesophagal sphincter and cause gastro oesophagal reflux. During labour and postpartum period gastric empty time is delayed. Progesterone decreases gastrointestinal contraction and peristalsis causing constipation in pregnancy. The most common symptom in the first trimester is nausea vomiting. Spider nevi and palmar erythema which is seen in liver pathology are commonly seen in pregnant women due to increased oestrogen. Plasma cholinesterase level decreases by 25% during 1^{st} trimester and maintain the same level till term.

Due to decreased tone of the lower oesophagal sphincter and increased intra abdominal pressure, makes pregnant women more prone to aspiration. Rapid sequence induction is preferred during general anaesthesia to prevent aspiration.

Nervous system changes:

Blood supply to the brain is increased due to low cerebral vascular resistance. The permeability of the blood brain barrier increases. The threshold to pain is increased at full term and labour due to increase in endorphin and progesterone levels in plasma. Compression of the gravid uterus on IVC causes dilation of epidural venous plexus. There is decrease in epidural space and CSF volume and increase in epidural fat.

The requirement of local anaesthetic dose in SAB is decreased due to change in epidural space anatomy and increased sensitivity of neural tissue to progesterone. Sympathetic blockade during neuraxial block produces more hypotension in pregnant women.

Renal system changes:

Renal plasma flow and glomerular filtration rate increases and no changes in the number of nephrons are seen. Blood urea and serum creatinine are decreased due to increase in glomerular filtration rate. Increase in progesterone and renin-angiotensin- aldosterone level lead to retention of water and decreases plasma osmolality. Progesterone cause ureteric smooth muscle relaxation leading to urinary stasis making pregnant women more prone to urinary tract infection. There is an increase in the volume of distribution of drugs requiring a higher dose than normal

dose. Due to hypoalbuminemia protein binding drugs like thiopentone sodium, midazolam, phenytoin and digoxin free levels are increased.

Endocrine system changes:

Increased vascularity and follicular hyperplasia makes thyroid gland enlarged. Increase in thyroid- binding globulin leads to increase in total T3 and T4. Free T4 and T3 levels are unaltered. Level of thyroid- stimulating hormone falls during the first trimester and recover later. Subclinical hypothyroid and hyperthyroid can occurs without any adverse effects. Hyperprolactinaemia can occur due to rise in dopamine and placental lactogen. After carbohydrate load, there is increase in blood glucose level due to reduced sensitivity to insulin caused by placental lactogen. Starvation causes rapid hypoglycemia and ketoacidosis.

Musculoskeletal system changes:

Lumbar lordosis is increased to compensate for growing gravid uterus. Joint laxity is increased due to hormonal changes which make the delivery of foetus easy. Lordosis decreases intervertebral space making neuraxial block technique difficult. This makes ascending spread of local anaesthesia. It can be compensated by keeping a pillow underneath the shoulder.

PHARMACOLOGY OF LOCAL ANAESTHETICS

Local anaesthetic (LA) provides anaesthesia and analgesia for non- surgical and surgical procedures. It produce reversible blockade of impulse conduction when injected near neural tissue. It interrupts the transmission of impulses to the sensory,

motor, and autonomic nerves producing sensory anaesthesia, skeletal muscle paralysis and autonomic nerve block.

Molecular structure

LA consists of two groups, lipophilic and hydrophilic group. The lipophilic group is usually an aromatic benzene ring whereas the hydrophilic group is a tertiary amine. LA property of the drug is mainly due to lipophilic group. These two groups are connected by hydrocarbon chains like ester or amide linkage. Classification of LA drugs is based on the nature of these hydrocarbon chains.

Mechanism of action:[28,29]

LA blocks the voltage- gated sodium (Na^+) channel in neural tissue and prevents the entry of Na^+ ions during depolarization of action potential. As the LA concentration increases, action potential fails to reach the maximum threshold and block the nerve impulse conduction. Blockade of Na^+ channel in 2-3 nodes of Ranvier interrupts the impulse conduction. LA is partially ionized at physiological pH. The pka value of LA determines the balance between ionized and unionized form. The basic form of the drug penetrates the axon. However, the cationic form of the drug binds more easily to the receptor on the Na^+ channel. The degree of blockade depends on the frequency of stimulation.

The onset of action depends on the pka value of LA. Drugs like Mepivacaine, Lignocaine have low pka with a fast onset of action. At a pH of 7.4, 30-40% of the drug is in the basic form which easily penetrates the axon. Drugs like Procaine, Bupivacaine, Tetracaine are slow acting with high pka value. At a pH of 7.4, only 15% of these drugs are in unionized form.

The diameter of the nerve fibers and the type of fibers determine the sensitivity of LA. Smaller nerve fibers are more sensitive than large fibers. The myelinated fibers are blocked first before the non- myelinated fibers. Sensitivity to LA also depends on the critical length of the axon. 2-3 nodes of Ranvier form the critical length of the axon. LA enters the axon easily in this part. The smaller fibers have a short critical length than the larger fibers. The concentration of Na^+ channel is more in nodes of Ranvier. Autonomic nerve fibers are the first one to get blocked followed by sensory and motor nerve fibers. The order of blockage among the somatic fibers is pain, temperature, touch and deep pressure.

Adding Adrenaline to LA cause vasoconstriction of the vessel and prolongs the duration of action of the LA. It decreases the absorption of the drug from site of infiltration and increases the concentration of the drug at that site.

Systemic action:

Central nervous system

Accidental intravenous injection or overdose of the drug can produce stimulation of central nervous system followed by depression.

The signs and symptoms observed with LA toxicity are numbness around the oral cavity, tingling sensation in the tongue, drowsiness, blurring of vision, tinnitus followed by dysphoria and lethargy. A still higher dose can produce restlessness, excitation, agitation, convulsion and finally loss of consciousness.

Cardiovascular system

LA does not produce any effect on the heart at the usual dose. At a higher dose, it acts as a cardiac depressant by reducing cardiac excitability, automaticity, and contractility. It also prolongs the Effective refractory period. It has antiarrhythmic action like Quinidine. Bupivacaine is more cardiotoxic and can produce tachycardia, fibrillation and cardiac arrest.

Blood vessel

LA produces hypotension by blocking the sympathetic nervous system. But at a higher dose, it produces arterial smooth muscle relaxation at the injection site. Bupivacaine produces more vasodilation than lignocaine. Prilocaine has least vasodilatory action.

Pharmacokinetics

Since LA act near the site of administration, efficacy is not determined by the pharmacokinetics of the drug. Toxicity and systemic effects are markedly influenced from the place where they enter.

LA like amide (eg-lidocaine) is directly absorbed from mucous membrane and abraded skin but not from intact skin. However, prilocaine is not absorbed from the mucous membrane. Blood flow to the particular area also determines the rate of absorption of the drug. Since LA is highly lipophilic it is widely distributed in the tissue and quickly enters the high vascular organ like heart, brain, kidney and liver.

Procaine is less likely to bind to plasma protein. Whereas amide LAs bind to alpha 1 glycoprotein. Ester LAs are hydrolysed by pseudocholinesterase in the plasma. Amide LAs undergoes dealkylation and hydrolysis in the liver.

Adverse effects

Systemic adverse effects occur after accidental IV injection or overdose of the drug.

- Central nervous system complications are shivering, abnormal movement, twitching, light headedness, drowsiness, disorientation and confusion.
- Cardiovascular adverse effects occur as hypotension, bradycardia, arrhythmia, and cardiac arrest.
- Local tissue toxicity is rare to occur. Addition of adrenaline to LA can cause local tissue necrosis.
- Some patients can develop a hypersensitivity reaction to LA. It manifests as rashes, dermatitis, angioedema, asthma and anaphylaxis. Ester group of drugs are more likely to produce an allergic reaction. Hypersensitivity occurs mainly to methylparaben preservative added to LA.

BUPIVACAINE

Bupivacaine belongs to the amide group of LA. It is highly potent and longer acting LA. It is used in various procedures like spinal anaesthesia , epidural anaesthesia and nerve block because of its longer duration of action (fig. 6).

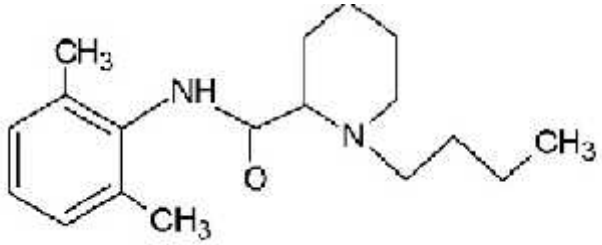


Figure 6 Chemical structure of bupivacaine

It is a potent cardiotoxic drug. It produces prolonged QTc interval, tachycardia and cardiac depression. The cardiotoxicity of bupivacaine is treated by lipid emulsion.

Changes during pregnancy[28]

The protein binding capacity of bupivacaine is altered during pregnancy resulting in more unbound drug in the plasma. Both progesterone and bupivacaine binds to alpha 1 glycoprotein but at a different site.

Potency

It is 3-4 times more potent than lignocaine and mepivacaine.

Onset and duration

The onset of action takes about 5 to 7 min and complete action is achieved by 15 to 25min.

Duration of action depends on the type of block

Epidural anaesthesia- 2.5 to 4 hr

Spinal anaesthesia- 2 to 3 hr

Spinal anaesthesia

Spinal anaesthesia is injection of LA into subarachnoid space. The principal site of action of LA is preganglionic fibres in the anterior rami of the spinal cord. The differential blockade occurs as the concentration of LA in CSF decreases from the site of injection. The sensitivity to LA differs according to the type of nerve fibres.

The spread of LA in CSF depends on the specific gravity of the solution injected. The specific gravity of the solution increases more than CSF when glucose is added to the LA solution (hyperbaric). The specific gravity of the LA solution is decreased by adding distilled water to it (hypobaric).

PHARMACOLOGY OF FENTANYL[30,31]

Fentanyl is a synthetic derived opioid. It is five hundred times more potent than morphine. In 1959, Dr Paul Jansen introduced fentanyl to the world. It has potent analgesic and anaesthetic properties. The various derivatives of fentanyl are sufentanil, alfentanil, remifentanil. They all vary in their analgesic potency.

Chemical structure

It is a phenylpiperidine derivative with a chemical name N-(1-2phenethyl-4-piperidyl) propinanilide citrate and empirical formula of $C_{22}H_{28}N_2O.C_6H_8O_7$ (fig. 7). Molecular weight is 528.9 gm/mol. Its melting point is 154-156^oC.

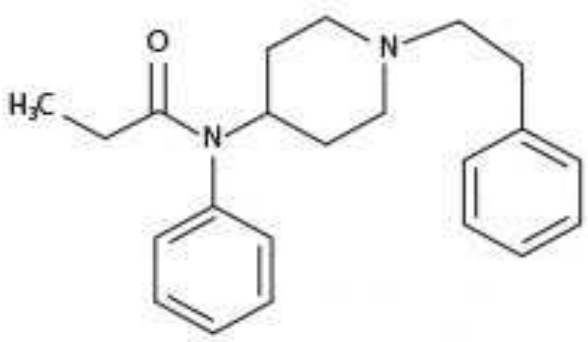


Figure 7Chemical structure of fentanyl

Mechanism of action

Fentanyl acts as a pure agonist at opioid receptor. Its action is mainly on Mu receptor present on the spinal cord, brain and smooth muscle. It also acts on kappa and delta opioid receptor. Binding on the Mu receptor causes respiratory depression, suppression of cough reflex and miosis. The analgesic and sedative effect of fentanyl is due to its action on the Mu receptor.

The opioid receptors are coupled with G- proteins. The activation of these receptors results in various activities like the closing of voltage- gated calcium channel and increase in the influx of potassium ion resulting in hyperpolarization and reduce cAMP. This decreases the nociceptive impulse transmission and neural cell excitation.

Pharmacokinetics

Absorption

It has a quick onset of action after IV administration and duration of action lasting for a short period. The time taken for equilibration between brain and blood is 6.4 min.

Distribution

It is widely distributed in the tissue due to its high lipid solubility. First, it enters highly perfused organ like brain, heart, lungs, skeletal muscle and fat. Initially, 75% of the drug undergoes first-pass metabolism in the lungs. Its volume of distribution is 4±0.4 l/kg.

Metabolism

Fentanyl is metabolized in the liver by cytochrome P450 3A4 and produce norfentanyl.

75% of the injected drug undergoes first- pass metabolism in the lung. 80% of the drug binds to plasma protein among which 15% binds to alpha 1 glycoprotein.

Elimination

After IV administration 75% of the drug is eliminated in the urine within 72 hr. Less than 7-8% of the drug is passed unchanged in the urine and 1% in faeces. The plasma clearance is about 0.5L/hr/kg.

Adverse effects

Cardiovascular system: produce syncope, hypotension and dose- dependent bradycardia.

Central nervous system:

It causes dose- dependent respiratory centre depression and reduces the carbon dioxide dependent ventilatory drive. Myoclonus occuring during drug administration can resemble tonic-clonic seizures. Action on the Mu receptor produces miosis.

Pruritus can occur when a drug is administered into CSF along with LA. This is due to the upward spread of the drug in the CSF and interaction with the Mu receptor.

Gastrointestinal system:

Decrease in gastric motility and an increase in smooth muscle tone produce constipation.

Allergic reaction

Hypersensitivity reaction occurs due to histamine release caused by opioid action. It manifests as itching, urticaria, hypotension and bronchospasm.

Tolerance and dependence

Tolerance to opioid occurs when there is a decreased effect of the drug after repeated administration.

Dependence to the opioid develops after over usage of the drug. Patients develop various psychological and physical signs and symptoms.

Effects on pregnancy and neonate

The opioid can cross the placenta if administered IV during labour and produce respiratory depression in the neonate.

Adding adjuvant in regional anaesthesia[32]

Adding adjuvant like an opioid to bupivacaine in SAB prolongs the duration of analgesia. Opioid binds to the receptor on the dorsal horn of the spinal cord and suppress the nociceptive stimulus. The decreased ascending spread of the opioid drug in the CSF produces minimal side effects.

Combining bupivacaine and opioid in the neuraxial block increases the duration of analgesia. Pain at two different pathways is blocked. Bupivacaine produces analgesia by blocking pain impulse generation at the dorsal root ganglion and nerve roots whereas opioid act at opioid receptor at substantiagelatinosa and decrease the nociceptive impulse.

Intrathecal administration of 10-25 µg of fentanyl and hyperbaric bupivacaine, increase the duration of analgesia in the parturient undergoing LSCS.[7,33] This minimal dose of fentanyl is safe for the mother and neonate.

MATERIALS AND METHODS

KLE'S Dr.PrabhakarKore Hospital and Medical Research Centre, Nehru nagar, Belagavi, in patients undergoing caesarean section under subarachnoid block between January 2019 to December 2019.

Study design: A one year hospital based randomized controlled trial.

Selection Criteria:

Inclusion Criteria:

- Patients undergoing elective C- section delivery under subarachnoid block.
- ASA physical status- I and II.
- Age between 18-40 years.
- Height between 140-170 cm.

Exclusion Criteria:

- Patient undergoing emergency caesarean section.
- Multiple pregnancies.
- PIH and Eclampsia.
- Contraindications including bleeding diathesis, severe hypotension, increase intracranial pressure, infection at the site, cardiac problems like severe ventricular out flow obstruction, infections like polio, skeletal disorders like ankylosing spondylitis.

Sample size:

A total sample size of 80 patients separated into 2 groups.

Group B: 40 patients received single dose of spinal anaesthesia with 2ml of 0.5% bupivacaine heavy and 0.2 ml of fentanyl.

Group F: 40 patients received fractionated dose of spinal anaesthesia with 2ml of 0.5% bupivacaine heavy and 0.2 ml of fentanyl.

Sample size calculation:

- The minimum sample size formula based on mean and standard deviation is

$$n = \frac{(z_\alpha + z_\beta)^2 (s_1^2 + s_2^2)}{(\bar{X}_1 - \bar{X}_2)^2}$$

Where z_α is linked with the level of significance and z_β is linked with the power of the test.

For 5% level of the significance z_α =1.96 and z_β =0.84 for 80% power of the test.

$\bar{x}_1$ is the mean of MAP in the first group (95.2) and $\bar{x}_2$ is the mean of MAP in the second group (92.4).

S1 is the standard deviation of the first group (3.1) and S_2 is the standard deviation of the second group (2.5).

With these values the sample size obtained is 16.

But to make the study more confirmative the sample size has be increased to 40 in each group.

Methodology:

After obtaining the departmental research committee and institutional ethical board approval, written informed consent was taken from 80 patients undergoing elective c- section delivery under subarachnoid block. After meeting inclusion and exclusion criteria patients were separated into two groups using a computer generated random number table.

In preoperative holding area, 18 - Gauge intravenous (IV) cannula was secured. Patient was administered with ranitidine 1mg/kg and ondansetron 0.1mg/kg. Preloading was done with ringer lactate 10-15 ml/kg. After shifting inside operation theatre standard non- invasive monitors like blood pressure, pulse oximeter, electrocardiogram (ECG) were attached. Baseline Blood pressure, heart rate, oxygen saturation were measured.

Patient was positioned in left-lateral position. Under sterile aseptic precautions, parts were painted and draped, L3-L4 intervertebral space identified. Skin was infiltrated with local injection with lignocaine 2%. Using 23 gauge quincke spinal needle 2ml of 0.5% hyperbaric bupivacaine plus 0.2ml (10µg) of fentanyl was injected into L3-L4 subarachnoid space according to group B or group F. For Group B patient drug was administered intrathecally as continuous bolus dose for 10sec. Group F patient received the drug in fractionated dose. In which from total dose two third of the drug was given initially. Patient was maintained in same lateral position with spinal needle in situ, after 90 sec remaining one third of the drug was administered. Both the doses of drug were injected at the rate of 0.2 ml/ sec.

After injection of the drug, patient was put in supine position. Left uterine displacement was done by keeping pillow under right hip. Supplied with oxygen through face mask at 5L/min. The onset and level of motor and sensory block assessment were done. The sensory block level was assessed by performing pin prick test at mid axillary line. The sensory block onset was taken from the time of administration of the drug intrathecally to highest sensory level achieved. The motor block level was assessed with modified bromage scale. The motor block- onset was taken as time to achieve bromage score of 3 from the time drug was injected into intrathecal space.

Score	Bromage scale
0	The patient is able to move the hip , knee and ankle
1	Patient is unable to move the hip but is able to move the knee and ankle
2	Patient is unable to move the hip and knee but is able to move the ankle
3	Patient is unable to move the hip knee and ankle

The procedure was converted to general anaesthesia if desired sensory or motor level fails to achieve and patient was excluded from the study.

The blood pressure and heart rate were recorded immediately after giving spinal anaesthesia. There after it was recorded every 2 min for 10 min and then every 5min till 50 min. Hypotension was considered if blood pressure falls more than 20% from baseline reading and was treated with IV mephentermine 6mg. For each patient, the usage of mephentermine and episodes of hypotension were noted. Bradycardia was treated with 0.6mg of IV atropine.

Immediately after baby delivery, 10U of IM oxytocin was given and another 10U of IV oxytocin was given in 500 ml of normal saline. Apgar score was noted at 1 and 5 min after baby delivery. Developments of side effects like shivering, pruritus, respiratory depression, nausea, vomiting and urinary retention were observed.

Post operatively, vitals were recorded. The duration of motor, sensory block and analgesia were noted. The sensory block- duration was considered from the time drug was injected intrathecally to S2 segment regression. The motor block duration was taken from the time drug was injected into subarachnoid space till the time to achieve bromage score zero in post operative period. Visual analogue scale (VAS) was used to assess the pain. The duration of analgesia was time interval from LA injected into subarachnoid space till the requirement of rescue analgesia. Intravenous 75mg of diclofenac was used as rescue analgesia.

Statistical analysis

The study was focused on comparison of two groups. For the continuous quantitative variables mean and standard deviation were calculated. The intergroup continuous variables were compared using suitable tools of statistics like student's unpaired t test. Two quantitative variables within a group were compared using student's paired t test. Discrete variables were represented by median. Suitable graphs were used to depict the comparison. For the entire test the value of P less than 5% (0.05) was considered significance.

RESULTS

one year randomized clinical trial, conducted during in KLE'S Dr. PrabhakarKore Hospital and Medical Research Center, Nehru Nagar, Belagavi during January 2019 to December 2019.

A total of 80 patients were studied, who underwent elective lower segment caesarean section under subarachnoid block. They were allocated into one of the two groups according to computer generated randomized table.

GROUP B: subarachnoid block was given with 2ml of 0.5% hyperbaric bupivacaine and 0.2ml (10µg) of fentanyl in a single bolus dose injection.

GROUP F: subarachnoid block was given with 2ml of 0.5% hyperbaric bupivacaine and 0.2ml (10µg) of fentanyl in fractionated dose.

Data collected were coded and analyzed below.

Table 1: **Mean Age, Height and Weight**

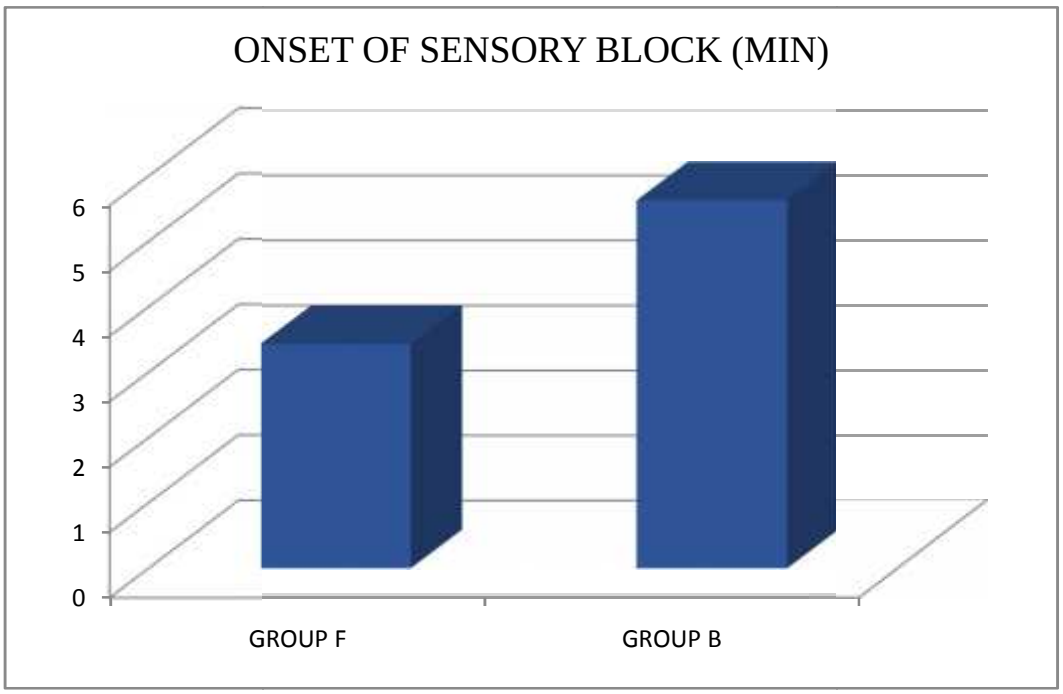
	GROUP F		GROUP B		P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION	
AGE (years)	27.48	3.77	26.65	3.45	0.3105
HEIGHT (cm)	152.85	3.68	151.8	3.11	0.1721
WEIGHT (kg)	60.38	5.24	60.65	6.07	0.8289

The demographic profiles among the both groups were comparable. The mean of age in group F was 27.48 years and in group B was 26.65 years. The mean height in group F and B were 152.85 cm and 151.80 cm respectively. The mean weight of patients in group F and group B were 60.38 kg and 60.65 kg respectively.

Table 2: Mean onset of sensory block

ONSET OF SENSORY BLOCK (MIN)				
GROUP F		GROUP B		P VALUE
MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION	
3.45	0.96	5.66	0.69	<0.001

Graph 1: Onset of sensory block

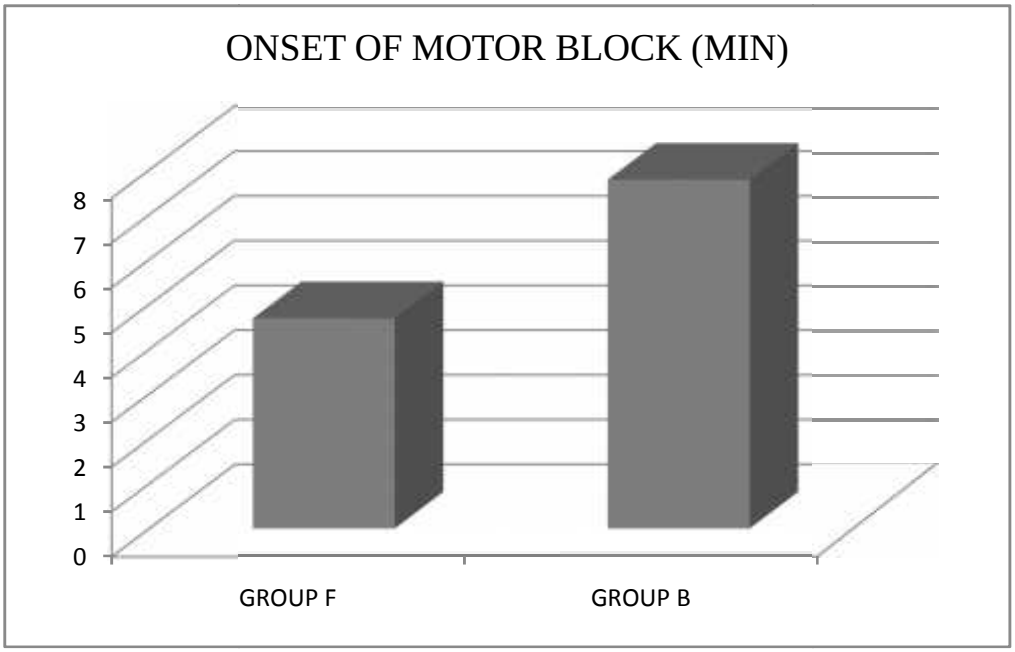


Group F patients, onset of sensory block was earlier than group B patients (3.45 $\pm$ 0.96 min and 5.66 $\pm$ 0.69 min respectively). This was statistically significant with P value of < 0.001.

Table 3: Mean onset of motor block

ONSET OF MOTOR BLOCK (MIN)				
GROUP F		GROUP B		P VALUE
MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION	
4.70	0.80	7.80	0.78	<0.001

Graph 2: Onset of motor block



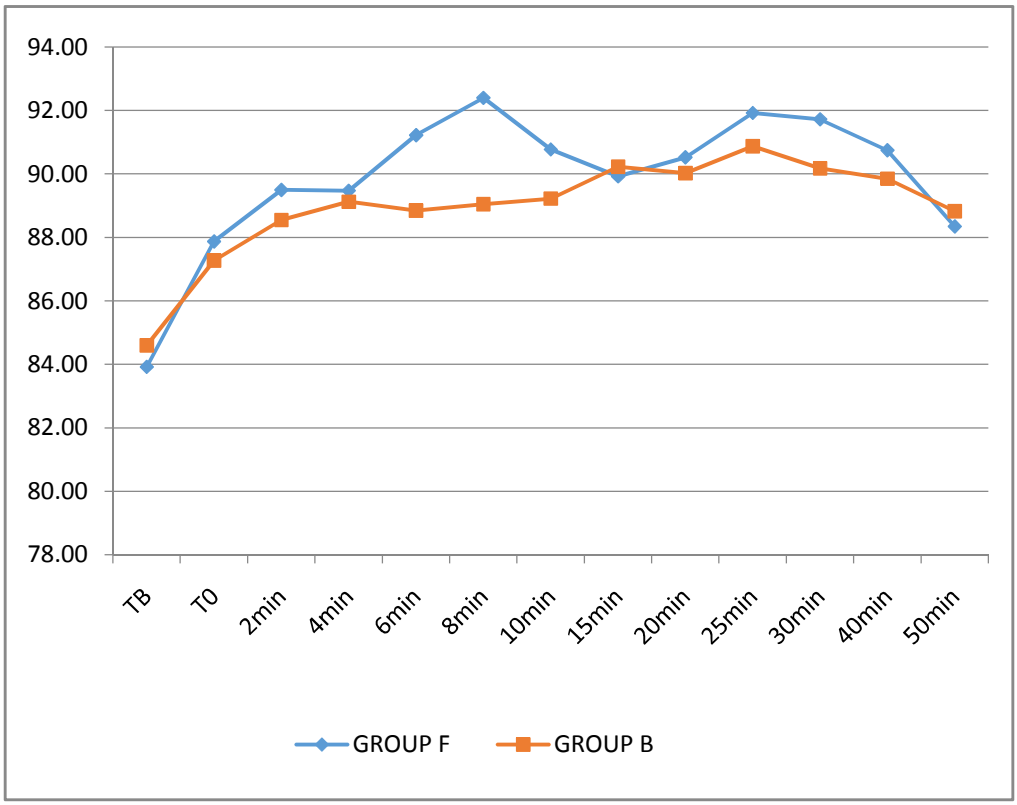
P value of < 0.001 was statistically highly significant for motor block onset. Motor block onset in group F was 4.70 $\pm$ 0.80 min and in group B was 7.80 $\pm$ 0.78 min.

Table 4: Comparison of heart rate at different time intervals (bpm)

INTERVALS	GROUP F		GROUP B		P VALUE
	MEAN	SD	MEAN	SD	
TB	83.93	7.73	84.60	6.46	0.6729
T0	87.88	7.56	87.28	6.48	0.7040
2min	89.50	7.28	88.55	6.05	0.5274
4min	89.48	7.33	89.13	6.01	0.8160
6min	91.23	6.40	88.85	5.87	0.0878
8min	92.40	5.87	89.05	5.56	0.0106*
10min	90.78	5.96	89.23	5.70	0.2381
15min	89.93	6.74	90.23	5.54	0.8284
20min	90.53	6.94	90.03	6.06	0.7323
25min	91.93	5.92	90.88	6.44	0.4498
30min	91.73	5.91	90.18	5.60	0.2323
40min	90.75	5.51	89.85	4.67	0.4333
50min	88.35	5.77	88.83	4.91	0.6930

Graph 3: Comparison of mean heart rate at different intervals (bpm)

MEAN HR (BPM)



The heart rates in group F were on the higher range than group B. At 8min, the mean heart rate of group F was 92.40 ± 5.87 bpm and group B was 89.05 ± 5.56 bpm. This was statistically significant with P value of 0.01.

Table 5: Comparison of Mean arterial pressure (MAP) at different time intervals (mmHg)

INTERVALS	GROUP F		GROUP B		P VALUE
	MEAN	SD	MEAN	SD	
TB	85.35	7.95	84.90	9.35	0.8173
T0	83.90	7.48	83.20	8.89	0.7041
2min	80.38	6.46	78.15	11.22	0.2805
4min	78.00	6021	75.13	11.33	0.1632
6min	77.45	6.26	75.63	9.93	0.3287
8min	78.18	6.28	76.70	9.21	0.4050
10min	79.10	6.38	78.33	8.93	0.6563
15min	79.33	5.82	78.83	8.01	0.7503
20min	80.55	5.76	79.25	6.48	0.3460
25min	79.33	3.47	80.28	6.00	0.3886
30min	78.88	3.20	80.50	5.29	0.1002
40min	80.25	3.60	79.55	4.81	0.4633
50min	81.35	3.60	79.18	4.61	0.0211

Graph 4: Comparison of Mean arterial pressure (MAP) at different time intervals (mmHg)

MAP (mmHg)

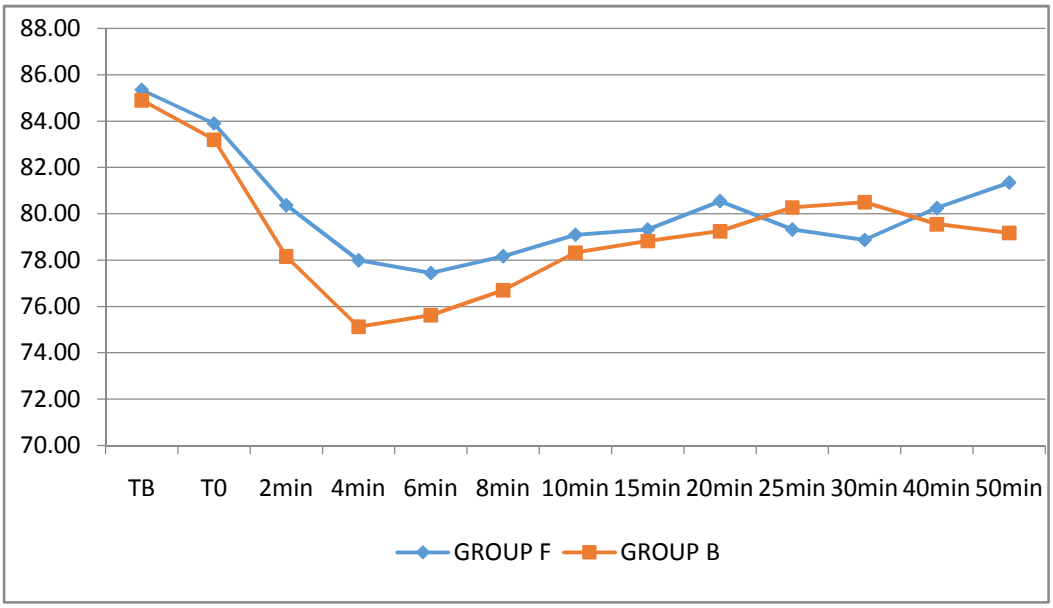


Table 6: Number of patients requiring mephentermine

GROUP F		GROUP B		P VALUE
MEAN	PERCENTAGE	MEAN	PERCENTAGE	
6	15	17	42.5	0.0066

Patients in group F were haemodynamically stable than group B. The mean arterial pressure values in group F were on higher range than group B but they were statistically not significant.

The number of patients requiring intraoperative mephentermine in group F and group B were six and seventeen respectively with P= 0.0066.

Table 7: Sensory block regression (min)

GROUP F		GROUP B		P VALUE
MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION	
182.93	6.34	174.85	8.36	<0.0001

Graph 5: Sensory block regression (min)

SENSORY BLOCK REGRESSION (MIN)

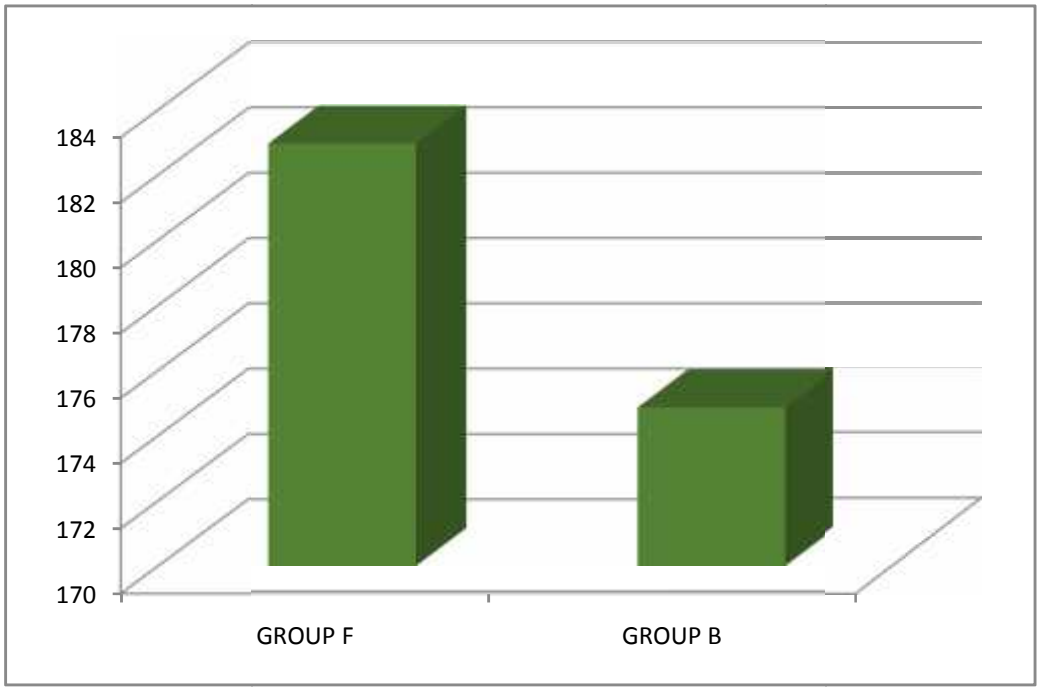
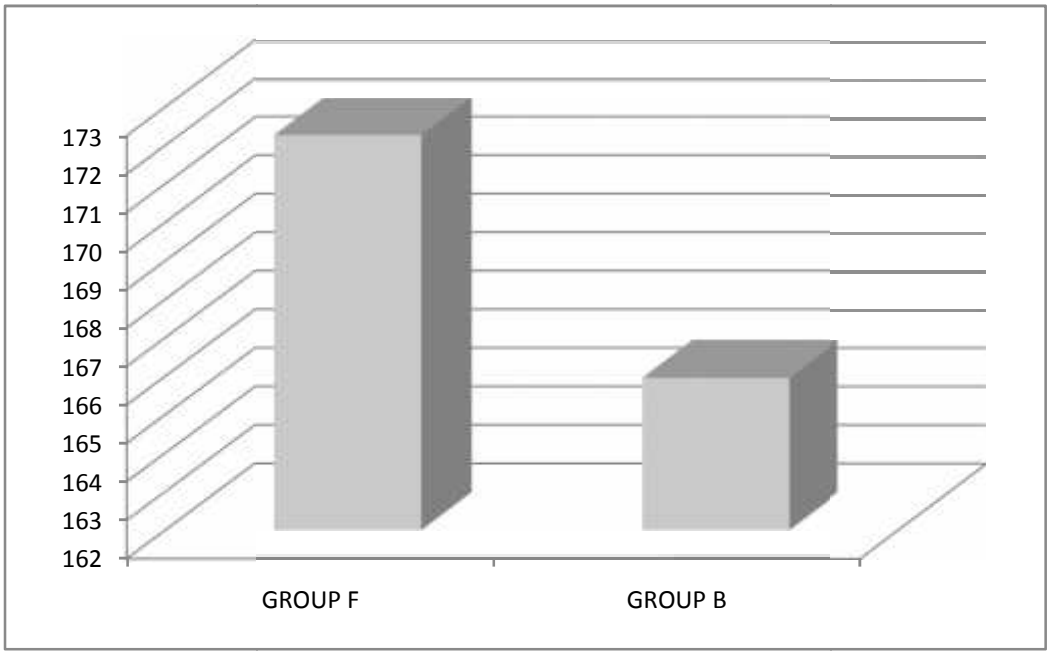


Table 8: Motor block regression (min)

GROUP F		GROUP B		P VALUE
MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION	
172.25	7.86	165.95	8.27	0.0008

Graph 6: Motor block regression (min)

MOTOR BLOCK REGRESSION (MIN)



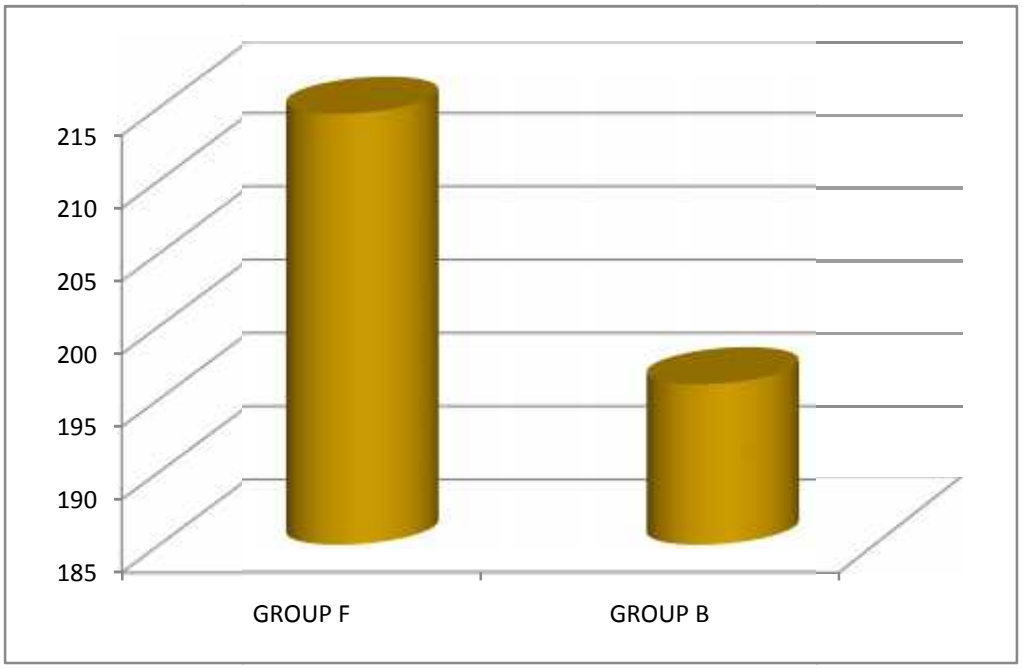
The time taken for sensory and motor block regression in group F (182.93 $\pm$ 6.34 min and 172.25 $\pm$ 7.86 min) were delayed than group B (174.85 $\pm$ 8.36 min and 165.95 $\pm$ 8.27 min) with was highly significant.

Table 9: Duration of analgesia (min)

GROUP F		GROUP B		P VALUE
MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION	
214.40	15.48	195.95	8.98	< 0.0001

Graph 7: Duration of analgesia (min)

DURATION OF ANALGESIA (MIN)



Patients in group F had longer pain free period than group B. Group F and group B had duration of analgesia of 214.40 + 15.48 min and 195.95 + 8.98 min respectively (P < 0.0001). The need for rescue analgesia was earlier in group B patients.

Table 10: APGAR score at 1min

GROUP F		GROUP B		P VALUE
MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION	
7.225	0.53	7.05	0.55	0.1524

Graph 8: APGAR score at 1min

APGAR SCORE AT 1 MIN

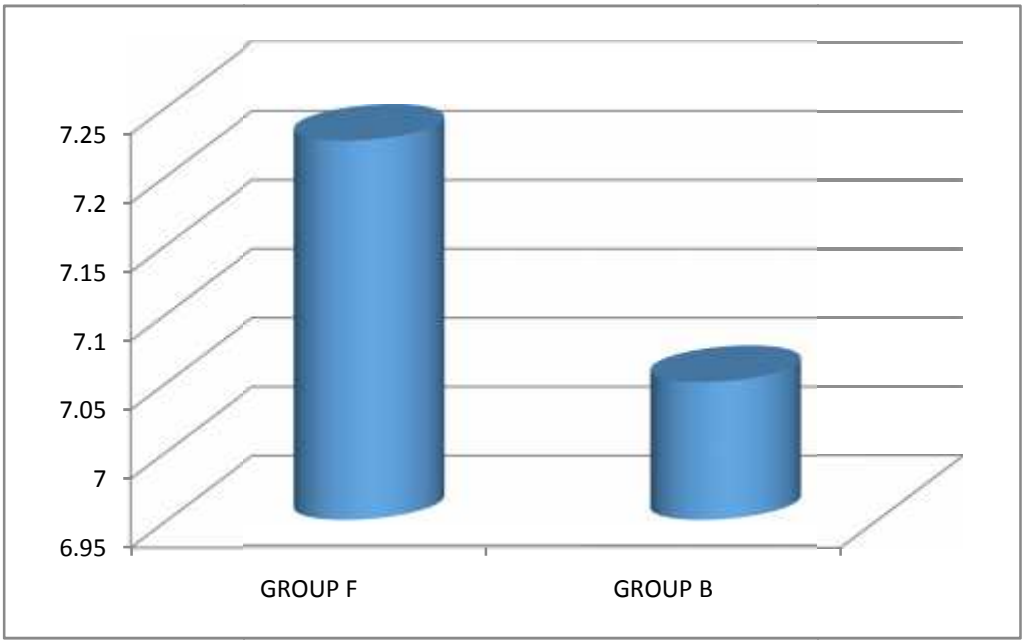
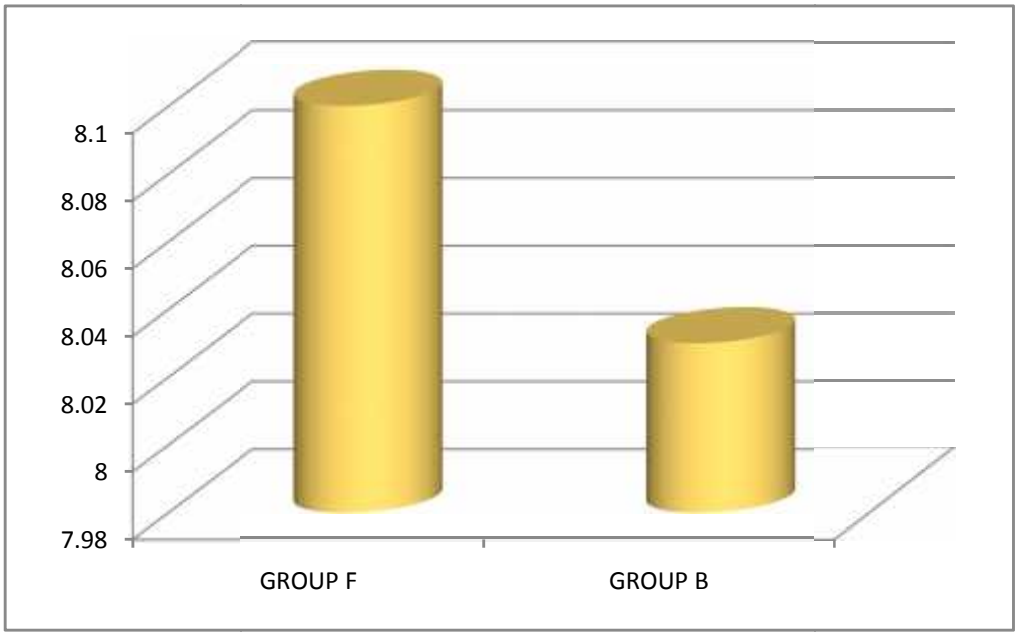


Table 11: APGAR score at 5min

GROUP F		GROUP B		P VALUE
MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION	
8.10	0.44	8.03	0.53	0.4939

Graph 9: APGAR score at 5min

APGAR SCORE AT 5MIN



APGAR score at 1 and 5 min were not statistically significant in both the groups. The adverse effects like respiratory depression, pruritus and headache were not observed in both the groups.

DISCUSSION

The subarachnoid block is the anaesthetic method of choice for pregnant women undergoing LSCS. It provides a quicker onset of action with adequate sensory and motor block. But the main disadvantage of this technique is maternal hypotension with adverse neonatal outcome. The incidence of maternal hypotension after the subarachnoid block is 75%.[34] Various non -pharmacological and pharmacological methods were studied to prevent hypotension in the mother after SAB.

Various studies were conducted to prevent the occurrence of maternal hypotension after SAB. Preloading and co-loading with colloids/crystalloids prevent maternal hypotension to some extent. Among the vasopressors, phenylephrine is found to be more effective than ephedrine. A Recent study showed prophylactic norepinephrine infusion was also effective in preventing maternal hypotension.[38]Despite of all these medical management, the occurrence of maternal hypotension is high. This suggests the need for multimodal treatment to decrease the occurrence of hypotension and increase the outcome of pregnant women.

Our study was conducted to analyze the haemodynamic stability with single bolus dose of bupivacaine with fentanyl to divided dose (fractionated dose) of bupivacaine with fentanyl in SAB for pregnant women undergoing LSCS, and the quality of sensory and motor block among them.

Badheka JP et al[10] conducted a study comparing fractionated and bolus dose injection of spinal anaesthesia in pregnant women. He found that patients in fractionate group were haemodynamically more stable than bolus dose group patients. Five patients required vasopressor in fractionated group whereas fourteen patients

needed the same in bolus group. The study concluded that giving LA in divided dose provides dense block leading to haemodynamic stability in fractionated group.

In a study conducted by Monika Gandhi et al[11]haemodynamic parameters were analyzed between fractionated and bolus dose injection of bupivacaine in SAB. They concluded that patients were haemodynamically more stable in fractionated group than bolus dose group. The number of people who required vasopressor in fractionated and bolus dose group were 15 and 39 respectively. Another randomized control trial was conducted by RamasaliManjula V et al[14] compared haemodynamic parameters like HR, blood pressure and MAP between fractionated group and bolus dose group. The study was done on 60 patients undergoing elective LSCS. They concluded that HR, blood pressure and MAP of the patients in fractionated group were on a higher level than bolus group.

Fahmyet al[4] conducted a study comparing circulatory effect and duration of analgesia in divided dose and single-dose subarachnoid block. From the study, they obtain that patient in divided dose group had better circulatory effect than single-dose group. The duration of analgesia was longer in fractionated group.

Favarel JF et al[36] compared the haemodynamic effect of the single-dose versus divided dose SAB in the old patients undergoing hip surgery. They found that elderly patients were haemodynamically stable in divided dose than single-dose group.

In our study, pregnant women in fractionated group were haemodynamically more stable than in bolus dose group. Even though it was not statistically significant, the blood pressures in the fractionated group were on higher range. Six persons required vasopressor in fractionated group whereas in bolus group seventeen persons

required the same. Injecting bupivacaine with fentanyl in fractionated dose into subarachnoid space provides dense block. This explains the haemodynamic stability in fractionated group.

The onsets of sensory and motor blockade were faster in our study. The sensory block onset in fractionated and bolus dose was 3.45 ± 0.96 min and 5.66 ± 0.69 min respectively. The motor block onset was 4.70 ± 0.80 min and 7.80 ± 0.78 min in fractionated and bolus dose group respectively. This result correlates with the study performed by Monika Gandhi et al.[11] The sensory block onset was early in fractionated group (71.53 ± 5.66 sec) than bolus group (88.950 ± 4.51 sec). The motor block onset was also early in the fractionated group than bolus group (88.95 ± 4.51 sec and 116.20 ± 2.56 sec respectively).

The time taken for sensory regression in our study was 182.93 ± 6.34 min in fractionated group which was delayed than bolus group (174.85 ± 8.36 min). In Badheka JP et al[10] study, the sensory regression was delayed in fractionated group (236 ± 42 min) than bolus dose group (161 ± 29 min). In another study conducted by Deepak K et al[13] found delay in sensory regression in fractionated group than bolus group which was significant statistically ($P < 0.00001$).

In a study conducted by Nugroho AM et al[12]haemodynamic effect and level of sensory block were compared between fractionated and single-dose SAB for patients with hypertension associated with pregnancy. No difference was found in the MAP between the groups. The level of sensory block in fractionated group and single dose group were 52.4% and 42.9% respectively (not significant). This was explained by excessive vasoconstriction and vascular resistance in preeclampsia patients due to increased activation of inflammatory cytokines. In these patients, BP was maintained

by excessive vasoconstriction despite of sympatholytic activity after SAB. So fractionated dose effect was limited here.

Adding adjuvant like an opioid to bupivacaine in SAB provides longer duration of analgesia. It even reduces the dose of bupivacaine and maintains the volume of drug to achieve an adequate level of block. 10 to 25 µg of intrathecal fentanyl produced prolonged sensory block and analgesia.[30] Bupivacaine and fentanyl produce synergic action on intrathecal injection.[5,37] Fentanyl blocks the nociceptive impulse by acting on a specific opioid receptor in the spinal cord. It modulates the C and A-delta fibers by opening potassium channel and causes hyperpolarization. Bupivacaine acts by blocking Na^+ channel in the axon. The combined action of these drugs on nerve fibers produce an enhanced sensory block and increase the duration of analgesia with minimal side effects. This also reduces the volume of bupivacaine and produce haemodynamic stability.[37]

In our study, adding fentanyl to bupivacaine in both the groups increased the duration of analgesia. In the fractionated group, the duration of analgesia was longer than bolus dose group (214.40 $\pm$ 15.48 min vs 195.95 $\pm$ 8.98 min respectively). The longer duration of analgesia in the fractionated group was explained by the combined action of dense block produced by fractionated dose and intrathecal fentanyl. Lakshmi sowmya N et al[15] compared duration of analgesia in fractionated and bolus dose group patients undergoing lower limb surgery. They found that fractionated group had prolonged duration of analgesia than bolus dose group. Sowmya N et al[17] conducted a study, comparing two different doses (10 µg and 15 µg) of fentanyl with 10mg of heavy bupivacaine for caesarean section. They concluded that 15µg of intrathecal fentanyl produced quicker onset of sensory block and prolonged analgesia. In our

study, we decided to use 10µg of intrathecal fentanyl to avoid possible adverse effects related to them.

In a study done by Jain K et al[38] compared different dose of fentanyl with bupivacaine in pregnant women with pregnancy induced hypertension (PIH). The longer duration of analgesia was found in the group which received 20µg of intrathecal fentanyl. The side effects like respiratory depression, pruritis and nausea vomiting were less in both 10µg and 20µg of intrathecal fentanyl. In our study, no side effects occurred to 10µg of intrathecal fentanyl.

There was no difference in the Apgar score at 1 and 5min between the groups, in our study. This was supported by the study conducted by Maayan – Metzger A et al.[39] They studied the effects of maternal hypotension on the foetal outcome and found no difference in the outcome of the foetus born to a hypotensive mother. Another comparative study was conducted by Kumar R et al[16] on 120 parturients undergoing LSCS. They analyzed the effect of maternal hypotension on neonatal outcome after giving two different doses of fentanly and bupivacaine in SA. They found no difference in the outcome of the foetus between the groups. This assures that hypotension for a short duration does not have any effect on the newborn.

CONCLUSION

To conclude, this study demonstrated that giving subarachnoid block in fractionated dose is better than usual single- bolus dose for pregnant women undergoing elective caesarean section delivery in terms of

- Providing better haemodynamic parameters like HR, blood pressure and MAP
- Faster onset of motor and sensory block
- Longer duration of analgesia

Adding opioid like fentanyl to bupivacaine increases the analgesia period. It provides prolonged postoperative pain-free periods and decreases the need for rescue analgesia. This newer technique is better than the usual method for maintaining intraoperative haemodynamic stability and better anaesthesia and analgesia.

SUMMARY

In this current study titled "COMPARISON OF FRACTIONATED DOSE VERSUS BOLUS DOSE INJECTION OF HEAVY BUPIVACAINE WITH FENTANYL IN SPINAL ANAESTHESIA FOR PATIENTS UNDERGOING ELECTIVE CAESAREAN SECTION: ONE YEAR RANDOMIZED CLINICAL TRIAL" we compared the new fractionated dose technique of injecting bupivacaine with fentanyl into subarachnoid space with the usual bolus dose technique in terms of haemodynamic stability, the onset of motor and sensory block and duration of analgesia.

This study was done on 80 parturients undergoing elective LSCS with SAB. Mothers aged between 18- 40 years and ASA physical status I and II were included in the study after meeting the inclusion criteria. According to computer randomization, they were separated into two groups. Group F (n=40) received 2ml (10mg) of 0.5% hyperbaric bupivacaine with 10µg of fentanyl in fractionated (divided) dose. In which, from the total dose two-third was given initially. After 90 sec remaining one-third of the dose was given. Group B (n=40) received 2ml (10mg) of 0.5% hyperbaric bupivacaine with 10µg of fentanyl in usual bolus dose.

The data were collected and analyzed. The demographic details like age, height and weight were similar between the groups. The haemodynamic parameters like HR, BP and MAP were better in group F than group B. The number of patients who required vasopressor in group F were six and in group B were seventeen. The sensory and motor block onsets were faster in group F (3.45 $\pm$ 0.96 min and 4.70 $\pm$ 0.80 min respectively). The time taken for sensory regression was delayed in group F

than group B (182.93 ± 6.34 min and 174.85 ± 8.36 min). There was a prolonged analgesia period in group F (214.40 + 15.48 min) than group B (195.95 + 8.98 min). There was no change in the neonatal outcome between the groups.

Overall, based on the result of this study it may be concluded that giving fractionated dose with bupivacaine and fentanyl in spinal anaesthesia provides better haemodynamic stability and quicker sensory and motor block onset in the pregnant women undergoing LSCS. They also increase the analgesia period when compared to the usual bolus dose of SA. This newer technique should be considered for the better maternal outcome.

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ANNEXURE I

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mrs/Miss. _____ we are requesting you to enrol yourself in **"COMPARISON OF FRACTIONATED DOSE VERSUS BOLUS DOSE INJECTION OF HEAVY BUPIVACAINE WITH FENTANYL IN SPINAL ANAESTHESIA FOR PATIENTS UNDERGOING ELECTIVE CAESAREAN SECTION: ONE YEAR RANDOMIZED CLINICAL TRIAL"** Conducted by _____, Post Graduate in M.D. Anaesthesiology under the guidance of _____., Professor, Department of Anaesthesiology, J.N. Medical College, Belagavi under KAHER university, Belagavi.

Respected Sir/Madam we request you to enrol yourself to participate in our study as you are eligible for participating in the study. During the study you will be asked some questions regarding your present complaint and you are supposed to answer to the best of your knowledge.

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

Purpose of the study:

The purpose of research is to compare the fractionated and bolus dose of a drug in spinal anaesthesia in patient undergoing elective caesarean section, so as to study mean arterial pressure and duration of analgesia so as to provide hemodynamic stability.

Procedure Involved:

If you agree to enrol in my study, I will ask your present and past medical history. You will be clinically examined in detail and routine investigations like Haemoglobin, Platelet Count, will be done accordingly. You will be allotted into one of the two groups randomly using computer generated software. One group will receive fractionated dose of spinal anaesthesia with heavy bupivacaine and fentanyl in which two-third of the calculated dose given initially followed by one-third dose after time gap of 90 s and another group will receive bolus dose of spinal anaesthesia with heavy bupivacaine and fentanyl.

Benefits and Risks:

Fractionated dose of spinal anaesthesia provides greater hemodynamic stability and adding adjuvant to them prolongs the duration of analgesia in patient undergoing elective caesarean section.Intrathecal administration of fentanyl can cause pruritus, nausea, vomiting and respiratory depression which is not desirable in pregnant patients.

Voluntary Participation/Withdrawal:

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

Alternatives:

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

Privacy and Confidentiality:

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

1. In emergency to protect your rights and welfare.

2. If required by law.

Authorization to Publish Results:

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

Financial Incentives for participation:

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

Compensation:

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

Queries/ Contact details

If you have any queries about your rights as a study subject, you may call Dr. RoopaBellad$_{MD}$, Professor, Department of Pediatrics and Chairman, J.N. Medical College Institutional Ethical Committee for Human Subjects Research, Phone number-9448113403 J.N. Medical College, Belagavi.

Consent for participation in research trial.

"COMPARISON OF FRACTIONATED DOSE VERSUS BOLUS DOSE INJECTION OF HEAVY BUPIVACAINE WITH FENTANYL IN SPINAL ANAESTHESIA FOR PATIENTS UNDERGOING ELECTIVE CAESAREAN SECTION: ONE YEAR RANDOMIZED CLINICAL TRIAL". I, Mr/Ms/Mrs_____ voluntarily agree for the participation of myself as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left Thumb Print of patient : _____

Signature or the Left Thumb Print of legally authorized relative: _____

Date:

Witness Name : _____ Signature:_____

Date:

Investigators Name: _____ Signature:_____

Date:

Place : _____

ANNEXURE II

PROFORMA

"COMPARISON OF FRACTIONATED DOSE VERSUS BOLUS DOSE INJECTION OF HEAVY BUPIVACAINE WITH FENTANYL IN SPINAL ANAESTHESIA FOR PATIENTS UNDERGOING ELECTIVE CAESAREAN SECTION: ONE YEAR RANDOMIZED CLINICAL TRIAL"

Name & Address of the patient:

_____

_____

Age of the Patient: _____ IP. No. _____

Weight of Patient: _____ Sex.

Height of patient: _____

Anaesthesiologist: _____ Surgeon: _____

PREANAESTHETIC EVALUATION:

Chief Complaints:

Past History:

- History of Diabetes Mellitus/Hypertension/Asthma/Tuberculosis
- Drug Therapy:
- Previous Anaesthetic procedure/Previous surgeries:

- History of renal disease, hepatic disease and neurological diseases.

Family History:

General Physical Examination:

Weight: Temperature: Pallor: Height:

Cyanosis: Pedal Oedema: Clubbing:

Pulse : B.P: RR:

Airway Assessment:

Mouth Opening: Teeth:

Jaw Movements: MP Grading:

SYSTEMIC EXAMINATION:

Cardiovascular System:

Respiratory System:

Per Abdomen:

Central Nervous system:

Spine assessment:

INVESTIGATIONS:

Hb%: Platelet count:

Any Other:

ASA STATUS: Grade 1 / 2

Diagnosis:

Proposed Surgery:

Inclusion Criteria:

- Patients undergoing elective caesarean section under spinal Anaesthesia.
- ASA physical status I and II.
- Age between 18 to 40 years.
- Height between 140 to 170 cms.

Exclusion Criteria:

- Patient undergoing emergency caesarean section.
- Multiple pregnancies.
- PIH and Eclampsia.
- Contraindications including bleeding diathesis, severe hypotension, increase ICP, infection at the site, cardiac problems like severe ventricular out flow obstruction, infections like polio, skeletal disorders like ankylosing spondylitis.

Observations:

Technique used: _____.

Group: _____.

Time	Blood pressure	Heart rate	Spo2

SENSORY BLOCK

TIME	ONSET	DURATION	REGRESSION

MOTOR BLOCK

TIME	BROMAGE SCORE	REGRESSION

Duration of analgesia:

Apgar score at 1min:

Apgar score at 5min:

Side Effects/ complications

Signature of staff in charge:

ANNEXURE III – ETHICAL CLEARANCE CERTIFICATE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http//www.jnmc.edu
E-Mail : domc@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/14 **Date: 24/11/2018**

REG NO. BA0118002

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"COMPARISON OF FRACTIONATED DOSE VERSUS BOLUS DOSE INJECTION OF HEAVY BUPIVACAINE WITH FENTANYL IN SPINAL ANAESTHESIA FOR PATIENTS UNDERGOING ELECTIVE CAESAREAN SECTION: ONE YEAR RANDOMIZED CLINICAL TRIAL"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

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

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

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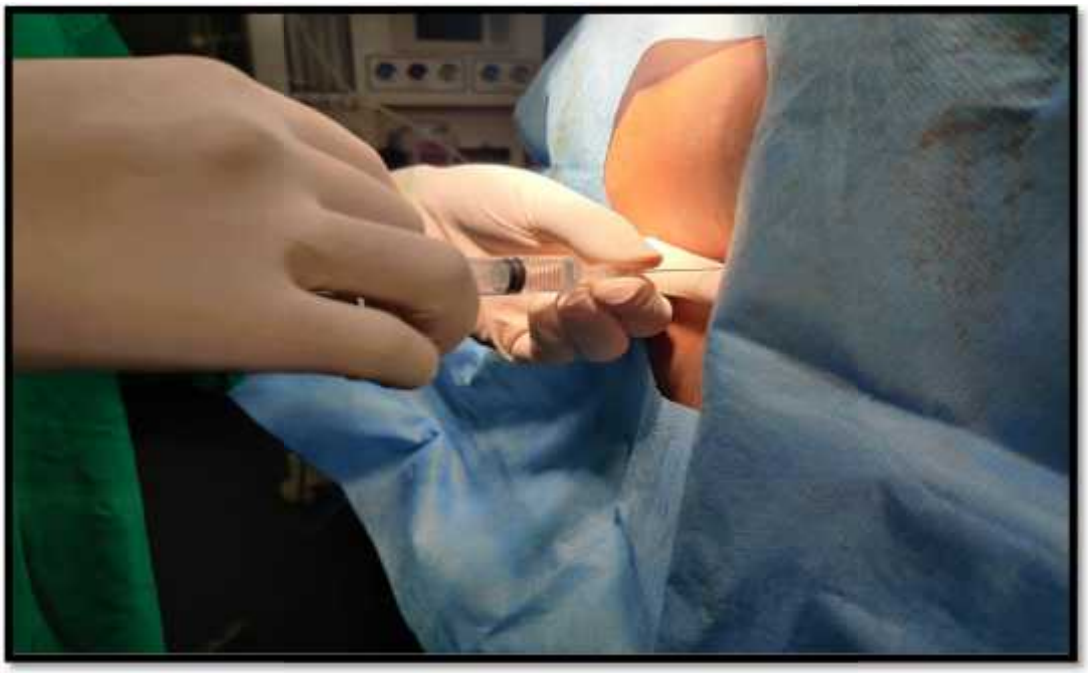
ANNEXURE IV – PHOTOGRAPHS

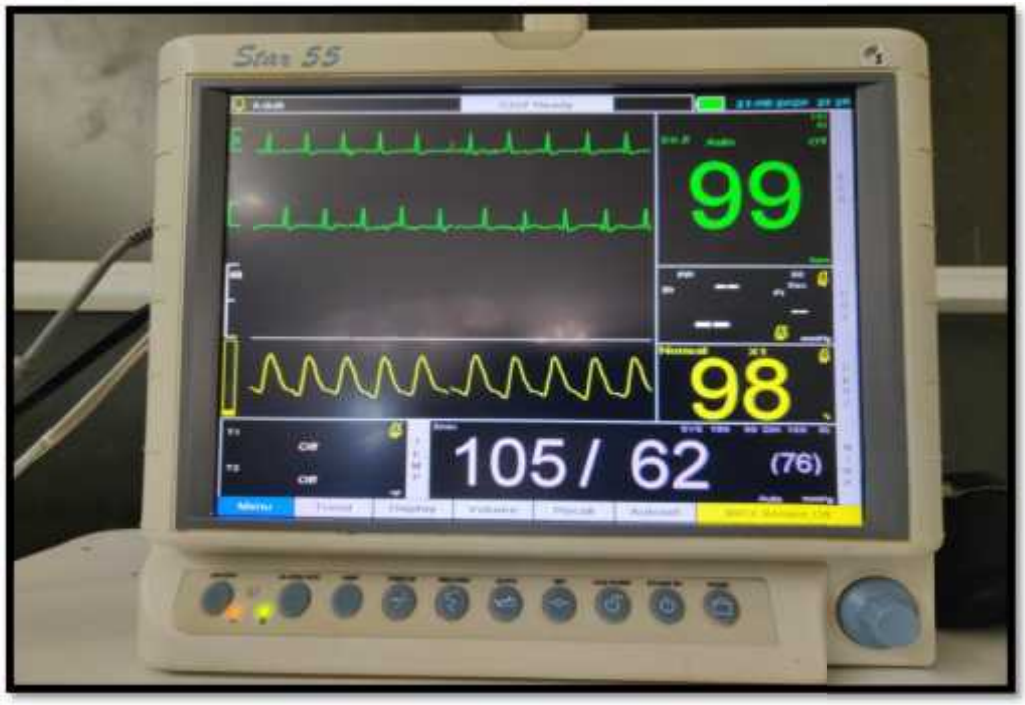
Photograph 1 0.5% hyperbaric bupivacaine ampoule

Photograph 2 Fentanyl ampoule

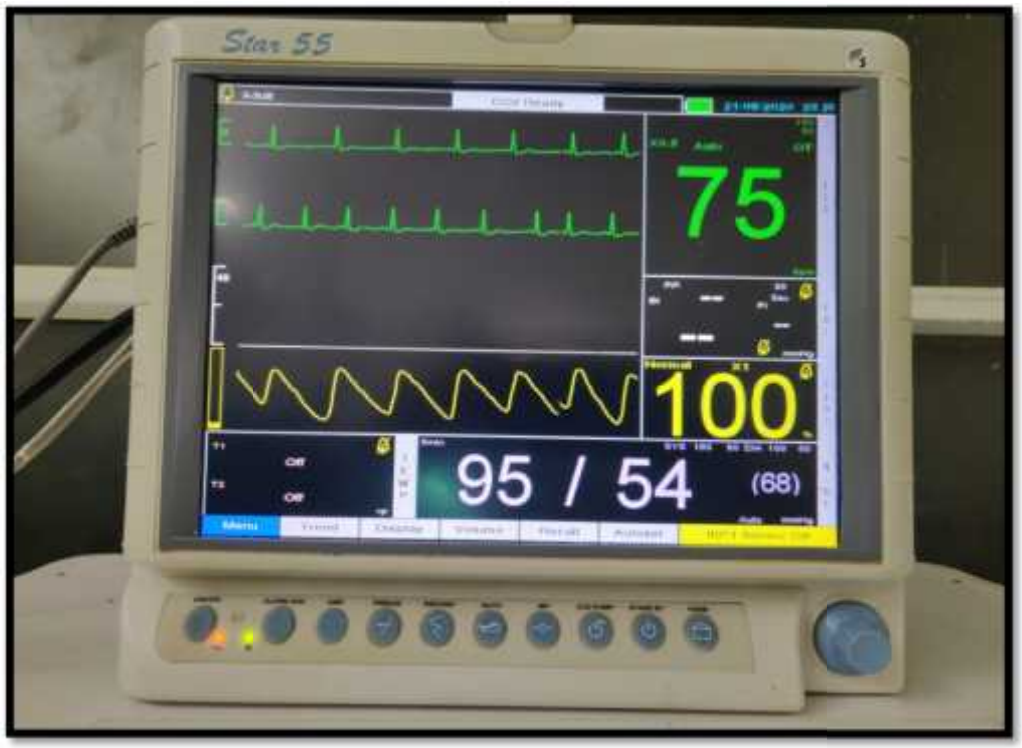
Photograph 3 Procedure of fractionated dose subarachnoid block



Photograph 4 Procedure of bolus dose subarachnoid block



Photograph 5Monitor after fractionated dose



Photograph 6 Monitor after bolus dose

ANNEXURES V - MASTER CHART

GROUP F

S.NO	NAME	AGE	SEX	HEIGHT (cm)	WEIGHT (kg)	HR (bpm)												SBP (mmHg)												DBP (mmHg)												MAP											
						TB	TO	2min	4min	6min	8min	10min	15min	20min	25min	30min	40min	50min	TB	TO	2min	4min	6min	8min	10min	15min	20min	25min	30min	40min	50min	TB	TO	2min	4min	6min	8min	10min	15min	20min	25min	30min	40min	50min	TB	TO	2min	4min	6min	8min	10min	15min	20min	25min	30min	40min	50min
1	Asha	22	F	152	58	84	88	89	90	92	94	93	89	84	88	84	94	90	117	116	114	109	104	112	108	110	114	112	112	119	126	70	68	63	62	66	62	66	63	69	64	65	66	66	86	84	80	78	79	79	80	79	84	80	81	84	86
2	Shobha N	29	F	155	55	90	94	96	99	99	99	101	95	92	94	90	97	89	123	124	118	112	112	120	116	126	118	116	112	114	123	81	77	73	71	73	70	75	72	74	63	64	66	61	95	93	88	85	86	87	89	90	89	81	80	82	82
3	Savita J	31	F	158	54	76	80	82	80	80	84	86	89	90	87	89	94	91	127	132	121	124	128	126	128	128	120	124	126	129	130	86	82	82	74	71	73	75	74	80	74	72	73	74	100	99	95	91	90	91	93	92	96	91	90	92	93
4	Drakshayani G	21	F	156	60	78	79	80	76	84	86	85	88	86	90	90	96	95	118	128	124	127	124	124	123	121	124	118	124	126	128	80	75	71	67	65	65	69	71	71	68	64	67	66	93	93	89	87	85	85	87	88	89	85	84	87	87
5	Sheethal	19	F	152	58	86	84	80	81	78	80	84	78	84	86	88	85	80	106	108	102	100	92	99	99	104	110	104	108	104	116	64	60	58	55	57	55	57	57	59	59	60	66	62	78	76	73	70	69	70	71	73	76	74	76	79	80
6	Mukta D	23	F	160	54	90	96	98	90	92	94	96	90	94	87	92	86	74	121	110	110	106	108	108	108	104	109	112	110	108	114	71	71	65	64	63	61	60	59	59	64	63	66	63	88	84	80	78	78	77	76	74	76	80	79	80	80
7	Savitha	26	F	156	50	94	100	101	98	98	99	97	102	109	96	94	92	89	136	134	116	120	126	128	126	124	128	118	118	110	119	85	81	78	73	75	71	75	73	75	68	70	71	68	102	99	91	89	92	90	92	90	93	85	86	84	85
8	Ankita	23	F	155	56	75	76	79	83	84	89	85	78	88	90	92	86	90	126	129	118	118	118	124	118	113	122	116	112	113	110	70	67	67	62	61	61	68	72	71	63	64	68	69	89	88	84	81	80	82	85	86	88	81	80	83	83
9	Sunita	25	F	154	57	80	90	92	95	94	94	92	74	80	76	74	84	76	110	108	108	106	101	110	108	110	114	106	110	110	110	62	64	58	58	62	59	63	63	63	61	62	65	65	78	79	75	74	75	76	78	79	80	76	78	80	80
10	Geetha	30	F	158	61	98	101	94	97	98	98	100	95	94	96	90	97	90	114	107	104	102	100	108	104	102	108	109	114	112	114	63	63	62	60	61	58	62	60	60	64	63	65	72	80	78	76	74	74	75	76	74	76	79	80	81	86
11	Kalyani P	28	F	160	60	78	74	80	85	90	92	94	78	84	90	94	88	86	119	102	102	101	96	100	104	108	112	105	106	112	109	59	61	61	57	57	56	57	63	65	61	59	61	62	79	75	75	72	70	71	73	78	81	76	75	78	78
12	Anita	26	F	154	66	84	88	88	86	89	88	89	96	82	89	90	92	88	106	106	110	104	101	104	109	110	112	114	112	116	118	68	67	63	62	62	59	62	65	68	69	67	60	61	81	80	79	76	75	74	78	80	83	84	82	79	80
13	Akansha	27	F	151	53	68	74	75	76	84	85	83	80	82	87	91	96	92	108	108	104	98	100	107	106	101	106	112	110	112	113	64	63	57	56	56	59	61	59	61	64	63	64	68	79	78	73	70	71	75	76	73	76	80	79	80	83
14	Sindhu	29	F	153	58	74	79	81	80	84	86	85	90	96	102	105	95	95	121	110	108	100	108	119	110	109	118	104	106	109	112	70	72	69	70	67	63	65	62	65	60	61	64	62	87	85	82	80	81	82	80	78	83	75	76	79	79
15	Deepthi P	25	F	156	60	88	96	99	99	96	97	95	98	94	100	103	93	89	119	112	110	106	110	116	116	114	118	105	100	108	110	65	70	66	65	65	65	66	69	64	61	61	61	62	83	84	81	79	80	82	83	84	82	76	74	77	78
16	Gayathri	30	F	156	62	84	80	82	83	84	85	88	94	90	96	99	95	93	126	128	130	118	114	121	124	122	124	118	113	113	121	88	80	74	74	75	68	71	74	74	70	68	71	70	101	97	93	89	88	86	89	90	91	86	83	85	87
17	Basavamma	33	F	151	54	88	86	84	80	78	80	82	84	80	89	89	86	84	124	124	128	119	112	120	128	126	120	116	109	110	118	77	76	66	68	68	67	66	66	67	62	62	63	59	93	92	87	85	83	85	87	86	85	80	78	79	79
18	Neha	27	F	154	55	79	88	90	91	88	90	89	86	83	88	88	87	86	122	121	112	101	104	109	118	110	120	110	110	112	114	60	62	62	63	60	58	59	62	60	63	62	58	64	81	82	79	76	75	75	79	78	80	79	78	76	81
19	Bharati D	28	F	152	59	89	90	92	89	94	95	96	99	104	102	102	110	100	108	108	102	100	99	106	104	108	112	112	108	114	110	61	60	58	56	58	58	59	60	61	64	61	61	63	77	76	73	71	72	74	74	76	78	80	77	79	79
20	Ramya	32	F	148	65	83	87	85	84	86	85	83	95	88	86	84	90	91	121	110	106	103	102	100	102	109	100	110	105	106	112	62	65	64	62	60	58	60	62	56	57	61	56	62	82	80	78	76	74	72	74	78	71	75	76	73	79
21	kavitha	27	F	152	67	90	98	100	102	101	102	106	99	101	98	96	92	98	124	116	104	102	100	99	100	100	108	110	112	115	113	55	60	62	58	56	58	59	55	60	62	62	64	65	78	79	76	73	71	72	73	70	76	78	79	81	81
22	Roopa S	25	F	155	63	82	84	86	85	87	89	84	85	88	90	91	90	93	106	112	104	98	100	102	104	112	106	108	116	110	115	61	59	59	57	58	60	60	59	64	64	62	60	65	76	77	74	71	72	74	75	77	78	79	80	77	82
23	Lata K	28	F	150	58	78	79	85	87	89	92	89	88	85	89	90	89	90	108	106	101	94	96	98	98	98	104	107	104	112	108	64	58	54	56	52	53	53	56	57	60	59	61	60	79	74	70	69	67	68	68	70	73	76	74	78	76
24	Kauser Nadaf	34	F	148	53	86	93	96	95	94	96	94	89	90	88	86	92	89	128	114	123	119	110	122	110	108	109	114	103	110	109	71	75	66	65	66	62	65	63	64	63	62	62	62	90	88	85	83	81	82	80	78	79	80	76	78	78
25	Sharada H	24	F	148	57	77	88	87	89	93	93	89	90	88	96	92	90	88	132	126	131	126	121	126	118	116	120	118	114	115	119	84	81	74	72	73	69	70	69	70	64	63	70	65	100	96	93	90	89	88	86	85	87	82	80	85	83
26	Heena kauser	20	F	150	60	90	98	100	94	98	96	90	93	90	96	90	95	86	130	128	124	124	120	124	112	112	116	108	108	112	112	71	69	65	61	64	61	64	67	63	63	60	61	61	91	89	85	82	83	82	80	82	81	78	76	78	78
27	Manjula	35	F	148	67	89	84	86	90	92	93	89	89	95	92	90	88	94	126	116	110	112	108	108	109	110	110	109	106	104	110	61	63	63	59	60	63	64	65	62	64	62	59	57	83	81	79	77	76	78	79	80	78	79	77	74	75
28	Gouravva G	29	F	150	64	94	99	100	100	101	103	102	98	106	110	104	98	96	130	118	116	120	116	124	112	114	112	113	110	114	113	76	76	74	67	66	70	74	70	70	63	63	64	65	94	90	88	85	83	88	87	85	84	80	79	81	81
29	Kalpana	26	F	152	60	79	90	89	88	89	91	87	82	88	90	89	84	78	124	114	108	110	110	118	101	117	114	114	116	114	114	59	63	60	60	60	61	72	61	64	67	62	63	64	81	80	76	77	77	80	82	80	81	83	80	80	81
30	Fakiravva J	30	F	148	65	85	92	96	98	98	100	93	89	90	96	97	94	90	108	108	102	99	100	104	104	106	112	112	110	113	110	63	58	58	60	58	59	62	64	59	61	60	62	66	78	75	73	73	72	74	76	78	77	78	77	79	81
31	Aishwarya	28	F	156	64	88	98	100	102	100	101	98	90	99	95	96	88	83	110	108	101	92	101	100	101	104	109	107	109	110	110	65	60	59	59	57	56	57	59	59	57	58	60	60	80	76	73	70	72	71	72	74	76	74	75	77	77
32	Tanuja	32	F	159	56	92	94	98	97	99	98	95	91	94	96	95	89	90	106	114	116	108	104	106	106	119	114	110	101	115	116	71	72	65	64	62	64	65	60	67	63	66	62	65	83	86	82	79	76	78	79	80	83	79	78	80	82
33	Preeti	24	F	156	58	84	90	92	94	95	97	92	93	90	93	93	90	87	109	117	112	104	106	102	106	102	106	113	115	118	119	64	61	61	62	59	58	59	58	58	60	62	65	68	79	80	78	76	75	73	75	73	74	78	80	83	85
34	Mounica	25	F	148	60	94	90	94	98	100	99	90	96	95	90	94	89	93	121	120	114	114	110	116	116	114	109	112	116	120	116	76	73	66	63	65	66	62	61	62	64	63	66	66	91	89	82	80	80	83	80	79	78	80	81	84	83
35	Fathima	31	F	149	66	89	94	94	91	94	95	98	100	98	94	90	86	89	132	130	120	120	119	120	122	118	113	110	114	119	120	85	83	70	67	65	67	69	67	66	63	63	66	69	101	99	87	85	83	85	87	84	82	79	80	84	86
36	Laxmi	27	F	150	68	68	80	86	86	89	90	87	86	88	90	89	85	80	109	119	104	100	103	101	97	104	109	109	106	104	110	59	60	60	59	56	53	58	57	58	59	59	62	62	76	80	75	73	72	69	71	73	75	76	75	76	78
37	Dhanalaxmi	29	F	148	65	64	78	80	81	86	88	84	86	90	92	90	80	79	112	116	108	99	102	108	96	104	108	110	116	116	112	70	62	63	61	60	54	57	59	60	63	62	63	70	84	80	78	74	74	72	70	74	76	79	80	81	84
38	Deenamma	31	F	148	67	82	86	89	90	94	94	90	97	92	90	92	84	89	114	108	105	96	99	104	100	102	109	107	110	117	114	61	60	60	58	55	57	56	58	59	62	62	61	63	79	76	75	71	70	73	71	73	76	77	78	80	80
39	Durga	32	F	152	70	86	80	82	80	86	88	84	85	80	82	82	86	90	102	110	110	103	103	108	104	108	106	108	112	114	109	69	66	63	64	61	58	65	60	58	64	61	63	61	80	81	79	77	75	75	78	76	74	79	78	80	77
40	Kankia	28	F	156	72	94	90	93	90	92	91	87	93	90	91	95	98	84	106	110	109	100	101	108	104	109	110	109	117	110	113	65	62	59	61	59	57	60	59	60	59	61	60	65	79	78	76	74	73	74	75	76	77	76	80	77	81

GROUP B

S.NO	NAME	AGE	SEX	HEIGHT (cm)	WEIGHT (Kg)	HR (bpm)													SBP (mmHg)												DBP (mmHg)												MAP											
						TB	T0	2min	4min	6min	8min	10min	15min	20min	25min	30min	40min	50min	TB	T0	2min	4min	6min	8min	10min	15min	20min	25min	30min	40min	50min	TB	T0	2min	4min	6min	8min	10min	15min	20min	25min	30min	40min	50min	TB	T0	2min	4min	6min	8min	10min	15min	20min	25min	30min	40min	50min
1	Kavita	30	F	150	67	88	89	92	90	90	94	96	98	95	97	99	98	94	114	112	110	102	102	109	118	109	118	129	130	116	126	66	64	62	60	61	61	61	64	64	69	73	69	64	82	80	78	74	75	77	80	79	82	89	92	85	85
2	sheela	29	F	156	58	78	80	85	84	83	86	88	89	90	92	94	92	92	130	119	114	113	109	112	120	118	116	126	126	112	110	70	74	69	63	64	65	63	61	60	66	63	64	63	90	89	84	80	79	81	82	80	83	86	84	80	79
3	Sweety	23	F	148	55	89	88	89	90	89	88	89	90	92	86	85	89	88	125	113	112	108	106	110	116	116	119	128	124	122	129	63	66	62	58	61	62	62	66	68	69	68	72	64	84	82	79	75	76	78	80	83	85	89	87	89	86
4	Gowri	28	F	155	54	90	93	90	91	92	93	90	92	94	95	91	92	90	106	101	92	89	92	98	99	92	96	101	104	120	110	58	57	48	42	44	44	48	54	87	59	60	60	60	74	72	63	58	60	62	65	67	70	73	75	80	77
5	Laxmi	25	F	156	70	68	70	72	74	73	76	80	78	76	79	85	83	83	117	118	116	116	114	116	118	126	116	120	116	121	112	70	68	66	62	64	66	67	64	66	60	63	65	61	86	85	83	80	81	83	84	85	83	80	81	84	78
6	Swathi	32	F	157	68	88	90	89	90	89	88	89	90	91	89	86	86	86	121	120	119	115	119	114	120	125	112	122	114	110	118	71	69	65	62	63	67	67	63	64	63	63	62	61	88	86	83	80	82	83	85	84	80	83	80	78	80
7	Kavya	29	F	148	65	79	80	82	80	82	80	81	80	78	81	83	86	84	131	124	121	119	120	118	121	126	118	120	115	113	116	71	73	73	71	69	68	68	69	65	67	65	62	62	91	90	89	87	86	85	86	88	83	85	82	79	80
8	Sheetal	24	F	154	64	88	82	80	81	80	84	80	82	82	84	88	86	86	140	129	128	125	126	128	128	128	122	128	128	124	126	81	84	80	75	72	72	75	71	72	75	71	70	70	101	99	96	92	90	91	93	90	89	93	90	88	89
9	Gomati	25	F	155	56	86	89	90	92	91	90	90	93	90	87	88	86	85	126	120	113	106	110	109	108	117	120	123	112	113	121	63	64	65	62	62	58	63	61	61	64	64	60	61	84	83	81	77	78	75	78	80	81	84	80	78	81
10	Latha	30	F	157	54	91	89	93	90	94	96	98	99	96	99	97	95	95	108	104	96	92	92	106	99	99	101	104	109	116	122	60	59	57	51	53	47	54	57	59	60	61	62	65	76	74	70	65	66	67	69	71	73	75	77	80	84
11	Preeti	27	F	150	50	87	90	89	90	90	91	93	90	89	95	94	92	92	122	112	112	108	106	115	116	108	115	128	118	114	113	68	71	68	60	64	62	63	64	64	65	68	66	60	86	85	83	76	78	80	81	79	81	86	85	82	78
12	Chaitanya	25	F	151	67	69	76	80	82	80	79	80	84	84	89	86	87	87	120	113	101	101	104	99	98	102	108	118	112	112	112	61	62	60	54	56	52	56	58	61	61	65	64	62	81	79	74	70	72	68	70	73	77	80	81	80	79
13	Akkavva	19	F	148	66	79	84	83	83	85	86	87	89	90	93	89	90	85	112	110	102	104	101	100	101	103	106	100	106	102	109	61	60	61	59	57	55	59	61	61	58	59	57	59	78	77	75	74	72	70	73	75	76	72	75	72	76
14	Pooja	20	F	150	54	84	86	88	89	90	92	90	93	91	93	90	92	88	138	129	128	128	129	118	130	128	124	119	113	116	114	81	82	78	75	70	74	71	75	71	71	71	66	63	100	98	95	93	90	89	91	93	89	87	85	83	80
15	Gangavva	23	F	150	53	86	80	82	80	84	86	84	86	88	86	85	87	83	110	104	89	86	92	99	99	99	104	114	110	108	112	59	59	42	45	47	48	52	55	59	61	65	60	61	76	74	58	59	62	65	68	70	74	79	80	76	78
16	Parwati	27	F	152	58	90	86	85	86	85	84	80	81	78	80	81	79	79	104	104	91	88	90	98	99	99	102	106	110	119	116	59	60	44	43	45	48	54	57	58	59	62	60	63	74	75	60	58	60	65	69	71	73	75	78	80	81
17	Singawwa	26	F	154	60	92	90	92	90	89	90	88	90	90	92	89	94	90	119	113	104	102	101	106	101	96	98	102	104	110	114	63	62	60	55	57	58	59	55	56	58	60	62	63	82	79	75	71	72	74	73	69	70	73	75	78	80
18	Girwwa	29	F	160	62	86	91	95	96	95	93	94	96	95	98	95	92	92	130	125	122	119	124	126	129	126	123	123	113	112	115	83	80	77	74	70	70	73	72	69	66	63	61	65	99	95	92	89	88	89	92	90	87	85	80	78	82
19	Dundavva	25	F	149	67	89	92	92	95	95	97	98	95	97	94	90	88	88	136	128	125	128	129	129	126	124	120	126	119	120	112	85	81	78	71	73	75	72	71	67	70	72	66	64	102	97	94	90	92	93	90	89	85	89	88	84	80
20	Shaila	23	F	148	68	82	85	87	90	92	93	95	95	96	98	94	95	95	129	126	120	124	126	126	123	127	128	127	129	124	119	82	81	76	68	66	69	72	73	77	71	73	71	72	98	96	91	87	86	88	89	91	94	90	92	89	88
21	Rukmini	27	F	151	65	98	102	104	106	104	99	98	97	99	103	101	98	98	118	119	100	94	94	98	99	101	108	110	110	112	113	64	62	50	47	52	51	55	57	58	60	62	62	63	82	81	67	63	66	67	70	72	75	77	78	79	80
22	Maduri	32	F	156	60	75	78	84	80	81	85	86	88	84	89	83	90	88	114	120	118	115	110	108	102	102	100	106	108	108	109	69	69	67	67	62	58	58	60	58	59	60	57	56	84	86	84	83	78	75	73	74	72	75	76	74	74
23	Yashodha	30	F	154	50	85	89	93	94	90	92	94	93	89	92	94	90	90	108	101	101	100	106	102	106	103	99	106	107	110	108	60	60	57	55	55	58	59	59	57	58	60	63	58	76	74	72	70	72	73	75	74	71	74	76	79	75
24	Tanima	29	F	148	55	94	96	95	97	96	96	98	100	101	104	99	97	97	131	128	119	119	123	122	129	119	123	108	114	109	108	77	75	75	72	72	74	73	74	61	63	63	59	60	95	93	90	88	89	90	92	89	82	78	80	76	76
25	Chinnavva	28	F	148	54	78	80	84	86	89	90	92	90	92	90	94	96	96	102	100	96	86	90	96	96	92	96	101	96	110	110	58	55	48	44	45	49	52	56	57	60	57	62	65	73	70	64	58	60	65	67	68	70	74	70	78	80
26	Shivamma	31	F	154	70	88	94	98	97	95	94	93	96	97	100	97	95	95	121	118	97	86	91	94	97	94	102	109	106	102	104	67	64	49	45	47	53	53	58	58	62	61	58	53	85	82	65	59	62	67	68	70	73	78	76	73	70
27	Padmavati	24	F	150	64	86	90	89	91	85	84	84	86	87	89	90	88	88	141	129	124	129	124	124	128	129	126	124	121	114	117	81	81	79	72	70	73	75	70	70	68	73	70	67	101	97	94	91	88	90	93	90	89	87	89	85	84
28	Rajeshwari	22	F	153	69	90	95	94	93	94	90	89	91	90	94	89	89	89	117	113	97	92	96	94	98	95	101	110	114	110	110	63	62	47	44	46	50	50	56	56	62	61	59	60	81	79	64	60	63	65	66	69	71	78	79	76	77
29	Sonali	26	F	153	63	89	90	88	90	91	89	90	90	89	87	90	91	89	121	119	118	109	116	124	118	114	119	118	118	112	65	65	61	62	62	61	61	66	60	67	64	61	64	84	83	80	78	80	82	80	82	80	84	82	80	80
30	Savita	25	F	150	62	94	101	100	98	96	97	96	98	96	90	86	85	85	105	110	109	102	108	106	109	112	118	119	120	123	118	61	62	59	58	58	61	64	64	64	71	67	67	70	76	78	76	73	75	76	79	80	82	87	85	86	86
31	Chandramati	28	F	148	58	82	94	98	96	94	92	93	95	98	101	104	98	98	110	113	106	103	98	99	99	101	108	98	101	97	100	62	62	61	56	56	52	55	59	60	56	57	56	55	78	79	76	72	70	68	70	73	76	70	72	70	70
32	Geeta	33	F	152	64	84	89	87	89	90	94	95	96	99	97	95	93	93	138	126	124	127	126	124	126	120	127	114	110	120	116	85	85	82	74	72	71	72	72	65	63	66	63	68	103	99	96	92	90	89	90	88	86	80	81	82	84
33	Deepa	29	F	150	52	78	84	86	88	90	91	90	89	91	87	85	86	83	103	98	98	89	90	98	92	99	101	104	104	102	104	59	57	45	44	48	48	54	55	57	59	60	58	57	74	71	63	59	62	65	67	70	72	74	75	73	73
34	Prema	30	F	152	58	82	87	89	90	92	94	89	85	80	81	86	84	84	101	90	96	96	99	100	100	98	102	108	116	116	108	57	58	48	52	52	53	55	57	60	63	62	66	63	72	69	64	67	68	69	70	71	74	78	80	83	78
35	Shakuntala	25	F	151	59	87	89	90	92	90	90	93	92	86	84	85	83	83	136	130	126	124	122	121	122	123	122	114	118	110	106	82	82	79	73	71	70	72	70	66	63	62	59	61	100	98	95	90	88	87	89	88	85	80	81	76	76
36	Sushila	24	F	149	60	76	84	86	90	93	89	84	86	89	88	86	90	88	110	109	101	110	112	120	120	126	124	112	114	110	108	63	61	62	62	62	60	63	64	71	61	63	62	63	79	77	75	78	79	80	82	85	89	78	80	78	78
37	Mahadevi	20	F	148	63	78	80	82	84	80	78	80	81	83	82	89	87	87	110	104	96	98	98	97	95	94	102	99	101	96	96	62	60	49	41	45	52	54	56	58	55	56	57	55	78	75	65	60	63	67	68	69	73	70	71	70	69
38	Shabana	25	F	151	66	80	82	85	86	84	85	83	86	90	94	96	94	94	116	121	108	107	102	106	112	108	110	110	110	118	110	62	61	63	59	58	59	61	61	63	65	68	68	65	80	81	78	75	73	75	78	77	79	80	82	85	80
39	Rajashree	28	F	152	68	85	87	86	87	83	80	82	87	89	84	81	85	80	119	119	113	118	119	118	116	116	114	112	113	108	106	65	65	63	67	62	61	63	66	63	61	63	58	58	83	83	80	84	81	80	81	83	80	78	80	75	74
40	Tahera	31	F	154	50	86	90	89	88	89	87	90	93	90	92	88	86	86	112	112	104	98	102	108	104	102	110	113	110	113	114	64	61	60	56	58	58	63	60	59	60	65	65	66	80	78	75	70	73	75	77	74	76	78	80	81	82

GROUP F

S.NO	NAME	DURATION OF SURGERY (MIN)	ONSET OF SENSORY BLOCK (MIN)	ONSET OF MOTOR BLOCK (MIN)	SENSORY REGRESSION (MIN)	MOTOR REGRESSION (MIN)	DURATION OF ANALGESIA (MIN)	APGAR SCORE AT 1MIN	APGAR SCORE AT 5MIN
1	Asha	50	2	3	180	174	206	7	8
2	Shobha N	62	3	3	188	175	240	8	9
3	Savita J	65	2	2	198	188	236	7	8
4	Drakshayani G	55	2	2	178	166	195	8	8
5	Sheethal	50	3	4	180	176	220	7	8
6	Mukta D	52	4	4	187	175	212	7	7
7	Savitha	64	2	4	180	173	230	6	8
8	Ankita	60	1	2	188	180	220	7	8
9	Sunita	66	3	4	192	183	228	8	9
10	Geetha	68	2	2	192	180	246	8	8
11	Kalyani P	65	3	3	181	173	240	7	8
12	Anita	54	3	4	178	162	200	7	8
13	Akansha	55	2	4	173	161	198	8	8
14	Sindhu	54	2	3	180	172	208	7	8
15	Deepthi P	60	3	3	190	182	226	7	8
16	Gayathri	62	3	2	189	176	230	6	8
17	Basavamma	65	3	4	190	182	235	7	9
18	Neha	70	2	3	187	175	234	8	8
19	Bharati D	68	4	3	178	168	210	7	8
20	Ramya	66	3	4	174	163	196	7	8
21	kavitha	68	2	3	183	170	200	7	7
22	Roopa S	65	2	3	178	160	198	8	8
23	Lata K	55	1	2	185	174	215	7	8
24	Kauser Nadaf	52	4	2	189	176	208	7	8
25	Sharada H	54	3	3	187	174	218	7	8
26	Heena kauser	45	4	4	178	166	208	8	8
27	Manjula	50	2	4	180	170	204	7	8
28	Gouravva G	55	2	3	175	162	195	7	8
29	Kalpana	60	3	3	174	160	190	7	8
30	Fakiravva J	62	3	4	178	165	208	8	9
31	Aishwarya	65	3	3	180	172	210	7	8
32	Tanuja	60	2	3	190	185	234	7	8
33	Preeti	62	4	4	172	160	198	8	9
34	Mounica	55	2	3	182	174	202	7	8
35	Fathima	65	3	2	178	166	206	7	8
36	Laxmi	70	3	4	179	162	200	7	8
37	Dhanalaxmi	64	3	3	186	178	224	7	8
38	Deenamma	68	4	4	190	186	220	8	9
39	Durga	55	3	4	192	180	232	7	8
40	Kankia	60	3	3	178	166	196	7	8

GROUP B

S.NO	NAME	DURATION OF SURGERY (MIN)	ONSET OF SENSORY BLOCK (MIN)	ONSET OF MOTOR BLOCK (MIN)	SENSORY REGRESSION (MIN)	MOTOR REGRESSION (MIN)	DURATION OF ANALGESIA (MIN)	APGAR SCORE AT 1MIN	APGAR SCORE AT 5MIN
1	Kavita	55	3	4	170	160	185	7	8
2	sheela	45	3	3	160	155	190	7	8
3	Sweety	62	4	3	166	158	192	6	7
4	Gowri	62	4	4	162	154	190	7	8
5	Laxmi	64	2	2	178	160	200	7	8
6	Swathi	65	2	2	180	170	202	8	9
7	Kavya	70	2	3	182	175	195	8	9
8	Sheetal	68	1	3	163	155	180	7	8
9	Gomati	52	1	4	158	148	188	7	8
10	Latha	68	2	3	178	165	198	7	8
11	Preeti	72	1	4	182	172	205	6	7
12	Chaitanya	58	2	4	178	165	208	7	8
13	Akkavva	62	3	4	190	179	215	7	8
14	Pooja	60	4	3	174	165	194	7	8
15	Gangavva	65	3	4	180	176	200	8	9
16	Parwati	64	3	5	178	166	204	7	8
17	Singawwa	72	2	3	178	169	198	7	8
18	Girwwa	65	2	4	184	178	205	7	8
19	Dundavva	70	2	3	184	174	210	7	8
20	Shaila	50	1	3	192	181	200	6	7
21	Rukmini	58	4	2	186	178	208	7	7
22	Maduri	56	3	5	169	160	190	7	8
23	Yashodha	55	3	3	165	158	198	8	8
24	Tanima	62	2	3	180	172	206	8	8
25	Chinnavva	60	2	2	184	176	210	7	8
26	Shivamma	65	2	4	178	172	204	7	8
27	Padmavati	48	4	3	164	158	185	7	8
28	Rajeshwari	45	1	4	172	162	188	8	9
29	Sonali	60	2	3	179	172	190	7	8
30	Savita	68	2	2	178	169	188	7	9
31	Chandramati	65	2	4	169	160	190	7	8
32	Geeta	60	3	4	170	164	182	6	8
33	Deepa	55	3	3	164	158	185	7	7
34	Prema	58	2	2	176	170	196	7	8
35	Shakuntala	65	3	2	180	172	202	8	9
36	Sushila	72	2	3	172	161	195	7	8
37	Mahadevi	68	4	3	182	174	200	6	8
38	Shabana	62	2	4	168	155	186	7	8
39	Rajashree	56	2	3	166	158	180	7	8
40	Tahera	50	2	3	175	164	196	7	8

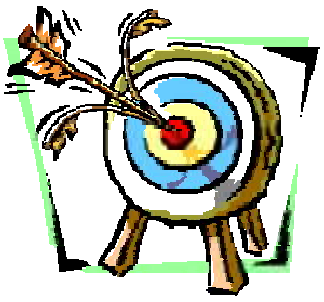
	GROUP F	GROUP B
NO. of patients required intraoperative mephentermine	6	17

ANNEXURE-VI

KEY TO MASTER CHART

F	–	Female
cm	–	Centimetre
Kg	–	Kilogram
Min	–	Minute
HR	–	Heart rate
SBP	–	Systolic blood pressure
DBP	–	Diastolic blood pressure
MAP	–	Mean arterial pressure
mmHg	–	Millimetre of mercury

Introduction



Objectives

Review of Literature

Basic Sciences

Methodology

Results

Discussion

Conclusion

Summary

Bibliography

Annexure-I

Annexure-II

Annexure-III

Annexure-IV

Annexure-V

Annexure-VI