A COMPARATIVE STUDY ON EFFECTS OF SPINAL ADDITIVES FENTANYL AND CLONIDINE WITH HYPERBARIC BUPIVACAINE

Dissertation submitted

In partial fulfillment for the award of

M.D. DEGREE EXAMINATION

M.D. ANESTHESIOLOGY AND CRITICAL CARE – BRANCH X

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APRIL 2011.

CERTIFICATE

This is to certify that this dissertation titled **"A COMPARATIVE STUDY ON EFFECTS OF SPINAL ADDITIVES FENTANYL AND CLONIDINE WITH HYPERBARIC BUPIVACAINE"** has been prepared by **Dr.V.PHILITSEN** under my supervision in the Department of Anesthesiology and Critical Care, Government Kilpauk Medical College, Chennai during the academic period 2008 – 2011 and is being submitted to The Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the university regulation for the award of the Degree of Doctor of Medicine (M.D. Anesthesiology) and his dissertation is a bonafide work.

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DECLARATION

I, Dr.V.Philitsen, solemnly declare that the dissertation, **"A COMPARATIVE STUDY ON EFFECTS OF SPINAL ADDITIVES FENTANYL AND CLONIDINE WITH HYPERBARIC BUPIVACAINE"** is a bonafide work done by me in the Department of Anesthesiology and Critical care, Government Kilpauk Medical College, Chennai under the guidance of Prof.Dr.P.S.Shanmugam, M.D.,D.A., Professor and HOD, Department of Anesthesiology and Critical Care, Government Kilpauk Medical College, Chennai.

Place: Chennai Signature

Date: (V. PHILITSEN)

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I also like to thank my Prof.Dr.Gunasekaran and Assistant Professors and tutors in anesthesiology in Kilpauk Medical College for their support during my study period. I also like to thank my colleague postgraduates for their support. I also like here to thank the theatre staff and assistants for their co-operation in conducting the study.

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CONTENTS

INTRODUCTION

The history of spinal anesthesia dates back since August 15, 1898 when Gustav August Bier performed the first spinal anesthesia with cocaine. Then came Arthur E. Barker who determined several factors involved in the spread of local anesthetic in subarachnoid space. It was Rudolph Matas who first used a spinal additive morphine with cocaine to enhance neuraxial anesthesia.

Several factors have been determined since the introduction of spinal anesthesia, till date and in evolution that modify the effects, extent or duration of spinal anesthesia.

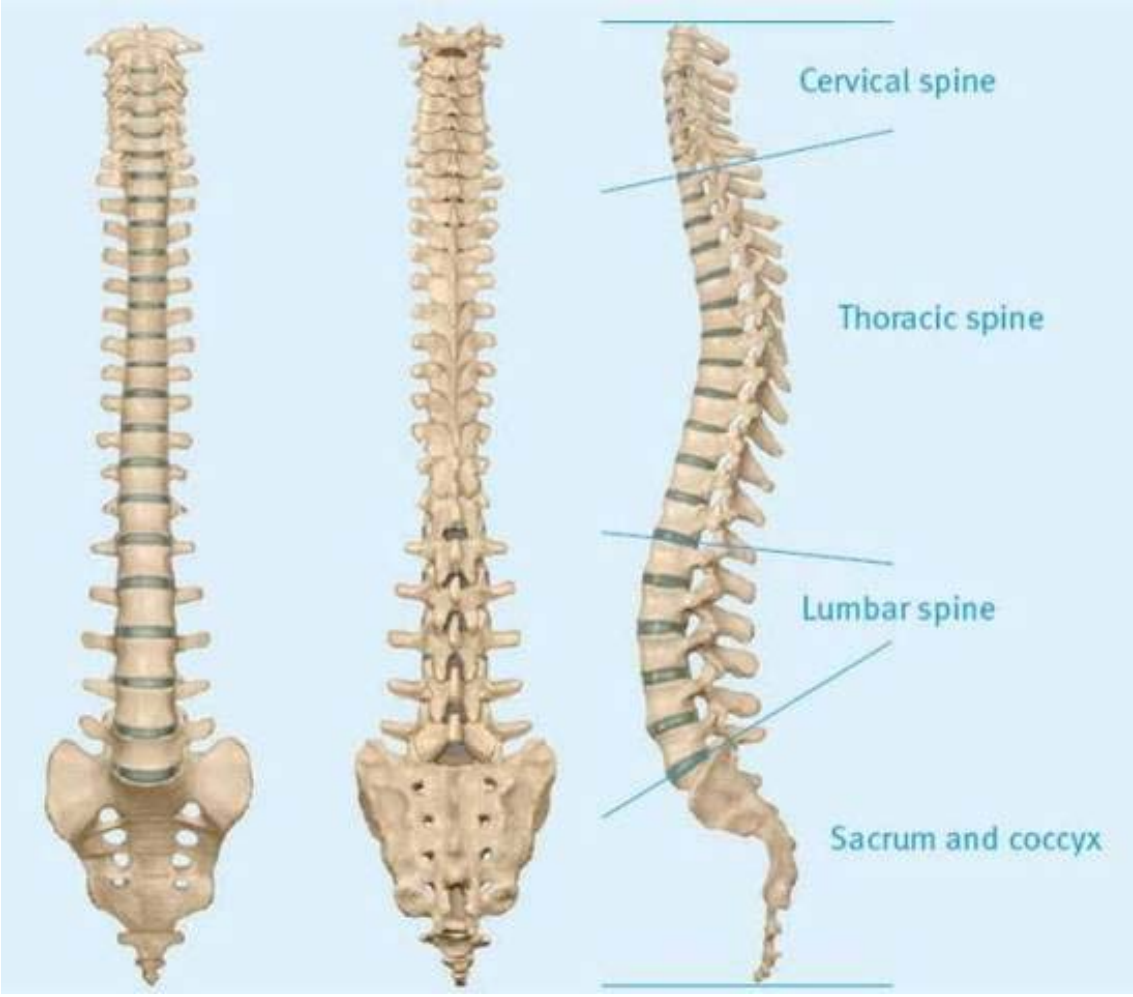
Bupivacaine is the commonly used local anesthetic in spinal anesthesia and several spinal additives, commonly the opioids are added to enhance the block and duration of spinal anesthesia. Each of the drug added as spinal additive has its own advantages and disadvantages. The ease of administering spinal anesthesia and its superior analgesic property has gained popularity over general anesthesia.

AIM OF THE STUDY:

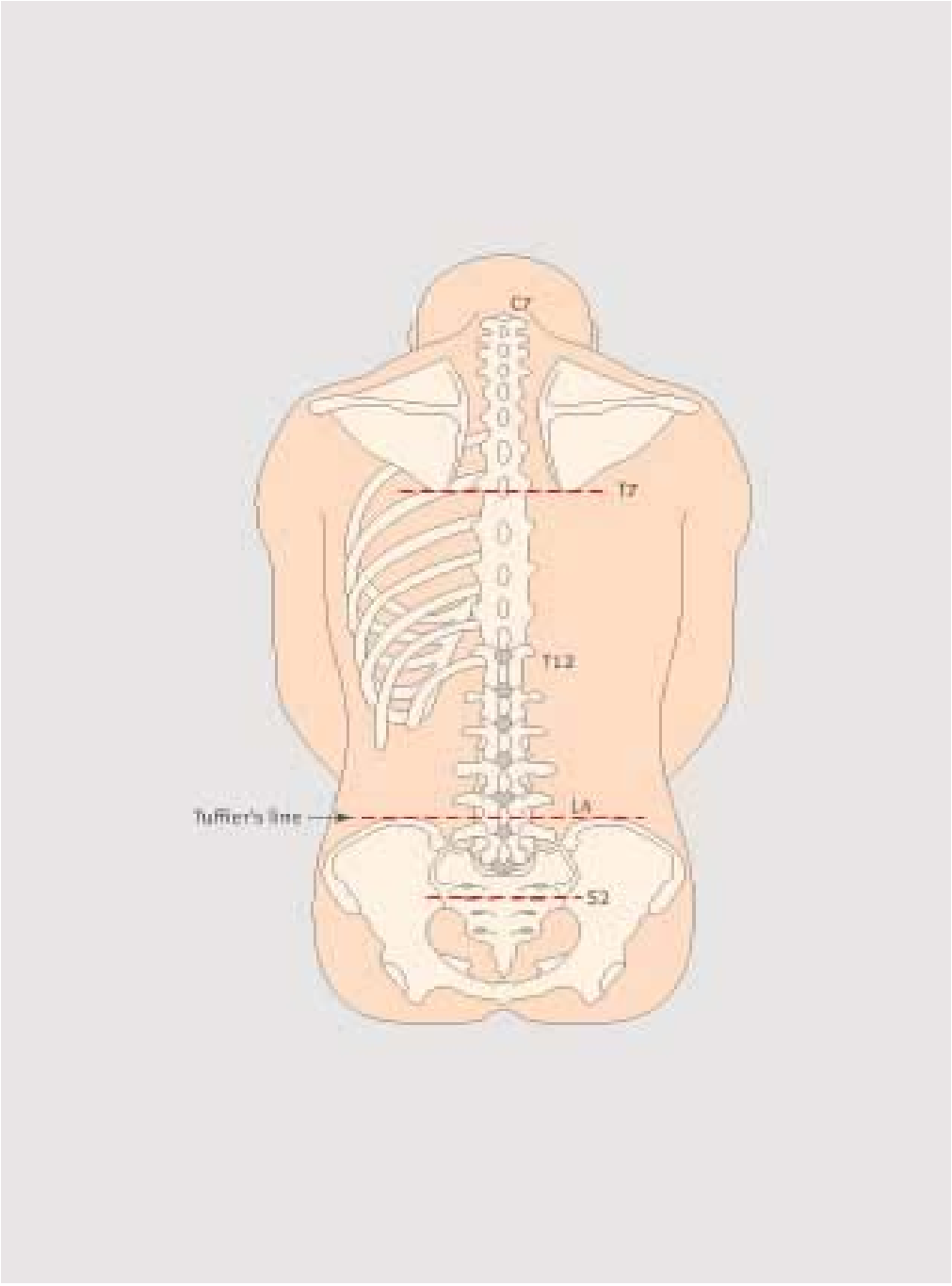
To compare the effects of intrathecal fentanyl with 0.5 % Hyperbaric Bupivacaine and clonidine with 0.5% Hyperbaric Bupivacaine with control group of patients who received only 0.5% Hyperbaric Bupivacaine.

ANATOMY FOR SUBARACHNOID BLOCK

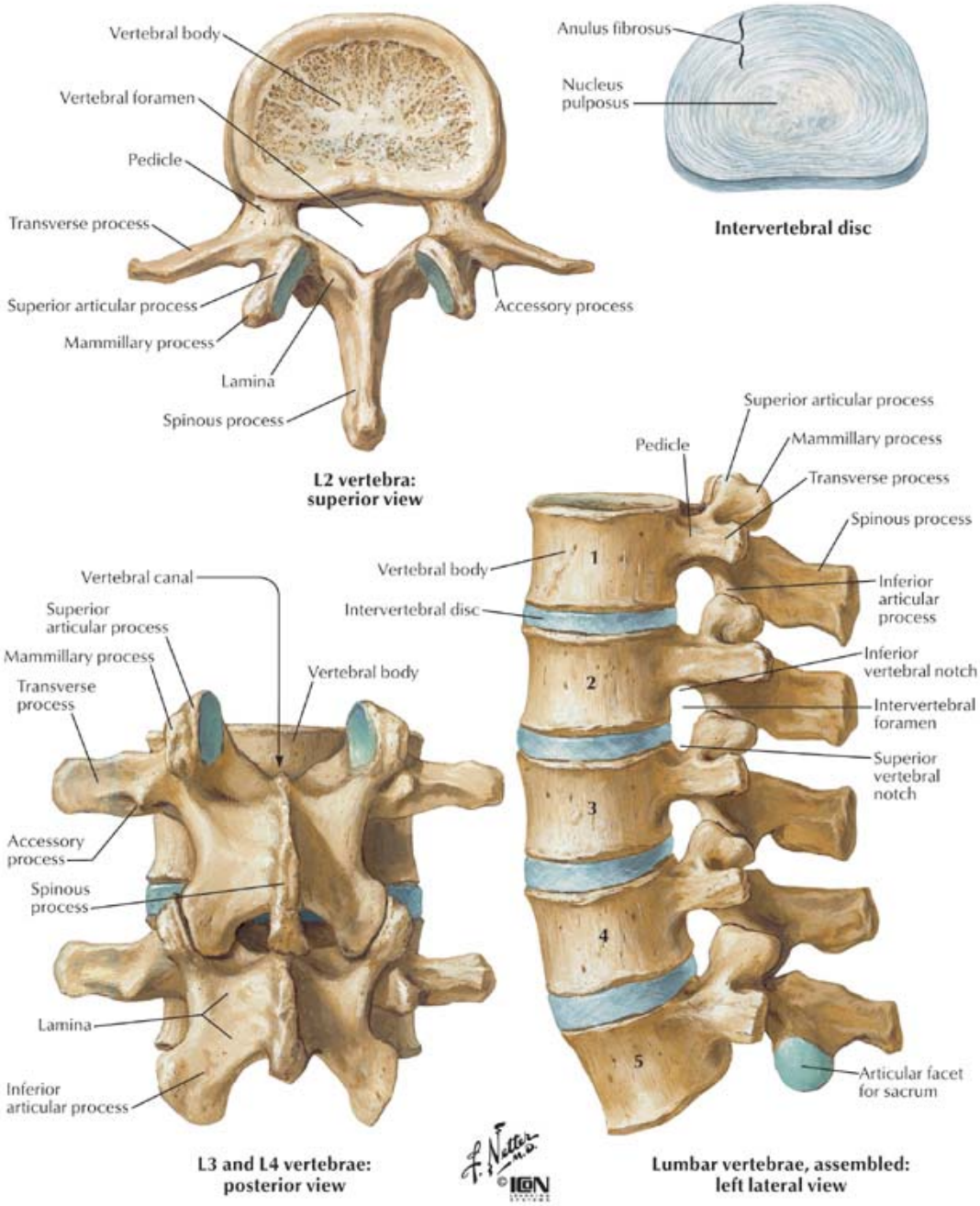
The **vertebral column** is made up of 33 vertebras 7 cervical, 12 thoracic, 5 lumbar, 5 sacral (fused), 3 or 4 coccyx (fused). It has two primary curvatures determined in utero and 2 secondary curvatures of developmental origin. The importance is that in supine position the highest point is L3 and lowest point is T5.



Line of TUFFIER - It is a topographic landmark for spinal anesthesia where a line drawn along the crests of iliac bone passes through spine of L4 in sitting position and L4-5 interspace in lateral position.



A **lumbar vertebra** contains a broad kidney shaped body, a thick and notched pedicle connecting body with the slender and long transverse process, short and broad laminae and a horizontal spine. The superior articular facets face backwards and inwards while the inferior articular facets face forwards and outwards



Ligaments – The supraspinous ligament is a strong, thick, fibrous band connecting the apices of spine from C7 to sacrum. In the cervical region it is specialized as ligamentum nuchae and extends from occipital protruberance to C7.

The interspinous ligament is a thin fibrous structure connecting adjascent spines which blends anteriorly with ligamentum nuchae and posteriorly with supraspinous ligament.

The ligamentum flavum is a yellow elastic tissue extending between antero-inferior surface of upper laminae to antero-superior surface of lower laminae.

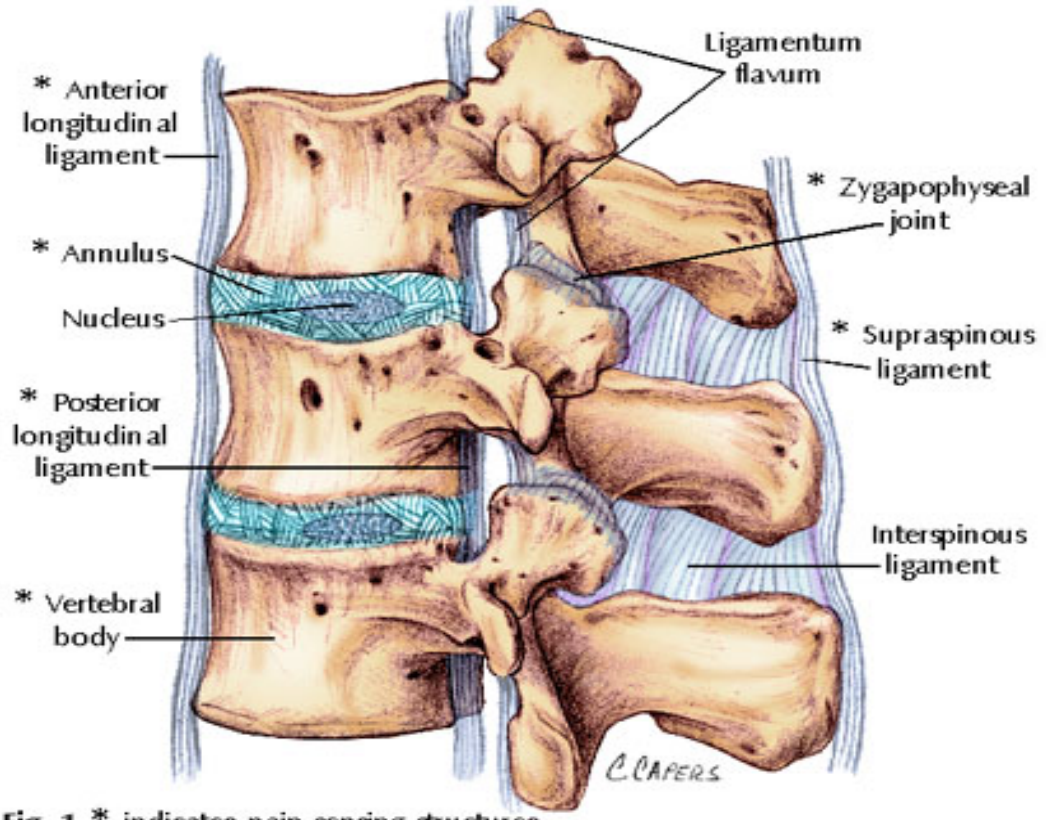


Fig. 1 * indicates pain-sensing structures

The **spinal cord** has three covering **meninges** – the outer dura mater, the pia mater internally and the arachnoid mater inbetween. The dura mater is an extension of cranial dura which is attached above to the foramen magnum and posterior aspect of C2,3 cervical vertebra, anteriorly to the posterior longitudinal ligaments, posteriorly it is free. Laterally it prolongs along with the nerve roots and blends with the epineurium of nerve roots and inferiorly it ends at the level of S2.

The arachnoid membrane is a an avascular delicate membrane which is resistant to the penetration of drugs. It is an extension from the cranial arachnoid membrane and it lines along with the dural sheath.

The pia mater is a vascular membrane which closely invests the brain and spinal cord along its fissures, sulci and gyri. The pia is thickened anteriorly to form linea splendens along the length of anterior median fissure. The denticulate ligaments are folds of pia mater attached lataerally to the dural sheath and they act as struts to hold the spinal cord. Filum terminale is an extension of pia mater from end of conus medullaris to coccyx.

The compartments formed by the spinal meninges are the subarachnoid space, the subdural space, and the epidural space out of which our space of interest is subarachnoid space.

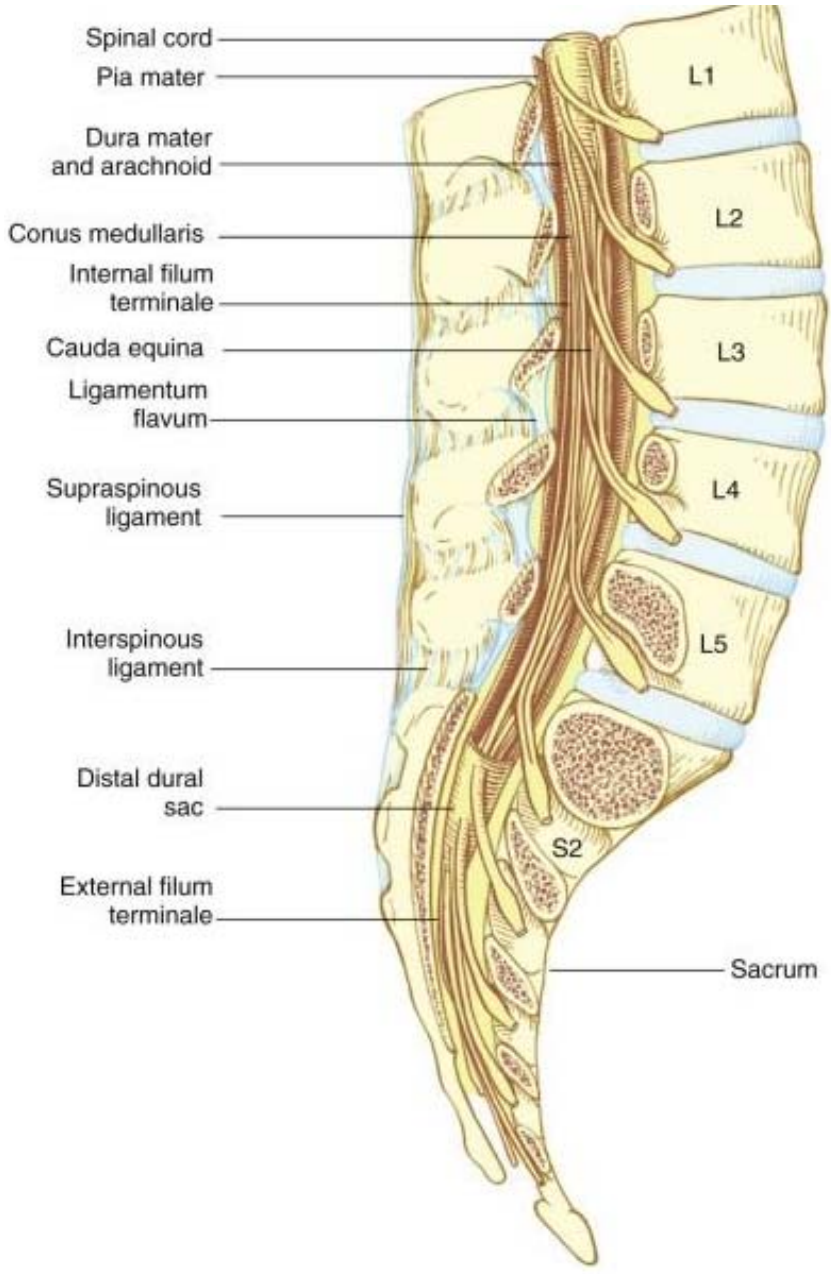
The subarachnoid space contains CSF, spinal nerve roots, blood vessels, and by incomplete trabecula – the posterior subarachnoid septum, And also traversed by ligamentum denticulatum. This space extends upto S2.

Fate of local anesthetic in this space is

- Dilution and mixing in CSF
- Uptake and fixation by neural tissues
- Vascular absorption and elimination

Spinal cord is about 45 cm. In length extending upto L1 in adults and L3 in infants. Upto the 3rd month of intrauterine life spinal cord extended through out the vertebral column. The spinal cord is enlarged at the cervical and lumbar level corresponding to the nerve supply of upper and lower limbs. The tapering end of the spinal cord is the conus medullaris .The blood supply of spinal cord is with one anterior spinal artery formed by fusion of two branches from either side of vertebral artery which runs in anterior median fissure supplying anterior two thirds of spinal cord. Two posterior spinal arteries formed from corresponding sites of posterior inferior cerebellar artery supplies posterior one third of spinal cord. Communicating branches from corresponding segmental arteries called radicular arteries from vertebral, ascending cervical, posterior

intercostals, spinal lumbar, lateral sacral arteries. Arteria radicularis magna is the largest of the contribution which is a branch from descending Aorta. Venous drainage is through plexus of veins in the pia mater, there are 6 longitudinal plexiform channels.



Site of Action of spinal anesthesia:

The local anesthetic injected in subarachnoid space acts on the spinal nerve roots and blocks its conduction. Hence the posterior nerve root carrying somatic and visceral sensation and anterior nerve roots carrying motor and autonomic outflow are blocked.

Contraindications for spinal anesthesia:

Absolute

- Patient refusal
- Infection at the site of injection
- Coagulopathy
- Severe hypovolemia
- Severe aortic stenosis
- Severe mitral stenosis
- Herniation of cerebellar tonsils (↑ICT)

Relative

- Sepsis
- Uncooperative patient
- Pre-existing neurological deficits
- Demyelinating lesions
- Severe spinal deformity

Complications of spinal anesthesia:

Immediate

- Hypotension
- Bradycardia
- Cardiac arrest
- Dyspnoea
- Nausea
- Vomiting
- Shivering
- Anxiety and apprehension
- High spinal
- Traumatic spinal cord or nerve root puncture
- Broken needle

Delayed

- Post-operative urinary retention
- Post-dural puncture headache
- Backache
- Transient neurological symptoms
- Epidural hematoma
- Meningitis / arachnoiditis
- Epidural abscess

Factors affecting Block Height:

Patient factor

- Age
- Height
- Weight
- Gender
- Intra abdominal pressure
- Anatomy of spinal column

Technique of injection

- Site of injection
- Direction of needle and bevel
- Use of barbotage
- Rate of injection

Charecteristics of spinal fluid

- Volume
- Pressure
- Density

Charecteristics of anesthetic solution

- Density
- Amount
- Concentration
- Temperature
- Volume

PHARMACOLOGY OF THE DRUGS USED

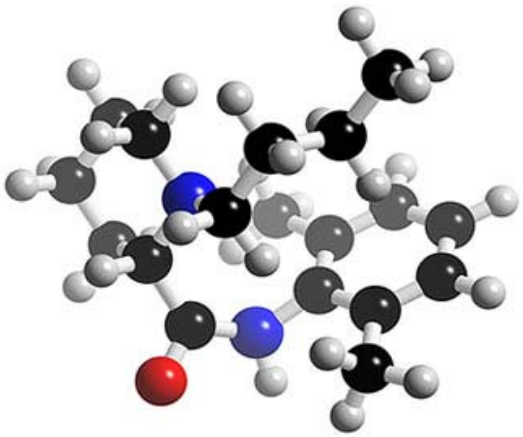
Bupivacaine:

It was first introduced by Evenstam

First came in to clinical use in 1963.

It is an amide Local Anaesthetic (1-butyl-N-(2, 6, dimethyll phenyl-piperidine – 2 – Carboxamide).

Structure:



Formulations:

As a clear 0.25%, 0.5%, 0.75% solution of bupivacaine hydrochloride. The hyperbaric solution used for subarachnoid block contains 80mg/ml of glucose.

Physiochemical Properties

Pka	:	8.1
Protein binding	:	96%
Lipid solubility	:	28
Elmination T½	:	210 mins
Clearance	:	0.47 l / min

Mechanism of action:

Local anaesthetics such as bupivacaine block the generation and the conduction of nerve impulses, presumably by increasing the threshold for electrical exitation in the nerve, by slowing the propagation of the nerve impulse, and by reducing the rate of rise of the action potential. In general, the progression of anaesthesia is related to the diameter, myelination and conduction velocity of affected nerve fibres. Clinically, the order of loss of nerve function is as follows.

- Autonomic
- Temperature cold before warmth
- Pain
- Touch
- Pressure

- Motor
- Vibration
- Proprioception

Routes of administration / dosage

Bupivacaine may be administered for infiltration, nerve blocks intrathecally, epidurally. The therapeutic dose of Bupivacaine is 2-3mg/kg (with or without adrenaline)

The drug acts within 10-20 mins and has a duration of action of 5-6 hours.

Pharmacokinetics

The absorption of Local Anaesthetic is related to

- The site of injection (intercostal > epidural > brachial plexus > Subcutaneous)
- The dose – a linear relationship exists between the total dose and the peak blood concentration achieved.
- The presence of vasoconstrictors which delay absorption

The possible pathway for metabolism of bupivacaine include aromatic hydroxylation, N-dealkylation, amide hydrolysis and conjugation. Only the N-dealkylated metabolite N-desbutyl bupivacaine has been measured in the blood or urine.

Alpha-1 acid glycoprotein is the most important protein binding site of bupivacaine. 5% of the dose is excreted in the urine as pipcolloxylidine. 16% is excreted unchanged clearance is 0.47 L/min and elimination T½ is about 210 min

Systemic Toxicity

Cardiovascular system:

Bupivacaine is markedly cardiotoxic. It binds specifically to the myocardial proteins. In toxic concentrations the drug decreases the peripheral vascular resistance and myocardial contractility producing hypotension and possible cardiovascular collapse. Cardiotoxic plasma concentrations of bupivacaine is 8-10 mcg/mL.

Central nervous system:

The principal effect of bupivacaine is reversible neural blockade. This leads to a characteristically biphasic effect in the CNS. During accidental over dosage or direct vascular injections the clinical signs are numbness of tongue, lightheadedness, visual and auditory disturbances, muscular

twitchings, tremors. The signs may progress to generalised convulsions of the tonic clonic nature. When plasma levels continue to rise, CNS excitation is rapidly superceded by depression drowsiness, disorientation & coma. The typical plasma concentration of Bupivacaine associated with seizures is 4.5 – 5.5 mcg/mL.

Clonidine:

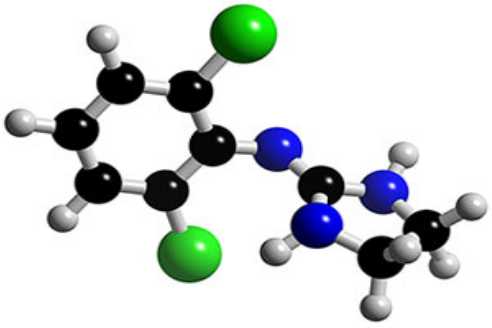
Clonidine is the prototype drug of alpha-2 adrenergic agonist.

The selectiveity ratio α2: α1 is 220:1.

Synthesized in early 1960 as a nasal decongestant.

The molecular formula is (2-(2, 6 – dicholorophenyl amino) – 2-imidazoline)

Structure:



Preparations:

Tablets – 0.1 mg, 0.2 mg, 0.3mg

Preservative free parenteral forms 75µg/ml

Trans dermal patch

Routes of administration:

As an oral premedication, intravenously, intrathecal and epidural additive, and additive for regional nerve blocks.

Pharmacokinetics:

Well absorbed orally with a bioavailability of 100%

Peak plasma concentration 60 - 90 min,

Elimination half time 9 - 12hrs.

50% metabolized in the liver rest excreted unchanged in the urine. Transdermally the therapeutic plasma concentration will take 48 hrs. The elimination half life is increased in patients with renal dysfunction.

Pharmaco dynamics:

Clonidine acts on various systems in the body.

Cardio Vascular System

Clonidine has got both central action and peripheral action.

Central Action

Activation of central α - 2 adrenergic receptors in medullary vasomotor centre inhibits the release of nor – epinephrine from the adrenergic neurons and reduces sympathetic outflow from the central nervous system. Further there is reduced discharge from the post ganglionic fibers of cardiac nerves and an increase in parasympathetic tone.

This results in decrease in blood pressure, heart rate, cardiac output, peripheral vascular resistance. Nucleus tractus solitarius, the site that modulates the autonomic control including vagal activity is an important central site for the action of clonidine. Other proposed sites of action are locus ceruleus, dorsal motor nucleus of vagus and nucleus reticularis lateralis.

Reduction in sympathetic tone is accompanied by lowering of plasma renin activity, decrease in renal vascular resistance and maintenance of renalblood flow even when the blood pressure is lowered. Vasopressor centers of the brainstem retain their sensitivity to baroreceptor control and hence postural hypotension is considerably less than the effects of drugs that act on the autonomic ganglia and peripheral adrenergic receptors.

The absence of fall in blood pressure when clonidine is given to tetraplegic with complete spinal cord transection above the level of sympathetic outflow also suggests a central site of hypotensive action.

Peripheral Action

These are mediated by inhibition of nor – epinephrine release from the peripheral pre-junctional nerve endings and by decreasing plasma concentration of nor-epinephrine.

Coronary Circulation

The direct effect of α-2 agonist on coronary vasculature is vasoconstriction. However, this is offset by the generalised reduction in sympathetic outflow.

Central Nervous System

Clonidine has got a sedative and anxiolytic action. The sedative effect of clonidine may be due to decreased tonic activity of the locus ceruleus which modulates the stimuli arriving in the central nervous system. It has got a potent spinal and supraspinal analgesic action. Clonidine has got opioid sparing effect and it reduces the anaesthetic requirements, reduces the MAC of halothane and isoflurane.

Respiratory System

Clonidine has minimal bronchodilating and respiratory depressant activity.

Endocrine System

Clonidine suppresses insulin secretion, decreases utilisation of glucose by tissues and may cause hyperglycemia. It inhibits the secretion of renin.

Gastrointestinal System

Clonidine decreases salivary flow. It prevents intestinal ion & water secretion in the large bowel.

Uses:

1. Pre-anesthetic medication

Clonidine in dose 3-5 mcg/kg orally 60-120 mins prior to induction given as a premedicant provides sedation, anxiolysis, antisialagogue effect, attenuates the hemodyanamic responses to largyngoscopy and intubation, decreases the intra operative lability of blood pressure, heart rate and decreases post anesthetic shivering.

2. Spinal & Epidural Analgesia

Preservative free clonidine injected epidurally (2-10mcg/kg) or in to subarachnoid space (0.3 – 1mcg/ kg) produces dose dependant analgesia. It acts on the substantia gelatinosa of the spinal cord, inhibits substance `p' release and nociceptive neuron firing produced by noxious stimuli.

3. Prolonging the effects of Reginal Anaesthesiao

When added to local anaesthetic solution prolongs the brachial plexus block and caudal analgesia.

4. Treatment of Post-anesthetic shivering.

Injection clonidine 75µg given intravenously inhibits or stops shivering mechanism by inhibition of central thermoregulatory control.

5. Diagnosis of Pheochromocytoma

Lack of suppression of plasma nor-epinephrine to less than 500 picogram / ml, 3 hours after a oral dose of 0.3 mg clonidine suggests Pheochromocytoma.

6. Treatment of Hypertension

It is not used as a first line antihypertensive

7. Induced hypotension

Clonidine is a useful adjunct in inducing deliberate hypotension.

Adverse Effects

Clonidine can cause bradycardia, hypotension, sedation and dry mouth occur in 50% of cases. It may cause dryness of nose and eyes. It may sometimes cause parotid swelling and pain. Less common side effects like sleep disturbances with vivid dreams or nightmares restlessness, depression and impotence may occur in some patients.

Clonidine withdrawal phenomena

Abrupt discontinuation of clonidine results in headache, apprehension, tremors abdominal pain, sweating, tachycardia hypertension. It occurs usually 18-24 hours after stopping the drug. It occurs because of increased sympathetic discharge resulting in increased plasma and urine catecholamine concentration. It is dose related, occurring rarely in patients taking a daily dose of clonidine 0.3mg or less and more frequently upon discontinuation of higher doses of > 1.2mg/day.

Drug Interactions

1) Diuretics potentiate hypotension caused by clonidine
2) Tricyclic antidepressants inhibit the antihypertensive effect of clonidine by a unknown mechanism.

Overdose

It results in depression of sensorium, transient hypertension followed by hypotension and bradycardia. It may cause respiratory depression and miosis resembling opioid overdose. Treatment is ventilatory support and circulatory support with crystalloids, colloids ionotropic support.

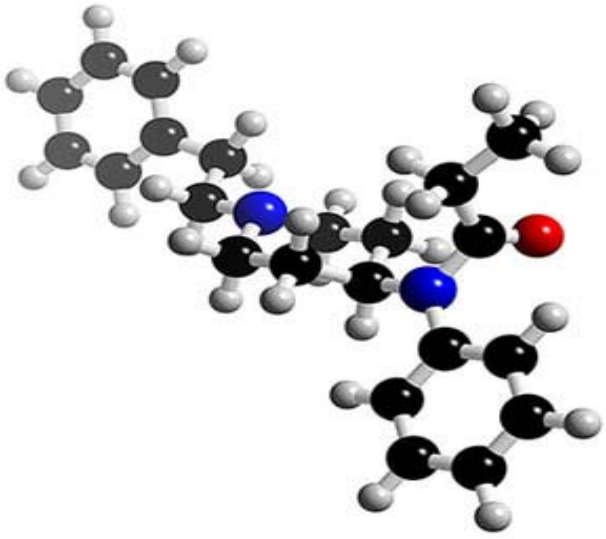
Fentanyl :

It is a synthetic opioid.

It is a phenylpiperidine derivative structurally related to pethidine.

It is a μ receptor agonist 75 – 125 times more potent than morphine, but has a shorter duration of action.

Structure:



Preparations:

Parenteral forms - preservative free 50μg/ml

Oral transmucosal fentanyl

Transdermal patch

Routes of administration:

Oral, intravenous, intramuscular, intrathecal, epidural, transdermal

Pharmacokinetics:

Property	**Value**
Pka	8.4
% of unionised at PH 7.4	<10
% bound to plasma protein	84
t½ μ	1-2 mins
Volume of distribution	0.5 – 1.0L/kg
Clearance	10-20mL/kg/min
Hepatic extraction ratio	0.8 – 1.0
Effect site equilibration time	6.4 min.

It is metabolized in liver, by N-demethylation to norfentanyl, hydroxyl propionyl fentanyl, and hydroxyl propionyl norfentanyl. The demethylated products have less pharmacologic activity, and is excreted unchanged in urine. Its short duration of action is due to its rapid

redistribution to fat and skeletal muscles .The lungs also serves as an inactive storage site with 75 % undergoing first pass pulmonary uptake.

Pharmacodynamic effects:

Neurophysiologic effects:

Analgesia – Mainly nociceptive pain but not neuropathic. Its analgesic action is both spinally as well as supraspinally mediated no matter in which route it is administered. Supraspinally it hyperpolarizes the second order neurons there by inhibiting ascending transmission of pain impulses. Spinally the mechanism is it decreases excitatory neurotransmitters like substance-p from the primary sensory neurons The opioid receptors are concentrated in the laminae-2 of the substantia gelatinosa. It decreases the MAC of inhalational agents. There will be no loss of consciousness except in high doses. Fentanyl produces chest wall rigidity. It also produces pruritis in face.

Cardiovascular system:

It decreases the heart rate and minimal decrease in cardiac output and blood pressure but relatively more hemodynamically stable than morphine as it does not release histamine.No effect on myocardial contraction . It decreases baroreceptor reflex in infants.

Respiratory system:

It is a respiratory depressant by acting on the medullary respiratory centre.depresses tracheal mucociliary outflow, and also depresses somatic and autonomic responses to intubation. It decreases hypoxic ventilatoty drive as well as carbon-dioxide stimulant effect. Its respiratory depressant effects can be effectively reversed by naloxone.

Endocrine system:

It decreases stress response by modulating nociception in the neuraxis. It also inhibits pituitary adrenal axis.

GIT:

Nausea and vomiting and it also delays gastric emptying time. It also produces biliary colic in conscious patients.

Renal:

It produces urinary retention by augmenting detrusor muscle tone and increasing vesical sphincter tone.

Placenta:

No placental barrier for opioids. The feto-maternal ratio is 0.57.

REVIEW OF LITERATURE

1. Mary Samuel MD, B.S.Sethi MD, Deepak et al in their study on the efficacy of low dose clonidine as an adjuvant to Bupivacaine in spinal anesthesia published in Indian Journal of anesthesia 2007;51(5), they have added Clonidine 1µg/kg with 12.5 mg of hyperbaric bupivacaine and concluded that Clonidine has a significant effect in extending the duration of sensory and motor blockade in spinal anesthesia. They have experienced hemodynamic variability and a good sedation level in Clonidine group.

2. I.Dobrydnjov, K.Axelson, S.E.Thorn, P.Mathiesan et al, in their study on Clonidine combined with small dose bupivacaine during spinal anesthesia for inguinal hernioraphy. A randomized double-blinded study published in Anesthesia Analgesia, May, 2003, vol.96. They have given 15 mg of Clonidine with 6 mg of hyperbaric bupivacaine

   Increases the spread of analgesia, prolongs the time to first analgesic request and decreases postoperative pain.

3. Stephen strebel MD, Jurg A. Gurzeler MD, Markus Schneider, Armin Aeschbach, Christopher H.Kindler in their study on small dose intrathecal Clonidine and isobaric bupivacaine for orthopedic surgery A dose response study published in Anesthesia Analgesia, 2004, October, vol.99. They have given three doses of Clonidine to

three groups 37.5 µg, 75 µg, 150 µg. there was significant prolongation in spinal anesthesia in a dose dependant manner and hemodynamic stability in all the groups.

4. F.Bonnet MD, A.Diallo MD, M.Saada MD, M.Belon MD, M.Guilbaud, O.Boico, in their study on prevention of tourniquet pain by isobaric Bupivacaine with Clonidine published in British Journal of Anesthesia 1998, 63, have added 150 µg of Clonidine with 15mg of 0.5% bupivacaine. They have given that "presence of Clonidine significantly prolonged the duration of sensory and motor block. Hypotension and bradycardia were not worsened by Clonidine".

5. Dr.B.N.Biswas, Dr.A.Rudra, Dr.B.k.Bose, Dr.S.Nath, Dr.S.chakrabarty, Dr.S.Bhattacharjee in their study on intrathecal fentanyl with hyperbaric bupivacaine improves analgesia during caesarean delivery and in early post-operative period, IJA 2002;46(6). They have added 12.5 µg of fentanyl with 10 mg of hyperbaric bupivacaine and concluded that fentanyl increases the duration of effective analgesia and had pruritis in 15 % of patients.

6. Kristina S.kuusnienni MD,Kalevi K.Pihlajamaki MD, Mikko T.Pitkanen MD, Hans Y.Helenius MSc, Olli A. Kirvela MD, in their study on The Use of Bupivacaine and Fentanyl for Spinal Anesthesia for Urologic Surgery published in Anesthesia Analgesia, December,

2000(91) have used 25 µg of fentanyl to 10 mg of bupivacaine and concluded prolongation of spinal anesthesia and improved quality of spinal anesthesia.

7. Ben-David, Bruce M.D.; Frankel, Roman M.D.; Arzumonov, Tatianna M.D.; Marchevsky, Yuri M.D.; Volpin, Gershon M.D.†In their study on Minidose Bupivacaine-Fentanyl Spinal Anesthesia for Surgical Repair of Hip Fracture in the Aged published in Anesthesiology: January 2000 - Volume 92 - Issue 1 they used 4mg of bupivacaine with 20 µg of fentanyl had a good anesthesia compared to using bupivacaine 10mg alone without any incidence of hypotension.

8. D.Fernandez-Galinski, Rue, V Morell, C Castells, M M Puig in their study on Spinal anesthesia with bupivacaine and fentanyl in geriatric patients published in Anaesthesia Analgesia September 1996(83) . They have added 25 µg of fentanyl to 12.5 mg of bupivacaine and there was a significant delay in the fentanyl group patients for request of further analgesics.

9. S. Y. Kim, J. E. Cho, J. Y. Hong, B. N. Koo, J. M. Kim and H. K. Kil Comparison of intrathecal fentanyl and sufentanil in low-dose dilute bupivacaine spinal anaesthesia for transurethral prostatectomy; British Journal of Anaesthesia 103 (5): 750–4 (2009), They have

conclude that the quality of spinal anesthesia with good hemodynamic stability prevailed when fentanyl or sufentanyl was added.

STUDY DESIGN

Prospective randomised control study

Ethical committee approval was obtained.

Pre – operative assessment done for all cases

Informed consent obtained from all patients

Inclusion criteria:

ASA PS – 1 & 2 patients

Both male and female patients

Age within 20 and 40 years

Patients who have given consent

Elective surgeries

Exclusion criteria:

Contraindication for spinal anesthesia

ASA PS 3, 4 & 5 patients

Patients who have not given consent

Age more than 40 years and less than 20 years

Drugs used:

- 0.5 % Hyperbaric Bupivaccaine
- Preservative free Fentanyl
- Preservative free Clonidine
- 0.9 % Normal Saline

Groups:

A – 15 mg of 0.5% bupivacaine (H) + 0.5ml of Normal Saline

B – 15 mg of 0.5% bupivacaine (H) + 25 µg of Fentanyl

C – 15 mg of 0.5% bupivacaine (H) + 50 µg of clonidine

Corrected to a volume of 0.5ml by adding Normal Saline

Study methodology:

45 Patients were assigned to 3 groups 15 each Randomisedly and after obtaining informed consents from all patients study was done. Preoperative vitals were recorded and all patients were standardly started with 18G Venflon and preloaded with 500ml of Ringer Lactate fluid 15 minutes before the time of spinal anesthesia. No patients were sedated intra operatively. Table was ensured to be horizontal before spinal

anesthesia. Under aseptic precautions spinal anesthesia was given to all patients in right lateral position, with 25G Quincke-Babcocks spinal needle, and in L3-4 space. Hypotension was defined as less than 20% from the basal mean arterial pressure and treated with ephedrine & intravenous fluids and bradycardia less than 60 and treated with atropine.

Monitors:

Noninvasive blood pressure for every five minutes in the first hour and every ten minutes thereafter, Continuous five lead Electrocardiogram, And pulse-oximeter.

Clinical parameters that were observed:

Maximum sensory level blocked (Until grade 3)

Time to achieve maximum sensory level

Sensory Regression time to L1 (Until grade 0)

Onset of grade 4 motor block

Regression time to grade 1 motor block

Sedation score

Assessment of sensory blockade:

Hollman's Scale

Grade 1 Normal sensation of pin prick

Grade 2 Pin prick felt as sharp pointed but weaker compared with the same area in other side.

Grade 3 Pin prick felt as touch with blunt object

Grade 4 No perception of pin prick

Assessment of sensory loss to pain was done by using 24 gauge intramuscular needle until the patient had grade 3 Sensory block.

Assessment of Motor Blockade:

Bromage score:

Grade	Criteria	Degree of Block
I	Free movement of legs and feet	(0%)
II	Just able to flex knees with free movement of feet	(33%)
III	Unable to flex knees, but with free movement of feet	(66%)
IV	Unable to move legs or feet	(100%)

Assessment of Sedation Level :

Ramsey Sedation Score:

1 - Anxious or agitated or restless

2 – Cooperative, oriented

3 – Responds only to commands but awake

4 – Asleep and brisk response to commands

5 – Asleep and sluggish response to commands

6 – No response to auditory stimulus

STATISTICAL ANALYSIS

Demographic details:

Age distribution

S.No.	Age Group in years	Group A	Group B	Group C
1.	20-25	4	3	3
2.	25-30	3	5	2
3.	30-35	2	4	4
4.	35-40	6	3	6

ANOVA

	Sig.
Between Groups Within Groups	.681

Here the significance value is >0.05. Implies there is no much statistical differences in the age distribution in all three groups.

Height

					95% Confidence Interval for Mean	
	N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound
1	15	165.60	6.243	1.612	162.14	169.06
2	15	165.20	6.213	1.604	161.76	168.64
3	15	164.67	5.367	1.386	161.69	167.64

ANOVA

	Sig.
Between Groups Within Groups	.912

The average height distribution in all three groups were around 165cm with not of much variation in the standard deviation. Here also the significance value is >0.05. Implies there is no much statistical differences in the height distribution in all three groups.

Weight

					95% Confidence Interval for Mean	
	N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound
1	15	70.53	7.549	1.949	66.35	74.71
2	15	69.07	5.934	1.532	65.78	72.35
3	15	70.33	8.191	2.115	65.80	74.87

ANOVA

	Sig.
Between Groups	.837
Within Groups	

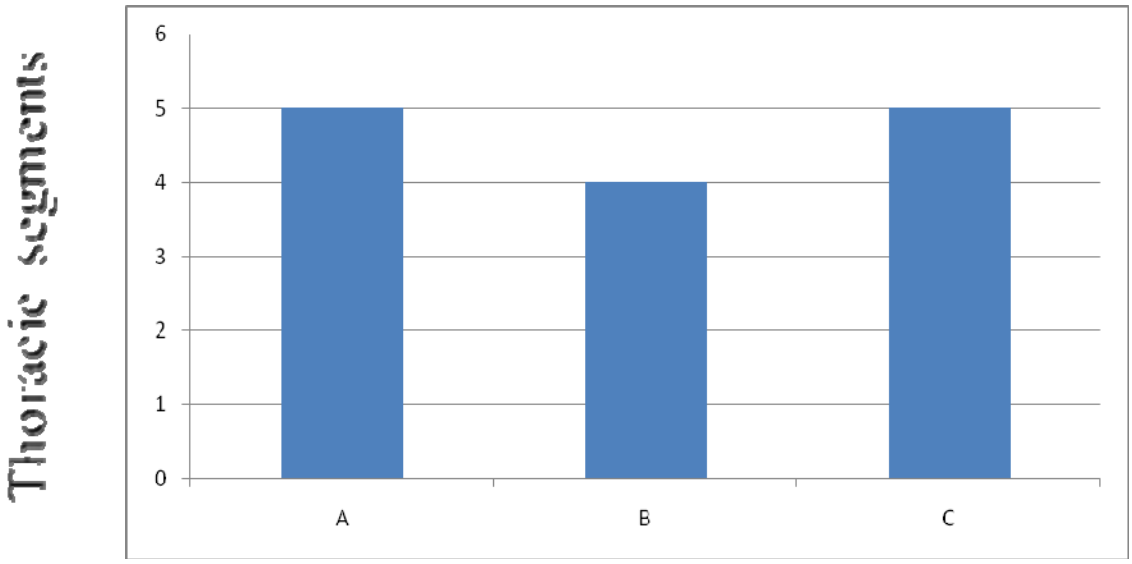
Since the study is a randomized study the demographic 'p' values were all insignificant. All these parameters age ,height and weight were all evenly distributed in all three groups.

Clinical parameters:

Maximum Sensory Level Blocked

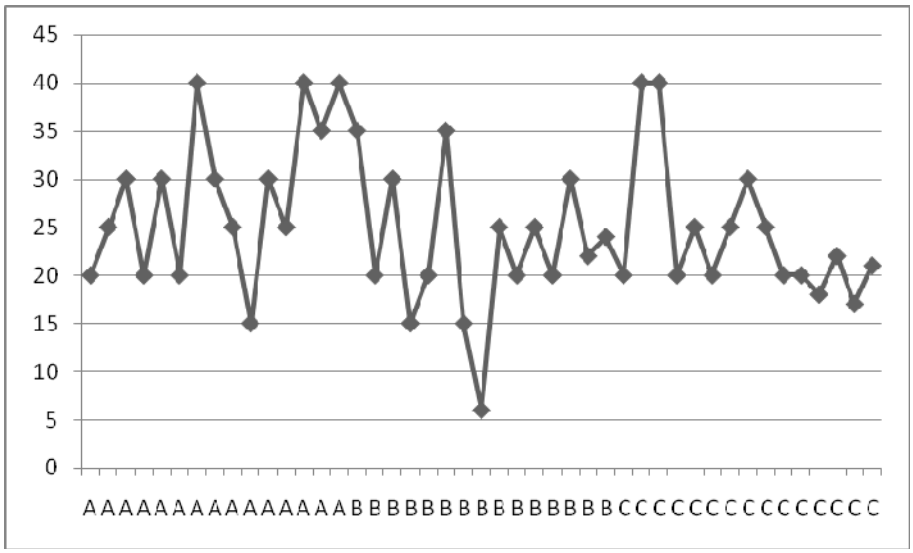
					95% Confidence Interval for Mean	
	N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound
1	15	5	1.424	.368	4.41	5.99
2	15	4	.884	.228	4.44	5.42
3	15	5.00	1.254	.324	4.31	5.69

	Sig.
Between Groups	.821
Within Groups	
Total	



Time to achieve maximum sensory level blocked:

					95% Confidence Interval for Mean	
	N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound
1	15	28.33	7.943	2.051	23.93	32.73
2	15	22.80	7.785	2.010	18.49	27.11
3	15	24.20	7.213	1.862	20.21	28.19



X – Groups.

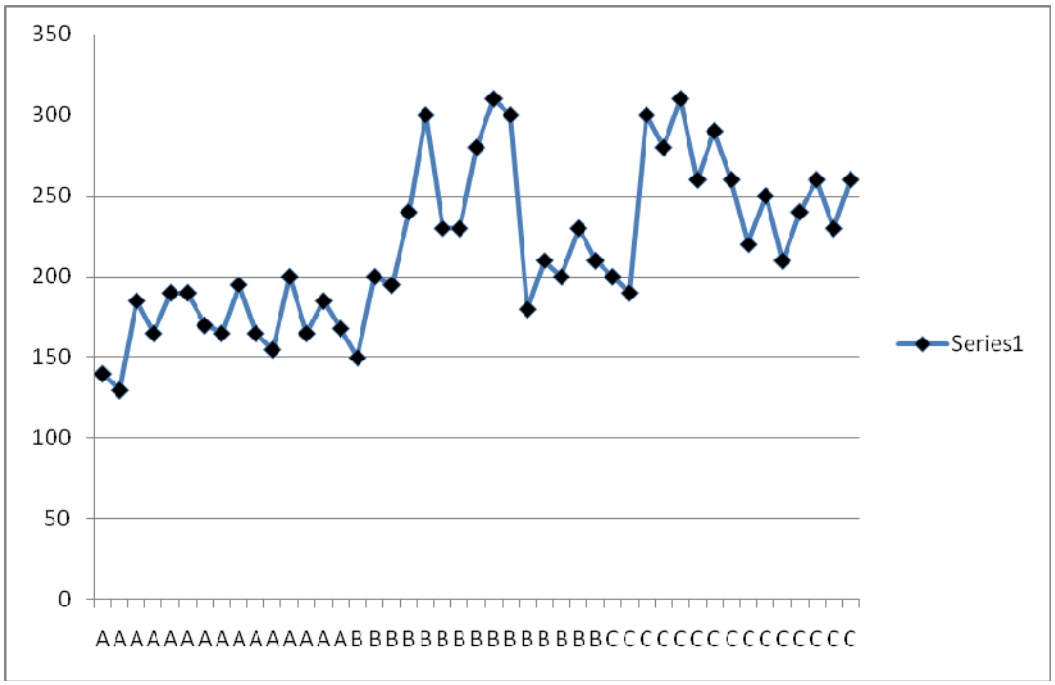
Y- Time.

p – value by ANOVA was .133 which shows that statistically it is insignificant but seeing the mean values the time to achieve this is short with group B.

Sensory Regression to L1 :

					95% Confidence Interval for Mean	
	N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound
1	15	171.20	19.969	5.156	160.14	182.26
2	15	231.00	47.442	12.249	204.73	257.27
3	15	250.67	35.950	9.282	230.76	270.57

.



p- value by ANOVA was 0 hence post hoc test was done to determine the intergroup significance level

POST HOC TEST

(I) GROUP	(J) GROUP	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
1	2	-59.800*	13.236	.000	-86.51	-33.09
	3	-79.467*	13.236	.000	-106.18	-52.76
2	1	59.800*	13.236	.000	33.09	86.51
	3	-19.667	13.236	.145	-46.38	7.04
3	1	79.467*	13.236	.000	52.76	106.18
	2	19.667	13.236	.145	-7.04	46.38

The mean difference is significant at the 0.05 level.

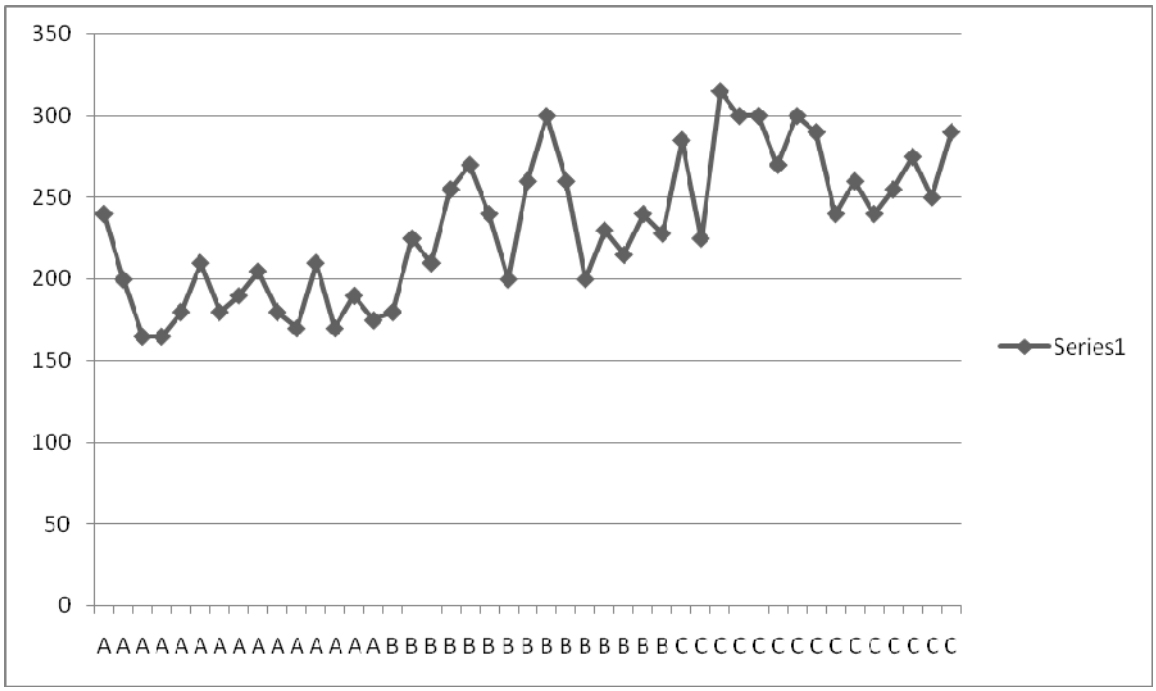
Here the p-value between Group B & C is 0.145 which is insignificant but between Group A and other groups it is 0

and so statistically significant. So sensory regression to L1 is

increased in B & C.

ONSET OF GRADE 4 MOTOR BLOCK IN MINUTES

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
1	15	10.00	2.619	.676	8.55	11.45
2	15	6.87	4.138	1.068	4.58	9.16
3	15	5.73	1.870	.483	4.70	6.77



The p – value by ANOVA was 0.001 and hence post hoc test was done to determine the intergroup significance level.

POST HOC TEST

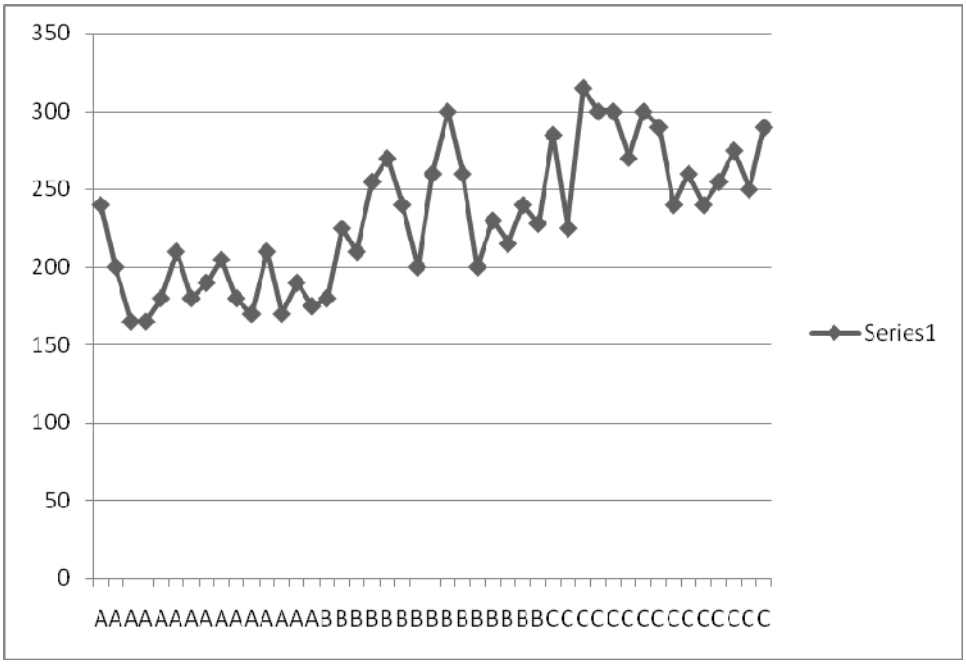
(I) GROUP	(J) GROUP	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
1	2	3.133*	1.105	.007	.90	5.36
	3	4.267*	1.105	.000	2.04	6.50
2	1	-3.133*	1.105	.007	-5.36	-.90
	3	1.133	1.105	.311	-1.10	3.36
3	1	-4.267*	1.105	.000	-6.50	-2.04
	2	-1.133	1.105	.311	-3.36	1.10

*. The mean difference is significant at the 0.05 level.

This test implies that the p-value between group B & C is 0.311 which is insignificant while group A compared to group B & C is significant.

Regression To Grade 1 Motor Block In Minutes

					95% Confidence Interval for Mean	
	N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound
1	15	188.67	20.999	5.422	177.04	200.30
2	15	234.20	31.412	8.111	216.80	251.60
3	15	273.00	26.979	6.966	258.06	287.94



X –Group
Y- Time (minutes)

The p- value by ANOVA is 0 and hence significant , so post hoc test Was done to determine intergroup significance .

POST HOC TEST

(I) GROUP	(J) GROUP	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
1	2	-45.533*	9.788	.000	-65.29	-25.78
	3	-84.333*	9.788	.000	-104.09	-64.58
2	1	45.533*	9.788	.000	25.78	65.29
	3	-38.800*	9.788	.000	-58.55	-19.05
3	1	84.333*	9.788	.000	64.58	104.09
	2	38.800*	9.788	.000	19.05	58.55

*. The mean difference is significant at the 0.05 level.

Here all the p values were significant and hence each and every group is also statistically proved to be significant and distinct.

Hemodynamic Variables:

BP at 15 min		N	Mean	Std. Deviation	Std. Error
SYSTOLIC	1	15	102.93	10.872	2.807
	2	15	98.00	6.928	1.789
	3	15	91.47	8.052	2.079
DIASTOLIC	1	15	58.00	7.635	1.971
	2	15	55.60	10.802	2.789
	3	15	47.20	6.625	1.710

BP AT 60 MIN					
		N	Mean	Std. Deviation	Std. Error
SYSTOLIC	1	15	108.56	10.795	2.787
	2	15	100.20	6.201	1.601
	3	15	96.33	5.150	1.330
DIASTOLIC	1	15	68.20	7.183	1.855
	2	15	65.00	7.241	1.870
	3	15	52.40	4.212	1.088

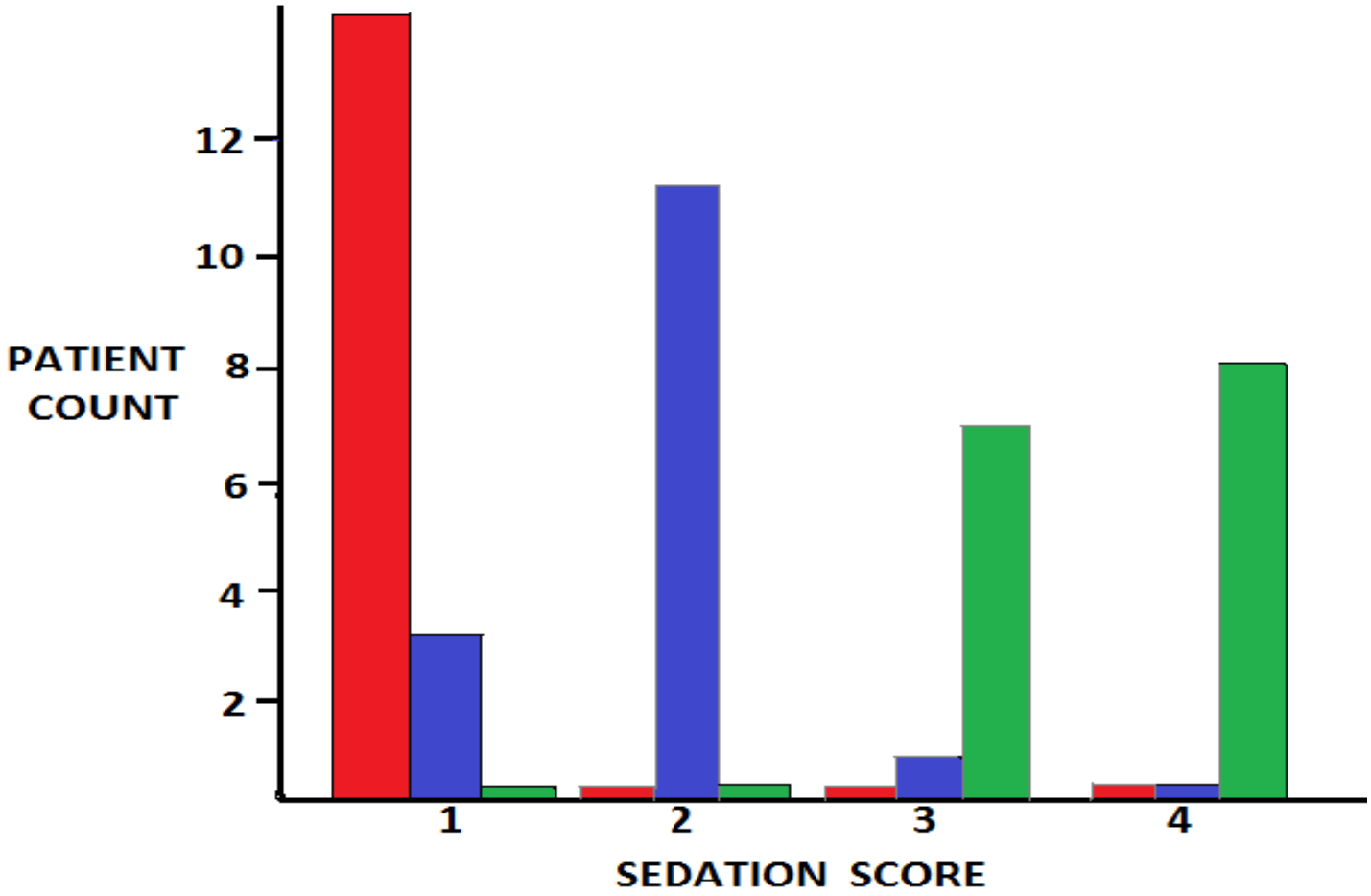
HEART RATE		N	Mean	Std. Deviation	Std. Error
At 15 min.	1	15	77.07	9.823	2.536
	2	15	73.13	8.123	2.097
	3	15	64.47	7.210	1.862
At 30 min.	1	15	89.07	9.354	2.415
	2	15	73.87	11.438	2.953
	3	15	70.80	8.833	2.281

HEART RATE		N	Mean	Std. Deviation	Std. Error
At 60 min.	1	15	85.01	12.823	2.536
	2	15	84.13	9.123	2.097
	3	15	71.36	5.210	1.862

RAMSEY SEDATION SCORE

Score	GROUP		
	1	2	3
1	15	3	0
2		11	0
3		1	7
4		0	8
Total Count	15	15	15

Here the p value is 0 and hence the test is significant.


PATIENT COUNT
12
10
8
6
4
2
0
1
2
3
4
SEDATION SCORE

RESULTS

- Onset of grade 4 motor block was shorter in group 2 and 3 with an average of around 5 to 7 minutes.
- Regression to grade 1 motor block is significantly prolonged In group 3 and 2 but group 3 is longer than 2.
- Sensory regression to L1 is prolonged in the additive groups but not significantly prolonged while comparing these two groups.
- Maximum height of dermatomal block was not significant in all these groups and the time to achieve it was also not significant.
- Hemodynamic variables were relatively lower in clonidine group.
- All the patients in clonidine group were well sedated.

DISCUSSION

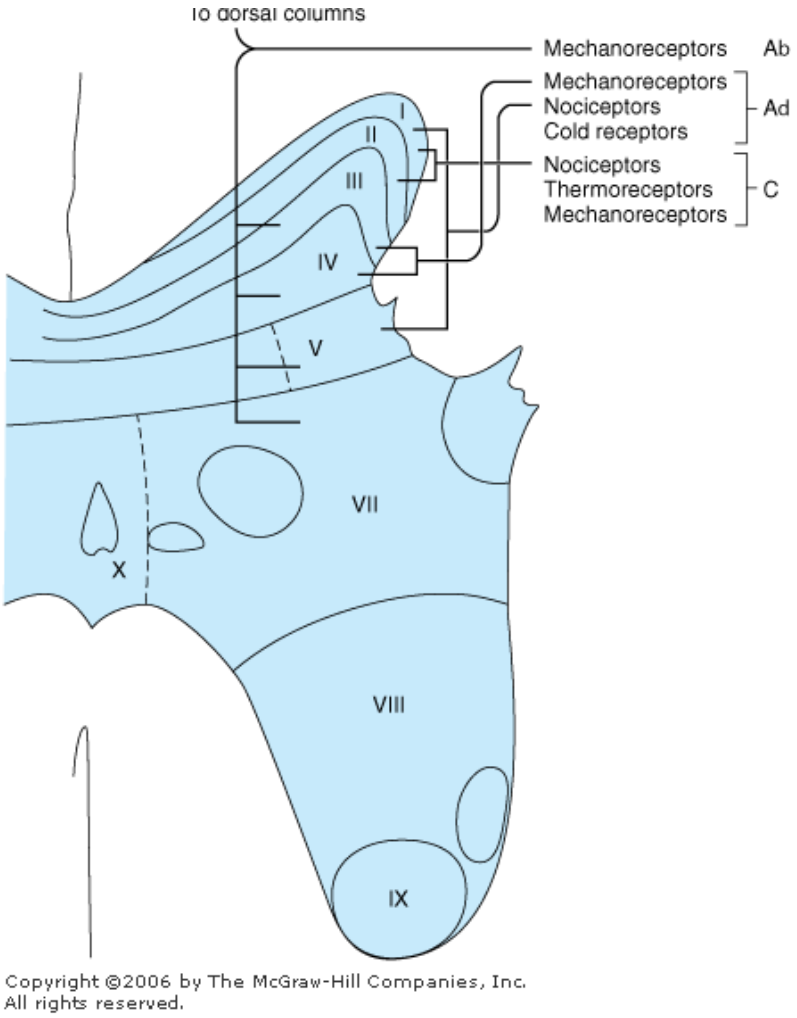
The study results show significant prolongation of sensory and motor blockade with clonidine. The average duration of motor blockade was 273 minutes which is ahead by 40 minutes compared to the average value with fentanyl and 85 minutes ahead with control group. The average duration of sensory blockade was 250.67 minutes in clonidine group while in fentanyl group it is 231 minutes and in control group 171 minutes. Even though there is a minimal blood pressure variability with clonidine which have been managed with ephedrine and intravenous fluids there was no significant bradycardia.

With clonidine it has an additional advantage of sedating thepatient compared with fentanyl and it also lacks other side effects and respiratory depression that an intrathecal opioid will have. The sedative property of clonidine can be observed in any route the drug is given intrathecal, epidural, and nerve blocks.

Clonidine a selective partial agonist for α-2 adrenoreceptors centrally and peripherally. The analgesic effect following its intrathecal administration is mediated spinally through activation of post-synaptic α-2 adrenoreceptors in the substantia gelatinosa of spinal cord and it works by blocking the conduction of C and Aδ fibres. The sedative property of the drug is due to its agonist action in α-2A receptors in the locus ceruleus of

the brain stem. Even though both the drugs fentanyl and clonidine produced an intense sub-arachnoid block clonidine is statistically significant in prolonging the blockade. Van der werff and C.J.Kalkmann in their study in using clonidine with hyperbaric bupivaccaine for caesarean section had a conclusion of prolonging sub-arachnoid blockade with no relevant maternal and neonatal side effects. In another study by Stephen strebel et al compared various doses of clonidine as spinal additive to hyperbaric bupivaccaine 37.5, 75, and 150 microgram and the results were prolongation of spinal anesthesia in a dose dependant manner but the sedation score was not different. The hemodynamic variables had more variability in higher doses.

Fentanyl a lipophilic opioid acts directly on the μ receptor In the laminae 2 of the substantia gelatinosa of spinal cord where by it provides pre-synaptic inhibition of the neurotransmitter release although minimal post-synaptic inhibition also occurs by hyperpolarizing the second order neurons. The side effects of intrathecal opioids which is lacked by the α-2 agonists are pruritis in the face, neck and upper thorax, nausea and vomiting, urinary retention, depression of ventilation which is not usually observed in such low doses of fentanyl and also due to its lipophilicity.



Rexed's spinal cord laminae. Note the termination of the different types of primary afferent neurons.

To summarize clonidine and fentanyl prolongs the duration of spinal anesthesia but clonidine has a longer duration than fentanyl and there is beneficial property of sedation with clonidine and it also lacks the adverse property of intrathecal opioids.

CONCLUSION

CLONIDINE when used as a spinal additive to hyperbaric bupivacaine in healthy adults it qualitatively prolongs the duration of both sensory and motor block of spinal anesthesia with insignificant hemodynamic variation which can be easily managed. Whereas fentanyl also prolongs the spinal Anesthesia but not to the extent of Clonidine, without any significant hemodynamic changes. Clonidine has an additional advantage of arousable sedation.

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PROFORMA

Group : 1 2 3

Name :

Age : (20 - 40 years only)

Sex :

I.P. No. :

Unit :

Diagnosis :

Surgical procedure :

Pre- operative Examination:

Routine H/O

Height

Weight

Pulse rate

B.P.

R.R.

C.V.S.

R.S

Investigations:

Hb%

Blood sugar

Serum Urea

Serum Creatinine

B.T.

C.T.

ASA – PS Grade: (1&2 only)

Procedure:

Date & Time of SAB:

Maximum sensory level blocked:

Time to achieve max.sensory block:

Motor block - Bromage score

Grade	Criteria	Degree of Block
I	Free movement of legs and feet	Nil (0%)
II	Just able to flex knees with free movement of feet	Partial (33%)
III	Unable to flex knees, but with free movement of feet	Almost Complete (66%)
IV	Unable to move legs or feet	Complete (100%)

Onset of Grade 4 block:

Sensory regression to L1 time:

Regression time to Grade 1 block:

Duration of surgery:

Sedation score:

Intra-0perative vitals:

Time in Min.	5	10	20	30	40	50	60	70	80	90	100	110	120	140
P.R														
B.P														
SpO2%														

Intravenous fluid replacement:

Blood no. of units used:

Post-operative vitals:

Time in hrs.	1	2	3	4	5	6
P.R						
B.P						
Spo2%						

CONTROL GROUP

S.No.	Heart rate 5 min.	Heart rate 10 min.	Heart rate 15 min.	Heart rate 30 min.	Heart rate 60 min.	HR at 90 min	Bp at 5 min	BP at 10 min	BP at 15 min	BP at 30 min	BP at 60 min	BP at 90 min	Ramsey Sedation Score	Ephedrine (mg)	Atropine (mg)
1	89	80	78	88	90	92	100/60	110/68	130/70	110/50	132/70	130/70	1	0	0
2	88	90	90	98	95	100	130/80	100/60	140/80	104/76	110/80	120/80	1	6	0
3	85	87	88	90	100	96	110/70	112/64	120/80	100/60	110/80	110/76	1	0	0
4	70	75	67	80	85	82	90/50	110/68	120/70	90/60	120/70	120/72	1	12	0
5	74	79	77	79	80	78	110/68	120/78	130/90	120/70	120/80	128/78	1	0	0
6	60	68	60	110	99	95	90/60	100/60	100/70	80/40	102/70	110/70	1	24	0.6
7	80	82	84	90	98	95	100/60	120/68	120/70	100/60	120/70	120/74	1	0	0
8	74	76	72	80	85	84	92/68	120/72	120/70	102/60	110/70	110/70	1	6	0
9	85	90	89	100	94	92	98/50	110/48	120/60	90/50	124/76	125/78	1	6	0
10	78	84	80	90	96	91	140/90	140/80	140/80	110/60	132/80	132/80	1	0	0
11	64	68	65	76	84	82	100/56	120/70	150/80	100/60	120/70	120/70	1	6	0
12	80	77	78	88	90	86	140/90	130/70	140/80	112/58	110/60	110/60	1	0	0
13	80	84	90	97	106	98	130/60	100/66	140/70	118/60	130/60	130/66	1	6	0
14	71	76	70	90	88	88	100/70	90/66	110/80	100/50	110/60	110/70	1	6	0
15	66	70	68	80	97	95	130/82	120/80	134/80	110/70	110/70	120/70	1	0	0

S.No.	Heart rate 5 min.	Heart rate 10 min.	Heart rate 15 min.	Heart rate 30 min.	Heart rate 60 min.	HR at 90 min	Bp at 5 min	BP at 10 min	BP at 15 min	BP at 30 min	BP at 60 min	BP at 90 min	Ramsey Sedation Score	Ephedrine (mg)	Atropine (mg)
1	89	80	78	88	90	92	100/60	110/68	130/70	110/50	132/70	130/70	1	0	0
2	88	90	90	98	95	100	130/80	100/60	140/80	104/76	110/80	120/80	1	6	0
3	85	87	88	90	100	96	110/70	112/64	120/80	100/60	110/80	110/76	1	0	0
4	70	75	67	80	85	82	90/50	110/68	120/70	90/60	120/70	120/72	1	12	0
5	74	79	77	79	80	78	110/68	120/78	130/90	120/70	120/80	128/78	1	0	0
6	60	68	60	110	99	95	90/60	100/60	100/70	80/40	102/70	110/70	1	24	0.6
7	80	82	84	90	98	95	100/60	120/68	120/70	100/60	120/70	120/74	1	0	0
8	74	76	72	80	85	84	92/68	120/72	120/70	102/60	110/70	110/70	1	6	0
9	85	90	89	100	94	92	98/50	110/48	120/60	90/50	124/76	125/78	1	6	0
10	78	84	80	90	96	91	140/90	140/80	140/80	110/60	132/80	132/80	1	0	0
11	64	68	65	76	84	82	100/56	120/70	150/80	100/60	120/70	120/70	1	6	0
12	80	77	78	88	90	86	140/90	130/70	140/80	112/58	110/60	110/60	1	0	0
13	80	84	90	97	106	98	130/60	100/66	140/70	118/60	130/60	130/66	1	6	0
14	71	76	70	90	88	88	100/70	90/66	110/80	100/50	110/60	110/70	1	6	0
15	66	70	68	80	97	95	130/82	120/80	134/80	110/70	110/70	120/70	1	0	0

FENTANYL GROUP

S.No	Name/I.P.No.	Age/Sex	Procedure	ASA status	Height	Weight	Level of SAB	Maximum Sensory Level Blocked	Time to achieve maximum sensory level	Onset of Grade 4 motor block	Sensory regression to L1	Regression to Grade 1 motor block
1	Elumalai 921498	22/M	Right IMIL nailing	1	170	65	L3-4	T6	35	5	150	180
2	Raghu 924475	37/M	Left Femur DHS fix	1	168	70	L3-4	T5	20	4	200	225
3	Ganesamoorthy 924929	38/M	Right tibia Ilizarov ring application	2	158	75	L3-4	T6	30	20	195	210
4	Murugan 924469	35/M	Left Ilizarov ring revision	1	160	70	L3-4	T4	15	4	240	255
5	Gunasekar 922767	30/M	Left tibia IMIL nailing	2	171	59	L3-4	T5	20	5	300	270
6	Duraibabu 924304	40/M	Right tibia ORIF and plating	1	169	67	L3-4	T5	35	7	230	240
7	Solomon 919749	24/M	Left tibia IMIL nailing	1	174	82	L3-4	T5	15	10	230	200
8	Rhuthrakumar 917926	26/M	Right Ilizarov ring revision	1	159	70	L3-4	T6	6	3	280	260
9	Dinesh 913249	32/M	Left Ilizarov ring application	2	157	65	L3-4	T5	25	6	310	300
10	Shanthakumari 940319	30/F	Right femur IMIL nailing	1	164	70	L3-4	T5	20	5	300	260
11	Pooja 925789	23/F	Right tibia IMIL and Left patellaTBW	2	166	74	L3-4	T6	25	10	180	200
12	Elumalai 931890	33/M	Left femurDHS fix.	1	170	74	L3-4	T4	20	7	210	230
13	Ramesh 915682	29/M	Left IMIL nailing	1	156	60	L3-4	T3	30	5	200	215
14	Manimegalai 918273	32/F	Right femoral condylar screw fix.	1	167	65	L3-4	T4	22	6	230	240

15	Senthamarai 937281	30/F	Right tibia IMIL nailing	2	175	70	L3-4	T5	24	6	210	228

S.No	Heart rate at 5 min	Heart rate at 10 min	Heart rate 15 min.	Heart rate 30 min.	Heart rate 60 min.	Heart rate 90 min	BP 5 min	BP 10 mkin	BP at 15 min	BP at 30 min	BP at 60 min	BP at 90 min.	Ramsey Sedation Score	Ephedrine (mg)	Atropine (mg)
1	60	76	70	84	80	82	110/66	100/60	110/70	100/50	116/70	120/72	2	0	0.6
2	84	86	88	92	90	92	100/50	110/74	122/80	112/76	120/84	120/80	2	0	0
3	60	68	66	80	75	77	100/58	110/80	120/80	90/60	136/70	140/72	1	6	0.6
4	63	72	70	75	74	76	94/68	100/68	118/70	90/50	128/70	130/70	3	6	0
5	68	70	65	70	79	86	110/76	120/78	130/80	102/70	130/80	128/68	2	0	0
6	64	70	67	75	80	82	112/78	110/76	124/80	100/60	124/76	128/80	1	0	0
7	70	75	74	97	100	90	110/78	90/66	126/80	92/50	120/80	120/80	2	6	0
8	60	86	90	104	99	98	100/62	100/65	114/76	90/40	110/72	112/76	2	24	1.2
9	58	88	87	100	98	96	100/60	110/58	112/60	96/50	110/60	110/68	2	6	0.6
10	66	69	64	70	78	80	110/68	100/66	110/70	100/66	110/70	110/70	2	0	0
11	80	78	74	90	88	84	108/70	110/68	120/70	100/60	120/70	120/70	2	0	0
12	80	82	78	89	90	90	90/58	110/78	120/80	110/66	112/68	120/70	2	6	0
13	72	69	64	70	77	78	100/70	108/70	110/70	90/40	110/70	112/70	1	12	1.2
14	74	78	70	75	80	82	120/69	100/66	124/78	100/50	100/70	100/78	2	12	0

15	75	78	78	88	98	95	110/70	100/60	112/80	98/46	110/60	112/64	2	6	0

CLONIDINE GROUP

S.No	Name/I.P.No.	Age /Sex	Procedure	ASA status	Height	Weight	Level of SAB	Maximum Sensory Level Blocked	Time to achieve maximum sensory level	Onset of Grade 4 motor block	Sensory regression to L1	Regression to Grade 1 motor block
1	Thanikachalam 914570	27/M	Right femur IMIL nailing	1	169	65	L3-4	T7	20	5	200	285
2	Kuppan 922553	40/M	Left Tibia Ilizarov ring fix.	1	156	80	L3-4	T6	40	5	190	225
3	Ravi 926492	34/M	Left femur DHS fix.	2	173	69	L3-4	T5	40	3	300	315
4	Manimaran 922619	34/M	Right tibia IMIL nailing	1	168	75	L3-4	T7	20	4	280	300
5	Annamalai 930614	40/M	Left tbia Ilizarov ring revision	1	172	84	L3-4	T5	25	6	310	300
6	Vishal 925616	38/M	Right Tibia IMIL nailing	2	165	80	L3-4	T4	20	7	260	270
7	Pooammal 924310	35/F	Left Tibia IMIL nailing	1	157	75	L3-4	T5	25	5	290	300
8	Priya 933646	24/F	Right Ilizarov ring fix.	1	162	70	L3-4	T5	30	8	260	290
9	Jagan 923414	21/M	Left tibia IMIL nailing	1	168	74	L3-4	T4	25	6	220	240
10	Divya 936610	28/F	Left femur IMIL nailing	1	163	58	L3-4	T2	20	10	250	260
11	Manoharan 937879	38/M	Left tibia IMIL nailing	2	158	55	L3-4	T5	20	4	210	245
12	Girija 937910	40/F	Left Ilizarov ring revision	1	160	62	L3-4	T6	18	5	240	255
13	Flora 915674	36/F	Right femur DHS fix.	1	164	66	L3-4	T5	22	6	260	275
14	Jeeva 9118903	32/M	Left Tibia IMIL nailing	1	170	72	L3-4	T4	17	4	230	250
15	Somesh 934562	25/M	Left tibia ORIF and plating	1	165	70	L3-4	T5	21	8	260	290

S.No	Heart rate 5 min	Heart rate 10 min	Heart rate 15 min.	Heart rate 30 min.	Heart rate 60 min.	Heart rate 90 min	BP at 5 min	BP at 10 min	BP at 15 min	BP at 30 min	BP at 60 min	BP at 90 min.	Ramsey Sedation Score	Ephedrine (mg)	Atropine (mg)
1	60	60	62	64	66	66	90/50	94/56	102/50	96/46	100/60	110/62	3	12	1.2
2	54	52	50	60	58	59	90/62	80/46	96/60	70/40	112/70	112/68	4	30	1.2
3	62	64	64	68	70	72	90/50	90/43	114/62	80/50	118/60	120/60	4	24	0
4	68	68	70	87	75	74	90/60	100/58	110/60	100/50	116/72	120/72	3	6	0
5	78	72	73	90	80	82	94/58	92/62	124/66	100/60	124/66	120/60	3	6	0
6	66	66	68	70	74	70	98/56	100/60	112/60	90/50	110/70	110/68	4	12	0
7	67	69	65	73	76	72	86/42	98/50	110/64	92/44	110/60	110/60	4	18	0
8	68	65	68	69	70	70	90/48	100/66	112/60	90/40	124/80	112/78	4	18	0
9	72	72	74	78	70	73	90/50	90/48	92/66	90/60	120/70	120/78	3	6	0
10	68	68	70	70	65	68	100/58	100/60	110/60	100/50	110/60	110/70	3	6	0
11	59	57	58	60	64	62	100/58	110/66	120/70	90/50	120/70	118/70	4	24	0.6
12	67	69	66	70	72	70	110/70	100/68	110/70	90/46	110/58	110/68	4	12	0
13	62	68	69	75	71	70	100/68	120/76	136/80	96/40	124/60	120/60	4	18	0
14	54	54	52	63	59	60	90/60	100/60	124/78	98/42	112/60	114/70	3	24	1.2
15	54	55	58	65	62	64	92/68	100/64	120/78	90/40	100/58	110/60	3	18	1.2