A COMPARATIVE STUDY ON TWO DOSES OF CLONIDINE ADDED TO HYPERBARIC BUPIVACAINE IN SPINAL ANAESTHESIA

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M.D. ANAESTHESIOLOGY—BRANCH X

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CERTIFICATE

This is to certify that this dissertation titled **"A COMPARATIVE STUDY ON TWO DOSES OF CLONIDINE ADDED TO HYPERBARIC BUPIVACAINE IN SPINAL ANAESTHESIA"** has been prepared by **Dr. K.B.Kayalvizhi** under my supervision in the Department of Anaesthesiology ,Chengalpattu Medical College & Hospital, Chengalpattu during the academic period 2007-2010 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(Branch X-MD Anaesthesiology) and her dissertation is a bonafide work.

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DECLARATION

I, **Dr. K.B.Kayalvizhi**, solemnly declare that the dissertation **"A COMPARATIVE STUDY ON TWO DOSES OF CLONIDINE ADDED TO HYPERBARIC BUPIVACAINE IN SPINAL ANAESTHESIA"** is a bonafide work done by me in the Department of Anaesthesiology, Chengalpattu Medical College & Hospital, Chengalpattu, after getting approval from the Ethical committee ,under the able guidance of Prof.R.S.VIJAYALAKSHMI, M.D, D.A, Professor and HOD, Department of Anaesthesiology, Chengalpattu Medical College, Chengalpattu.

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CONTENTS

AIM OF THE STUDY

To compare the effect of addition of two doses of clonidine (40µg and 60µg) to 0.5% hyperbaric bupivacaine 2.75 ml, intrathecally for sub umbilical surgeries .

To evaluate :

Time to onset of sensory and motor block

Duration of sensory and motor block

Duration of effective post operative analgesia

Side effects

INTRODUCTION

Spinal anaesthesia is commonly used for abdominal, perineal, gynaecological and lower limb operations. It offers excellent anaesthesia and fewer side effects than General anaesthesia .It is easy to perform and provides faster onset and effective sensory and motor block. Bupivacaine produces long lasting spinal anaesthesia without Transient neurological symptoms. Recently there has been an interest in using additives to intra thecal local anasesthetics to decrease the dose of local anaesthetics and also provide effective post operative analgesia. Various studies have been conducted to evaluate the addition of clonidine to hyperbaric bupivacaine.

The alpha 2 adrenergic agonist clonidine has a variety of actions including the ability to potentiate the effect of local anesthetics .It prolongs sensory blockade and also reduces requirement of post operative analgesics.

This study was designed to evaluate the addition of two doses of clonidine(40 µg and 60µg) added to hyperbaric bupivacaine (0.5%) 2.75ml in spinal anaesthesia for sub umbilical surgeries.

SPINAL ANAESTHESIA AND ADJUVANTS

Spinal (subarachnoid /intrathecal) anaesthesia is a form of central neuraxial block in which a temporary interruption of nerve transmission is achieved following injection of local anaesthetic and / adjuvant solutions into subarachnoid space.

Subarachnoid block is one of the most commonly performed methods of regional anaesthesia.

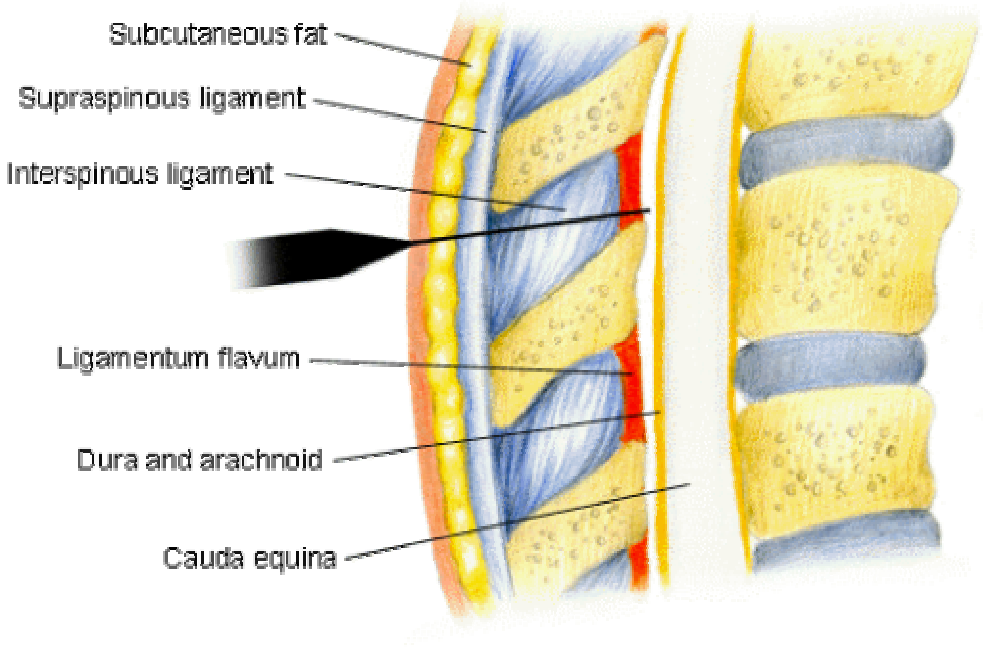
ANATOMY

The vertebral canal extends from foramen magnum to the sacral hiatus. Its boundaries are the dorsal spine, pedicles and laminae of successive vertebrae(7 cervical ,12 thoracic , 5 lumbar and 5 sacral) .The vertebrae are held together by overlapping ligaments namely, anterior & posterior longitudinal ligaments,ligamentum flavum, interspinous ligament ,supraspinous ligament and the intervertebral discs.

The spinal cord a direct continuation of medulla oblongata begins at the upper border of atlas and terminates distally in the conus medullaris. The distal termination , because of the differential growth rates between the bony vertebral canal and spinal cord varies from L3 in the infant to lower border of L1 in the adult.

Surrounding the spinal cord in the bony vertebral column are 3 membranes (from within to periphery) : the pia mater , arachnoid mater and the dura mater.The piamater is a highly vascular membrane that closely invests the spinal cord.The arachnoid mater is a delicate non vascular membrane closely attached to outermost dura mater.

STRUCTURES TO BE PIERCED FOR SUBARACHNOID BLOCK



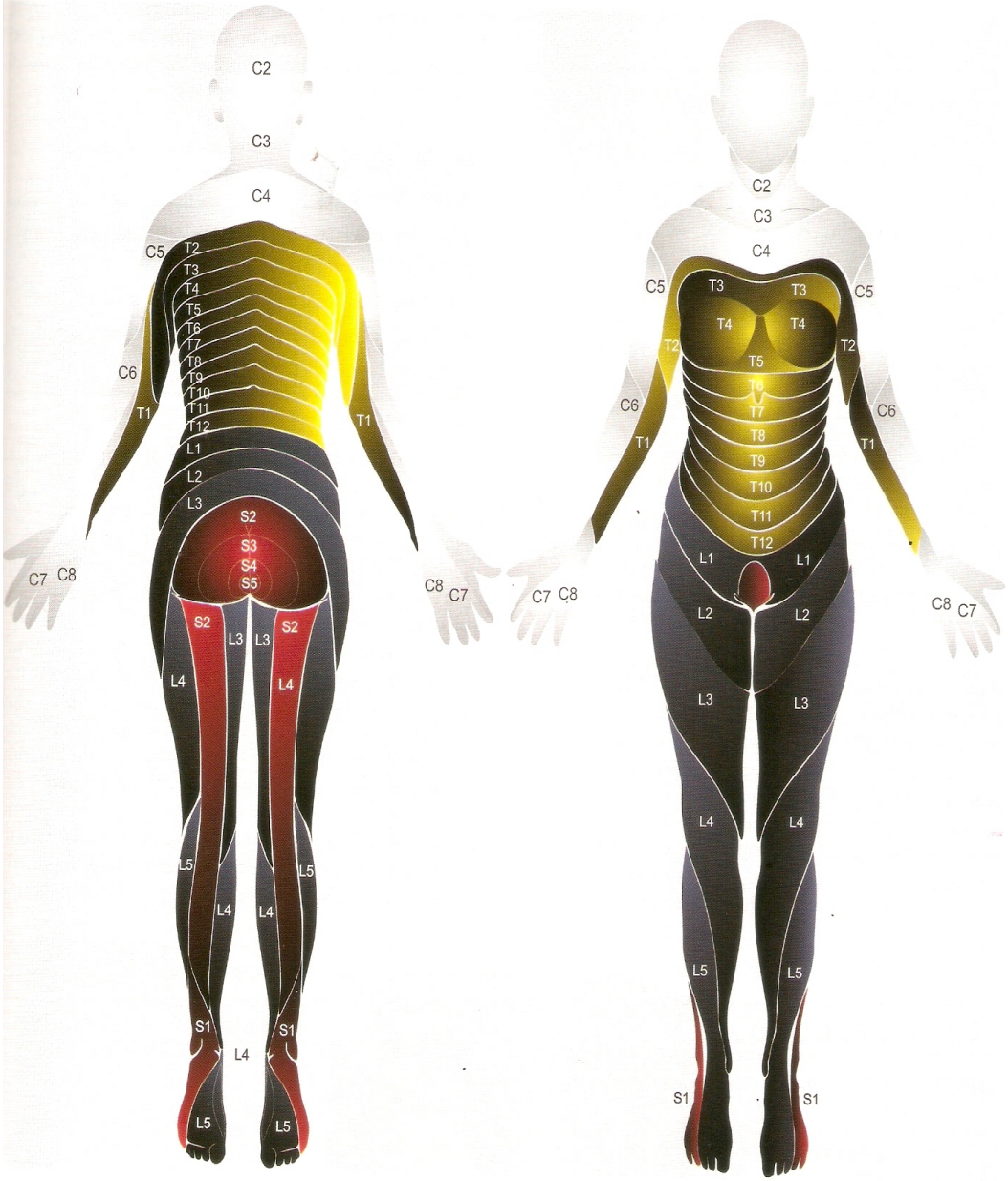
Between the 2 innermost membranes is the subarachnoid space . In this space , cerebrospinal fluid (CSF) ,spinal nerves , blood vessels that supply the spinal cord and dentate ligaments are present. Although the spinal cord ends at lower border of L1 in adults , the subarachnoid space continues upto S2.The outermost membrane in the spinal cord is the longitudinally organised fibroelastic membrane ,the dura mater. This

layer is the direct extension of cranial dura mater and extends as spinal duramater from foramen magnum to S2, where filum terminale blends with periosteum of subdural space which contains small amounts of serous fluid to allow dura and arachnoid to move over each other.

Surrounding the dura mater is the epidural space which extends from foramen magnum to sacral hiatus.Posterior to the epidural space is ligamentum flavum.Immediately posterior to the ligamentum flavum is interspinous ligament.Extending from external occipital protruberance to the coccyx ,posterior to this structure is the supraspinous ligament.

Lumbar puncture is routinely performed below L2 vertebrae down to the L5 –S1 interspace to avoid damage to the spinal cord which ends at lower border of L1 vertebra in adults.

DIAGRAM OF DERMATOMES



PHYSIOLOGY OF SUBARACHNOID BLOCK

CEREBROSPINAL FLUID

The cerebrospinal fluid is an ultrafiltrate of blood plasma which is in hydrostatic and osmotic equilibrium.It is clear , colourless fluid found in spinal and cranial subarachnoid space and in ventricles of brain . The average volume in adults ranges from 120 to 150ml of which 35ml in the ventricles , 25ml is in the cerebral subarachnoid space and 75ml is in the spinal subarachnoid space.It is secreted by choroid plexus at a rate of 0.3 -0.4ml/minute.

PHYSICAL CHARACTERISTICS OF CEREBROSPINAL FLIUD

pH	**7.4**
Specific gravity	1.007
Density	1.0003
Baricity	1.000
Pressure	8-12 mmHg / 70- 80 cmH20
Cells	3- 5 /cu.mm
Proteins	20mg/dl
Glucose	45 -80 mg/dl

The cerebrospinal fluid plays an important role in spinal anaesthesia as a media for dispersion of the local anaesthetic drug to the spinal nerve. An important factor determining the spread of drugs in subarachnoid space is specific gravity of the injected solution compared with that of CSF.

MECHANISM OF SPINAL ANAESTHESIA

Injection of local anaesthetics into the spinal CSF allows access to sites of action both within the spinal cord and the peripheral nerve roots. The nerve roots leaving the spinal canal are not covered by epineurium and are readily exposed to the local anaesthetic within CSF. Therefore afferent impulses leaving via ventral nerve roots are blocked during spinal anaesthesia . Spinal local anaesthetics block sodium channels and electrical conduction in spinal nerve roots. Local anaesthetics can exert sodium channel block within the dorsal and ventral horns inhibiting the generation and propagation of electrical activity.

The order in which nerve fibres are blocked in spinal anaesthesia is preganglionic sympathetic B fibres followed by temperature fibres (cold before warmth) , fibres carrying pin prick sensation , touch, deep pressure and finally proprioception. Recovery is in the reverse order.

The major factors determining the level of blockade after subarachnoid block are the baricity of the local anaesthetic solution, the position of the patient before and after injection and dose of the anaesthetic injected.

FATE OF LOCAL ANAESTHETICS IN SUBARACHNOID SPACE

Following injection of local anesthetic solution into subarachnoid space ,its concentration falls rapidly. The initial steep fall is due to mixing with CSF and subsequent absorption into nerve roots and spinal cord.

Depending on the type of drug used , it is metabolized in plasma by pseudocholinesterase or in the liver. The addition of a vasopressor to the local anesthetic will retard the absorption of the drug and thus increase the duration of anaesthesia.

Indications for subarachnoid block

Spinal anaesthesia can be administered whenever a surgical procedure can be done with a sensory level of anaesthesia that does not produce adverse patient outcome which includes,

- Lower abdominal surgeries
- Lower limb surgeries
- Urological procedures

- Obstetric & gynaecological procedures
- Perineal and rectal surgeries

Contra indications for subarachnoid block

An absolute contraindication for subarachnoid block is patient refusal .

Other contraindications are :

- Local sepsis
- Uncorrected coagulopathy
- Uncontrolled blood loss / shock
- Fixed cardiac output states
- Documented allergy to local anaestehtics
- Raised intracranial pressure
- Neurological disease
- Major spine deformities /previous surgery on the spine
- Severe cardiac disease.

SPINAL ANAESTHESIA TECHNIQUE

The first step in successful application of spinal anaesthesia is proper patient selection. This is accomplished by pre- anaesthetic evaluation of the patient through history, physical examination ,laboratory data and communication with patient and surgical staff about details of the procedure. Reliable intravenous access through a

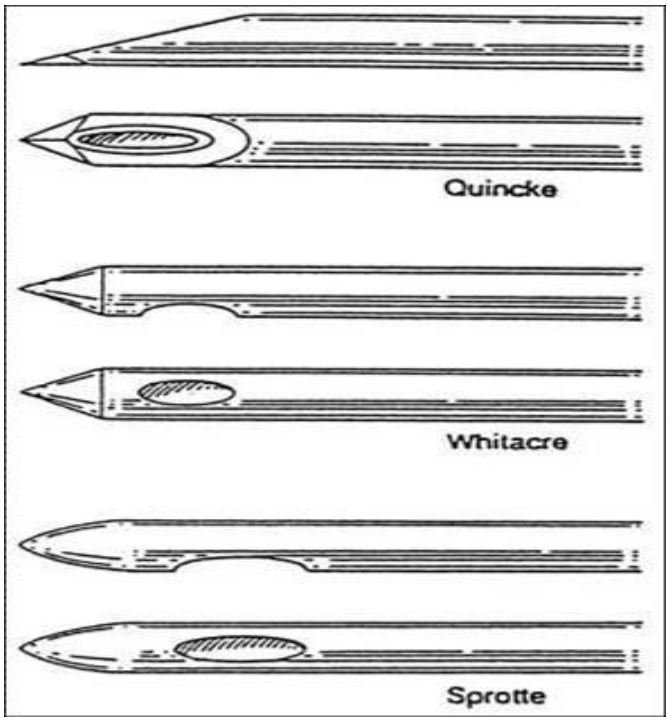
large bore intravenous canula(18G /16G) is mandatory. Preloading limits the hypotension that may result from sympathetic block. The recommended standards for airway management and emergency drugs are kept in readiness.

PROCEDURE

PREPARATION

Preparation of equipment and drugs is essential for performing a subarachnoid block. The choice of drug is based on duration of block desired, the surgical procedure and patient variables. Spinal needles of various diameters with various types of points are available.Spinal needles fall into two main categories: those that cut the dura and those that are designed to separate the dural fibres.The former includes the Quincke –Babcock needle and the latter include the Greene , Whitacre and Sprotte needles. In order to keep the incidence of post dural puncture headache to a minimum , small bore needles with a rounded non –cutting bevel are preferred.

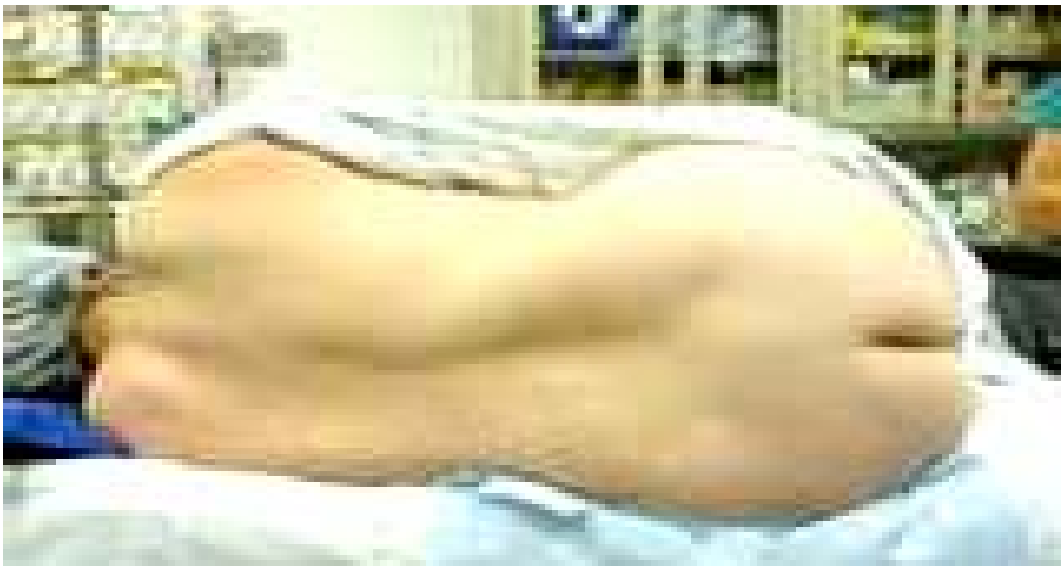
SPINAL NEEDLES



Position

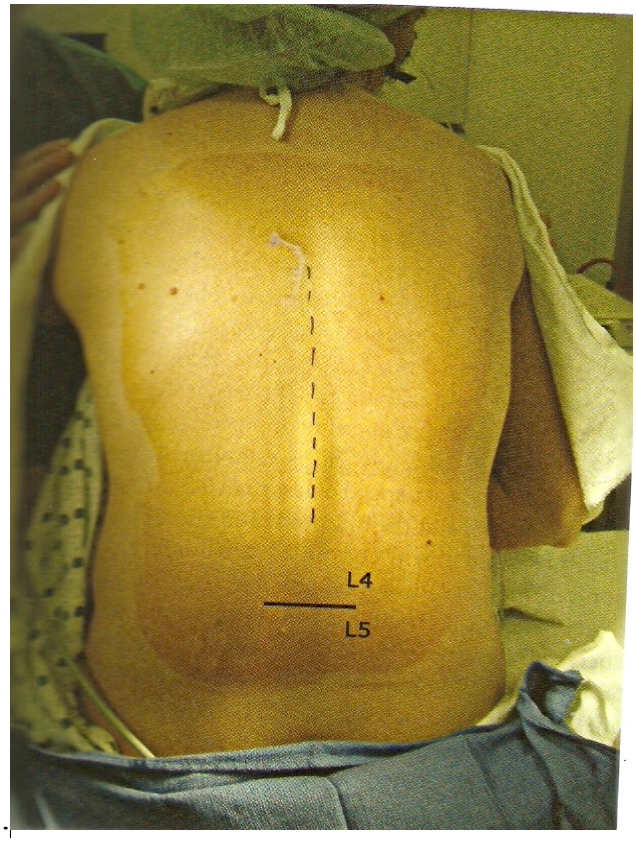
The choice of position of the patient for performing the subarachnoid block depends on a number of factors- the proposed surgery being the most important .

LATERAL DECUBITUS POSITION



In the lateral decubitus position, the patient is placed with back parallel to the edge of the operating table nearest the anaesthesiologist with thigh flexed upon the abdomen and neck flexed

SITTING POSITION



The sitting position is chosen when low lumbar and sacral levels of anaesthesia are adequate for the surgical procedure or when obesity or scoliosis makes identification of midline anatomy difficult in lateral decubitus position or when orthopaedic problems of hip and knee exist.

Projection & Puncture

The spinal puncture can be performed either by a midline or a paramedian approach ,usually at the L2 –L3, L3-L4, L4-L5 interspaces. The procedure is carried out under strict aseptic conditions.The patients

back is prepared with an antiseptic solution and sterile drapes are applied.A line from the highest point of iliac crest paases through either spinous process of L4 or the L4-L5 interspace. The midline approach with the patient in sitting position /right lateral decubitus position is used in our study. Depending on the interspace and approach selected, subcutaneous skin wheal is raised over the intended puncture site with local anaesthetic solution. The needle is inserted in the middle of the interspace with bevel parallel to the longitudinal dural fibres. After traversing the skin and subcutaneous tissue , the needle is advanced in a slightly cephalad direction with the long axis of the vertebral column. The stylet is removed and appearance of cerebrospinal fliud at the hub of the needle confirms correct position of the needle tip.Stylet is reinserted to prevent excess leakage of CSF.The hub of the needle is firmly held between the thumb and index finger of the anaesthesiologist's non dominant hand and back of hand held against patients back to steady the needle , while syringe containing anaesthetic solution is firmly attached to the needle.

After confirming free flow of spinal fluid by aspiration, the anaesthetic solution is injected. The patient is placed in supine position. Cardiovascular and respiratory functions are monitored. Analgesia is

checked by loss of sensation to pin prick.Motor block assessed by modified Bromage score .

In the recent past various additives have been added to local anaesthetic solution – vasopressors, alpha 2 adrenergic agonists and acetyl choline esterase inhibitors. These produce prolongation of analgesia after subarachnoid block and reduce the dose requirement of local anaesthetics.

COMPLICATIONS OF SUB ARACHNOID BLOCK

Immediate

1. Hypotension
2. Bradycardia
3. Toxicity due to intravascular injection
4. Allergy to local anaesthetic
5. Hypoventilation (brainstem hypoxia)

Late

1. Post dural puncture headache
2. Retention of urine
3. Backache
4. Meningitis
5. Transient lesions of cauda equina
6. Sixth nerve palsy
7. Anterior spinal artery syndrome

PHARMACOLOGY OF BUPIVACAINE

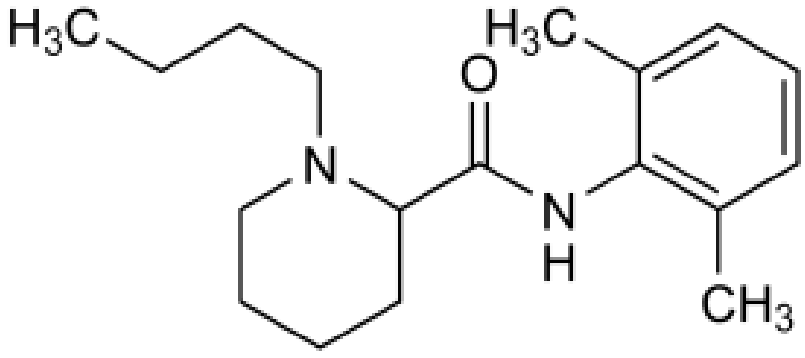
Bupivacaine is an amide local anaesthetic synthesised by A.F.Ekenstam in 1957 and brought into clinical use in 1963.

It is produced for clinical use in a racemic mixture containing equal proportions of the 'S' and 'R' enantiomers. It is supplied for clinical use as hydrochloride salt.

Chemical structure

Description : + 1- butyl –N- (2,6-dimethylphenyl)-2-piperidine Decarboxamide Hydrochloride monohydrate.

BUPIVACANE HYDROCHLORIDE



Physico-chemical profile

Molecular weight (base)	-	288
pKa	-	8.1

Solubility In

alcohol	-	1 in 8
water	-	1 in 25
octanol/water partition coefficient	-	high
lipid solubility	-	28
plasma protein binding	-	95%

Mechanism of action

Bupivacaine exerts its effect by inhibition of sodium channels. It acts to block conduction in nerves by decreasing or preventing the large transient increases in permeability of cell membrane to sodium ions that follows depolarisation of the membrane. Bupivacaine also reduces the permeability of the resting nerve membrane to potassium as well as sodium ions.

Pharmacodynamics

Bupivacaine by virtue of its pharmacological effects has a stabilizing action on all excitable membranes. The clinical profile of nerve blockade produced by bupivacaine differs from that of lignocaine.

It is 4 times more potent than lignocaine, but the onset of action is slower. The duration of action is considerably longer. The sensory block produced by bupivacaine tends to be more marked than the motor block.

Pharmacokinetics

Bupivacaine is rapidly absorbed from the site of injection. The rate of rise in plasma bupivacaine concentration and the peak plasma concentrations depend on the route of administration. There is also some interindividual variation and peak systemic concentrations may occur 5 and 30 mins after administration. The addition of vasoconstrictor delays absorption and results in lower plasma concentrations of bupivacaine.

Pharmacokinetic profile [6]

Volume of distribution at stedy state (Vdss)	72 litres
Clearance	0.47L/min
t1/2α	2.7 min
t1/2β	28min
t1/2 γ	3.5hrs

Metabolism

Possible pathways for metabolism of bupivacaine include aromatic hydroxylation , N dealkylation , amide hydrolysis and conjugation. Only the N–dealkylated metabolic N –desmethyl bupivacaine has been

measured in blood and urine after epidural and spinal administration. The degradation of bupivacaine takes place in the liver. Renal disease is unlikely to alter the kinetics of bupivacaine to any great extent.Less than 10% of the drug is excerted unchanged in urine[6].

Clinical applications :

- Infiltration anaesthesia
- Peripheral nerve blocks
- Central neuraxial blocks (intrathecal, epidural, caudal)

Contraindications

- Paracervical block (in obstetrics)
- Known hypersensitivity to amide local anaesthetics
- Intra venous regional anaesthesia (IVRA)

Preparations available:

0.25% ,0.5% solutions in 10ml and 20ml vials

5mg/ml (0.5%)bupivacaine and 80mg dextrose in 4ml ampoules for intrathecal injection (baricity 1.0207)

Recommended safe dose

Concentration used	Max permitted dose
0.125% - 0.5 %	3mg/kg body weight
0.75%(not to be used in obstetric epidurals)	Max over 4 hrs - 150mg Max during 24hrs -4000mg
0.5% plain/hyperbaric(intrathecal use)	20mg

Adverse reactions

Adverse reactions are associated with excess plasma levels of the drug which may be due to overdosage, unintentional intravascular injection or slow metabolic degradation.

CNS Reactions

Excitation characterised by restlessness, anxiety, dizziness, tinnitus, blurred vision or tremors possibly proceeding to convulsions, followed by drowsiness unconsciousness and cardiac arrest.

CVS

Part of the blockade that occurs from high plasma concentrations of bupivacaine occurs because of blockade of cardiac sodium channels. Accidental intravenous injection of bupivacaine causes cardiac

dysarrythmias, atrioventricular block, refractory ventricular tachycardia and ventricular fibrillation.pregnancy increases the sensitivity of cardiotoxic effects of bupivacaine.

Bupivacaine binds and inhibits cardiac voltage gated calcium and potassium channels at concentrations greater than those at which binding to sodium channel is maximal.

Unlike other local anaesthetics ,bupivacaine dissociates from blocked sodium channels at a much slower rate , resulting in prolongation of maximal rate of depolarization (Vmax) and creating the potential for re entrant type of ventricular arrhythmias.

Allergic reactions

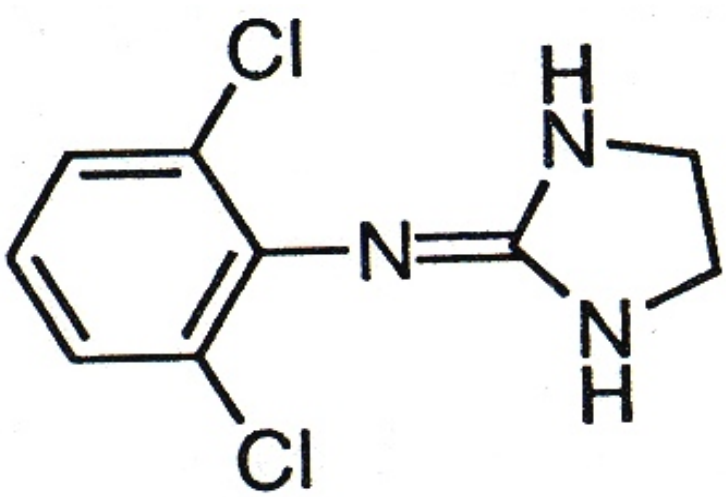
Manifests as urticaria, pruritis,angioneurotic edema etc. Cross sensitivity among members of amide local anaesthetics has been reported.

PHARMACOLOGY OF CLONIDINE HYDROCHLORIDE

Clonidine a imidazoline derivative is a selective partial agonist for alpha 2 adrenergic receptors.It is known to increase sensory and motor block of local anaesthetics.

Its action is mediated spinally through activation of post synaptic alpha 2 receptors in the substantia gelatinosa of spinal cord.

STRUCTURE OF CLONIDINE



Clonidine

Physical chemistry

C9H9N3CI2HCL

2,6 DichloroN-2 imidazolidinyiedlenebenzenamine : hydrochloride

1.	Molecular weight(freebase)	266.6(230.1)
2.	pKa	8.05
3.	Solubility in alcohol	1 in 25
4.	Solubility in water	1 in 13
5.	Octanol/water partition co efficient	3.02

Clonidine hydrochloride is a white crystalline, odourless powder with a bitter taste. It is produced by chemical synthesis.

Pharmacology

Clonidine is a partial agonist at alpha adreno receptors both within the central nervous system and in the periphery. It is more specific for alpha 2 than for alpha 1 with a ratio of affinities at these sites at approximately 300:1.Within the CNS alpha 2 adrenoreceptors are located both presynaptically on terminals of neurons which release a variety of transmitters(nor epinephrine ,epinephrine, serotonin and acetylcholine) and post synaptically on noradrenergic neurons.

Mechanism of clonidine as an adjuvant in central neuraxial blockade

Intrathecal clonidine increases the duration of both sensory and motor block.The mechanism of clonidine induced potentiation of sensory block in spinal anaesthesia is mediated by presynaptic (inhibition of transmitter release) and post synaptic (enhancing hyperpolarisation)

The reason for potentiation of motor block seems to be hyperpolarisation of ventral horn neurons of spinal cord .This is dose related[21].

Clonidine blocks conduction of C and A delta fibres and increases potassium conductance in neurons and also intensifies conduction block of local anaesthetics. Clonidine may cause local vasoconstriction[12].

EFFECTS ON ORGAN SYSTEMS

Cardiovascular System

Oral or intra venous administration of clonidine causes a dose dependent fall in blood pressure and heart rate in both supine and erect position , with the orthostatic response being most prominent

Clonidine affects blood pressure in a complex fashion.In nucleus tractus solitarius and locus ceruleus of brain stem activation of post synaptic alpha 2 adrenoreceptors reduces sympathetic drive.In addition it activates noradrenergic binding sites in lateral reticular nucleus thereby producing hypotension and antiarrythmogenic action.The magnitude of hypotensive effect is greater in hypertensive than in normotensive subjects[12].

The brainstem and peripheral effects of alpha 2 adrenoreceptor stimulation are counter balanced by direct peripheral vasoconstriction from circulating concentrations of clonidine. As a result the dose response for clonidine by neuraxial or systemic administration is U shaped, with peripheral vasoconstriction from circulating drug concentrations at high doses opposing central sympatholysis.

Neuraxial administration of clonidine directly inhibits sympathetic preganglionic neurons in spinal cord. Degree of hypotension is related to spinal level of injection.

The pressor effect of high dose of clonidine is due to peripheral vasoconstriction mediated by stimulation of post synaptic alpha 1 and or alpha 2 adrenoreceptors on vascular smooth muscle[21].

RESPIRATORY SYSTEM

The respiratory depressant effect of clonidine is not remarkable unless massive doses are given.The effect of clonidine is less potent than that of opiate narcotics[23].

CENTRAL NERVOUS SYSTEM[20]

Sedation is one of the most consistent effects mediated by central alpha 2 receptors. The locus ceruleus was shown to be the principal

region responsible for sedative effect. Another characteristic effect of alpha 2 agonists is anxiolysis which is comparable to the response produced by benzodiazepine compounds.

Clonidine has a potent analgesic action that cannot be reversed by naloxone, an opioid antagonist, indicating that clonidine and opioid mediate analgesia through independent recptor mechanism.Clonidine may potentiate the effects of bupivacaine by reducing spinal cord blood flow and prolonging the effective availability of bupivacaine.

There is a 50% decrease in MAC of inhalational anesthetics and decreased anaesthetic requirements of opioids. At doses of 75µg iv, it prevents shivering.clonidine is also effective in suppressing signs and symptoms of withdrawal from opioids ,benzodiazepines and ethanol.

ENDOCRINE

Endocrine and metabolic effects mediated by alpha2 adrenoreceptor stimulation are 1. Increased TSH and GH secretion 2.Decreased ACTH and ADH secretion and 3.Inhibition of glucose stimulated insulin release , but this does not result in severe hyperglycemia in a clinical setting.

GIT

Stimulation by clonidine of peripheral presynaptic alpha2 adrenoreceptors on post ganglionic noradrenergic or cholinergic neurons contributes to reduced salivary flow, intestinal motor activity and gastric acid secretion.

Pharmacokinetics

Oral absorption	100%
Pre systemic metabolism	0- 25%
Elimination half life	20 -25h
Volume of distribution	2L /kg
Plasma protein binding	20 -40%

Clonidine is approximately 60% excreted unchanged in urine. The remaining 40% elimination is by oxidative metabolism predominantly in the liver .There is no evidence that any metabolites possess significant biological activity. Clearance of clonidine is linearly related to dose over 75 – 300mcg. Total plasma clearance is 3ml/kg/min, while renal clearance accounts for 1.8ml/kg. Clearance may be reduced in the presence of abnormal renal functions. Although clonidine may cross the placenta it does not appear to reach concentrations sufficient to affect the fetus.

METABOLISM

Clonidine is approximately cleared by metabolism predominantly in the liver to five inactive metabolites.the predominant pathways are: hydroxylation of the phenyl ring ,and opening up of the imidazoline ring following an initial reductive step with subsequent oxidative cleavage. The hydroxylated metabolites are subjected to secondary conjugation with sulphate or glucoronide prior to urinary excretion.

DOSAGE OF CLONIDINE IN VARIOUS ROUTES

S.No.	Route	Bolus	Cont infusion
1	Oral	4- 5mcg/kg	
2	IM	2mcg/kg	
3	IV	4- 5mcg/kg	
4	Epidural	75- 450mcg	12.5 – 70mcg/hr
5	Intrathecal	30- 225mcg	8 -400 mcg/day

USAGE

1. Antihypertensive agent
2. Anaesthesia -prolongation of action of local anaesthetic after neuraxial administration ,pre- medication and post anaesthetic shivering
3. Opiate withdrawal syndrome
4. Glaucoma (apraclonidine and brimonidine)

5. Migraine prophylaxis
6. Provocative tests of growth hormone secretion, in the investigation of short stature
7. Diagnosis of phaeochromocytoma
8. Psychiatric disorders
9. Menopausal symptoms
10. Chronic diarrhoea.

CONTRAINDICATIONS

Disorders of cardiac impulse generation and conduction like Sino atrial disease (sick sinus syndrome) , Atrioventricular node disease and patients with cardiac pacemakers.

ADVERSE REACTIONS

Common symptomatic effects are sedation (35- 100%) , dry mouth (25 – 90%), bradycardia, constipation and contact dermatitis(transdermal clonidine) .Less common effects include postural hypotension, dizziness, fluid retention (weight gain , oedema), sleep disturbances (insomnia, sleep reversal, nightmares, hallucinations, reduction of REM sleep), impotence ,parotid swelling and depression. Uncommon effects are rash, pruritis, angioedema, hepatitis,

gynecomastia, raynauds phenomenon, thinning of hair, urinary retention and agitation.

Withdrawal syndrome which is characterised by a rapid rise in blood pressure, with marked blood pressure lability, symptoms such as headache, flushing , sweating , insomnia , agitations, emotional lability , tremor .nausea and vomiting presents 18- 72 h after the last dose of clonidine. The syndrome can be prevented by gradual withdrawal of clonidine over days to weeks and , if present controlled by reintroducing clonidine treatment or by inhibiting peripheral sympathetic nervous activity, with alpha and beta adrenoreceptor antagonists.

Disturbance of cardiac impulse generation and conduction in the presence of pre existing SA and AV node disease can lead to symptomatic bradycardia and impairment of atrio ventricular (AV) nodal conduction (wenkebach phenomenon , AV dissociation) which have been occasionally described.

PREPARATIONS

Oral forms

1. Catapres tablets (Boehringer Ingelheim UK) containing clonidine hydrochloride 100mcg, 200mcg or 300mcg.

2. Dixarit tablets (Boehringer Ingelheim ,UK) containing clonidine hydrochloride 25 mcg.

Transdermal form

Catapres TTS delivering clonidine 100mcg , 200mcg , or 300mcg daily for 1 week

Parenteral form

1. Catapres injection (Boehringer Ingelheim, UK) containing clonidine hydrochloride 150mcg/ml ampoules

2. CLONEON (Neon labs ltd, thane) containing clonidine hydrochloride 150 mcg /ml ampoule.

ASSESSMENT OF BLOCKADE AFTER SPINAL ANAESTHESIA

Following subarachnoid block assessment of motor & sensory block is done in the following manner.

SENSORY BLOCK

Sensory block was assessed by loss of sensation to pinprick using 23G sterile needle. The assessment was started immediately after injection and continued every 15 secs till loss of pinprick sensation at L2 level. Onset of sensory block was taken as time from intrathecal injection to loss of pinprick sensation at L2. At 20mins interval after SAB , the dermatomal level of sensory block noted and this was considered as maximum level of sensory block.

MOTOR BLOCK

Motor block was assessed using modified BROMAGE score

Grade 1 : free movement of legs and feet

Grede 2 : just able to flex knees with free movement of feet

Grade 3 : unable to flex knees but with free movement of feet

Grade 4 : unable to move legs and feet

Assessment of motor block was started immediately after the intrathecal injection. It was tested every 15 secs till BROMAGE SCORE of 1 was reached. Onset of motor block was taken as time taken to achieve BROMAGE score of 1 from Subarachnoid block.The degree of motor block after 20mins of injection was noted and this was considered maximum degree of motor block.Thereafter motor block regression was noted and duration of motor block was taken as time from SA injection to return of BROMAGE score to 1

ASSESMENT OF SEDATION AND PAIN :

Sedation was assessed using **Ramsay sedation score** and pain was assessed using **visual analogue scale**.

Level 1 : Anxious And agitated ,or restless or both

Level 2 : Co Operative , oriented and tranquil

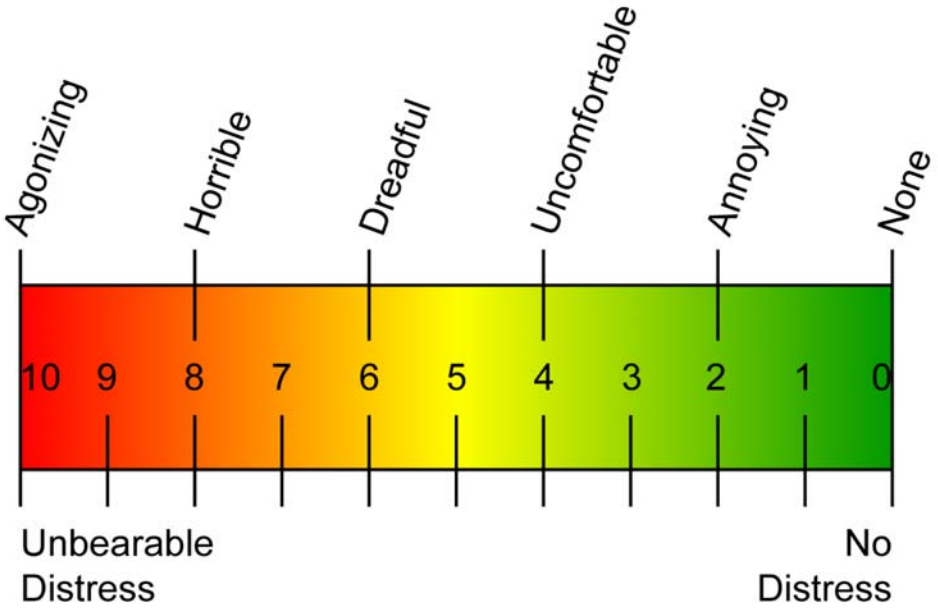
Level 3 : Responds to commands only

Level 4 : Brisk response

Level 5 : Sluggish response

Level 6 : No Response.

Pain was assessed using visual analogue scale.



Task _____

Date _____ *Start* _____ *End* _____

REVIEW OF LITERATURE

Clonidine combined with local anaesthetics in spinal anaesthesia:

van tuiijl et al[34] investigated the effect of addition of clonidine to hyperbaric bupivacaine on post operative morphine consumption after caessarian section .

A group of 106 patients were randomly allocated to receive spinal anaesthesia with either 2.2ml of 0.5%bupivacaine heavy with 0.5ml NS 0.9% total 2.7ml (Gp B) or to receive 2.2ml of 0.5% bupivacaine heavy with clonidine 0.5ml – 75µg diluted in 0.9% NS total of 2.7ml (Gp BC).The time for first analgesic request was 129 mins in the BC gp compared to 55mins in the B gp.In the BC gp 58% had a MAP < 70 mmHg compared to 9% in gp B. Clonidine added to bupivacaine in caessarian section prolongs the duration of analgesia and motor block .It did not result in reduced morphine consumption in the first post operative day.

Wu CI et al[32] studied the effect of adding clonidine to hyperbaric tetracaine spinal anaesthesia in 60 ASA class I - II patients .The subjects were randomly allotted to 4 groups.All patients received tetracaine 10mg in 10% glucose solution 2 ml. Patients in group I received the above medication and were the control group, patients in other group received

tetracaine plus increasing doses of clonidine : 15 µg(gp 2) ,30µg (gp 3) and 45µg(gp 4).The three clonidine groups had significant increase in sensory regression time to L1 level(by 42 ,47 , 60% respectively), and also had significantly increased motor complete recovery time , but the incidence of hypotension and bradycardia was increased in clonidine 45µg group.He concluded that addition of 15µg or 30µg may be useful as a means of increasing the duration of hyperbaric tetracaine spinal anaesthesia.

NIEMI[29] studied the analgesic and circulatory effects of intrathecal clonidine in patients undergoing knee arthroscopy under spinal anaesthesia.Forty ASA I & II patients were randomly divided into 2 group. One group received clonidine 3 µg /kg mixed with 0.5% bupivacaine and the other group an identical saline volume mixed with bupivacaine as above in a double blinded fashion.Oxycodone 0.14mg/kg i.m or ketoprofen 100mg p.o was administered when needed. The duration of sensory analgesia, was longer in clonidine group (mean 215 mins) than in control group (mean 160 mins) ($p<0.05$) . Duration of motor blockade was also longer in clonidine group (mean 161mins) ($p<0.05$).Mean arterial pressure and heart rate were significantly lower in the clonidine group compared to control group.More patients in the

clonidine group were sedated 3 – 6 hrs after the injection ($p<0.05$). Addition of clonidine prolonged the bupivacaine spinal block.

De Negri P et al[10] studied to determine whether intrathecal administration of clonidine can reduce the dose of local anesthetic , and the effects of clonidine on cardiovascular system and on arousal level.In 56 patients scheduled for minor surgical procedure (spermatic vein ligature) under unilateral spinal anesthesia with hyperbaric bupivacaine 1% one half of patients received clonidine 150µg in addition to bupivacaine .Cardiac output ,stroke volume ,ejection fraction were measured by thoracic electric bio impedance method, baseline and until 1 hr after surgery. In clonidine treated group, variations of cardiovascular parameters were observed, In the same group sensory block , motor block were significantly prolonged. A higher sedation level and a significant post operative analgesia were also observed.The addition of clonidine to hyperbaric bupivacaine seems to be particularly useful in unilateral spinal anesthesia, exerting minimal influence on hemodynamic parameters and guaranteeing a satisfactory postoperative analgesia.

Seah ys et al[31] studied the prolongation of analgesic effect of hyperbaric bupivacaine spinal anestehsia with clonidine . 40 AS A class I & II patients scheduled for TURP were randomly classified into 2

groups pof 20 each. In the saline group, 3ml of 0.5% hyperbaric bupivacaine + 1ml NS was given. In the clonidine group, 1ml of (150µg) clonidine in addition to 3ml of 0.5% bupivacaine was given. The mean time for two segment regression to L2 were significantly greater in clonidine group than in the saline group .Motor block was also prolonged in the clonidine group than in the saline group. Side effects such as hypotension and bradycardia commonly occurred in clonidine group , but all patients could be effectively treated with ephedrine and atropine respectively.

Clonidine as sole analgesic in spinal anaesthesia

Filos kriton[14] et al studied to evaluate the effect of intrathecal clonidine as the sole analgesic on pain following caessarian section. Twenty patients who underwent elective caessarian section receive 45 mins after GA either 150µg clonidine(n=10) or saline (n=10) intrathecally.Pain scores were lower in clonidine than saline treated patients .Pain relief in terms of the first supplemental analgesic requested by patients lasted 414 mins after clonidine and 181 mins after saline. The results suggest that 150µg clonidine is effective in pain following caessarian section but is not free of side effects like hypotension, sedation and dryness of mouth.

Goudas Leonidas et al[19] studied to evaluate the dose response hemodynamics and analgesic profiles of intrathecal clonidine .30 women who underwent LSCS under GA 45 mins after tracheal extubation, a lumbar puncture was performed and patients received 150µg (gp 1) ,300µg(gp 2) and 450µg (gp 3) clonidine. Pain relief lasted 402 ±75 mins in group 1,570± 76 mins in gp 2 , 864± 80 mins in gp 3 . Sedation was found in all three groups. The results demonstrated dose dependent analgesia after intrathecal clonidine at doses as great as 450 µg .A relative hemodynamic stability is observed suggesting a pressor effect at peripheral sites.

Clonidine combined with opioids and local anesthetics in spinal anesthesia

Chiari astrid et al[7] evaluated the dose response potency of intrathecally administered clonidine during 1st stage of labour along with sufentanil . 36 parturients received 50µg, 100 µg and 200 µg of intrathecal clonidine.

The duration of analgesia was significantly more in 200µg gp. Duration and quality of analgesia were more pronounced in 100µg, 200µg gps than with 50µg gp. The high incidence of hypotension requires caution with use of 200µg for labour analgesia.

Gautier Philippe E et al[20] studied the efficacy of low doses of intrathecal clonidine (15 µg & 30 µg)combined with sufentanil . 93 parturients received one of the following intrathecal solutions, either 15 µg clonidine (n=10), 30µg clonidine (n=10), 2.5µg sufentanil & 15 µg clonidine(n=13), and 5 µg ufentanil with 30 µg clonidine (n=13). Patients receiving 30 µg intrathecal clonidine with 2.5 or 5 µg sufentanil had significantly long lasting analgesia .30 µg intrathecal clonidine with 2.5 or 5 µg intrathecal sufentanil had significantly increased the duration of analgesia during the first stage of labour without adverse maternal or fetal effects.

Benhamou Dan et al[2] studied 78 pregnant women at term scheduled for elective caessarian section to compare the analgesic efficacy and side effect profile of a spinal block with hyperbaric bupivacaine alone (group B) or combined with 75 µg clonidine (group BC) or with clonidine 75 µg and fentanyl 12.5 µg (group BCF) . Adding a small dose of intrathecal clonidine to bupivacaine increases the quality of intraoperative analgesia and decreases pain during cesarian section . Combining clonidine with fentanyl further improved analgesia.

Acalovschi lurie et al[1] studied the effects of intrathecally administerd epinephrine and clonidine on the duration and quality of

meperidine spinal block. 45 patients scheduled for orthopaedic surgery divided into 3 groups, received spinal anaesthesia with 1mg/kg meperidine 5% alone or with 200 µg epinephrine or 2 µg /kg clonidine.

The duration and degree of motor block were increased by addition of both epinephrine and clonidine. A tendency toward bradycardia and decrease in MAP was potentiated by clonidine. The co administration of clonidine or epinephrine with meperidine enhances the duration and degree of spinal anaesthesia and that adding clonidine prolongs duration of post operative analgesia.

Owen MD et al[30] studied to determine whether the addition of clonidine and neostigmine to intrathecal bupivacine fentanyl would increase the duration of analgesia without increasing side effects for patients in labour.45 healthy parturients in active labour received 2ml intrathecal dose of one of the following dextrose containing solutions : 1. Bupivacaine 2.5mg and fentanyl 25 µg (BF) 2. BF + Clonidine 30 µg. 3. BFC + neostigmine 10 µg(BFCN). Patients administered BFCN had significantly longer analgesia (165 ± 32 mins) than those who received BF (90 ±21mins) or BFC (123±21 mins)$p<0.001$. The addition of clonidine and neostigmine significantly increased the duration of analgesia but neostigmine caused more nausea

MATERIALS AND METHODS

This study was conducted at the Chengalpattu Medical College Hospital , Chengalpattu - between May 2009 to August 2009 on 60 patients of ASA physical status I and II undergoing infra umbilical surgeries .

This study was done after Ethical Committee approval and written informed consent obtained from all patients included in the study.

STUDY DESIGN

This study was done in a prospective double blinded randomized manner.

SELECTION OF CASES

Inclusion criteria

- Patients in age group of 20 to 50 yrs .
- ASA –PS I & II
- Infra umbilical surgeries .

Exclusion criteria

- ASA –PS III & IV
- Patient refusal

- Renal / hepatic dysfunction
- Allergy to drugs
- Contra indication to sub arachnoid block.

60 patients were included in this double blinded randomized controlled study. patients were divided into 3 groups.

Patients in **group B** received 2.75ml of 0.5% hyperbaric bupivacaine plus 0.4ml saline.

Patients in **group C1** received 2.75ml of hyperbaric bupivacaine with 40 µg of clonidine .

Patients in **group C2** received 2.75ml of hyperbaric bupivacaine with 60µg of clonidine.

PRE ANAESTHETIC EVALUATION

Patients included in the study underwent thorough pre operative evaluation which included the following

History

History of underlying medical illness, previous surgery, anaesthesia and hospitalization. Patients were advised overnight starvation.

CLONIDINE & BUPIVACAINE

Physical examination

1. GC of the patient
2. Vital signs
3. Height and weight
4. Examination of CVS , RS , CNS and vertebral columns
5. Airway assessment

Investigations

Hb , PCV, BT, CT, RFT, blood sugar , ECG, CXR , platelet count, Blood grouping and cross matching were done.Patients who satisfied the inclusion criteria were explained about the nature of the study and the anaesthetic procedure. Written informed consent were obtained from all patients included in the study.

HOW DOUBLE BLINDING WAS DONE

Allotment of cases was done by computerized lots. The Consultant who made the drug combination took no further part in the study. I performed the subarachnoid block and made intraoperative observations. Postoperatively in the recovery room, observations were done.

Technique

In the OT, appropriate equipment for airway management and emergency drugs were kept ready. Patient was shifted from premedication room to the OT after giving oral diazepam 5mg 2hrs prior to surgery.The horizontal position of the operating table was checked and patient shifted to the table I.V.line was started and intra venous fluids started. NIBP, SpO2 , ECG leads were connected to the patient.Pre operative baseline systolic and diastolic BP , PR, SpO2 and RR were recorded. SAB and done and observations were made in all the patients involved in the study. Under strict aseptic precautions a midline lumbar puncture was performed using a 24/ 25G Quincke needle in sitting position/right lateral decubitus position. The patient was then immedietly placed in supine position.Lumbar puncture was successful in first attempt in almost all patients.The time for intrathecal injection was

considered as 0 and the following parameters were observed - sensory blockade, motor blockade, duration of analgesia and sedation.

Vital signs and side effects

The PR, systolic and diastolic BP, SpO2 and RR were recorded every min for 5 mins and then every 5 mins throughout the intra operative period.The above vital signs at the completion of surgery were noted.

Hypotension defined as fall in systolic BP > 30 % from baseline or MAP <60 mmHg.This was managed with inj. Ephedrine 6mg increments.

Bradycardia was defined as HR <60 /min and this was managed with inj.atropine 0.01mg/kg i.v.

Respiratory depression defined as RR< 8/min and or SpO2 <85%.This was planned to be managed with bag and mask ventilation or intubation and IPPV if necessary. Blood loss more than the allowable loss was replaced with blood. The occurrence of sedation were assessed using Ramsay sedation scale

Assessment in Recovery Room

Patient was shifted to recovery room after completion of surgery, the vital signs were recorded, every 15 mins in the 1st hr after surgery and 30 mins interval for next 2 hrs and thereafter at hourly intervals for next 3

hrs. Sensory and motor block assessment were done every 15 mins till recovery of pin prick sensation to L1 and BROMAGE score of 1 respectively. Patients were shifted to post operative ward after complete resolution of motor blockade.

Assessment of pain and duration of analgesia

In the recovery room pain assessment using VAS were done every 15 mins . At the end of surgery, the degree of pain was assessed using VAS scale till VAS score >4 was reached. Whenever the patient complained of pain and rescue analgesic Inj. Diclofenac 75mg i.m was given. Duration of effective analgesia was defined as time interval between onset of SAB and the time to reach VAS >=4.

Patients were monitored for 24 hrs to detect the occurence of side effects - respiratory depression, nausea, vomiting ,dry mouth and pruritis. Patients were also enquired about the occurence of Transient neurological symptoms which was described as pain / paresthesia in the neck, buttocks, legs or pain radiating to lower extremities after initial recovery from SAB within 72 hrs.

OBSERVATIONS & RESULTS

STATISTICAL ANALYSIS:

All recorded data were entered using MS Excel software and analysed using STATA software for determining the statistical significance. Analysis of Variance was used to study the significance of mean of various study parameters between the three groups. Student's t test was used to compare the two groups on mean values of various parameters. The p-value taken for significance is 0.05.

DEMOGRAPHICS:

1.DISTRIBUTION OF MEAN AGE BY GROUPS

PARAMETERS	GROUP B	GROUP C1	GROUP C2	p- VALUE
No. Of cases	20	20	20	0.5075
Mean	38.5	35.25	36.25	
S.D	8.6	8.84	9.49	

2. DISTRIBUTION OF MEAN HEIGHT (cms) BY GROUPS

PARAMETERS	GROUP B	GROUP C1	GROUP C2	p- VALUE
No. Of cases	20	20	20	0.001
Mean	160.4	166	167.5	
S.D	4.0574	5.5345	7.3592	

3. DISTRIBUTION OF MEAN WEIGHT (Kgs) BY GROUPS

PARAMETERS	GROUP B	GROUP C1	GROUP C2	p-VALUE
No. Of cases	20	20	20	0.299
Mean	56.5	62.2	65.1	
S.D	5.9338	8.3766	6.3526	

The groups were comparable with respect to their age and weight. There is difference among groups with regard to height, it may be due to less sample size.

4. DURATION OF SURGERY

PARAMETERS	GROUP B	GROUP C1	GROUP C2	p-VALUE
No. Of cases	20	20	20	0.24
Mean	100.5	118.5	99.5	
S.D	39.53	45.11	33.64	

The mean duration of surgery is higher in Group-C1 compared to other two groups and Group-C2 has lower mean duration. However, there is no statistical significance among the groups.

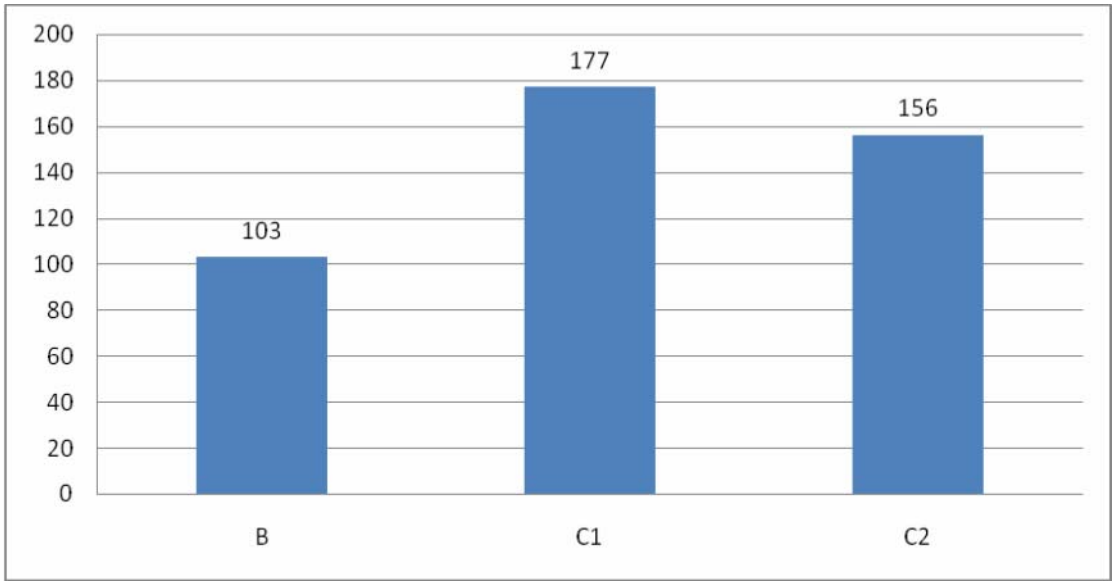
5. TYPE OF SURGERY BY GROUPS

SURGERY	GROUP B	GROUP C1	GROUP C2
# Both bones leg	2	4	3
DHS	3	2	3
Inguinal hernia	4	3	4
Epigastric hernia	1	-	2
# SOF	2	3	4
Appendicectomy	3	2	3
Implant exit	2	1	1
Diagnostic arthroscopy	3	3	-
Knee arthroplasty	-	1	-

6. DISTRIBUTION OF MEAN ONSET OF SENSORY BLOCK (secs) BY GROUPS

PARAMETERS	GROUP B	GROUP C1	GROUP C2	p-VALUE
No. Of cases	20	20	20	0.001
Mean	103	177.25	156.25	
S.D	10.809	43.542	32.23577	

ONSET OF SENSORY BLOCK

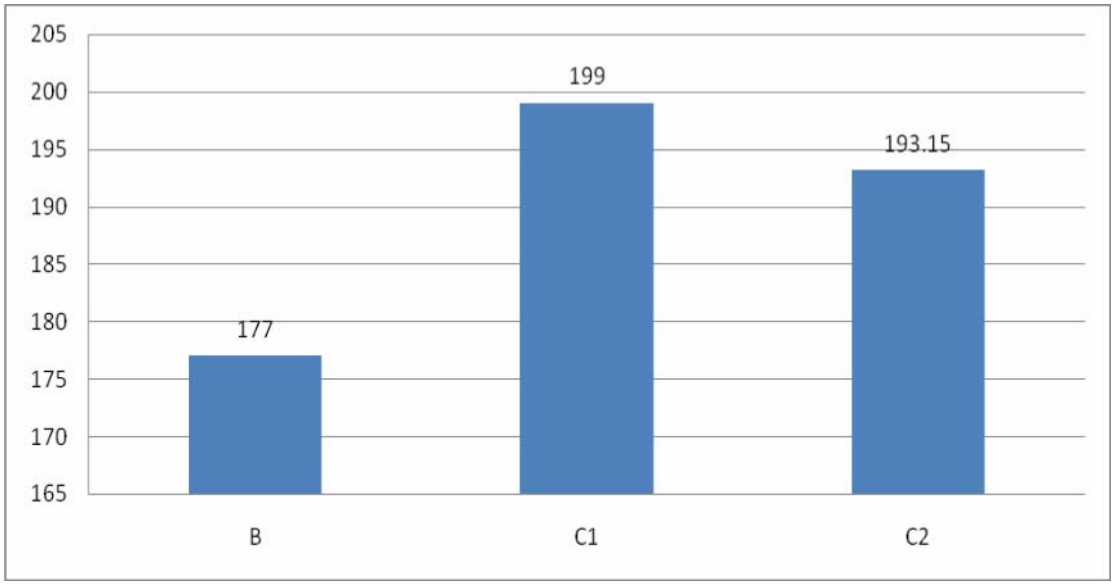


There is a significant difference between groups with regard to onset of sensory block ,with group C2 having a rapid onset compared to C1.

7. DISTRIBUTION OF MEAN ONSET OF MOTOR BLOCK (secs) BY GROUPS

PARAMETERS	GROUP B	GROUP C1	GROUP C2	p-VALUE
No. Of cases	20	20	20	0.001
Mean	177.25	199	193.150	
S.D	18.6007	15.61	11.663	

ONSET OF MOTOR BLOCK



There is significant difference between groups in the onset of motor block.Group C2 has a faster onset compared to C1.

8. DISTRIBUTION OF MAX. SENSORY BLOCK AMONG GROUPS

PARAMETERS	GROUP B		GROUP C1		GROUP C2	
	NO	%	NO	%	NO	%
T4	0	0	6	30	10	50
T5	1	5	1	5	0	0
T6	10	50	9	45	10	50
T8	9	45	4	20	0	0

Maximum sensory block of T4 was observed in 50% of cases in group C2 and 30% of cases in group C1

9. DISTRIBUTION OF CASE BY GROUPS AND GRADE OF MAXIMUM MOTOR BLOCK

PARAMETERS	GROUP B	GROUP C1	GROUP C2	p-VALUE
No. Of cases	20	20	20	
Mean	4	4	4	
S.D	0	0	0	

There is no difference between the groups in the grade of maximum motor block.

10. DISTRIBUTION OF MEAN TWO SEGMENTAL REGRESSION(mins) BY GROUPS

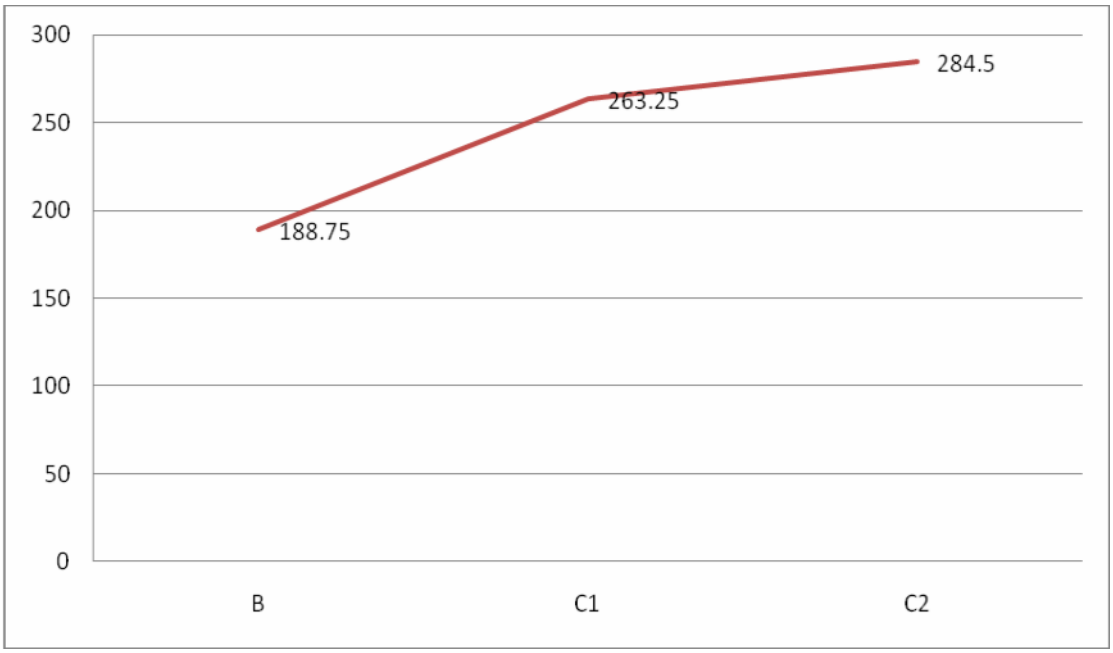
PARAMETERS	GROUP B	GROUP C1	GROUP C2	p-VALUE
No. Of cases	20	20	20	0.001
Mean	128	187.05	211	
S.D	16.091	8.846	21.250	

There is significant difference between groups in two segment regression –with C2 having a much longer time compared to C1.

11. DISTRIBUTION OF MEAN DURATION OF MOTOR BLOCK(mins) BY GROUPS

PARAMETERS	GROUP B	GROUP C1	GROUP C2	p-VALUE
No. Of cases	20	20	20	0.001
Mean	188.75	263.25	284.5	
S.D	13.848	12.904	16.693	

DURATION OF MOTOR BLOCK

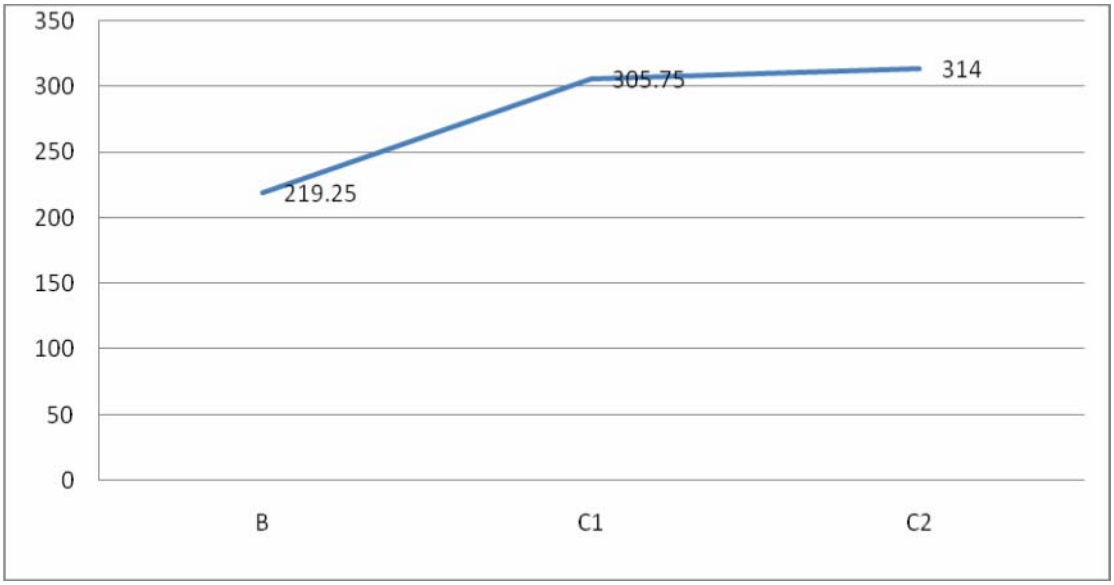


There is significant difference between groups in duration of motor block with group C2 having longer duration compared to C1.

12. DISTRIBUTION OF MEAN DURATION OF ANALGESIA BY GROUPS

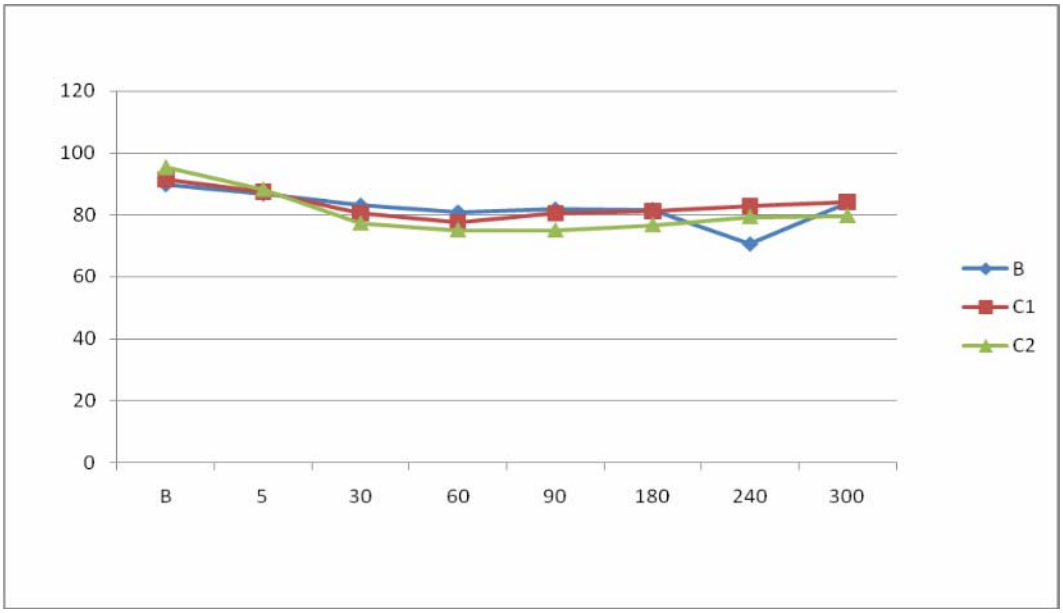
PARAMETERS	GROUP B	GROUP C1	GROUP C2	p-VALUE
No. Of cases	20	20	20	0.001
Mean	219.25	305.75	314	
S.D	9.215	17.341	28.635	

DURATION OF ANALGESIA

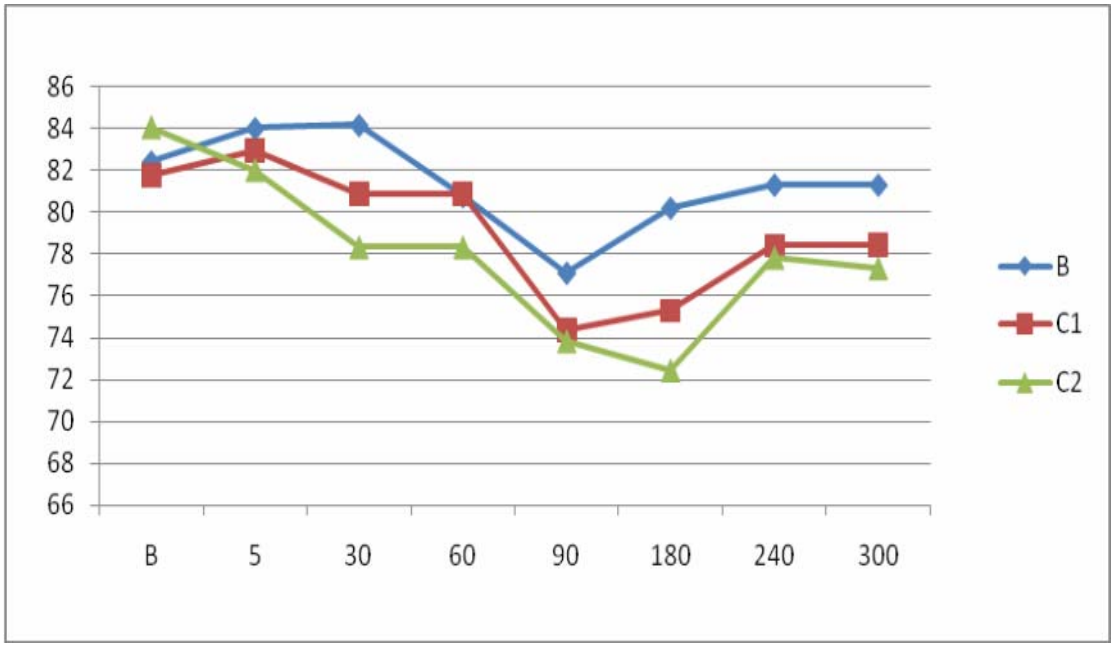


There is significant difference between groups in total duration of analgesia with C2 having a much longer duration compared to C1.

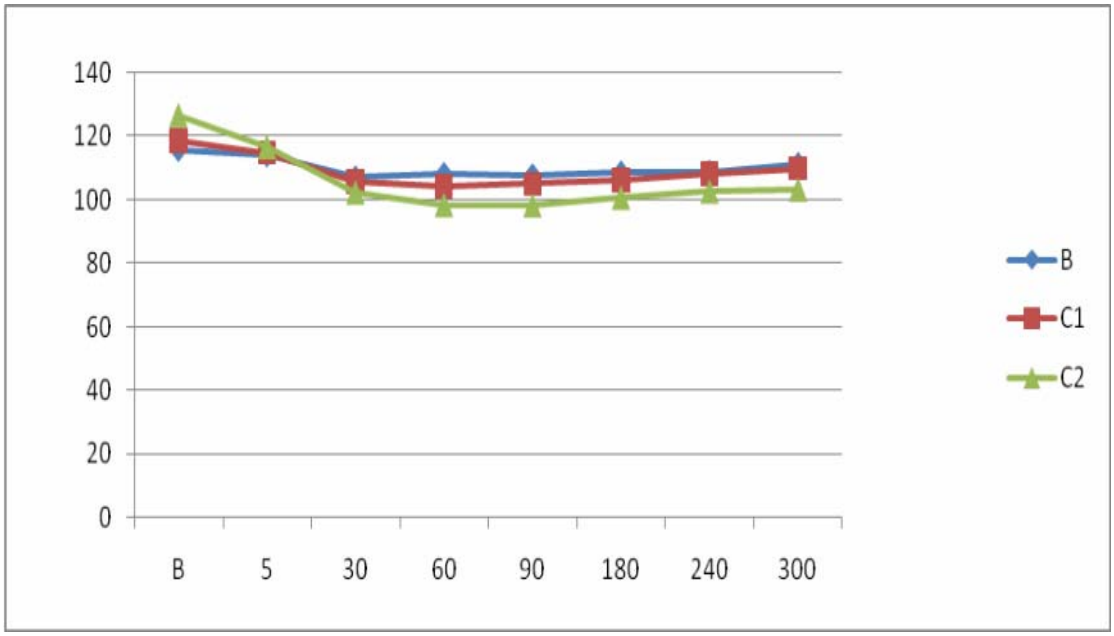
DISTRIBUTION OF MEAN ARTERIAL PRESSURE AMONG THE GROUPS



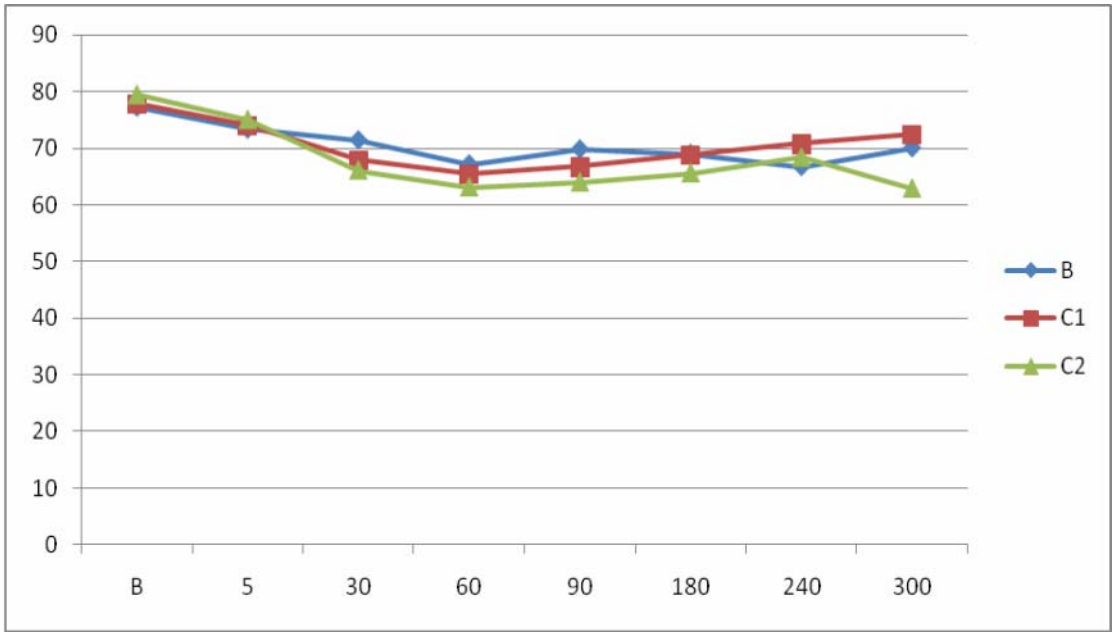
DISTRIBUTION OF HR AMONG GROUPS



DISTRIBUTION OF SBP



DISTRIBUTION OF DBP



There is no statistically significant difference among groups with respect to hemodynamics

DISTRIBUTION OF SIDE EFFECTS

EFFECTS	GROUP B		GROUP C1		GROUP C2	
	NO	%	NO	%	NO	%
HYPOTENSION	2	10	1	5	2	10
BRADYCARDIA	1	5	1	5	2	10
SEDATION	0	0	10	50	20	100
DRYNESS OF MOUTH	0	0	1	5	2	10

DISCUSSION

Alpha 2 agonist clonidine added to local anaesthetics have been shown to provide excellent surgical anaesthesia.

ONSET OF SENSORY BLOCK:

The mean time to onset of sensory block was 103secs in control group. It is 177.25secs in group C1 and 156.25secs in group C2 . Onset time is statistically significantly prolonged in group C1

Klimscha et al[23] studied intrathecally administered 0.5% bupivacaine 5mg and 150µg clonidine vs plain bupivacaine and showed there is no statistically significant difference between the groups.

ONSET OF MOTOR BLOCK :

The mean time to onset of motor block was 177 secs in control group . it was 199secs in group C1 and 193 secs in group C2. There is no statistically significant diference among the three groups .

This correlated with the study by Acalvoschi lurie et al[1] who found that addition of clonidine 2µg /kg with 1mg/kg meperidine intrathecally had no significant difference compared to meperidine with epinephrine 200µg in the onset of motor blockade.

MAXIMUM LEVEL OF SENSORY BLOCK:

There was no statistically significant difference among the groups in maximum level of sensory block.

De kock et al[9] in his study found that addition of intrathecal clonidine in increasing doses (15µg, 45µg, 75µg) with 8mg of ropivacaine increased the level of sensory block as the dose of clonidine increases.

MAXIMUM LEVEL OF MOTOR BLOCK:

The median of maximum grade of motor block measured using modified bromage scale was grade 4 in all the groups. There is no statistically significant difference among the two groups.

Klimscha et al[23] showed that intrathecal clonidine 150µg added to 0.5% bupivacaine significantly increased the intensity of motor block.

Bonnet et al[3] in his study found that intensity and duration of motor block was prolonged with increasing the dose of clonidine from 75µg to 150µg added to 0.5% tetracaine 15mg.

TIME FOR TWO SEGMENTAL REGRESSION:

The mean time taken for two segmental regression was 211mins in group C2 compared to 187.05 mins in group C1. group C2 had significantly prolonged time for two segmental regression compared to C1.

This correlated with the study by Fogarty et al[15] that addition of 75µg of clonidine with 2.75ml of 0.5% hyperbaric bupivacaine prolonged the time to two segment regression below L4 by 216+/- 97.1 mins compared with control of 138+/-59.9 mins.

Fakuda et al[16] found in their study that time to two segment regression of sensory block was significantly prolonged when clonidine 150µg was added to 0.5% tetracaine compared with 0.5% tetracaine alone.

MEAN DURATION OF MOTOR BLOCK :

The mean duration of motor block was 263 mins in group C1 compared to 284mins in group C2. This was statistically significant .

This correlated with the study by Dobrydnjov et al [11] where clonidine combined with small dose bupivacaine during subarachnoid

block for inguinal hernioraphy prolonged the duration of motor block compared to bupivacaine alone.

Study by Bonnet F et al[4] compared the effects of oral and subarachnoid clonidine on spinal anaesthesia with bupivacaine showed prolongation of motor block (175+/- 68mins) with spinal clonidine compared to oral clonidine (103±20mins) .

MEAN DURATION OF ANALGESA

The mean duration of analgesia was 305 mins in group C1 compared to 314 mins in group C2. The difference is statistically significant when compared with control group B.

This correlated with study by Stephen strebel[33] where he studied small dose intrathecal clonidine and isobaric bupivacaine for orthopaedic surgeries. There was significant prolongation of analgesia compared to control group.

Dobrydnjov et al[11] also showed in his study that clonidine added to small dose bupivacaine for inguinal hernioraphy had prolonged analgesia compared to control group.

Gautier et al[20] showed in study that clonidine combined with sufentanil for first stage of labour significantly prolonged analgesia compared with sufentanil alone.

Study by Mercier et al[27] showed addition of clonidine to intrathecal sufentanil for labour significantly prolonged analgesia.

Complications

Study by Chiari Astrid et al[7] on analgesic and hemodynamic effects of intrathecal clonidine as a sole analgesic agent during 1st stage of labour showed hypotension was produced with increasing doses of clonidine.

Study by Filos kriton et al[14] found that hypotension is the main side effect.

Studies done by Freedman JM et al[17] and Hampl KF et al[22] showed an increased occurrence of TNS in patients undergoing spinal anaesthesia with lignocaine.

In our study ,patients in both clonidine groups had sedation with RSS score ≤ 3 , which did not require any active intervention.

With respect to hemodynamic parameters , incidence of bradycardia and hypotension were not significantly higher in clonidine groups compared to control group.Hypotension and bradycardia were observed in 5-10% of patients in clonidine group.

Hypotension was treated with ephedrine and bradycardia with atropine

CONCLUSION

In conclusion the addition of clonidine as an adjuvant to bupivacaine in subarachnoid block prolongs duration of both sensory and motor block.

I conclude that 60µg of clonidine hydrochloride added to local anaesthetic in subarachnoid block has proved to be a better adjuvant in prolonging the sensory and motor blockade intra operatively and duration of effective post operative analgesia compared to 40µg , without significant adverse effects.

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PROFORMA

Name :

Age /sex

Duration of surgery

Pre op assessment

ASA	HEIGHT	WEIGHT

Airway

Drug therapy

INVESTIGATIONS

Hb	PCV	BT	CT	RBS	CREAT	PLATELETS

MONITORS

ECG	NIBP	SPO2	TEMP

IV ACCESS	PRELOADING

SAB

SPACE	NEEDLE	SIZE	APPROACH/ POSITION	GROUP

BLOCK CHARACTERISTICS

TIME	1”	3”	5”	8”	10”	15”	30”	60”	1Hr 30”
Motor									
Sensory									
Vas score									

INTRA OP FLUIDS

INTRA OP BLOOD LOSS

INTRA OP HEMODYNAMICS

TIME	1”	3’’	5’’	10”	15”	30”	45”	60”	1hr30”
HR									
SBP									
DBP									
MAP									
SPO2									
RR									

POST OP

Time for demand of analgesia

Total duration of post op analgesia

PERIOPERATIVE COMPLICATIONS

	INTRA OP	POST OP	TREATMENT DETAILS
EXCESS SEDATION			
HYPOTENSION			
RESP DEPRESSION			
BRADYCARDIA			
URINARY RETENTION			
SHIVERING			
NAUSEA, VOMITING			
HEADACHE			
CONFUSION			
ANXIETY			
NEUROLOGICAL			
OTHERS			

	BASE LINE				5 MIN				10 MIN			
S.No	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP
1	76	124	80	95	88	123	78	93	88	100	62	75
2	86	110	76	87	90	98	58	71	92	100	60	73
3	82	120	70	87	86	120	70	87	90	130	70	94
4	82	130	90	103	84	126	88	101	92	120	80	93
5	82	110	80	90	84	112	80	91	80	112	80	91
6	68	110	70	83	68	110	70	83	64	110	64	79
7	82	120	74	89	78	120	72	88	78	116	70	85
8	80	120	82	95	82	120	80	93	80	120	80	93
9	78	110	80	90	68	110	80	90	68	114	80	90
10	66	110	74	86	64	110	70	83	62	106	70	82
11	84	126	80	95	84	126	80	95	76	110	64	79
12	97	117	80	93	100	114	80	91	98	110	72	82
13	72	126	80	95	72	110	70	83	76	110	64	79
14	94	130	80	97	92	104	60	75	92	104	60	75
15	84	118	74	89	92	117	70	86	98	118	74	89
16	74	110	70	83	74	110	70	83	72	106	70	82
17	100	120	80	93	102	120	80	93	100	120	80	93
18	90	137	86	103	82	122	76	91	84	116	67	83
19	74	110	70	83	78	102	68	79	80	102	68	78
20	84	114	80	91	91	120	80	93	80	114	86	95

15 MIN				20 MIN				25 MIN				
HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR
78	101	66	78	74	104	66	79	78	100	70	80	78
90	102	62	75	90	102	64	77	90	110	70	83	88
82	130	70	83	84	130	70	83	86	108	60	76	96
90	118	76	90	78	118	74	89	76	116	72	87	74
82	112	80	91	82	110	70	83	84	110	80	90	84
58	110	68	82	60	110	70	83	64	126	78	94	64
80	116	68	84	76	120	70	87	78	120	70	83	80
84	122	80	94	82	120	80	93	84	110	80	90	86
62	112	80	91	66	110	80	90	64	112	80	91	58
68	102	64	77	62	106	54	71	64	110	77	88	60
74	100	60	73	72	92	60	71	78	100	80	87	74
96	106	72	83	96	100	70	80	97	94	65	75	78
74	100	60	73	72	92	60	71	68	96	60	72	74
94	704	66	79	92	100	66	77	96	106	48	67	96
90	120	58	79	98	94	43	60	100	116	72	87	116
72	100	76	84	76	100	74	83	72	100	74	83	76
88	100	72	81	88	90	70	77	88	90	70	77	92
82	108	64	79	92	109	64	79	90	101	59	83	83
88	100	68	79	90	100	64	76	92	88	66	73	98
78	112	70	81	76	114	74	87	68	110	74	86	62

GROUP B

30 MIN			35 MIN				45 MIN				60 M	
SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP
100	70	80	70	100	70	80	74	106	70	82	86	100
110	70	83	86	112	72	85	80	110	58	75	76	112
90	60	70	106	110	70	83	92	120	70	87	86	110
114	70	85	78	116	72	87	74	120	70	87	68	114
90	56	67	82	110	80	90	84	110	56	74	82	96
126	78	94	72	120	70	87	68	100	80	97	60	116
120	74	90	72	116	72	84	68	108	68	81	68	110
114	74	87	82	120	80	93	82	110	80	93	80	113
114	76	89	60	120	70	87	58	120	68	85	60	110
114	70	85	62	110	70	83	70	99	62	75	64	103
104	80	88	60	104	80	88	56	90	70	77	52	110
91	65	74	82	92	62	72	82	91	64	73	73	91
112	60	77	66	114	60	78	62	110	60	77	60	90
106	50	69	92	94	53	67	90	110	62	78	93	93
116	67	83	110	114	73	87	92	110	62	78	93	108
100	74	83	78	102	74	84	72	100	74	83	64	96
80	64	69	92	70	62	65	90	70	62	65	64	90
109	64	79	86	108	68	81	82	116	66	83	90	101
90	60	70	100	94	68	77	77	100	100	68	90	104
110	74	86	70	112	74	87	76	114	76	85	78	114

JP B

VIN		75 MIN				90 MIN				120 MIN		
DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP
67	78	92	99	66	77	78	106	78	88	78	106	70
68	83	80	112	68	83	88	110	70	83	83	112	72
70	83	86	110	70	83	88	110	70	83	86	120	74
72	86	62	110	72	85	68	116	74	88	64	104	68
58	71	78	110	64	79	84	110	62	78	80	110	60
74	88	66	120	70	87	64	128	74	92	66	126	70
68	82	66	114	70	85	68	116	70	85	70	120	76
74	87	78	116	62	80	80	110	68	82	86	100	64
62	78	64	110	62	78	58	110	70	83	64	110	70
66	78	62	101	66	79	74	95	64	74	66	107	74
72	85	49	100	70	80	52	106	70	82	70	96	70
64	73	92	116	72	87	76	76	62	93	100	92	66
50	63	68	90	60	70	80	100	60	73	90	102	60
48	63	88	109	63	78	86	106	67	80	82	106	73
65	79	82	100	56	71	88	99	56	70	89	94	57
74	81	60	96	74	81	62	100	70	80	80	84	60
58	69	64	90	52	65	72	90	50	65	70	106	55
54	70	74	97	56	70	68	101	58	69	68	98	53
70	66	88	104	74	84	84	106	70	82	82	102	68
74	87	76	112	70	84	68	402	70	81	72	106	64

JP B

	150 MIN				180 MIN				210 MIN			
MAP	**HR**	**SBP**	**DBP**	**MAP**	**HR**	**SBP**	**DBP**	**MAP**	**HR**	**SBP**	**DBP**	**MAP**
82	76	110	76	87	80	106	70	82	90	110	70	83
85	82	110	70	83	78	110	64	79	80	110	68	82
89	86	126	76	93	84	120	70	87	88	130	74	93
80	72	108	68	81	30	112	72	85	76	112	72	85
77	86	404	68	80	82	110	74	86	82	112	76	88
89	68	116	74	88	68	110	70	83	66	114	70	85
91	70	108	70	83	72	116	70	85	68	106	68	81
76	86	112	68	83	80	106	64	78	84	114	70	85
83	60	108	70	83	60	112	74	87	62	106	70	82
85	64	110	70	80	76	116	76	89	86	119	72	88
79	68	96	70	79	72	100	76	84	72	100	74	83
75	106	92	64	73	90	92	64	73	88	92	68	76
74	88	100	64	76	86	100	60	73	74	102	74	84
84	80	109	67	81	84	103	69	80	88	109	64	79
68	86	98	70	79	84	100	70	81	82	112	80	91
68	76	90	60	70	72	100	74	83	74	109	63	78
73	70	106	54	71	70	100	55	70	74	110	73	83
68	76	98	58	71	78	100	60	73	68	101	58	73
79	88	114	74	87	86	100	70	80	88	100	70	80
78	76	112	64	80	74	110	74	86	76	106	70	82

JP B

240 MN				270 MIN				300 MIN			
HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP
76	98	72	81	80	110	76	86	84	110	70	83
82	110	64	79	88	106	72	82	88	112	72	85
84	110	74	86	84	126	78	94	86	120	74	84
74	106	74	82	78	112	68	83	74	114	74	87
86	110	74	86	84	112	70	84	85	110	74	86
74	126	78	89	76	120	74	89	70	120	80	93
66	114	70	85	66	114	70	85	70	108	73	84
80	112	70	84	84	110	68	82	84	114	74	87
64	112	70	84	68	110	70	83	60	116	74	88
82	120	74	89	82	120	74	89	82	110	72	85
70	94	70	78	70	110	72	85	74	110	74	85
90	94	70	78	96	92	64	73	98	92	68	76
74	102	74	84	92	90	60	70	74	100	70	80
86	101	64	76	82	110	64	79	80	106	60	75
180	116	80	93	78	106	72	83	78	110	70	83
78	110	74	83	78	110	83	83	74	110	86	86
74	110	73	83	74	100	80	90	76	110	80	90
78	91	55	67	72	99	61	74	74	101	56	71
92	112	64	80	92	106	70	82	88	110	72	85
78	112	70	84	68	106	70	84	70	112	74	87

	BASE LINE				5 MIN				10 MIN			
S.No	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP
1	80	110	70	83	90	96	58	71	92	100	60	73
2	92	110	70	83	90	96	58	71	92	100	60	73
3	80	120	82	95	82	122	80	94	82	122	80	94
4	91	125	80	95	82	123	78	93	88	101	63	76
5	98	116	80	92	96	116	78	91	91	100	67	78
6	82	120	74	89	78	120	72	88	78	116	70	85
7	90	130	80	97	96	130	80	97	96	130	78	95
8	89	120	70	87	86	120	70	81	90	130	70	90
9	78	126	82	97	80	126	80	97	86	126	82	97
10	72	100	78	82	78	102	68	79	90	102	68	79
11	98	110	80	90	96	116	70	86	100	110	70	83
12	76	124	80	95	88	123	78	93	88	100	62	75
13	80	110	70	83	90	96	58	71	92	100	60	73
14	70	110	70	83	74	110	70	83	68	100	70	87
15	90	110	80	90	68	112	82	92	68	114	80	91
16	82	110	80	90	84	112	80	91	84	112	80	91
17	68	100	70	80	72	110	70	83	60	110	70	83
18	82	130	90	103	84	126	88	101	88	124	82	96
19	70	106	70	82	86	102	68	81	90	102	68	81
20	80	126	88	101	80	120	80	93	82	126	82	97

15 MIN				20 MIN				25 MIN				
HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR
90	102	62	75	90	102	64	77	96	106	66	79	92
84	120	84	96	90	102	67	79	80	122	80	94	82
84	120	84	96	80	120	80	94	80	122	80	94	82
102	100	67	78	70	98	68	78	76	107	75	86	76
100	108	74	86	98	90	65	74	98	90	65	75	90
80	116	68	84	76	120	70	87	78	120	70	87	74
92	130	76	94	84	130	70	90	86	108	60	76	98
82	130	70	90	84	130	70	90	86	108	60	76	98
82	122	78	93	88	122	78	93	92	120	78	92	88
90	100	66	77	92	100	66	77	92	100	64	76	96
102	100	68	79	98	98	64	75	96	94	64	74	100
78	101	6	78	74	104	66	79	78	98	62	74	70
90	110	60	77	90	102	68	81	96	100	68	81	92
66	124	70	88	68	112	76	88	66	112	70	84	68
62	112	80	91	60	100	80	87	60	112	80	91	56
82	110	80	90	82	112	80	91	82	110	80	90	82
62	110	68	72	58	110	88	72	58	110	88	87	65
84	126	88	91	90	122	84	97	92	120	80	93	92
92	100	66	79	86	85	56	66	98	90	60	90	102
88	120	78	92	120	120	82	95	88	116	76	89	88

GROUP C1

30 MIN			45 MIN				60 MIN				75M	
SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP
108	66	80	86	110	70	83	80	112	64	80	82	110
120	80	94	82	120	80	93	82	96	48	64	86	106
120	83	93	82	120	80	93	82	96	48	64	86	106
100	70	80	73	99	70	80	83	117	76	90	81	106
95	65	75	100	99	66	77	100	100	66	77	100	100
116	72	87	68	106	68	81	66	110	70	82	68	110
90	60	70	82	130	70	90	78	110	76	87	86	120
90	60	70	110	130	70	90	88	110	70	83	88	110
128	82	95	88	120	80	93	78	116	74	88	70	119
88	56	67	100	98	66	77	96	102	70	81	90	104
96	76	83	100	100	66	77	98	100	62	75	92	100
100	70	80	74	106	70	82	86	100	67	78	92	99
108	66	80	88	114	74	87	86	112	50	75	88	106
106	70	82	74	102	64	77	70	106	68	81	68	128
110	80	90	52	120	68	85	52	110	62	78	52	110
110	80	90	84	80	50	60	84	110	80	90	80	110
126	78	94	70	130	90	103	64	124	78	93	62	126
118	76	90	74	114	76	89	82	118	74	89	82	118
94	62	73	98	100	65	77	88	104	70	81	88	104
118	76	90	70	120	70	87	72	110	70	83	98	116

MIN		90 MIN				120 MIN				150 MIN		
DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP
64	80	78	102	60	74	76	110	64	80	80	114	68
62	77	80	113	74	87	80	110	64	81	80	112	76
62	77	84	106	62	77	78	116	64	81	80	112	76
73	84	86	100	68	79	69	114	70	85	84	112	68
68	79	82	100	72	82	86	100	72	82	88	110	76
66	81	68	120	76	91	68	110	66	81	80	104	74
74	89	88	114	68	83	88	114	68	83	88	114	70
70	83	84	100	74	83	83	110	70	83	88	110	58
74	89	70	119	80	93	80	130	88	102	76	110	76
70	81	88	104	70	81	88	104	70	81	88	114	70
70	80	88	100	70	80	92	100	77	75	88	110	58
66	77	78	108	78	88	74	110	80	83	76	110	76
64	78	76	110	64	70	80	106	70	82	84	114	70
80	96	68	112	74	87	72	114	74	87	76	112	70
60	77	56	110	68	82	54	110	70	83	50	110	70
80	90	80	80	56	60	84	110	82	91	80	80	58
76	93	64	128	72	89	66	126	70	89	68	114	76
74	89	60	114	72	86	68	114	72	77	68	116	74
70	81	86	104	70	81	88	114	70	85	86	100	70
74	88	78	110	68	85	81	110	70	83	80	104	74

	180 MIN				210 MIN				240 MN			
MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP	HR	SBP	DBP	MAP
83	82	112	64	80	88	110	70	83	86	106	70	82
88	88	110	68	82	82	112	68	83	86	106	64	78
88	88	110	68	82	82	112	68	83	86	106	64	78
83	78	106	68	81	76	112	74	87	78	116	70	85
82	88	106	64	78	90	106	62	77	88	110	58	75
84	88	110	74	86	78	106	70	82	74	112	68	83
85	86	104	70	81	90	100	70	80	90	112	60	77
75	90	114	64	81	90	116	68	84	92	110	64	79
87	80	106	74	85	90	110	70	83	76	98	72	81
85	56	104	70	71	90	100	70	80	90	112	60	77
75	90	114	64	81	90	116	68	84	92	110	64	79
87	80	106	74	85	90	110	70	83	76	98	72	81
82	88	110	70	83	92	108	66	80	96	102	64	77
84	78	104	60	75	72	112	70	84	76	112	70	84
83	58	112	70	84	56	110	70	83	50	108	70	83
65	82	110	68	82	84	100	80	90	86	110	62	78
89	66	114	76	89	68	120	68	85	68	116	70	85
88	62	110	70	83	64	108	68	81	70	114	74	87
80	88	100	70	80	92	112	68	83	92	106	70	82
84	88	110	74	86	78	106	70	82	74	112	68	83

270 MIN				300 MIN			
HR	SBP	DBP	MAP	HR	SBP	DBP	MAP
84	116	70	85	86	112	72	85
86	112	68	83	82	106	64	78
86	112	68	83	82	116	62	80
74	112	70	84	76	111	76	88
90	114	64	81	90	116	68	84
83	110	72	85	78	112	64	80
92	106	72	82	90	110	74	87
84	110	64	78	90	110	74	86
80	110	76	87	82	110	74	87
92	106	70	82	90	112	74	87
84	110	62	78	88	100	74	83
80	110	76	87	84	110	70	83
86	112	68	83	86	112	56	75
78	120	70	87	72	110	70	83
60	112	64	80	62	112	70	84
82	110	74	86	86	110	74	86
66	114	70	85	68	126	78	94
72	108	68	81	70	110	64	79
92	114	74	87	92	110	70	83
78	110	72	85	72	110	72	85

GROUP C1

S.No	NAME	AGE	SEX	DURATION OF SURGERY	GROUP	MAXIMUM MOTOR BLOCK	MAXIMUM SENSORY BLOCK	RSS SCORE	ONSER MOTOR BLOCK	ONSET SENSORY BLOCK	TWO SEGMENTREGRESSION(MINS)	TOTAL DYRATION OF MOTOR BLOCK	DURATION 0F ANALGESIA	SIDE EFFECTS
1	sundarajan	35	m	120	c1	4	t8	2	130	185	190	270	270	
2	harish	45	m	100	c1	4	t5	1	230	220	180	260	300	
3	tatchiyammal	35	f	140	c1	4	t4	2	120	180	170	240	300	
4	elangovan	34	m	60	c1	4	t4	2	150	195	180	270	320	Hypotension
5	shanti	40	f	120	c1	4	t4	2	230	200	180	265	280	
6	prakash	20	m	60	c1	4	t4	2	140	195	196	250	300	
7	eluamlai	45	m	50	c1	4	t4	2	150	200	185	265	300	
8	kanaan	45	m	75	c1	4	t8	2	145	190	180	250	310	
9	durai	25	m	70	c1	4	t4	2	200	210	200	270	340	
10	kuppan	24	m	150	c1	4	t6	1	230	200	185	250	290	
11	thangalelu	50	m	150	c1	4	t6	1	200	210	200	250	280	
12	jayanmani	32	m	190	c1	4	t6	1	125	185	180	250	310	
13	thyagu	26	m	150	c1	4	t6	1	230	210	200	280	320	Bradycardia
14	radha	26	f	90	c1	4	t6	1	230	240	200	285	315	
15	kathikeyan	25	m	75	c1	4	t6	1	220	210	195	280	315	
16	arjunan	40	m	180	c1	4	t6	1	145	195	180	270	330	
17	kumaraswamy	35	m	140	c1	4	t6	1	130	190	180	250	320	
18	mani	48	m	150	c1	4	T6	1	230	210	190	280	300	Dryness of Mouth
19	palani	35	m	195	c1	4	t8	2	160	175	185	260	300	
20	kumari	40	f	105	c1	4	t8	2	150	180	185	270	315	

GROUP B

S.No	NAME	AGE	SEX	DURATION OF SURGERY	GROUP	MAXIMUM MOTOR BLOCK	MAXIMUM SENSORY BLOCK	RSS SCORE	ONSER MOTOR BLOCK	ONSET SENSORY BLOCK	TWO SEGMENTREGRESSION(MINS)	TOTAL DYRATION OF MOTOR BLOCK	DURATION 0F ANALGESIA	SIDE EFFECTS
1	madhavan	36	m	70	B	4	t6	1	100	180	130	180	210	
2	venkatesan	50	m	100	B	4	t6	1	100	180	140	200	220	
3	mohanavel	46	m	45	B	4	t6	1	120	175	145	180	220	
4	anjalatchi	50	f	100	B	4	t6	1	100	180	135	210	230	
5	raja	36	m	45	B	4	t6	1	110	200	145	200	230	Hypotension
6	meenakashi	40	f	120	B	4	t6	1	110	190	145	220	235	
7	lund mary	36	f	120	B	4	t6	1	110	180	135	180	220	
8	agasan	45	m	70	B	4	t6	1	120	200	140	200	230	
9	padmanathan	45	m	60	B	4	t6	1	90	170	130	180	215	
10	velu	40	m	210	B	4	t6	1	100	280	145	210	200	
11	aravind	26	m	140	B	4	t8	1	110	185	150	180	215	
12	mani	45	m	135	B	4	t8	1	80	170	110	170	220	
13	rajesh	36	m	120	B	4	t8	1	100	180	110	180	220	Hypotension
14	subramani	46	m	105	B	4	t8	1	110	180	110	185	215	
15	ravishankar	26	m	70	B	4	t8	1	110	175	115	185	215	
16	neelankandan	21	m	80	B	4	t8	1	100	195	115	180	210	
17	ramesh	24	m	90	B	4	t8	1	100	175	110	175	230	
18	lavanya	38	f	130	B	4	t5	1	110	180	110	180	210	
19	ravi	39	m	70	B	4	t8	1	80	160	100	180	210	
20	ayyaswamy	45	m	130	B	4	t8	1	100	110	140	200	230	

GROUP C2

S.No	NAME	AGE	SEX	DURATION OF SURGERY	GROUP	MAXIMUM MOTOR BLOCK	MAXIMUM SENSORY BLOCK	RSS SCORE	ONSER MOTOR BLOCK	ONSET SENSORY BLOCK	TWO SEGMENTREGRESSION(MINS)	TOTAL DYRATION OF MOTOR BLOCK	DURATION 0F ANALGESIA	SIDE EFFECTS
1	parthasarathy	50	m	120	c2	4	t6	2	135	190	210	300	340	
2	venu	28	m	100	c2	4	t6	2	120	196	215	295	350	
3	partahasarathy	50	m	120	c2	4	t4	2	160	190	230	290	350	
4	mala	36	f	120	c2	4	t4	2	200	190	220	295	355	
5	perumal	42	m	60	c2	4	t4	3	150	200	210	290	360	Hypotension
6	ramani	36	f	120	c2	4	t4	3	230	210	240	300	320	
7	magala	46	f	70	c2	4	t4	3	140	185	200	280	350	
8	sarath	37	m	90	c2	4	t4	3	130	180	140	260	270	
9	vijatsarathi	20	m	140	c2	4	t6	2	145	200	210	280	310	Hypotension
10	madhavan	29	m	60	c2	4	t6	2	135	180	190	285	280	
11	raja	35	m	60	c2	4	t4	2	140	180	220	260	300	
12	murugan	25	m	120	c2	4	t4	2	145	206	215	275	315	Dryness of mouth
13	nithyanandam	22	m	150	c2	4	t6	2	140	200	225	295	315	
14	chellamuthu	50	m	120	c2	4	t6	2	145	220	215	275	275	
15	gunasekaran	38	m	120	c2	4	t6	2	145	186	230	270	310	Bradycardia
16	marimuthu	45	m	60	c2	4	t4	2	210	190	200	310	290	
17	logonathsn	38	m	80	c2	4	t6	2	225	210	190	310	280	
18	devbararath	22	m	60	c2	4	t4	2	145	185	230	300	310	Dryness of mouth
19	iniyan	40	m	160	c2	4	t6	1	140	180	220	265	310	
20	madhivani	36	f	60	c2	4	t6	1	145	185	210	255	290	Bradycardia