A COMPARATIVE STUDY OF 0.25% BUPIVACAINE WITH CLONIDINE, FENTANYL, MIDAZOLAM, AS ADJUVANTS FOR BRACHIAL PLEXUS BLOCK

Dissertation Submitted in partial fulfillment of

M.D. DEGREE EXAMINATION

M.D. ANAESTHESIOLOGY—BRANCH X

GOVERNMENT KILPAUK MEDICAL COLLEGE, CHENNAI

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

MARCH 2O1O

CERTIFICATE

This is to certify that this dissertation titled **"A Comparative Study Of 0.25% Bupivacaine With Clonidine, Fentanyl And Midazolam As Adjuvants For Brachial Plexus Block"** has been prepared by **Dr. C. SUGANTHALAKSHMI** under my supervision in the Department of Anaesthesiology, Government Kilpauk Medical College, Chennai during the academic period 2008-2010 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 (MD Anaesthesiology) and her dissertation is a bonafide work.

Prof. Dr. V. Kanagasabai, M.D.
DEAN
Government Kilpauk Medical College
& Hospital,
Chennai.

Prof. Dr. P.S.Shanmugam, M.D., D.A.
Professor & HOD
Department of Anaesthesiology
Government Kilpauk Medical College
& Hospital,
Chennai.

CONTENTS

ACKNOWLEDGEMENT

I wish to express my sincere thanks to **Dr.V. Kanagasabai, MD,** Dean Government Kilpauk Medical College, Chennai for having kindly permitted me to utilise the facilities of the hospital for the conduct of the study.

My heart felt thanks to Professor and Head of the Department of Anaesthesia Kilpauk Medical College and Hospital **Dr. P.S.Shanmugam M.D., D.A.,** for his motivation, valuable suggestions, constant supervision and for providing all necessary arrangements for conducting the study.

I thank Department of Plastic Surgery and Department of Orthopaedics KMCH and their faculty members for their kind cooperation and permitting me to use the hospital facilities for the study.

I express my sincere thanks to the other Professors of Anaesthesiology Department **Dr. M.Vasanthi M.D., D.A.,** and **Dr.S.Gunasekar M.D., D.A.,** Dr. Soundarapandian, M.D., D.A., for their guidance and encouragement in carrying out this study.

I wish to express my gratitude to Prof. Dr. Azhar Hussian M.D., D.A., Registrar in Anaesthesiology, KMCH for his invaluable ideas and consisting support.

I thank all the Assistant Professors and Tutors of Anaesthesiology KMC & Royapettah Hospital for their keen interest and support without which this study would not have been possible.

I also thank all my colleague Postgraduates for supporting me through out the study.

I also thank the theatre personnel for their co-operation and assistance. I also thank my family members and friends for their constant encouragement and help through out the study.

I also thank statistician Mr.Padmanabhan for his work on statistics. I wish to thank all the patients whose willingness and patience made this study possible.

I finally thank God Almighty for HIS blessings in successfully completing the study.

INTRODUCTION

Regional anaesthesia as the name implies is the blocking of peripheral nerve conduction in a reversible manner by using local anaesthetic agents thereby one region of the body is made insensitive to pain and is devoid of reflex response to surgical stimuli. The central nervous system is spared, so the patient is conscious during the surgical procedure.

Regional anaesthesia offers many advantages over general anaesthesia for surgery on upper extremities particularly in emergency operations.

Advantages of Regional over General Anaesthesia

- Completely attenuates rather blocks stress response and attended stress hormones release.
- Causes least disturbance to the normal physiology than any other type of anaesthesia.
- Proven to be safe for high risk patients who are in greater risk due to stress imposed by general anaesthesia.
- Only method of anaesthesia, which prevents all afferent impulses from the site of surgery reaching the central nervous

system. Hence the need for polypharmacy and its attented risks are eliminated.

- Along with complete pain relief and total muscle relaxation, it produces vasodilatation, which improves blood circulation and prevents tissue hypoxia.
- Many intraoperative and post operative complications of general anaesthesia are avoided.
- Postoperative pain relief is ensured for a longer duration by using long acting local anaesthetics and for several days if continuous block using catheter technique is employed.
- It is cost effective & safe
- Avoids theatre pollution.
- Safest technique for patients with full stomach.
- All adverse effects of airway manipulation can be avoided.

Brachial plexus can be blocked by different approaches [1-4], but the ones frequently employed for blocking brachial plexus include.

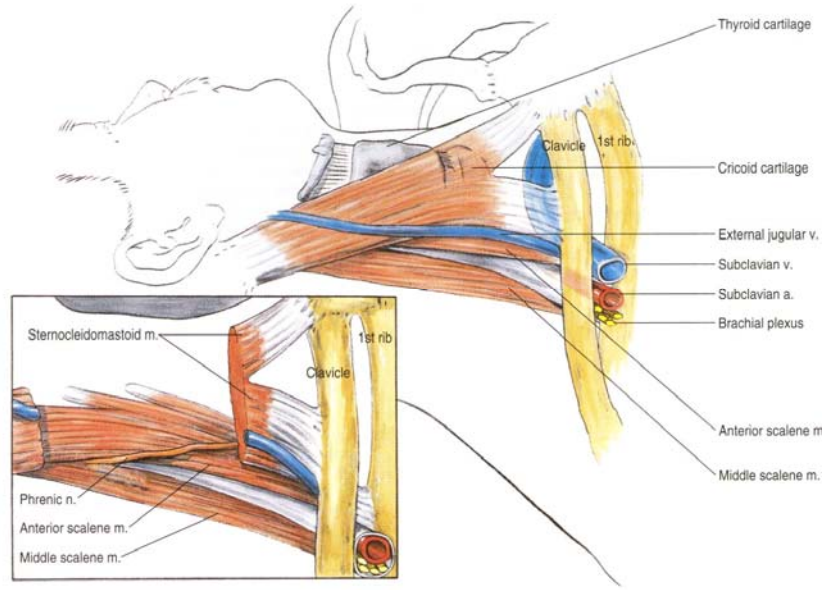
(a) Inter scalene approach

(b) Supraclavicular approach

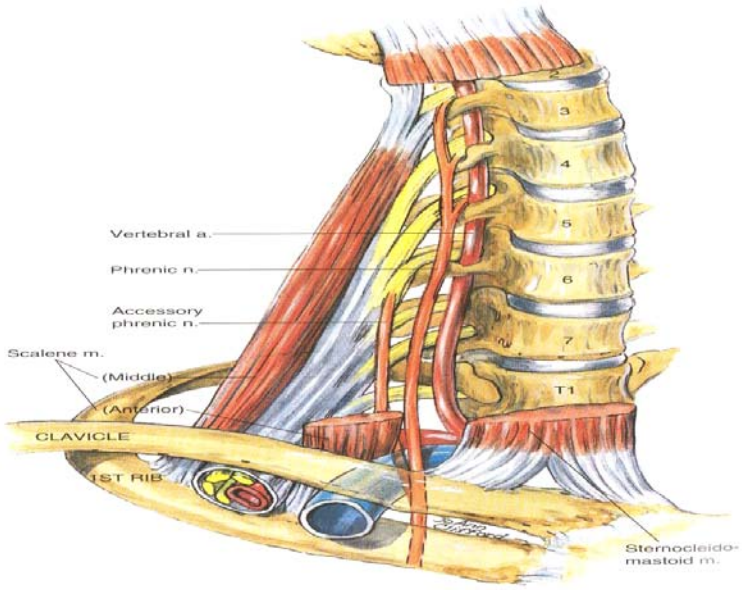
(c) Infraclavicular approach

(d) Axillary approach

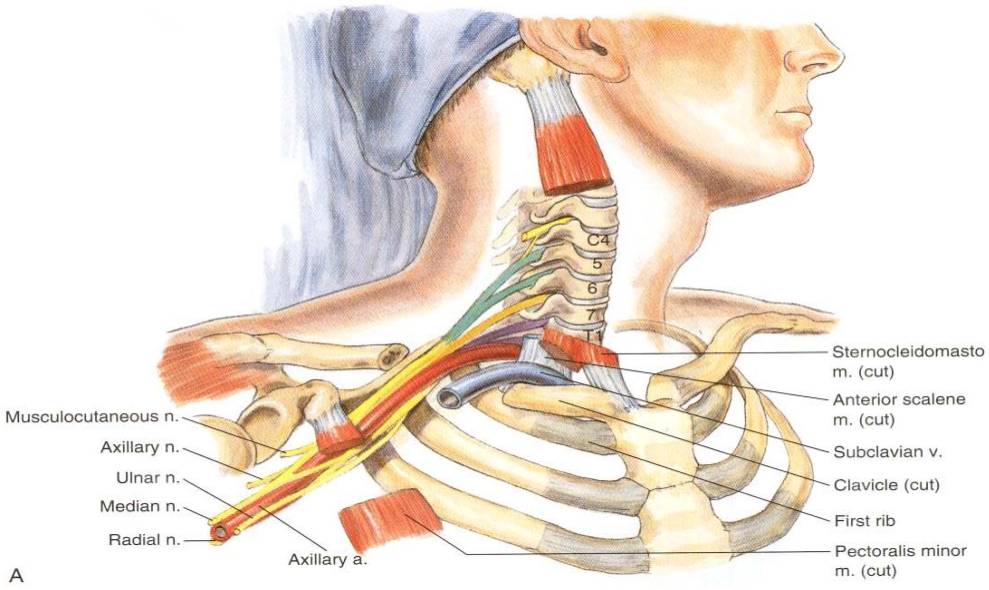
Interscalene approach



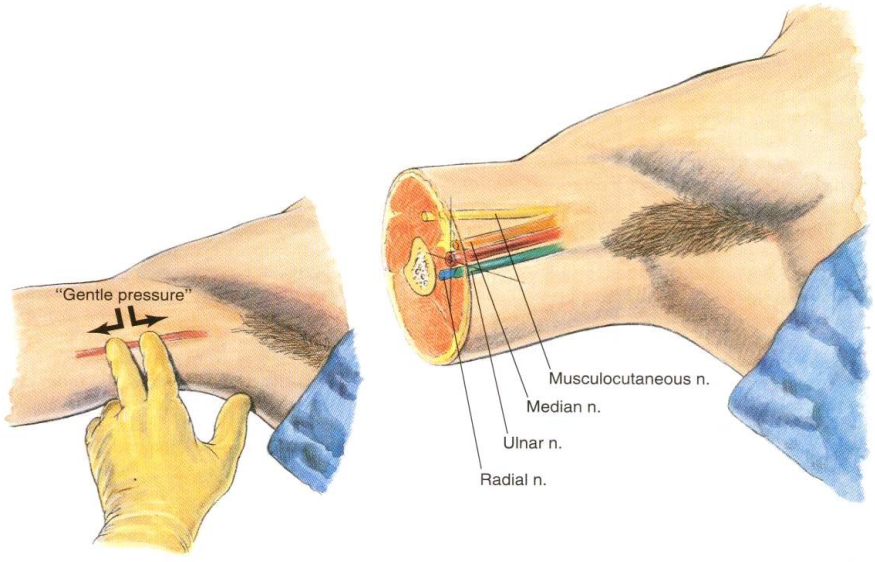
Supraclavicular approach



Infraclavicular approach

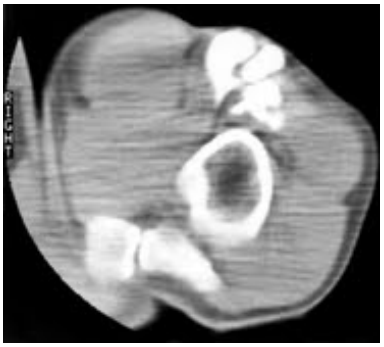


Axillary approach



Axillary[1] approach has the lowest incidence of serious complications and can be performed with ease. But there are limitations associated with axillary approach like

- Unlike in paediatric age group each and every nerve is enclosed in separate sheaths in adults.
- It is inadequate for operations on the arm & shoulder
- It is difficult to block the musculocuteneous nerve predictably with resultant sparing of the radial aspect of forearm and dorsum of the hand.
- Tourniquet pain is not well tolerated.
- Also abducting the arm by 90° for giving the block may be painful and even dangerous in traumatic lesions of the upper extremity.



CT of axillary block showing contrast medium to remain in three separate compartments

The brachial plexus is approached at the level of the trunks and the compact arrangement of trunks at supraclavicular level gives a high success rate with minimum local anaesthetic drug volume and a dense and fast onset block. Hence the supraclavicular approach is the method of choice for blocking the brachial plexus.

William Steward Halsted first performed brachial plexus block is 1885. In 1911 Kulemkampff and Hirschel described the first percutaneous brachial plexus block by supraclavicular and axillary routes respectively.

Since then several techniques of brachial plexus block have been described with the purpose of improving the efficacy and success rate and minimizing the risk and rate of complications. Of the various techiques the most widely used methods are classical technique described by Patrick (1940), Vertical plump bob approach described by Brown, 1st rib walk over technique described by Bonica & Moore and subclavian perivascular technique described by Winnie and Collins (1964).

Of the several local anaesthetic drugs used for brachial plexus block, Bupivacaine is used most frequently as it has a long duration of action varying from 3 – 8 hours.

To prolong the duration of analgesia various drugs have been studied as adjuvants to local anaesthetic solution and techniques like the continuous catheter placement in the plexus have evolved. These adjuvant drugs ideally are expected to prolong the analgesic effect without causing any systemic side effects or prolonging motor blockade. Commonly used additives to local anaesthetic solutions are epinephrine, clonidine and opioids [40,41], benzodiazepines and phenylephrine.

Clonidine [8-12] an α2 adrenergic agonist has been extensively studied as an adjunct to general and regional anaesthesia. It has been shown to produce this effect by activation of postsynaptic adrenergic receptors [13].

Fentanyl an μ-receptor agoinst has also been used widely in intrathecal, extradural and peripheral nerve plexus blockade[33-38].

Midazolam, a water soluble benzodiazepine, is known to produce antinociception [48,49] and to enhance the effect of local anaesthesia when given epidurally or intrathecally [50-54]. Midazolam produces this effect by its action on GABA – A receptors [48,51,54]. The presence of GABA receptors in peripheral nerves is also demonstrated [44,46,55].

This study is intented to determine and compare the effects of adding additives like clonidine, fentanyl and midazolam to bupivacaine in brachial plexus blockade by supraclavicular approach with regard to onset, and blockade duration of blockade along with its analgesic efficacy and quality of analgesia and sedation.

AIM OF THE STUDY

The aim of the present study is to evaluate the effects of addition of 1 mcg / kg of preservative free clonidine to the maximum of 75 mcg, 1 mcg / kg of preservative free fentanyl to the maximum of 50mcg and 50mcg / kg of preservative free midazolam to 30ml of 0.25%. Bupivacaine solution in supraclavicular brachial plexus block with regard to

- Onset of blockade
- Duration of blockade
- Quality of analgesia
- Sedation
- Hemodynamic stability
- Complications if any

ANATOMY OF THE BRACHIAL PLEXUS[1-4]

Knowledge of the formation of brachial plexus and of its distribution is absolutely essential for the precise and effective use of brachial plexus analgesia for surgeries of the upper limb. A thorough understanding of the vascular, muscular and fascial relationships of the plexus thoroughout its formation and distribution is equally essential in order to master the various techniques of brachial plexus analgesia.

In its course from the inter vertebral foramina to the arm, the fibres that constitute the plexus are composed consecutively of roots, trunks, divisions, cords and terminal branches which are formed through complex process of combining, dividing, recombining and finally redividing.

The brachial plexus is formed by the union of anterior primary rami of the fifth to eighth cervical nerve and first thoracic nerve with occasional contributions from the fourth cervical nerve (prefixed) above and second thoracic nerve (post fixed) below. These nerves unite to form trunks, which lie in the neck above the clavicle. Its roots pass through the fascia enclosed space between the scalenus anterior and the scalenus medius accompanied by the subclavian artery and invaginate the scalene fascia to form a neurovascular bundle. This fascia becomes axillary sheath in the axilla.

Relations of Brachial plexus

Anterior relations

The skin, superficial fascia, platysma, and supraclavicular branches of the superficial cervical plexus, the deep fascia and external jugular vein. The clavicle is in front of the lower part and scalenus anterior is in front of the upper part.

Posterior Relations

Scalenus medius and the long thoracic nerve of bell.

Inferior relations

Related to the first rib

Superior relations

Lies first above and then lateral to the subclavian artery.

Sympathetic contribution to the plexus

Close to their emergence, the 5^{th} & 6^{th} cervical nerves, each receive a grey ramus from the middle cervical sympathetic ganglion. The 7^{th} and 8^{th} cervical nerves receive a grey ramus from the inferior cervical ganglion.

Roots

Anterior primary rami of C5-C8 and T1(Occasionally C4 & T2)

Trunks

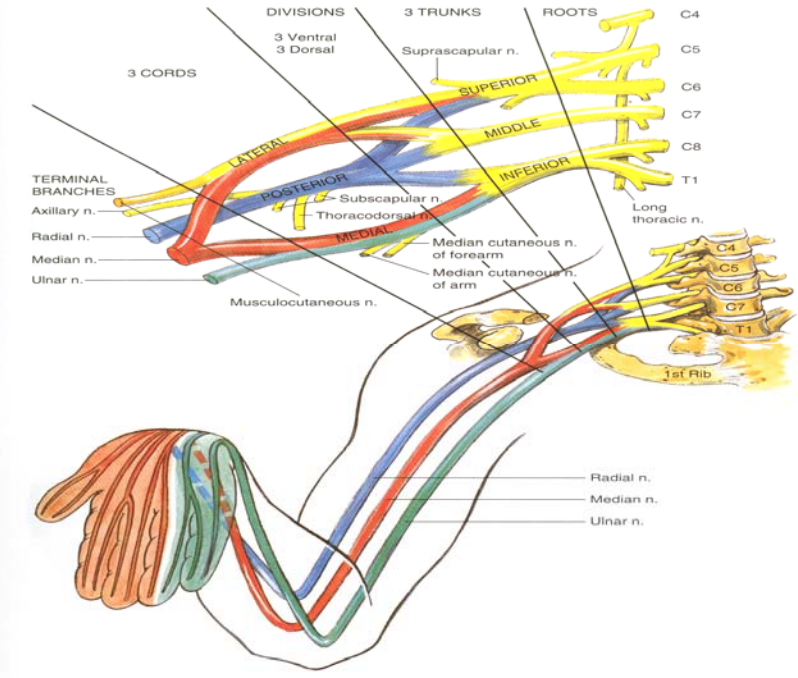
- Upper trunk – anterior rami of C5 and C6
- Middle trunk – anterior rami of C7
- Lower trunk – anterior ramus of C8 and T1

Divisions

Behind the clavicle, each trunk divides into anterior and posterior divisions.

Cords

- Lateral cord - Anterior divisions of upper and middle trunks (C5-C7)
- Medial cord - Anterior division of lower trunk (C8-T1)
- Posterior cord - Posterior divisions of all the three trunks (C5-T1)



Branches

From Roots

- Nerve to serratus anterior (C5-C7)
- Muscular branches to longus cervices C5-C8
- Nerve to three scalene C5-C8
- Nerve to Rhomboids C5
- A twig to phrenic nerve C5.

From Trunks

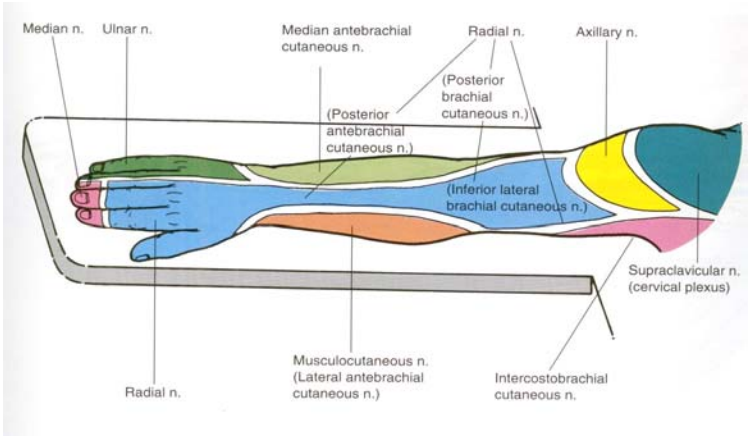
- Supra scapular nerve C5 & C6
- Nerve to subclavius C5 & C6

From Cords

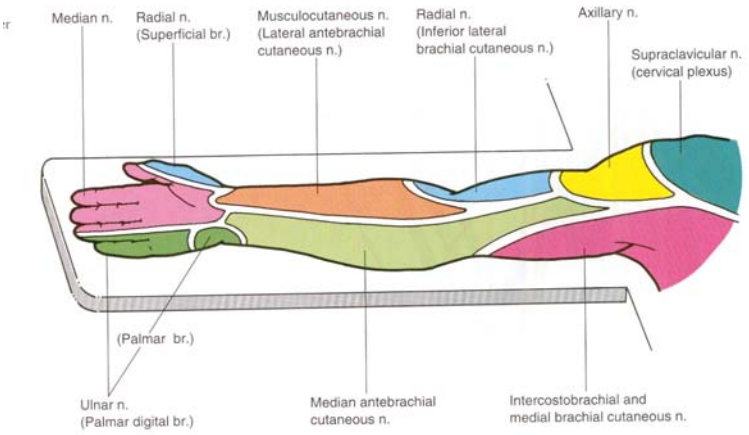
- Lateral cord
  - Lateral pectoral nerve C5-C7
  - Lateral Root of Median nerve C5-C7
  - Musculo cuteneous nerve C5-C7

- Medial cord
  - Medial pectoral nerve C8-T1
  - Medial root of median Nerve C8-T1
  - Medial Cuteneous Nerve of Arm C8-T1
  - Medial Cuteneous Nerve of forearm C8-T1
  - Ulnar nerve C8-T1

- Posterior cord
    - Radial nerve C5-T1
    - Axillary nerve C5-C8
    - Thoracodorsal nerve C6-C8
    - Upper and lower subscapular (C5-C6)



Sensory innervation of arm



Familiarity with the perineural structures that surround and accompany the brachial plexus as it leaves the vertebral column on its course to the upper arm is important as the knowledge of the formation

and distribution of the neural plexus it self. Palpable muscular and vascular landmarks allow accurate location of the plexus per cuteneously. An appreciation of the fascial relations is absolutely essential since this is the basis for all the perivascular techniques.

After leaving the intervertebral foramina, the anterior primary rami of the nerves destined to become the brachial plexus travel in the gutter formed by the anterior and posterior tubercles of the corresponding transverse process of the cervical vertebra. After leaving the transverse process, the roots of the plexus descend in front of the middle scalene muscle, which arises from the posterior tubercles of the transverse process of the lower six cervical vertebra. The insertion of this muscle on the first rib is separated from that of the anterior scalene muscle by the inferior trunk of the brachial plexus. The anterior scalene muscle arises from the anterior tubercles of the transverse process of 3^{rd} – 6^{th} cervical vertebra & inserts on the scalene tubercle of the first rib, thus separately subclavian artery from the subclavian vein.

The fascia covering both the scalene muscles is derived from prevertebral fascia which splits to invest these muscles and then fuses again at their lateral margins to form an enclosed interscalene space. Therefore, as the roots leave the transverse process they emerge between

two walls of the facia covering the anterior and middle scalene muscle. In their descent toward the first rib to form the trunks of the plexus, the roots may be considered to be sandwiched between anterior and middle scalene muscles, the fascia of which serves as a sheath of the plexus. As the trunks approach the first rib, they are rearranged as superior, middle and inferior trunks.

As the trunks of the plexus cross the first rib, they are joined by the subclavian artery, which lies in a plane anterior to the trunks, so that the inferior trunk lies behind the artery in the subclavian groove with the middle and superior trunks above the level of the vessel. At this level the artery and trunks are moving laterally across the ribs and invaginate the scalene fascia to form the subclavian perivascular space, which is continuous medially and superiorly with the inter scalene space and inferiorly and laterally with axillary perivascular space.

The important concept is that there is a continuous fascia enclosing the perineural and perivascular space extending from cervical transverse process to several centimeters beyond the axilla. This space has been divided in to an axillary perivascular space and an inter scalene space. The existence of such a continuous perineural space renders brachial plexus block simple. The space described may be entered at any level,

and the volume of the anaesthetic injected at that level would determine the extent of anaesthesia. Thus, the technique to be used in any case should be determined on the basis of the surgical site, the required level of anaesthesia, the physical status and habitus of the patient.

The upper medial aspect of the arm is not anaesthetised by any brachial plexus block technique, since this area is innervated by the intercosto brachial nerve T2. This nerve can be blocked by subcutaneous infiltration across the upper medial aspect of the arm using 3-5 ml of local anaesthesia solution for surgical anasthesia or tourniquet.

The brachial plexus can be blocked at the level of the roots, trunks, cords or peripheral branches. The block at each level has a distinct distribution of anaesthesia, advantages, disadvantages and complications.

CLINICAL PHARMACOLOGY

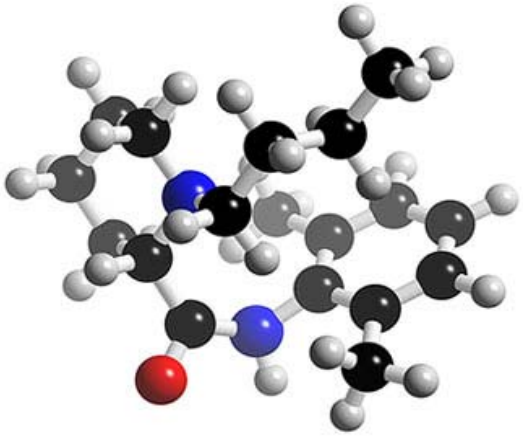
Bupivacaine

Sythesised by Evenstam in 1957 in Sweden

First came in to clinical use in 1963.

Bupivacaine is an anilide compound

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



Presentation

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	:	0.4 7 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.

(1) Pain
(2) temperature
(3) touch
(4) Proprioception and
(5) Skeletal muscle tone.

The analgesic effects of bupivacaine are thought to be due to its binding to the prostaglandin E2 receptors, subtype EP1, (PGE2 EP1] which inhibits the production of prostaglandins thereby reducing fever, inflammation and hyperalgesia.

Routes of administration / doses

Bupivacaine may be administered topically by infiltration, 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 > Subcuteneous)
- The dose – a linear relationship exits between the total dose and the peak blood concentration achieved.
- The presence of vasoconstrictors which delay absorption.

The addition of adrenaline to bupivacaine does not influence the rate of systemic absorption as,

- The drug is highly lipid soluble and therefore uptake into fat is rapid.
- The drug has a direct vasoconstrictor effect.

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.

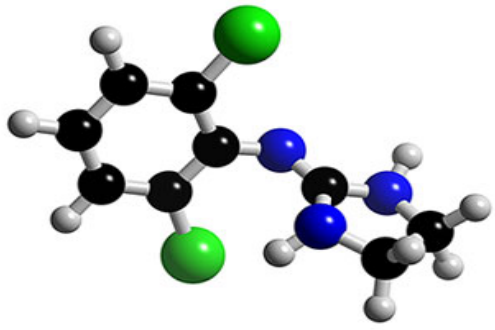
CENTRAL NERVOUS SYSTEM

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.

Pharmacology of Clonidine

Clonidine is a prototype, partially selective alpha-2 adrenoreceptor agonist (alpha 2; alpha-1) 220:1. It is a centrally acting imidazole compound. It was synthetised in the early 1960's as a vasoconstricting nasal decongestant.

STRUCTURAL FORMULA



MOLECULAR FORMULA

(2-(2,6 – dicholorophenyl amino) – 2- imidazoline)

Physical Property

Molecular Weight : 226.56

Preparations

i. Tablets – 0.1mg, 0.15mg, 0.2mg, 0.3mg

ii. Injection (parenteral) 0.15mg /ml ampoule (1ml)

iii. Injection (preservative free) For epidural & spinal injection (0.1mg/ml)

iv. Transdermal Therapeutic Patch release

Routes of Administration

It can be given as oral tablets, intraveneous injection, subarachnoid or epidural injection, as an additive for regional nerve blocks.

Pharmacokinetics

Oral clonidine is well absorbed with a bio-availability of nearly 100%. The onset of action starts from 30-60 minutes. The peak effect is between 60 to 120 minutes and its action lasts for upto 8 hours. Clonidine has a low to moderate protein binding capacity (20-40%) It has an elimination half-life of 6-24 hours with a mean duration of about 12

hours. The elimination half life is increased upto 40 hours in patients with renal dysfunction.

There is good correlation between plasma concentration of clonidine and its pharmacological effects.

Plasma Concentration of clonidine mg/ml	Pharmacological effects
About 1	Salivary flow reduced
> 1.5 – 2	Sedation to sleep
upto 1.5-2	Hypotension
> 2	Vasoconstriction to Hypertension

METABOLISM & ELIMINATION

Nearly 50% of clonidine is eliminated in the urine and remaining drug undergoes hepatic biotransformation. Biliary and faecal excretion is responsible for 20% of drug elimination.

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 renal blood 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 prejunctional nerve endings and by decreasing plasma concentration of nor-epirephrine.

Coronary Circulation

The direct effect of α-2 agonist on coronary vasulature 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 coeruleus 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. *Preanaesthetic 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 anaesthetic shivering.

2. *Spinal & Epidural Analgesia*

Preservative free clonidine injected epidurally (2-10mcg/kg) or in to subarachnoid space (0.3 – 3mcg/ 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 Anaesthesia*

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

4. *Treatment of Post anaesthetic shivering.*

Injection clonidine 3 mcg/kg 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, occuring 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 hypertension caused by clonidine
2) Tricyclic antidepressants inhibit the antihypertensive effect of clonidine by a unknown mechanism.

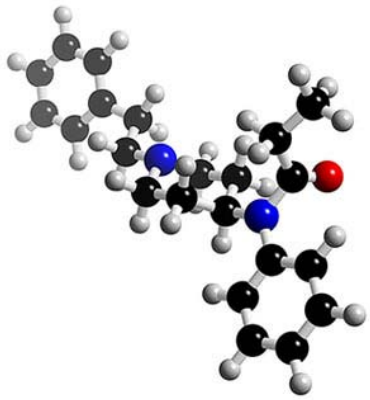
Overdose

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.

PHARMACOLOGY OF FENTANYL

Structure

4 anilinopiperidines that are structurally similar to pethidine.



Fentanyl is a synthetic opioid with morphine like actions. Act at μ receptor as a agonist. It is more specific, shorter acting & 80 – 100 times more potent than morphine.

PHARMACOKINETICS & PHYSIOCHEMICAL PROPERTIES

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

Pharmaco Dynamics of Fentanyl

Cardio Vascular System

Bradycardia – Vagal stimulation in high doses.

No effect on cardiac contractility

Hypotension in large doses due to bradycardia, venodilation and suppression of central sympathetic out flow.

Respiratory System

Dose dependant respiratory depression through direct effect on medullary respiratory centre. Effects are:

Apnoeic threshold increased.

Hypoxic drive decreased.

Delayed respiratory depression.

CNS

Analgesia, Euphoria, Sedation, Hypnosis, Miosis,

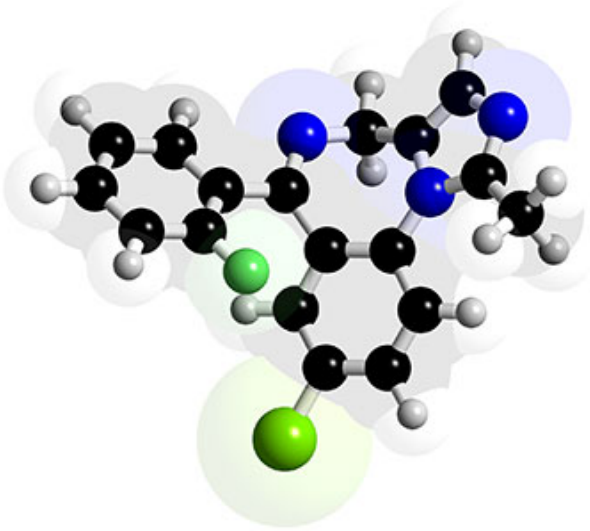
GIT – delays gastric emptying, produces biliary colic, nausea, vomiting.

Endocrine System : Attenuates the stress response

Side Effects : Pruritis, nausea, vomiting, urinary retention, apnoea, seizures, chest wall regidity.

Pharmacology of Midazolam

Midazolam is a water soluble imidazobenzodiazepine (8-chloro-6-(2-flurophenyl)-1-methyl – 4H – imidazo (1, 5 - 9) (1, 4) Benzodiazpine) and its unique feature being its PH dependant imidazole ring which opens at pH < 4 and accounts for its stability in aqueous solution and rapid metabolism. At pH > 4, the ring closes leading to increase in lipid solubility.



$C_{18}\ H_{13}\ ClFN_3$

Pharmaco Kinetics

- It has a PH of 3.5 with Pka of 6.15
- Protein binding : 96% - 98%
- Volume of distribution : 1-1.5l/kg
- Clearance: 6-8ml/Kg/min

- Elimination halftime : 1.4 hrs. Increased in elderly & obese
- Metabolised by hepatic microsomal enzyme cytochrome P-450 by hydroxylation to 1OH and 4OH midazolam.

Excreted in urine as glucuronide conjugates Erythromycin decreases its hepatic clearance leading to increased duration of action. Less than 0.02% is excreted unchanged. Therefore it is not affected by renal failure.

Mechanism of action

It is thought that the actions of benzodiazepines such as midazolam are mediated through the inhibitory neurotransmitter gamma-aminobutyic acid (GABA), which is one of the major inhibitory neurotransmitters in the brain. Benzodiazepines increase the activity of GABA, thereby producing a calming effect, relaxing skeletal muscles, and inducing sleep. benzodiazepines act as agonist at the benzodiazepine receptors, which form a component of the benzodiazepine GABA receptor – chloride ionophore complex. Most anxiolytics appear to act through atleast one component of this complex to enhance the inhibitory action of GABA.

Dosages & Routes of Administration

Routes: Oral, Nasal, IM, IV, intrathecal & epidural

Dosage

Sedation	:	0.05 – 0.1 mg/kg
Pre-medication	:	0.07 – 0.08 mg/kg
Induction	:	0.1 – 0.3 mg/kg
Infusion	:	2 – 5 mcg/kg/min
Intrathecal	:	0.3 – 2mg
Epidural	:	0.1 – 0.2 mg/kg.

Actions

Central Nervous System

Decreases cerebral blood flow, cerebral O_2 requirement and intra cranial pressure.

Sedation, Hypnosis, Anxiolysis, Antegrade amnesia, Anti convulsant.

Respiratory System

Transient apnoea occurs when administered in doses greater than 0.15mg/kg and in opiod premedicated patients.

Potent respiratory depressant especially in COPD patients.

Cardiovascular System

Decrease in peripheral vascular resistance and transient alteration of baroreceptor reflexes leading to hypotension and tachycardia. In

hypovolemic and elderly patients there is increased risk of significant hypotension.

Local effects

No venous irritation & thrombophlibitis.

Mechanism of pain relief in Central Neuraxial Blockade

It acts on spinal GABA receptors. There are 2 types of GABA receptors. GABA-A and GABA-B. Midazolam binds to the alpha subunit of the pentamer GABA-A receptors leading to its conformational change causing increased chloride ion conductance and hyperpolarisation and thereby acts potentiating the inhibitory neurotransmitter, GABA. This is mainly a post synaptic action while GABA-B receptors mainly have presynaptic antinociceptive effect by decreasing the excitatory neurotransmitter release.

Intrathecal midazolam positively modulates GABA-A/ Benzodiazepine receptor complex causing the release of an endogenous opioid acting at opioid receptors and also intrathecal midazolam causes anti-nociception by combining with three different receptor subtypes of GABA-A in the spinal cord.

PHARMACOKINETICS OF LOCAL ANAESTHETIC IN BRACHIAL PLEXUS BLOCKADE

When a local anaesthetic is injected around a nerve trunk, it will soak the trunk is an advancing front. Transmission in fibres situated in the periphery of the trunk (mantle fibres) will be first blocked and those in the centre of the trunk (core fibres) last. Further transmission, in peripherally placed fibres will be blocked over a longer length of time compared to central fibres. Thus analgesia will appear first and last longest in the territory supplied by peripheral fibres. If the pool of local anaesthetic is small or of the injection was not accurate or too dilute, the fibres in the centre of the trunk escape blockade.

Theory of Winnie

The trunks are arranged so that the central fibres are the longest, supplying the extremities of the limb while the shorter fibres are arranged more peripherally as their area of supply is more proximal. Winnie groups the fibres in to two: the peripheral mantle fibres which contain the motor fibres and core fibres which are mainly sensory. Peripheral motor fibres supply the muscles of the forearm and the central fibers carry sensation from the hand.

REVIEW OF LITERATURE

Technique and Drug

The supraclavicular brachial plexus block is one of several techniques of the brachial plexus. The block is performed at the level of brachial plexus trunks confined to a very small surface area. It produces rapid onset, predictable and dense anaesthesia. Kulenkmapff of Germany in 1911 performed the first precuteneous supraclavicular approach. This technique was later published in 1928 by Kulenkampff and Persky (Classic approach).

Clonidine in brachial Plexus Block

1. Daniel M. Popping, Nadir Elia et al.[13], in Anaesthisiology 2009 have said that use of clonidine 30-300mcg, mostly 150mcg added to Bupivacaine have observed that time to onset of sensory block was significantly reduced when using clonidine. Duration of sensory and motor block was significantly prolonged in clonidine group. Duration of postoperative analgesia was significantly increased in clonidine group.

2. Hutschala D, Mascher H, Sohmetterer L, Klimschaw, Fleck T, et al[5] have studied the effects of clonidine added to bupivacaine enhances and prolongs analgesia after brachial plexus block via a local mechanism in healthy volunteers. They studied the effects of clonidine 2 mcg /kg Plus 0.25% of Bupivacaine 1mg/kg in 7

healthy volunteers with a control treatment of local analgesic with 0.9% NaCl solution for the block and intra muscular injection of saline. The results were, the mean duration of sensory blockade was 270 mins in clonidine block when compared to `O' minutes for control treatment. Administration of clonidine was associated with sedation and a decrease in heart rate and blood pressure independent of the route of administration.

3. Carabine UA, Milligan KR, Moorej et al[11] of Department of Anaesthetics, Queen's University, Belfast have assessed the use of clonidine and bupivacaine for postoperative analgesia. Both drugs were administered via extradural route. The analgesia produced by clonidine was superior to that of bupivacaine alone.

4. Erlacher W, Schuschnig C, Koinig H, Marhofer P et al [6,7] of Department of Anaesthesia and IC Hospital Vienna, Austria have studied Clonidine as adjuvant for mepivacaine, ropivacaine and bupivacaine in axillary perivascular brachial plexus block. 120 trauma patients were randomly allocated in to six groups. Brachial plexus block was performed using 40ml of drug plus 1ml (0.150mg) of clonidine, with the control of 40ml of local anaesthetic solution + 1ml of NaCl 0.9%. They found that Mepivacaine groups showed a rapid onset and the ropivacaine and bupivacaine groups had a longer onset time. They concluded that addition of clonidine has a different impact on each of the three

local anaesthetics investigated in terms of onset and duration of block.

5. Duma A, Urbanek B, Sitzwohlc, Krieger A et al [9] have performed a randomised controlled study of clonidine as a adjuvant to local anaesthetic axillary brachial plexus block. 20 patients each were investigated using 40ml of levo bupivacaine 0.5% plus 0.150mg of clonidine and 40ml of levobupivacaine 0.5% plus 1ml of NaCl 0.9% and 40m of bupivacaine 0.5% plus 0.150mg of clonidine and 40ml of bupivacaine 0.5% plus 1ml of NaCl 0.9% respectively. There was a significant higher variance ($P < 0.001$) was found in the 2 group with clonidine than in two groups without clonidine.

6. Bhatnagar S, Mishra S, Madhurima S, Gurjar M, Mondal[10]AS Dept. of Anaesthesiolosy, Institute Rotary Cancer Hospital, AIIMS, New Delhi have performed randomized study of clonidine as adjuvant to continuous paravertebral bupivacaine for post – thorocotomy pain. They evaluated the effects of clonidine as an adjuvant to bupivacaine for continuous paravertebral intercostal nerve block, measuring pain and sedation scores and PFT. Thirty patients scheduled to undergo thorocotomy were randamized to receive either a bolus of 0.125%. Bupivacaine 2mg/kg or bupivacaine 2mg/kg with clonidine 2mcg/kg . They concluded that clonidine as an adjunct to bupivacaine for continuous paravertebral intercostal nerve block improves pain relief after thorocotomy, but

hypotension and sedation are adverse effects interfering with its clinical application.

7. El Saied, Stenyn et al[15] have observed that addition of clonidine 150mcg prolongs the effect of Ropivacaine for axillary brachial plexus blockade.

8. Jean J. Eledjan, Jacques Deschodt et al[12] have observed that addition of clonidine to Bupivacaine brachial plexus is a attractive alternative to epinephrine to prolong the duration of analgesia following upper limb surgeries under conduction anaesthesia.

FENTANYL IN BRACHIAL PLEXUS

1. Kohki Nishikawa MD, Noriaki Kanya, MD, Ph.D, Masayasu Nakayama et al [36,39] of Department of Anaesthesiology, Japan have evaluated the effects of fentanyl added to lignocaine for axillary brachial plexus block in 66 patients for elective hand and forearm study. In this double blinding study all patients received 40ml of 1.5% lignocaine with 1:200,000 epinephrine and randamized in to 3 groups receiving 2ml of normal saline, 100mcg of fentanyl in the block and 100mcg of fentanyl IV. They concluded that addition of fentanyl to lidocaine causes an improved success rate of sensory blockade. IV fentanyl had no effect on success rate, onset or duration of blockade.

2. Karakaya D, Buyukgoz F, Baris S et al[33] have evaluated the analgesic and anaesthetic effects of 40ml Bupivacaine 0.25% alone and 40ml of 0.25% Bupivacaine + 2.5 mg/ml of fenlantyl (BF) and 40ml of 0.125% Bupivacaine plus 2.5mcg/ml of fentanyl. The onset time, duration of sensory and motor blocks, duration of analgesia were noted. They found out that mean duration of sensory block and analgesia were longer in group BF. Hemodyanamic parameters similar in all groups. They concluded that addition of 100mcg/ml fentanyl to 0.25% Bupivacaine almost doubles the duration of analgesia following axillary brachial plexus block when compared with 0.25% Bupivacaine alone.

3. J.E.Bazin, C. Massoni, P. Bruelle, V. Fenis, et al.,[34] Department of Anesthesia France have compared the duration of analgesia produced by a mixture of lignocaine and bupivacaine either alone or combined with morphine (75mcg/kg), buprenorphine (3mcg/kg) or sufentanil (0.2 mcg/kg) in 80 patients after brachial plexus block for orthopedic surgery of the upper limb. They concluded that the addition of opoids to a local anaesthetic mixture lengthens the duration of analgesia.

4. Kardash K, Schools A, Concepcion M. et al[35] Department of Anaesthesia, Canada have examined the effects of adding fentanyl to mepivacaine supraclavicular blocks. They concluded that addition of 75mcg of fentanyl to mepivacaine has no significant effect on block characteristics. It may enhance postoperative analgesia, but the duration of this effect is too brief to be clinically useful.

5. Mostafa Abdel Hamid Abo Eltnin, Ismail Ewio et al. [37], have evaluated the effects of fentanyl to local anesthetic in Peribulbar block in patients undergoing vitrectomy due to vitreous haemorrhage. Fentanyl group receive 20mcg added to local anasthetic. The onset, duration of lid and globe akinesia were assessed. Fentanyl group had prolonged duration of analgesia 3.25 ± 0.67 hrs as compared to 1.85 ± 0.67 in control group. They concluded that addition of fentanyl to local anaesthetic mixtures fastens the onset and prolong the duration of akinesia and improve quality of postoperative pain in peribulbar block.

6. Power, I.B.Sc. Hons, F.C. Anaes, et.al.[38], have studied the effects of fentanyl, meperidine and diamorphine on A and C fiber conduction in an invitro rabbit nerve preparation was examined. The effect of fentanyl, meperidine and diamorphine were observed. Both fentanyl and meperidine potentiated the block produced by a low concentration of bupivacaine.

MIDAZOLAM IN BRACHIAL PLEXUS BLOCK

Peripheral GABA receptors

Brown et al [44,45] observed that extrasynaptic GABA receptors occur on both neuron somatic and unmyelinated axons in the mammalian peripheral nervous system Activation of these receptors leads to depolarisation, reduced spike amplitude, and slowed conduction probably mediated by increased chloride conductance.

Midazolam in Brachial Plexus

Koj Jarbo et al[61] observed that midazolam in combination with bupivacaine hastened onset of sensory and motor block and improved postoperative analgesia when used in brachial plexus block, without producing adverse effects.

Intrathecal midazolam

Batra et al [55] observed that addition of midazolam to bupivacaine intrathecally provided better postoperative analgesia without any adverse effects.

Kim et al[54] observed that intrathecal midazolam increases the analgesia effects of spinal blockade with bupivacaine in patients undergoing hemorroidectomy.

Epidural Midazolam

Nishiyama et al [51,53] observed that adding midazolam to continuous epidural infusion of bupivacaine for postoperative pain can provide a better analgesia, amnesia and sedation than bupivacaine alone.

MATERIALS AND METHODOLOGY

60 adult patients of both sexes in the age group of 20-60 years belonging to ASA I / II category and their weight ranging between 40-70 kgs posted for various types of upper limb surgeries at the Department of Orthopedics and Department of Plastic surgery Govt. KMCH formed the study group.

This study was designed as a prospective randamized comparitive study. After receiving the institutional ethical committee approval and informed consent, the patients were randomly allocated into 4 groups brachial plexus block with Nerve Stimulator was performed with supraclavicular block technique.

GROUPS:

1. BC – 15 patients received 30ml of 0.25% Bupivacaine with 1mcg/kg of preservative free clonidine to the maximum of 75 mcg.
2. BF – 15 patients received 30ml of 0.25% Bupivacaine with preservative free fentanyl 1 mcg /kg to the maximum of 50 mcg.
3. BM – 15 patients received 30ml of 0.25% Bupivacaine with preservative free midazolam 50 mcg/kg.
4. B – 15 patients received 30ml of 0.25% bupivacaine.

Inclusion Criteria

- ASA I & II.
- Age Group 20-60 years
- Weight 40 – 70 kgs
- Surgeries of the upper limb.

Exclusion Criteria

- Patients refusal
- Coagulopathy
- Infection at Injection site

Patients were all pre-operatively evaluated, clinically examined and investigations done prior to assessment Procedures were explained in detail and written consent obtained.

The procedure was carried out in the theatre where facilities for resuscitation were available.

Equipment

- Sterile tray
- Sterile towel with gauze packs.
- 10ml syringes with local anaesthetic.
- Sterile gloves with marking pen and surface electrode.
- 1.5 inch 25 G needle with syringe for skin infiltration.

- 3-5 cm long, short, bevel insulated stimulating needle.
- Peripheral nerve locator.

Drugs

- 0.25% Bupivacaine vial
- Preservative free midazolam 50mcg / ml
- Preservative free fentanyl ampoule 50mcg / ml
- Preservative free Clonidine 150mcg / ml

Intraoperative and Postoperative Monitor

- Pulseoximeter
- NIBP
- ECG

Initially the pre procedure parameters were recorded ie. PR, BP, SPO2, ECG. Then block was administered. All through the study, these parameters were monitered continuously except the NIBP which was recorded intermittently. Postoperatively they were monitered for 24 hours.

Patients were observed vigilantly for development of various complications.

SUPRACLAVICULAR BRACHIAL PLEXUS APPROACH

Indications

Surgical – Surgical procedure on the proximal humerus, elbow, forearm and hand.

Therapeutic – Chronic regional pain syndromes, post amputation pain, post herpetic neuralgias.

Surface Anatomy

Important landmarks for supraclavicular block include the interscalene groove behind the posterior border of the sternocleidomastoid muscle, the clavicle, subclavian pulse. The interscalene groove can be identified by placing a finger behind the sternocleidomastoid muscle and then rolling laterally. Maneuvers to help identify landmarks include asking the patients to lift their head against resistance to identify sternocleidomastoid muscle. Sniffing accentuates the scalene muscles. The groove can be followed towards the clavicle. The external jugular vein crosses the interscalene groove and posterior border of sternocleidomastoid muscle at the level of the cricoid cartilage. The needle insertion is immediately posterior to the subclavian pulse.

Patient is placed in the supine position with the head turned away from the side to be blocked. The arm and shoulder is depressed on that side.

The skin and subcuteneous tissue is infiltrated with local anaesthetic solution. The subclavian artery is palpated above the medial third of the clavicle. A 35mm 21G insulated needle is attached to the nerve locator set at 1-5mA and inserted through the weal created in downward, inward and backward direction, so that it is pointing to the spine of second to fourth thoracic vertebra. The superior trunk of the brachial plexus is usually located first. The needle position is adjusted while decreasing the current to 0.9mA with maintenance of the muscle response.

The response that results in the greatest block success is muscle contraction below the shoulder. A cough from the patient is a warning sign that the pleura is being contacted by the needle. Incremental injection of local anaesthetic is made with repeated aspiration.

After injecting the local anaesthetic the block is tested for both sensory (using Pin prick) and motor (using muscle power) and is compared with same stimulation or power in the contralateral arm. Motor block was evaluated by thumb abduction (Radial Nerve), thumb adduction (ulnar nerve), thumb opposition (Median Nerve) and flexion of the elbow in supination and pronation of the forearm (musculocuteneous).

The Hollmens scale is used in the study for assessing both sensory and motor blockade.

Hollmen's Scale

Sensory blockade (Grade)

1. 0 - Normal sensation of pin prick

2. + - Pin prick felt as sharp pointed but weaker compared with the same area in other extremity

3. ++ - Pin prick felt as touch with blunt object

4. +++ - No perception of pin prick.

Onset of blockade means minimum grade 2 and complete blockade means minimum grade 3

Motor Blockade (Grade)

1. 0 - Normal muscle function

2. + - slight depression in muscle function as compared with pre-anaesthetic power

3. ++ - Very weak muscle action persisting in muscle

4. +++ - Complete block with absent muscular function.

Onset of blockade means minimum grade 2 and complete blockade means minimum grade 3.

Nerves studied in the block

Sensory

Lateral Cuteneous Nerve of arm

Medial Cuteneous Nerve of arm

Medial Cuteneous Nerve of forearm

Posterior Cuteneous Nerve of forearm

Lateral Cuteneous Nerve of forearm

Median Nerve

Ulnar Nerve

Radial Nerve

Motor

Median Nerve

Radial Nerve

Ulnar Nerve

Musculocutenous Nerve

Evaluation was carried out for every minute after completion of injection and the time of onset was noted both for sensory and motor blockade.

Onset of blockade both sensory & motor is defined as a minimum of grade 2 in Hollmens scale. Block was considered complete when

sensory and motor scores were atleast grade 3 in Hollmens scale. Only patients with complete block are included in the study.

Duration of sensory blockade was considered as the time interval between local anaesthetic administration and the onset of paresthesia, while the duration of motor block was defined as the time interval between local anaesthetic administration and recovery of the block.

Sedation was assessed using Sedation scores by Culebras et al where sedation was graded on a scale of 1-5 as follows.

1. Awake & alert
2. Sedated, responding to verbal stimulus
3. Sedated, responding to mild physical stimulus
4. Sedated, responding to moderate or severe stimulus
5. Not arousable

MONITERING

Baseline vital signs PR/ RR/BP/ SPO2 were recorded and monitered every 5 mins till the procedures was over and thereafter every hour for 24 hours.

Onset, completion of blockade, duration of blockade was assessed.

Pain was assessed using visual analog scale.

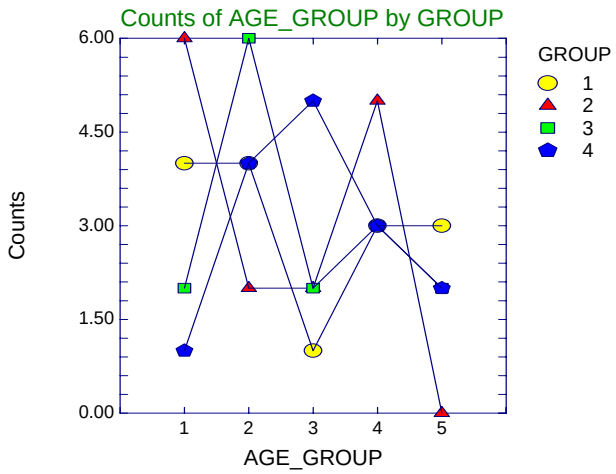
OBSERVATION

ANALYSIS OF AGE AMONG THE GROUPS

S.No.	Age Group in years	Group 1 (BC)	Group 2 (BF)	Group 3 (BM)	Group 4 (B)
1.	20-25	4	6	2	1
2.	26-35	4	2	6	4
3.	36-45	1	2	2	5
4.	46-55	3	5	3	3
5.	56-65	3	0	2	2

Using Chi Square Test

P value = 0.31967 : Not significant

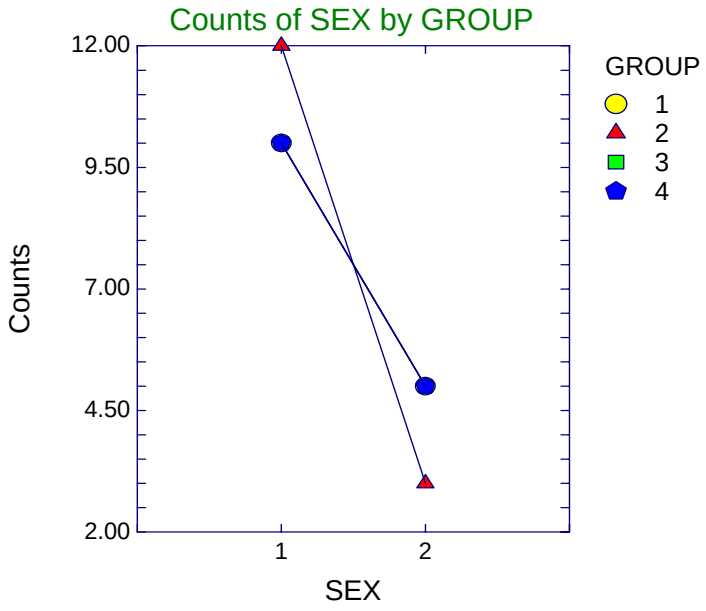


ANALYSIS OF SEX DISTRIBUTION BETWEEN THE GROUPS

S.No.	Sex	Group 1 (BC)	Group 2 (BF)	Group 3 (BM)	Group 4 (B)
1.	Male	10	12	10	10
2.	Female	5	3	5	5

Using Chi Square Test

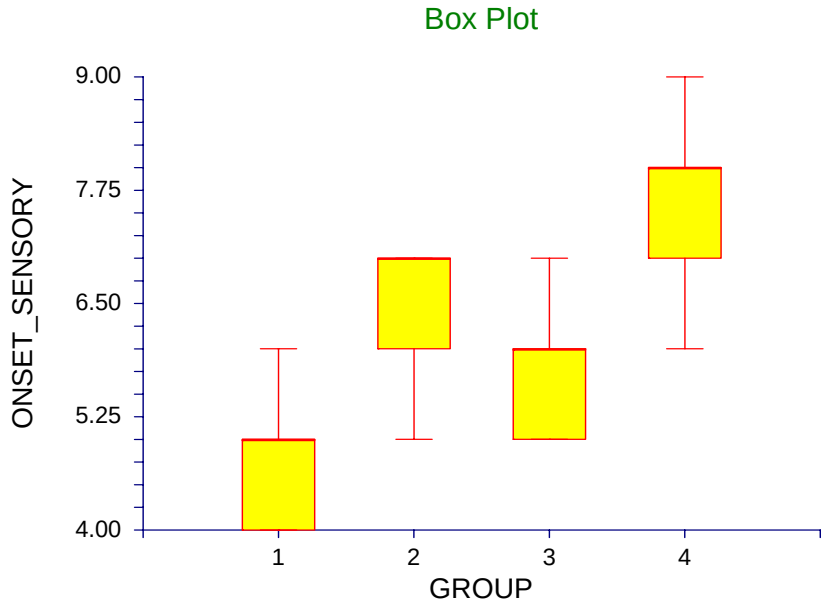
P value = 0.812772 : Not significant



ONSET OF SENSORY BLOCK

Group	Count	Mean	Standard Error
1 (BC)	15	4.733333	0.1972027
2 (BF)	15	6.466667	0.1972027
3 (BM)	15	5.8	0.1972027
4 (B)	15	7.6	0.1972027

P = 0.0000 < 0.005 Significant

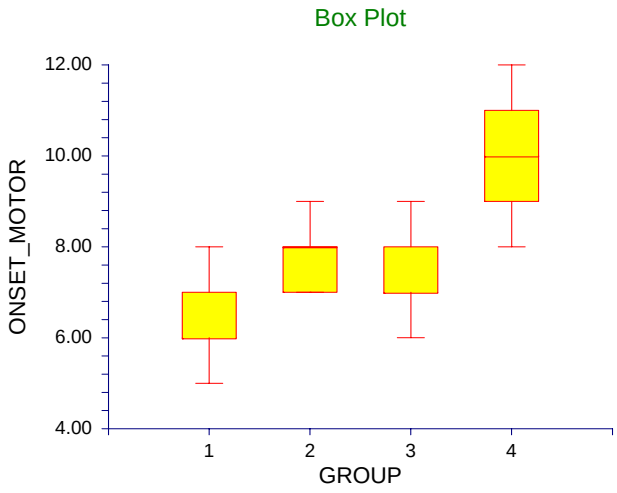


Using multiple comparison test group I (BC) was found to be very significant than the other three groups.

ONSET OF MOTOR BLOCK

Group	Count	Mean	Standard Error
1 (BC)	15	6.266667	0.2510296
2 (BF)	15	7.733333	0.2510296
3 (BM)	15	7.33333	0.2510296
4 (B)	15	10.13333	0.2510296

P = 0.0000 < 0.005 Significant

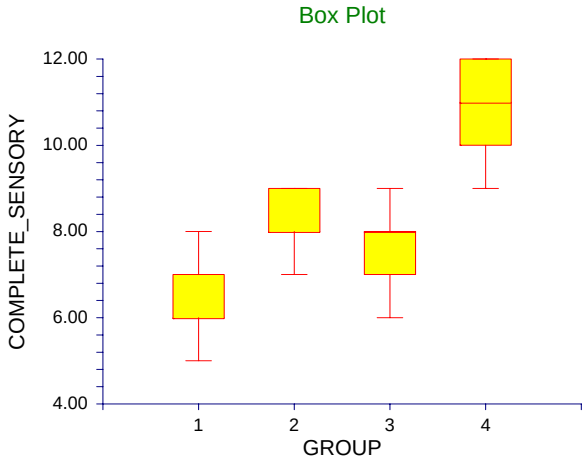


Using multiple comparison test group I (BC) was found to be very significant than the other three groups.

COMPLETION OF SENSORY BLOCK

Group	Count	Mean	Standard Error
1 (BC)	15	6.466667	0.2323107
2 (BF)	15	8.333333	0.23237107
3 (BM)	15	7.666667	0.2323107
4 (B)	15	10.73333	0.2323107

P = 0.0000 < 0.005, Significant

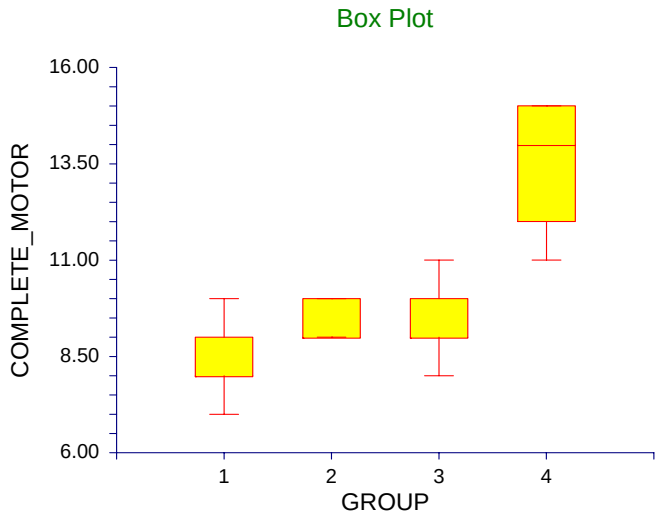


Using multiple comparison test group I (BC) was found to be very significant than the other three groups.

COMPLETION OF MOTOR BLOCK

Group	Count	Mean	Standard Error
1 (BC)	15	8.333333	0.2468854
2 (BF)	15	9.466666	0.2468854
3 (BM)	15	9.2	0.2468854
4 (B)	15	13.53333	0.2468854

P = 0.0000 < 0.005, Significant

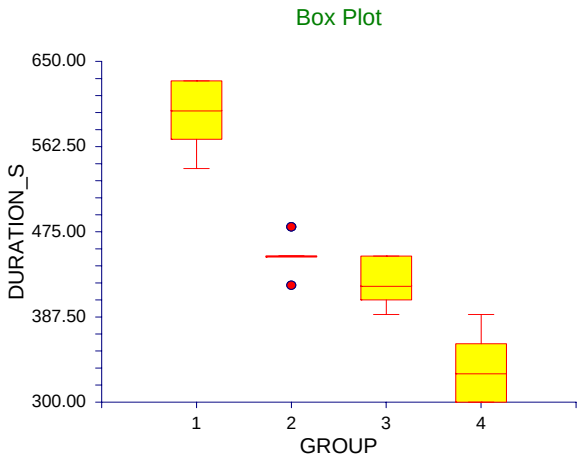


Using multiple comparison test group I (BC) was found to be very significant than the other three groups.

DURATION OF SENSORY BLOCK

Group	Count	Mean	Standard Error
1 (BC)	15	602	6.549264
2 (BF)	15	452	6.549264
3 (BM)	15	421	6.549264
4 (B)	15	332	6.549264

P = 0.0000 < 0.005 Significant

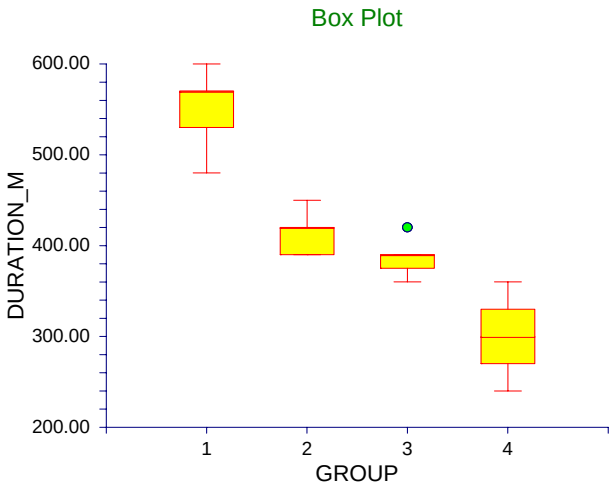


Using multiple comparison test group I (BC) was found to be very significant than the other three groups.

DURATION OF MOTOR BLOCK

Group	Count	Mean	Standard Error
1 (BC)	15	557.3333	7.245962
2 (BF)	15	414	7.245962
3 (BM)	15	389	7.245962
4 (B)	15	292	7.245962

P = 0.0000 < 0.005 Significant

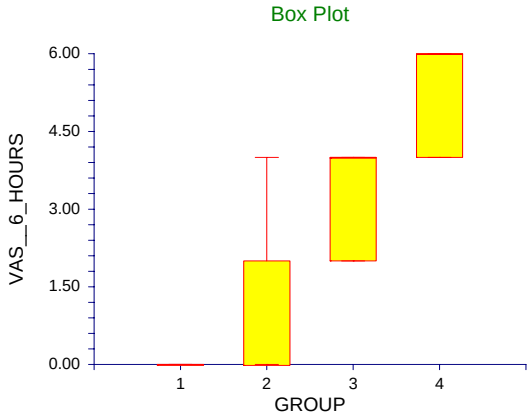


Using multiple comparison test group I (BC) was found to be very significant than the other three groups.

VISUAL ANALOG SCALE - 6 HOURS

Group	Count	Mean	Standard Error
1 (BC)	15	0	0.2606463
2 (BF)	15	0.9333333	0.2606463
3 (BM)	15	3.2	0.2606463
4 (B)	15	5.466667	0.2606463

P = 0.0000 < 0.005 Significant

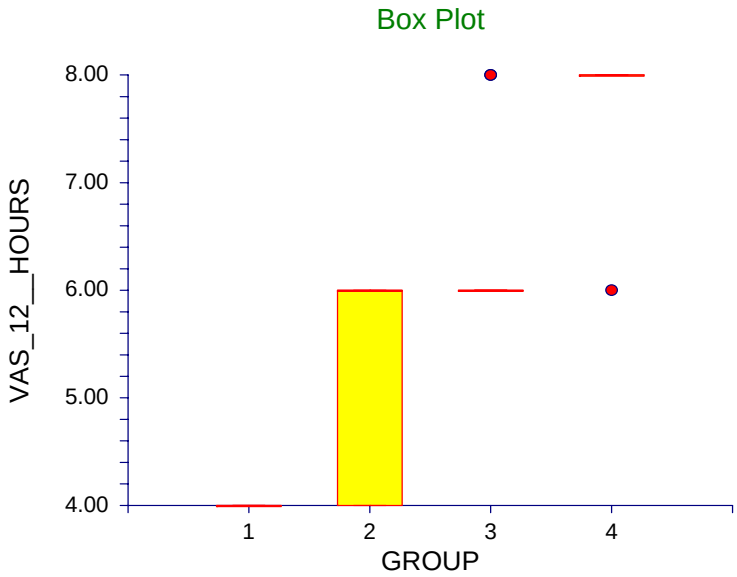


Using multiple comparison test group I (BC) was found to be very significant than the other three groups.

VISUAL ANALOG SCALE - 12 HOURS

Group	Count	Mean	Standard Error
1 (BC)	15	4	0.1690308
2 (BF)	15	5.333333	0.1690308
3 (BM)	15	6.266667	0.1690308
4 (B)	15	7.866667	0.1690308

P = 0.0000 < 0.005 Significant



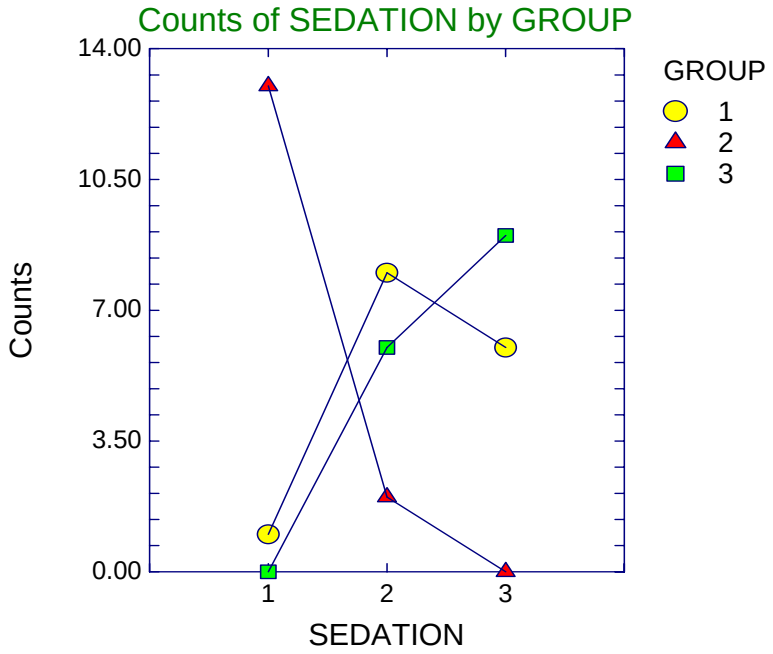
Using multiple comparison test group I (BC) was found to be very significant than the other three groups.

SEDATION SCORES

Sedation Scores	Group I (BC)	Group II (BF)	Group III (BM)
1	1 (67%)	13 (86%)	0 (0%)
2	8 (53.3%)	2 (13.3%)	6 (40%)
3	6 (40%)	0 (0%)	9 (60%)

60% of the patients in Group III (BM) were in sedation scores of 3

P = 0.000001, Significant



OBSERVATIONS OF HEMODYANAMIC VARIABLES

Variables		Group I (BC)	Group II (BF)	Group III (BM)	Group IV (B)
Pulse rate 15mins	Mean	78.06667	86.0667	83.93333	82.53333
	Standard Error	1.94463	1.94463	1.94463	1.94463
	Probability Level	**0.036908 Significant**			
Pulse rate 30mins	Mean	77.06667	85.4	83.4	81.6
	Standard Error	1.83541	1.83541	1.83541	1.83541
	Probability Level	**0.015791 Significant**			
Systolic BP 15mins	Mean	122.0667	128.2	132	128.6667
	Standard Error	2.790858	2.790858	2.790858	2.790858
	Probability Level	0.098164			
Systolic BP 30mins	Mean	118.3333	128.3333	130.7333	126.9333
	Standard Error	2.646321	2.646321	2.646321	2.646321
	Probability Level	**0.009869 Significant**			
Diastolic BP 15mins	Mean	77.93333	82.6	82.4	81.33334
	Standard Error	1.666	1.666	1.666	1.666
	Probability Level	**0.180946 Significant**			
Diastolic BP 30mins	Mean	76.46667	82.4	81.6	79.53333
	Standard Error	1.442	1.442	1.442	1.442
	Probability Level	**0.024695 Significant**			

DISCUSSION

Brachial plexus blockade offers an excellent alternative technique to general anaesthesia for upperlimb surgical procedures. Various approaches for successful performance of the blocks and for reducing the complication have been described.

The technique chosen in this study was supraclavicular brachial plexus technique. Kulenkampff in Germany in 1911 performed the first percuteneous supraclavicular approach. This technique was later published in 1928 by Kulenkampff and Persky (Classical) approach).

Supraclavicular technique was chosen for this study because it provides a rapid onset, dense and predictable anaesthesia with a high success rate.

Clonidine an $\alpha 2$ – adrenergic agoinst has been extensively used an adjunct to general anaesthesia and regional anaesthesia. When added to 1% mepivacaine[6] with 1:2,00,000 epinephrine 150mcg of clonidine prolongs the duration of both anaesthesia and analgesia after axillary brachial plexus blockade. The minimum dose of clonidine[8] required to prolong significantly the duration of analgesia and anaesthesia for brachial plexus block with 1% mepivacaine is respectively 0.1mcg/kg and 0.5mcg/kg. At this dose, clonidine may be used without important

reported adverse effects even in outpatients. In this present study 1mcg/kg to the maximum of 75mcg of clonidine is used.

It is postulated that clonidine added to local anaesthetics for peripheral nerve block prolongs postoperative analgesia and duration of block owing to a direct action on the nerve.[33,34]

Two mechanisms of action may be proposed. This effect might be due to clonidine mediated activation of postsynaptic adrenergic receptors leading to vasoconstriction thus prolonging local anaesthesia by decreasing the systemic absorption of the local anaesthetic. When applied on the rabbit cornea, clonidine is approximately 140 times more potent as a surface anaesthetic than procaine. This might indicate that C fibers or Aδ fibers, which exclusively innervate the rabbit cornea are especially sensitive to clonidine. Butterworth and Strichartz hypothesized that analgesia seen after neuraxial application of clonidine might result from direct inhibition of impulse conduction in primary afferent nerve fibres. They speculate that part of the efficacy of α2 – adrenergic agonists at producing analgesia after their regional injection may result from their local anaesthetic actions on A α and especially C fibers.

Fentanyl a synthetic opioid [35-41] and a μ receptor agonist has been extensively studied for its use in brachial plexus block.

Nishikawa et al [38] have concluded in their study that fentanyl improves analgesia but prolongs the onset of brachial plexus block by peripheral mechanism.

Mostafa et al [39] have studied the effects of addition of fentanyl to local anaesthetic in peribulbar block and concluded that addition of fentanyl to local anaesthetic mixtures fastens the onset and prolong the duration of akinesia and improve the quality of postoperative pain in peribulbar block.

Karakaya et al [35] have studied the analgesic and anaesthetic effects of fentanyl with 0.25% bupivacaine and concluded that addition of 100 mcg/ml fentantyl to 0.25% bupivacaine almost doubles the duration of analgesia following axillary brachial plexus block when compared to 0.25% bupivacaine alone.

Midazolam as an additive to local anaesthesia has been studied in intrathecal, epidural and caudal routes. It has been proved in these studies that midazolam is as useful additive by way of improved analgesia and with sedation. 50mcg/kg midazolam in central neuraxial blockade did not produce any significant adverse effects. Studies in animals have showed no neurotoxic effects of intrathecally administered midazolam [58,59,60]. Potentiation of analgesic effects of intrathecal fentanyl with midazolam in labouring patients has been demonstrated [61]. Intrathecal midazolam 2mg

did not increase the occurence of neurologic or urologic symptoms[62]. Hence 50mcg/kg dose was chosen in this study.

In this prospective randamised comparitive study, 60 patients satisfying the selection criteria underwent brachial plexus with or without adjuvants. Comparison of the onset, completion and duration of the block and sedation scores between the three groups and hemodyanamic variables were observed and statistically analysed.

The onset and completion of the sensory and motor blockade was quicker in group I (Bupivacaine + clonidine) followed by group II (Bupivacaine + fentanyl) and group III (Bupivacaine + midazolam).

Similarly the duration of sensory block was prolonged to last longer than motor block in group I (BC) followed by group II (BF) and group (III) (BM). This is in line with the observations made by Dejong et al who explained that large fibers require a higher concentration of local anaesthetic than small fibres. The minimum effective concentration of local anaesthetic for large motor fibres is greater than for small sensory fibres. Thus motor function return before pain perception and duration of motor block is shorter than the sensory block.

In this study, the pain scores as assessed by the visual analog scale were significantly lower in group I (BC) when compared to the other groups.

Sedation scores was higher in group III (BM) when compared to group I (BC) & group II (BF). This is due to partial vascular uptake of the drug and its transport to the central nervous system where it acts and produces sedation. The limited duration of sedation could be explained by the fact that it is highly lipophilic and diffuses faster in to the blood vessels, by its rapid clearance and short halflife. Highest sedation score was 3 ie patient was asleep and arousable by mild physical stimuli. No patient required airway compromise or required airway assistance due to sedation.

Hemodyanamic variables like pulse rate, blood pressure was found to altered much in group I (BC) than group II (BF) and group III (BM), during the first 30 mins of the intraoperative period. But no patient required vassopressor support. The hypotension was only mild and corrected only with intravenous crystalloids.

No complications with regard to the techniques or drug was observed.

SUMMARY

1. Onset and completion time for both sensory and motor blockade was quicker in the group I (Bupivacaine plus clonidine group) followed by group II (Bupivacaine plus fentanyl) and group III (Bupivacaine plus midazolam).

2. The mean duration of the sensory and motor blockade was significantly prolonged in group I (bupivacaine plus clonidine group)

3. Sedation was statistically significant in group III (Bupivacaine plus midazolam) in the intraoperative period.

4. Hemodynamic parameters was found to be altered much in group I (BC) than the other groups.

5. Patient's compliance and acceptance of the block is more with group I (BC) and group III (BM) followed by group II (BF) and group IV (B).

6. There was no complication due to addition of 1mcg/kg of clonidine to the maximum of 75 mcg and 1mcg/kg of fentantyl to the maximum of 50mcg and 50mcg/kg midazolam to bupivacaine.

CONCLUSION

In conclusion, clonidine 1mcg/kg to a maximum of 75mcg added to 0.25% Bupivacaine solution for supraclavicular brachial plexus block, quickens the onset of sensory and motor blockade, prolongs the duration of sensory blockade, improves the quality of postoperative analgesia when compared to fentanyl and midazolam group.

BIBLIOGRAPHY

1. Cornish PB. Greenfield LJ. Brachial Plexus anatomy Reg. Anaesth 1997, 22 : 106-107.

2. Williams PL, Warwick R, Dyson M, Bannister LH. The brachial plexus In : Gray's Anatomy 37th ed. London, Churchill Livingston, 1989: 1131-37 & 1150 – 1153.

3. Thompson GE, Rorie D.K. Functional anatomy of the brachial plexus sheath. Anaesthesiology 1983, 59 : 117-122.

4. Partridge B.L, Kartz J, Berishke K. Functional anatomy of the brachial plexus sheath – implication for anaesthesia Anaesthesiology 1987, 6 : 743-747.

5. Hutschala D, Mascher H, Schmetterer L, Fleck T. Clonidine added to Bupivacaine enhances and prolongs analgesia after brachial plexus block via a local mechanism in healthy volunteers. Eur J. Anaesthesiology 2004 Mar : 21(3) : 198-204.

6. Erlacher W, Schuschnig C, Koinig H, Marhofer P, Mayer N, Kapral S Clonidine as adjuvant for mepivacaine, ropivacaine, bupivacaine in axillary perivascular brachial plexus block. Can J Anaesth. 2001 Jun; 4 (6); 522-5.

7. Erlacher W, Schuschnig C, Orlicke F, MarhoferP, Koinig H, Kapral S. The effects of clonidine on ropivacaine 0.75% in axillary Perivascular brachial plexus block. Acta Anaesthesiol Scand 2000 Jan. 44(1) 53-7.

8. Singelyn FJ, Gouverner JM, Rober A. A minimum dose of clonidine added to mepivacaine prolongs the duration of anaesthesia and analgesia after axillary brachial plexus block. Anaesth Analg : 1996 Nov; 83(5) ; 1046-50.

9. Duma A, Urbanek B, Sitzwohl C, Kreiger A, Zimpfer M, Kapral S Clonidine as adjuvant to local anaesthetic axillary brachial plexus block. A randamized controlled study. Br. J. Anaesth 2005 Jan; 94(1); 112-6 E pub 2004 Oct. 29.

10. Bhatnagar S, Mishra S, Madhurima S, Gurjar M, Mondal AS Clonidine as an analgesic adjuvant to continuous paravertebral bupivacaine for post thorocotomy pain. Anaesth Intensive Care 2006 Oct. 34 (5) : 581-91.

11. Carbarine UA, Milligan KR, Moore J Extradural Clonidine and pubivacaine for post operative analgesia. Br. J. Anaesth 1992 Feb;68(2) ; 132-5

12. Jean J. Eledjam, Jacques Deschodt, Eric J. Viel, JeanF, Lubrano Brachial Plexus block with bupivacaine; effects of added α-adrenergic agonist. Comparison, between clonidine and epinephrine. Can J. Anaesth 1991 Nov. 38(7); 870-75.

13. Daniel M Popping MD, Nadia Elia MD, Emmanuel Marret, Martin R Tremor. Clonidine as an adjuvant to local anaesthetics for Peripheral nerve and plexus blocks. Anaesthesiology 2009 ; 111 406-15.

14. Darothee Gaumann, Alain Forster, Marthe griessen, Walid Habre, Dominique Delia Santa `Comparison Between Clonidine and epinephrine admixture to lignocaine in Brachial plexus block. Anaesth Analg 1992; 75 : 69-74.

15. A.H. El Saied, M.P. Steyn and J.M. Ansermino, `Clonidine prolongs the effect of ropivacaine for axillary brachial plexus blockade. Can Jr Anes 2000 Oct. 47(10); 962 – 67.

16. Fran CoisJ. Singelyn, Jean – Marie Gouverner, Annie Robert A minimum dose of clonidine added to mepivacaine prolongs the duration of anaesthesia and analgesia after axillary brachial plexus block. Anaesth Analg 1996; 83 : 1046-50.

17. Elia N, Culebras X, Mazza C, Schiffer E, Tramer MR : Clonidine as an adjuvant to intrathecal local anesthetics for surgery: Systematic review of randomized trails. Reg Anesth Pain Med 2008 ; 33 :159-67.

18. Elisenach JC, De Kock M, Klimscha W : Alpha (2) adrenergic agonists for regional anesthesia. A clinical review of clonidine (1984-1995). Anesthesiology 1996; 85:655-74.

19. McCartney CJ, Duggan E, Apatu E: Should we add clonidine to local anesthetic for peripheral nerve blockade? A qualitative systematic review of the literature. Reg. Anesth Pain Med 2007; 32:330-8.

20. Murphy DB, McCartney, CJ, Chan VW: Novel analgesic adjuncts for brachial plexus block: A systematic review. Anesth Analg 2000; 90 : 1122-8

21. Beaussier M, Weickmans H, Abdelhalim Z, Lienhart A; Inguinal herniorrhaphy under monitored anesthesia care with ilioinguinal-illiohypogastric block; The impact of adding clonidine to ropivacaine. Anesth Analg 2005: 101:1659-62.

22. Buttner J, Ott B, Klose R: The effect of adding clonidine to mepivacaine. Axillary brachial plexus blockade. Anaesthesist 1992: 41-548-54.

23. Singelyn FJ, Gouverneur JM, Robert A: A minimum dose of clonidine added to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. Anesth Analg 1996; 83 : 1046-50.

24. Antonucci S : Adjuvants in the axillary brachial plexus blockade. Comparison between clonidine, sufentanil and tramadol. Minerva Anestesiol 2001: 67-23-7

25. Bernard JM, Macaire P : Dose-range effects of clonidine added to lidocaine for brachial plexus block. Anesthesiology 1997: 87: 277-84.

26. Casati A, Magistris L, Fanelli G, Beccaria P, Cappelleri G, Aldegheri G, Torri G: Small-dose clonidine prolongs postoperative analgesia after sciatic-femoral nerve block with 0.75% ropivacaine for foot surgery. Anesth Analg 2000; 91:388-92.

27. Erlacher W, Schuschnig C, Koinig H, Marhofer P, Melischek M, Mayer N, Kapral S: Clonidine as adjuvant for mepivacaine, ropivacaine and bupvicaine in axillary' perivascular brachial plexus block. Can J Anaesth 2001; 48:522-5.

28. Fang L, Liu F, Li L, Wang TJ, Yang LS, Sun XX : Effects of clonidine combined with various local anaesthetics in brachial plexus block. Zhonghua Ui Xue Za Zhi 2004 : 84:1712-3.

29. Iskandar H, Guillaume E, Dixmerias F, Binje B, Rakotondriamihary S, Thiebaut R, Maurette, P: The enhancement of sensory blockade by clonidine selectively added to mepivacaine after midhumeral block. Anesth Analg 2001; 93-771-5.

30. Iskandar H, Benard A, Ruel-Raymond J, Cochard G, Manud B: The analgesic effect of interscalene block using clonidine as an analgesic for shoulder arthroscopy. Anesth Analg 2003; 96:260-2

31. Gaumann DM, Brunet PC, Jirounek P: Clonidine enhances the effects of lidocaine on C-fiber action potential. Anesth Analg 1992: 74:719-25.

32. Culebras X, Van Gessel E, Hoffmeyer P, Gamulin Z : Clonidine combined with a long acting local anaesthetic does not prolong postoperative analgesia after brachial plexus block but does induce hemodynamic changes. Anesth Analg 2001: 92:199-204.

33. Singelyn FJ, Dangoisse M, Bartholomes S, Gouverneur JM. Adding clonidine to mepivacaine prolongs the duration of anaesthesia and analgesia after axillary brachial plexus block. Reg Anesth 1992; 17:148-50.

34. Eledjam JJ, Deschodt J, Viel EJ, et al. Brachial plexus block with bupivacaine: effects of added alpha-adrenergic agonists: comparison between clonidine and epinephrine. Can J Anaesth 1991; 38:870-5.

35. Karakaya D, Buyukgoz F, Baris S, Addition of fentanyl to Bupivacaine doubles the duration of analgesia following axillary brachial plexus block. Reg. Anaesth Pain Med 2001 Sep – Oct. 26(5). 434-8.

36. J.E. Bazin, C. Massoni, P. Bruelle, V. Fenies, D. Groslier, P.Schoeffler. Addition of opioids to local anaesthetic mixture lengthens the duration of analgesia. Jr. of Association of Anaesthetists of great Britain and Ireland.

37. Kardash K, Schools A, Concepcion A : Effects of Brachial plexus fentanyl on supraclavicular block. Randamized double blind study. Reg. anaesth. 1995 Jul – Aug. 20(4), 311-5.

38. Nishikawa K, Kanaya N, Nakayama : Fentanyl improves analgesia but prolongs the onset of axillary brachial plexus block by peripheral mechanism. Anaesth Analg. 2000 Aug : 91(2) 384-7.

39. Mostafa Abdee Hamid Abo Eltnin, Ismail Eiwis. Effect of fentanyl addition to local anaesthetic in peribulbar block. IJA 2009; 5(1) ; 57-63.

40. Power, IBSC. Hons, F.C. Anaes, Brown, D.T.F.C. Anaes. The effects of fentanyl, Meperidine and diamorphine on nerve conduction in vitro. Reg Anaes & Pain Med. July / Aug. 1991-Vo1.16 issue 4.

41. Kohki Nishikawa MD, Moriaki Kanya, Masayasu, Nakayama. Anasth Analg 2000 : 91 : 834-387.

42. Joseph M. Neal, James R. Hebl, J.C. Gerancher, Quinn H. Hogan. Brachial Plexus Anaesthesia. Essentials of our current understanding. Regional anaesthesia and pain medicine Vol.27, 2002, 4 : 402-428.

43. J.C. Gerancher. upper extremity nerve blocks. Anaesthesiology clinics of North America. June 2000, Vol.18, No.2

44. De Jong RH, Wagman IH. Physiological mechanisms of Peripheral nerve block by local anaesthetics. Anaesthesiology 1963; 24 : 684-727.

45. Winnie AP, Tay C-H, Patel KP, Ramamurthy S, Durrani Z. Pharmacokinetics of local anaesthetics during brachial plexus blocks. Anaesth Analg 1977; 56 : 852-61.

46. Brown DA, Marsh S, Axonal GABA receptors in Mammalian Peripheral nerve trunks. Brain Res.1978; 156: 187-91.

47. Brown DA, Adams PR, Higgins AJ, Marsh S. Distribution of GABA receptors and GABA carriers in Mammalian nervous system J. Physiol (Paris) 1979; 75(6) : 667-71.

48. Bhisitkul RB, Villa JE, Kocsis JD. Axonal GABA receptors are selectively present on normal and regenerated sensory fibres in rat peripheral nerves. EXP. Brain Res. 1987; 66: 659-63.

49. Brain E. Cairns, Bary J. Sessle, James W. Hu. Activation of Peripheral GABA A receptors inhibits TM joint evoked jaw muscle activity. J. Neurophysiol 81 : 196-69; 1999.

50. Edwards M, Serrao JM, Gent JP, Goodchild CS. On the mechanism by which midazolam causes spinally mediated analgesia. Anaesthesiology 1990; 73 ; 273-7.

51. Good child CS, Guo Z. Musgreave A, Gent JP. Antinociception by intrathecal midazolam involves endogenous neurotransmitters acting at the spinal cord delta opioid receptors. Br. J. Anaes. 1996, 77 : 758-763.

52. Yegin A, Sanli S, Dosemecil, Kayacarin, Akbas M, Karsli B. The analgesic and sedative effects of intrathecal midazolam in perianal surgery. Eur.J. Anaesthsiology, 2004 Aug; 21(8); 658-62.

53. Nishiyama T, Yokoyama T, Haraoka K. Midazolam improves postoperative epidural analgesia with continuous infusion of local anaesthetics. Can J Anaesth 1998; 45(6) : 551-5.

54. Nishiyama T, Matsukawa T, Hanaoka K. Continuous epidural midagolam and bupivacaine for postoperative analgesia. Acta Anaesthesiol Scand. 1999 May ; 43(5) : 568 – 72.

55. Nishiyama T, Matsukawa T, Hanaoka K. Effects of adding Midazolam on postoperative epidural analgesia with two different doses of Bupivacaine J. Clin. Anaesth 2002 Mar; 14(2) 92-7.

56. Kim MH1 Lee YM. Intrathecal midazolam increases the analgesic effects of spinal blockade with bupivacaine in patients undergoing haemorroidectomy. Br. J. Anaesth 2001, 86:77-9.

57. Batra YK, Jain K, Chari P, Dhillon MS, Shaheen B, Reddy GM. Addition of intrathecal midazolam to bupivacaine produces better postoperative analgesia without prolonging recovery Int. J. Clin Pharmacol. Ther 1999; 37 : 519-23.

58. Serrao JM, Mackenzie JM, Goodchild CS, Gent JP. Intrathecal midazolam in the rat; an investigation of possible neuroloxic effects. EurJ. Pharmcol. 1990; 7 ; 115-22.

59. Nishiyama T, Matsukawa T, Hanaoka K. Acute phase histopathological study of spinally administered midazolam in cats. Anaesth Analg 1999; 89, 717-20.

60. Schweiger IM, Jerg – Costa M, Pizzolato GP, Foster A, Morel DR. Intrathecal midazolam reduces isoflurane. MAC and increases the apnoecic threshold in rats. Canj Anaesth 1994; 41:144-8.

61. Tucker AP, Mezzatesta J. Nadeson R, Goodchild CS. Intrathecal midazolam II: Combination with intrathecal fentanyl for labour pain. Aanesth Analg 2004; 98: 1521-7.

62. Tucker AP, Lai C, Nadeson R, Goodchild CS. Intrathecal Midazolam I a cohort study investigating safety. Anaesth : Analg 2004; 98 : 1512-20.

63. Koj Jarbo, Yatindra Kumar Batra, Nidhi Bidyut Pandr. Brachial Plexus block with midazolam and Bupivacaine improves analgesia. Can.J. Anaesth 2005; 52:8: 822-826.

PROFORMA – 1

Group IV (Bupivacaine)

S. No.	Age	Surgery Time in Mins	Sex	Wt in Kg	Onset mins		Complete mins		Duration in mins		Sedation Scores	Visual analog scale		
					Motor	Sensory	Motor	Sensory	Motor	Sensory		6 hrs	12 hrs	24 hrs
1.	29	180 mins	M	52 kg	12	9	15	11	300	330	-	6	8	10
2.	45	210 mins	M	61 kgs	9	7	12	10	270	300	-	6	8	10
3.	54	90 mins	M	65 kgs	10	8	14	12	330	360	-	6	8	10
4.	60	150 mins	M	50 kgs	11	9	15	12	270	330	-	4	6	10
5.	49	110 mins	F	65kgs	9	7	12	10	300	330	-	4	8	10
6.	37	130 mins	M	57 kgs	8	6	11	9	270	300	-	4	8	10
7.	26	170 mins	F	50 kgs	8	6	12	9	330	360	-	6	8	10
8.	57	210 mins	M	45 kgs	12	8	15	12	270	300	-	6	8	10
9.	38	155 mins	M	52 kgs	11	7	15	10	300	390	-	6	8	10
10.	27	130 mins	M	59 kgs	10	8	14	12	360	330	-	6	6	10
11.	23	160 mins	F	55 kgs	9	7	13	10	240	300	-	6	8	10
12.	41	120 mins	M	57 kgs	11	9	14	12	330	360	-	6	8	10
13.	55	150 mins	M	68 kgs	12	8	15	11	300	360	-	6	8	10
14.	39	180 mins	F	65 kgs	9	7	12	9	270	330	-	4	8	10
15.	35	130 mins	F	62 kgs	11	8	14	12	240	300	-	6	8	10

PROFORMA – 1

Group I (Bupivacaine + Clonidine)

S.No.	0 MINS				15 MINS				30 MINS			
	RR	PR	BP	SPO2	RR	PR	BP	SPO2	RR	PR	BP	SPO2
1)	15	88	140/94	99%	15	85	136/90	99%	15	86	135/88	99%
2)	14	88	124/79	99%	14	78	113/81	99%	15	79	98/75	99%
3	15	100	130/96	99%	15	96	121/82	99%	15	89	132/84	99%
4	15	102	110/72	99%	15	98	108/68	99%	15	95	106/72	99%
5	15	82	136/84	99%	15	74	135/82	99%	15	75	130/74	99%
6	14	84	130/90	99%	15	78	120/82	99%	15	80	118/72	99%
7	15	78	156/90	99%	15	75	140/80	99%	15	70	130/80	99%
8	16	74	110/80	99%	15	68	100/70	99%	15	70	104/72	99%
9	15	82	140/90	99%	15	79	135/84	99%	15	79	130/80	99%
10	16	72	118/72	99%	15	71	112/66	99%	15	69	110/72	99%
11	15	84	130/90	99%	15	80	114/82	99%	15	78	110/82	99%
12	15	88	146/90	99%	15	78	136/80	99%	15	76	126/78	99%
13	15	72	110/70	99%	15	65	96/62	99%	15	67	96/64	99%
14	15	74	150/90	99%	15	68	135/78	99%	15	67	120/74	99%
15	15	81	138/92	99%	15	78	130/82	99%	15	76	130/80	99%

PROFORMA – 1

Group – II (Bupivacaine + Fentanyl)

S. No.	Age	Surgery Time in Mins	Sex	Wt in Kg	Onset mins		Complete mins		Duration in mins		Sedation Scores	Visual analog scale		
					Motor	Sensory	Motor	Sensory	Motor	Sensory		6 hrs	12 hrs	24 hrs
1.	45	90 mins	M	60	7	6	9	8	420	450	1	0	4	10
2.	21	80 mins	M	55	8	7	9	8	420	480	1	0	4	10
3.	50	150 mins	M	65	8	7	10	9	420	450	1	0	4	10
4.	20	90 mins	M	50	8	7	10	9	420	450	2	2	4	8
5.	24	170 mins	F	50	8	7	10	9	420	450	1	2	4	10
6.	25	110 mins	M	55	7	5	9	8	450	480	1	0	4	8
7.	21	140 mins	M	45	9	7	10	9	390	480	1	0	6	8
8.	49	180 mins	M	60	8	7	10	9	420	450	1	2	6	8
9.	52	150 mins	M	65	8	7	9	8	420	450	2	0	6	10
10	10	210 mins	M	50	7	6	9	8	390	450	1	0	6	10
11.	20	130 mins	M	45	9	7	10	9	390	420	1	2	6	10
12.	48	190 mins	F	50	7	6	9	7	450	480	1	2	6	10
13.	45	70 mins	M	60	8	6	10	8	390	450	1	0	6	10
14.	35	150 mins	M	50	7	6	9	8	420	450	1	0	4	10
15.	35	180 mins	F	50	7	6	9	8	390	420	1	0	6	10

PROFORMA – 1

Group II (Bupivacaine + Fentanyl)

S.No.	0 MINS				15 MINS				30 MINS			
	RR	PR	BP	SPO2	RR	PR	BP	SPO2	RR	PR	BP	SPO2
1)	15	88	140/94	99%	15	87	136/92	99%	15	88	135/88	99%
2)	16	74	118/72	99%	15	72	115/72	99%	15	71	115/72	99%
3	15	85	140/92	99%	15	87	136/90	99%	15	88	140/92	99%
4	15	100	110/74	99%	15	100	114/72	99%	15	99	116/72	99%
5	15	90	130/80	99%	15	87	130/78	99%	15	85	126/74	99%
6	15	85	118/72	99%	15	88	120/76	99%	15	84	118/78	99%
7	17	88	124/82	99%	16	86	124/88	99%	16	85	126/84	99%
8	16	88	150/90	99%	16	88	147/45	99%	16	87	145/83	99%
9	16	90	140/84	99%	15	88	135/85	99%	16	89	137/84	99%
10	15	91	140/90	99%	15	90	141/88	99%	16	87	140/94	99%
11	16	74	115/74	99%	15	73	118/70	99%	16	71	118/78	99%
12	16	89	134/90	99%	16	87	127/88	99%	16	88	130/84	99%
13	16	89	130/90	99%	16	87	127/85	99%	16	88	127/88	99%
14	15	84	130/90	99%	15	83	125/85	99%	15	83	127/82	99%
15	16	90	128/90	99%	15	88	127/85	99%	15	88	125/83	99%

PROFORMA – 1

Group I (Clonidine + Bupivacaine)

S. No.	Age	Surgery Time in Mins	Sex	Wt in Kg	Onset mins		Complete mins		Duration in mins		Sedation Scores	Visual analog scale		
					Motor	Sensory	Motor	Sensory	Motor	Sensory		6 hrs	12 hrs	24 hrs
1.	29	110 mins	F	60kg	6	4	8	6	570	630	2	0	4	8
2.	35	170 mins	F	64	6	5	8	7	570	600	2	0	4	10
3.	48	130 mins	F	65	6	5	9	7	530	570	2	0	4	10
4.	23	70 mins	M	50	5	4	7	5	540	600	1	1	3	8
5.	20	130 mins	M	50	6	5	7	6	530	570	2	0	4	8
6.	29	190 mins	M	75	5	4	7	5	600	630	3	0	4	8
7.	60	170 mins	F	50	6	4	8	6	570	630	3	0	4	8
8.	65	160 mins	M	45	6	5	9	7	480	540	3	1	4	10
9.	55	90 mins	M	59	6	4	8	6	570	630	3	0	3	8
10	20	170 mins	M	50	6	4	8	6	570	630	2	0	4	10
11.	30	130 mins	M	60	7	5	9	7	600	630	2	0	4	10
12.	43	180 mins	M	55	7	5	9	7	530	570	2	1	4	8
13.	23	155 mins	F	50	7	6	9	8	530	570	2	0	4	8
14.	60	210 mins	M	75	7	5	9	6	600	630	3	0	4	10
15.	50	170 mins	M	60	8	6	10	8	570	600	3	0	4	8

PROFORMA – 1

Group III (Bupivacaine + Midazolam)

S. No.	Age	Surgery Time in Mins	Sex	Wt in Kg	Onset mins		Complete mins		Duration in mins		Sedation Scores	Visual analog scale		
					Motor	Sensory	Motor	Sensory	Motor	Sensory		6 hrs	12 hrs	24 hrs
1.	30	130 mins	M	55Kgs	7	6	9	8	390	420	3	6	8	10
2.	45	180 mins	M	70 kgs	9	7	10	8	360	390	2	6	8	10
3.	60	210 mins	F	50 kgs	9	7	11	9	390	420	2	6	8	10
4.	21	150 mins	M	60 kgs	7	6	9	8	390	420	3	4	8	10
5.	35	180 mins	M	55 kgs	7	5	9	7	420	450	3	6	8	10
6.	52	210 mins	M	60kgs	6	5	8	7	390	420	2	6	8	10
7.	48	160 mins	F	60 kgs	7	5	8	6	390	450	3	4	8	10
8.	45	130 mins	M	55 kgs	7	6	9	8	360	390	3	6	10	8
9.	48	110 mins	F	65 kgs	8	6	10	8	390	420	2	6	8	10
10	35	150 mins	F	60 kgs	7	5	9	7	420	450	3	4	8	10
11.	35	170 mins	M	59 kgs	7	6	9	8	360	390	2	4	8	8
12.	20	155 mins	M	50 kgs	8	6	10	8	390	420	2	4	10	8
13.	29	90 mins	F	55 kgs	7	6	9	8	375	405	3	6	10	10
14.	34	130 mins	M	61 kgs	7	6	9	7	420	450	3	6	8	10
15.	59	150 mins	M	53 kgs	7	5	9	7	390	420	3	6	10	10

PROFORMA – 1

Group III (Bupivacaine + Midazolam)

S.No.	0 MINS				15 MINS				30 MINS			
	RR	PR	BP	SPO2	RR	PR	BP	SPO2	RR	PR	BP	SPO2
1)	15	90	134/82	99%	15	88	132/82	99%	15	88	130/82	99%
2)	15	84	128/92	99%	15	85	130/90	99%	15	86	128/84	99%
3	15	74	150/90	99%	15	72	146/88	99%	15	73	144/86	99%
4	15	88	140/84	99%	15	86	138/86	99%	15	85	137/85	99%
5	15	91	130/90	99%	15	89	134/88	99%	15	88	134/87	99%
6	15	87	140/92	99%	14	88	138/90	99%	14	85	130/84	99%
7	15	85	134/92	99%	15	87	130/90	99%	15	85	128/88	99%
8	15	74	128/84	100%	15	76	127/80	99%	15	75	125/78	99%
9	16	78	115/72	99%	15	80	117/74	99%	15	79	118/70	99%
10	15	83	126/88	100%	15	82	128/86	99%	15	84	126/90	99%
11	14	92	133/71	99%	14	89	129/76	99%	14	90	130/78	99%
12	15	100	127/85	100%	15	97	130/82	99%	15	96	132/81	100%
13	15	79	131/82	99%	15	81	130/78	99%	15	79	131/79	99%
14	16	85	127/74	100%	16	87	130/76	99%	16	86	128/78	99%
15	15	69	148/74	100%	15	72	141/70	100%	15	72	140/74	100%

PROFORMA – 1

Group IV (Bupivacaine)

S.No.	0 MINS				15 MINS				30 MINS			
	RR	PR	BP	SPO2	RR	PR	BP	SPO2	RR	PR	BP	SPO2
1)	15	87	110/72	100%	15	89	112/78	100%	15	87	114/80	100%
2)	15	82	126/84	100%	15	85	124/80	100%	15	83	118/80	100%
3	16	79	130/90	100%	16	78	126/84	99%	15	81	127/83	100%
4	16	71	146/88	99%	16	70	140/80	99%	16	74	138/76	99%
5	15	88	136/82	100%	15	85	137/83	100%	15	83	130/81	100%
6	16	72	110/70	99%	16	74	112/72	99%	16	75	110/74	99%
7	15	74	138/84	100%	15	75	130/80	100%	15	77	132/81	100%
8	14	82	150/90	99%	14	83	146/84	99%	14	81	145/83	99%
9	15	75	110/82	99%	15	77	112/84	99%	15	79	110/80	99%
10	14	87	132/84	99%	14	89	136/82	99%	14	87	133/81	99%
11	15	91	140/85	100%	15	89	139/83	100%	15	85	137/80	100%
12	15	85	124/84	100%	15	84	120/85	100%	15	81	118/87	99%
13	15	96	128/82	99%	15	97	126/78	99%	15	100	128/74	99%
14	14	78	130/84	99%	14	80	130/87	99%	14	82	128/79	99%
15	15	81	142/84	100%	15	83	140/80	100%	15	79	136/74	99%

Name :
Age :
Sex :
Surgery :
Group :
Wt :

PROFORMA – II

Vital		0	5min	10 min	15	20	30 mins	1 hr	2	3	4	5	6	12	24 hrs
	PR														
	BP														
	SPO2														
	RR														
SENSORY AND MOTOR SCORE															
RADIAL NERVE	SENSORY														
	MOTOR														
MEDIAN NERVE	SENSORY														
	MOTOR														
ULNAR NERVE	SENSORY														
	MOTOR														
MUSCULOCUTENEOUS NERVE	SENSORY														
	MOTOR														
SENSORY SCORE															
Lateral Cuteneous Nr. of the arm															
Medial Cuteneous Nr. of the arm															
Lateral Cuteneous Nr. of the fore arm															
Medial Cuteneous Nr. of the fore arm															