# A COMPARATIVE STUDY OF INTRATHECAL LOW DOSE BUPIVACAINE WITH FENTANYL AND LOW DOSE LEVOBUPIVACAINE WITH FENTANYL IN TRANSURETHRAL RESECTION OF PROSTATE

**DISSERTATION SUBMITTED TO THE TAMILNADU**

**DR.M.G.R. MEDICAL UNIVERSITY, CHENNAI**

**In partial fulfilment of the requirements for the degree of**

**M.D. BRANCH – X**

**(ANAESTHESIOLOGY)**

**DEPARTMENT OF ANAESTHESIOLOGY**

**TIRUNELVELI MEDICAL COLLEGE HOSPITAL**

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*Dear Dr.M.SIVASANKARI, MBBS, The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during The IEC meeting held on 27.10.2017.*

**THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED**

| | | |
|---|---|---|
| 1. | TIREC Application Form | ☐ |
| 2. | Study Protocol | ☐ |
| 3. | Department Research Committee Approval | ☐ |
| 4. | Patient Information Document and Consent Form in English and Vernacular Language | ☐ |
| 5. | Investigator's Brochure | ☐ |
| 6. | Proposed Methods for Patient Accrual Proposed | ☐ |
| 7. | Curriculum Vitae of The Principal Investigator | ☐ |
| 8. | Insurance /Compensation Policy | ☐ |
| 9. | Investigator's Agreement with Sponsor | ☐ |
| 10. | Investigator's Undertaking | ☐ |
| 11. | DCGI/DGFT approval | ☐ |
| 12. | Clinical Trial Agreement (CTA) | ☐ |
| 13. | Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA) | ☐ |
| 14. | Clinical Trials Registry-India (CTRI) Registration | ☐ |

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1. The approval is valid for a period of 2 year/s or duration of project whichever is later
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   e. Approval for amendment changes must be obtained prior to implementation of changes.
   f. The amendment is unlikely to be approved by the IEC unless all the above information is provided.
   g. Any deviation/violation/waiver in The protocol must be informed.

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## CONTENTS

# INTRODUCTION

Benign prostatic hypertrophy(BPH) is common among elderly age groups for which transurethral resection of prostate is required in all symptomatic patients. Now a days increasing numbers of elderly patients coming for surgery due to longer life expectancy. This group of population has a greater anaesthetic risk because of coexisting cardiovascular and pulmonary diseases. Spinal anaesthesia is the technique of choice for Transurethral resection of prostate (TURP). It provides surgical anaesthesia and postoperative analgesia, and also had added advantage of preserving cerebral function which in turn allows earliest recognition of TURP syndrome.

Racemic hyperbaric Bupivacaine has been considered as local anaesthetic of choice for spinal anaesthesia. Recently Levobupivacaine, a pure S-enantiomer of racemic Bupivacaine is introduced as an attractive alternative to bupivacaine. Its cardiovascular and central nervous system toxicity is lower as compared to Bupivacaine. There are only few studies, about clinical use of Levobupivacaine in spinal anaesthesia.So this randomized, double blind, prospective study was planned. In this study the clinical effectiveness, hemodynamic effect, sensory and motor block characteristic of intrathecally administered isobaric 0.5% Levobupivacaine

is compared with hyperbaric 0.5% Bupivacaine in patients posted for Transurethral resection of prostate.

## AIMS AND OBJECTIVES:

To compare intrathecal low dose of Bupivacaine with fentanyl and low dose of Levobupivacaine with fentanyl in patients undergoing Transurethral resection of prostate with respect to

- Time of onset and resolution of sensory and motor blockade
- Intraoperative hemodynamics
- Quality of analgesia

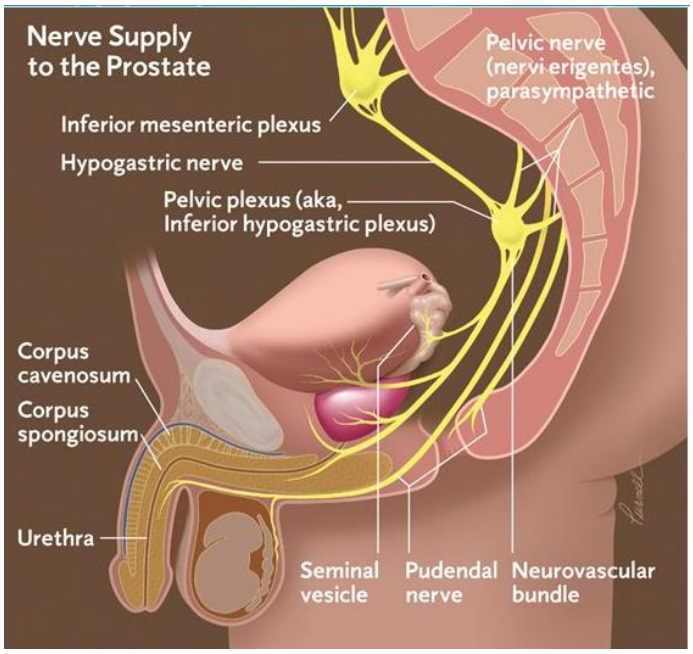
## ANATOMY OF PROSTATE GLAND

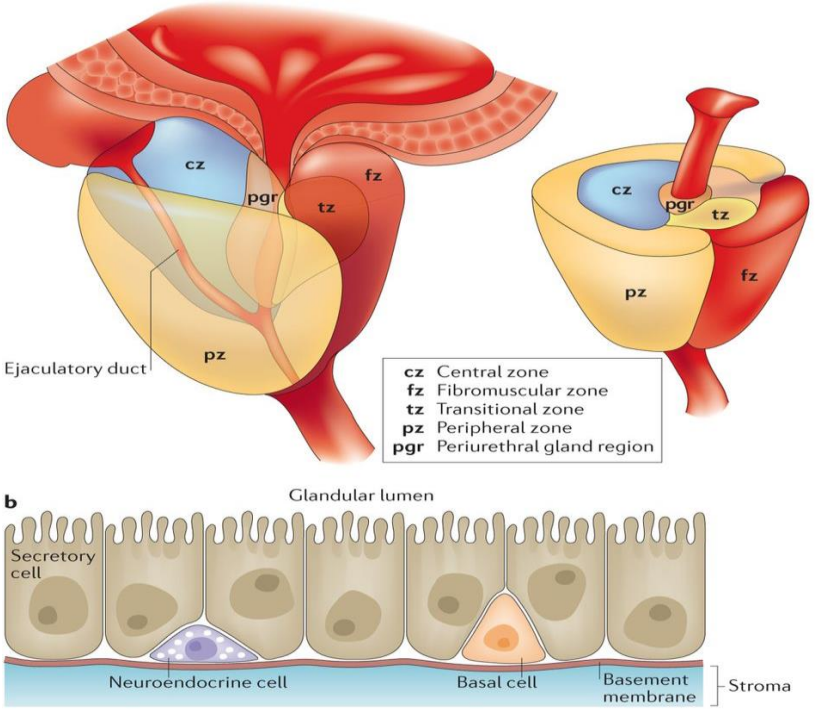
The prostate gland, encircles the urethra as it emerges from the base of the bladder. Its weight around 20g. It comprises glandular, which contains secretory acini and non-glandular, which has smooth muscle and fibrous tissue components enclosed by a fibrous capsule. It has a rich blood supply and venous drainage is via the large, thin-walled sinuses adjacent to the capsule.

It is described as having four histological zones also known as McNeal zones: the central, peripheral, anterior (fibromuscular), and transitional (periurethral) zones. The transitional zone comprises 5% of normal prostatic volume which surrounds the proximal urethra in two pear-shaped lobes and it is the common site of benign prostatic hyperplasia and also 10% of prostatic carcinomata. Twenty percent of the men aged 40 yrs have hyperplasia of the transition zone, increasing to 50% at 50 yrs and 70% at 60 yrs. The hyperplastic tissue encroaches on the proximal urethra, causing obstruction of normal urine flow. The prostatic tissue is compressed against the capsule, and it is often referred to as the ‘surgical capsule’.

The nerve supply of the prostate arises from the prostatic plexus, which originates from the inferior hypogastric plexus, and carries both sympathetic fibres from T11 to L2 and parasympathetic fibres from S2 to S4. Pain fibres from the prostate, prostatic urethra, and bladder mucosa

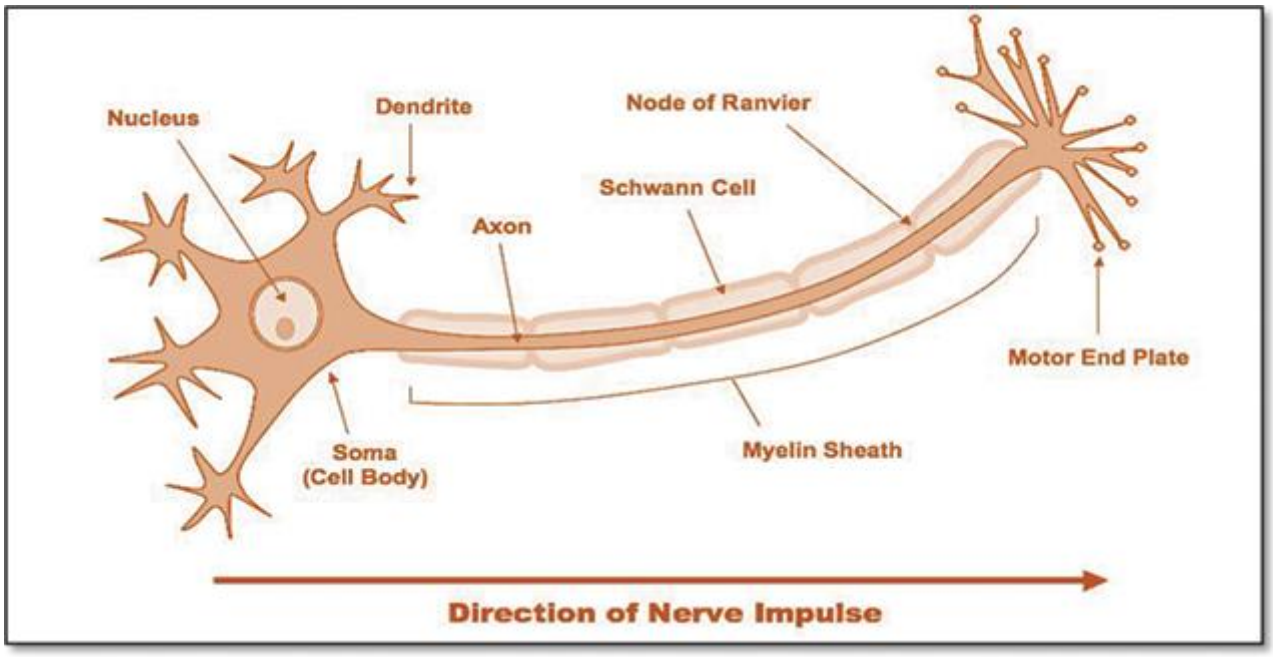
originate primarily from sacral nerves S2 to S4. Pain signals from bladder distension travel with sympathetic fibres and have their origin in T11–L2. The sensation of stretch in the bladder (proprioception) is carried by the parasympathetic fibres of S2–S4



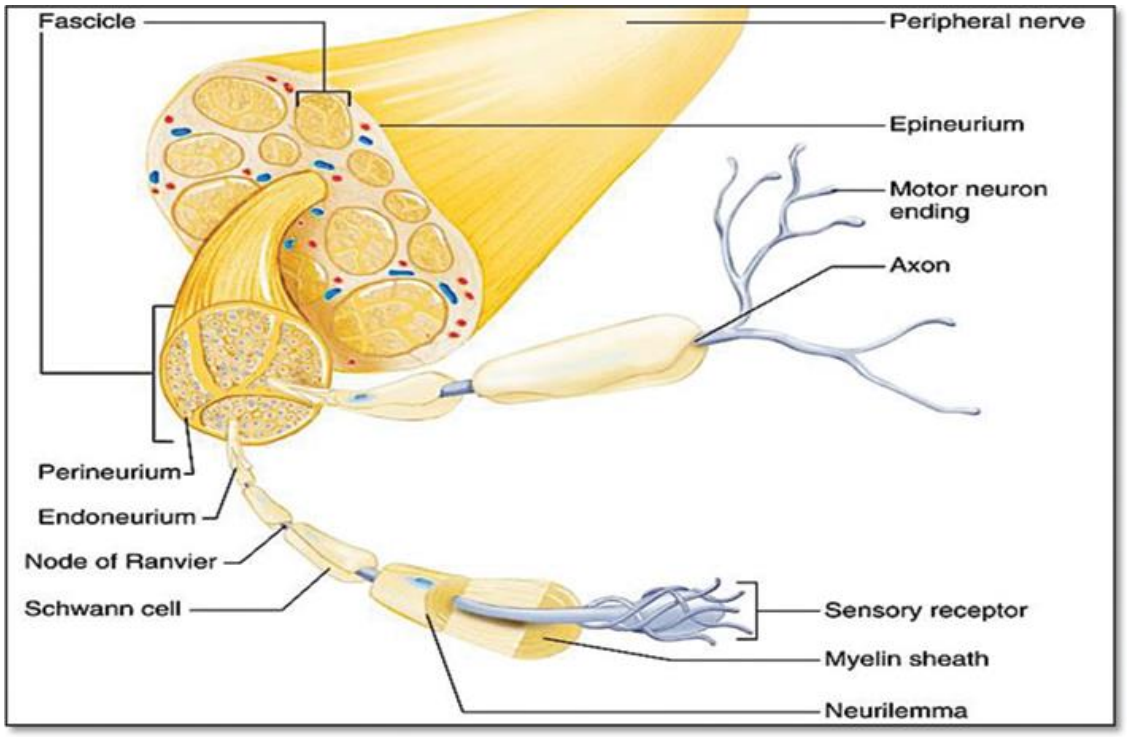
## NERVE ANATOMY

Neurons are the primary cells in the nervous system. The nervous system is made up of the central and the peripheral nervous system. It can also be looked at in terms of parasympathetic nervous and sympathetic nervous system. A group of neurons bundled together make up peripheral nerves.




The Peripheral nerves contains both the afferent and efferent fibres, which are bundled into one or more fascicles. Individual nerve fibres within the fascicle are surrounded by a layer of loose connective tissue called the endoneurium. The endoneurium houses the glial cells, fibroblasts and blood vessel capillaries, all of which are integral to the function of the nerve fibre. The fascicle is in turn surrounded by a dense layer of collagenous connective tissue called the perineurium. A cylindrical sheath

called the epineurium forms the outermost layer. The main function of these layers is to protect the nerve fibres and also it act as barriers to agents acting on the nerves including local anaesthetics.



## ELECTROPHYSIOLOGY OF NERVE CONDUCTION

The Resting membrane potential of a nerve cell is −60mV to −70 mV. At rest, neurons are more permeable to potassium ions due to the presence of leak potassium channels. So the resting neuronal membrane potential is closer to the equilibrium potential of potassium that is −80 mV. This ionic disequilibrium acts as the energy needed for propagation of action potentials on the cell surface. The intracellular milieu of the nerve cell is negatively charged relative to the extracellular environment. Upon excitation of the nerve fibres, the electrical impulse propagates along the axon due to changes occurring in the adjacent membrane alternating from negative to positive values of about +50 mV due to rapid influx of sodium ions. At an electrical potential of +50 mV, there is rapid efflux of potassium ions in an attempt to maintain electrical neutrality of the cell. To restore the resting membrane potential, the sodium/potassium ATPase pumps the sodium extracellularly, and the potassium ions intracellulary. The conduction of impulses along nerve fibres occurs as small brief, localised spikes of depolarisation on the surface of the cell membrane. Impulses travels in one direction as the axonal membrane that has just undergone depolarisation remains in the refractory state until the resting potential is restored by the Sodium/Potassium ATPase pumps.

## PHARMACOLOGY OF LOCAL ANESTHETICS

### HISTORY

1860 **Albert Niemann** isolated crystals from the coca shrub and he called it as "**cocaine**" and he found that it reversibly numbed his tongue.

**Sigmund Freud** found the mood altering properties of cocaine, and he thought it might be useful in curing morphine addiction. He obtained a supply of cocaine (from Merck) and shared it with his friend **Carl Koller**, a junior intern in ophthalmology at the University of Vienna

1884 Following preliminary experiments using conjunctival sacs of various animals species, **Koller** did first eye surgery in humans using cocaine as local anesthetic

1905 German chemist **Alfred Einhorn** produced the first synthetic **ester-type** local anesthetic -**novocaine** (**procaine**). And he found that it retained the nerve blocking properties, but lacked the powerful Central nervous system actions of cocaine

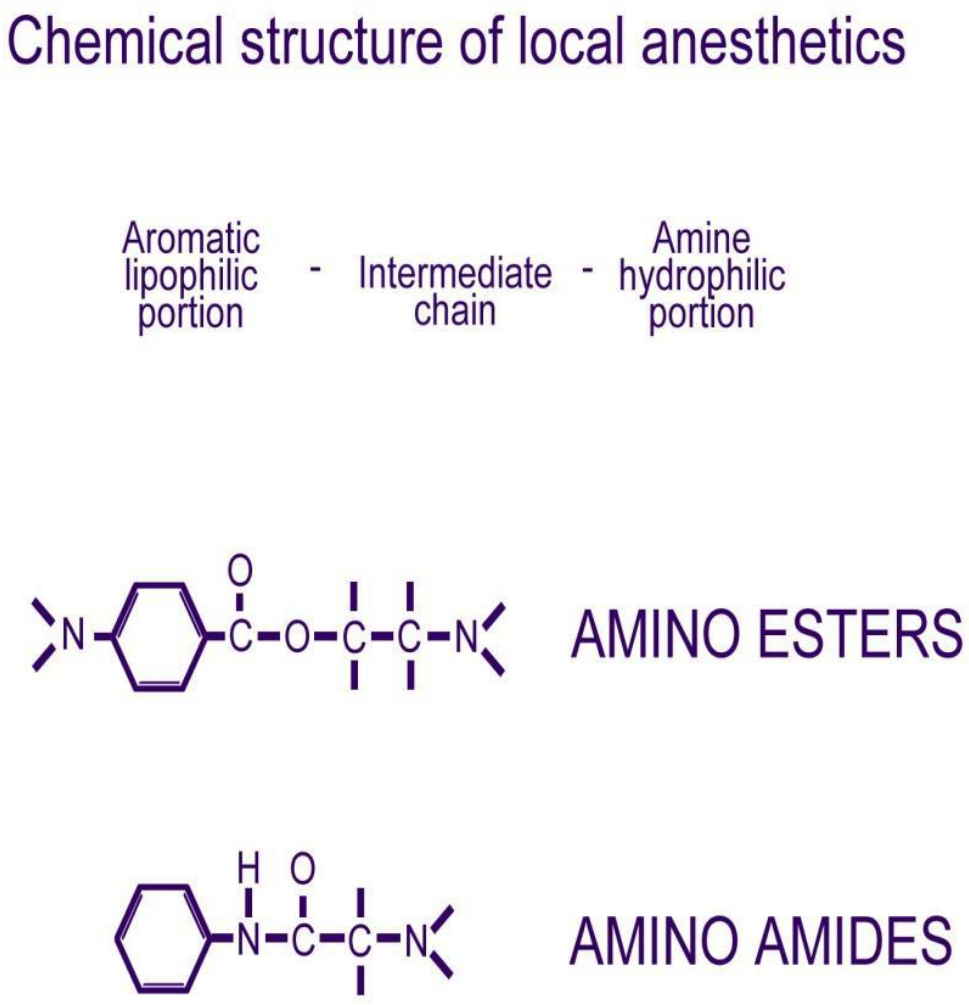
1943 Swedish chemist **Nils Löfgren** synthesized the first **amide-type** local anesthetic and it is marketed under the name of **xylocaine**(**lidocaine**)

**CHEMISTRY**

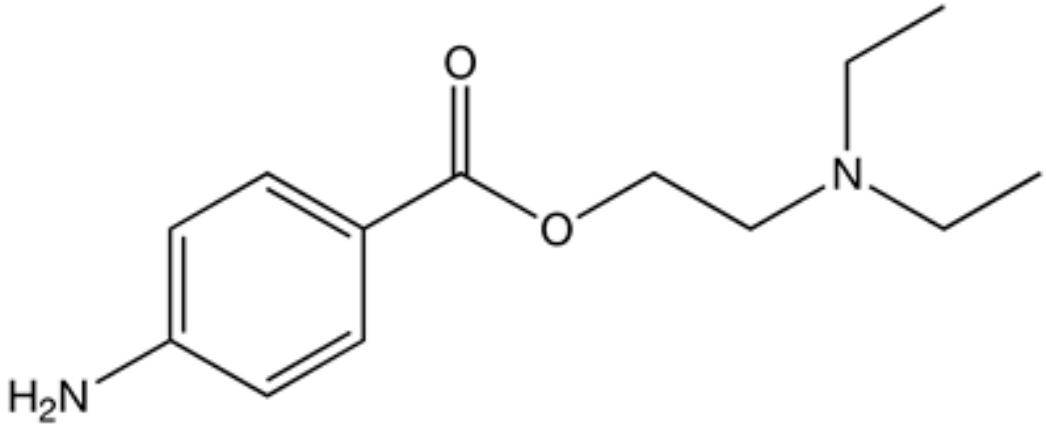
**Structure-Activity Relationships:**

All local Anesthetics contains three structural components:

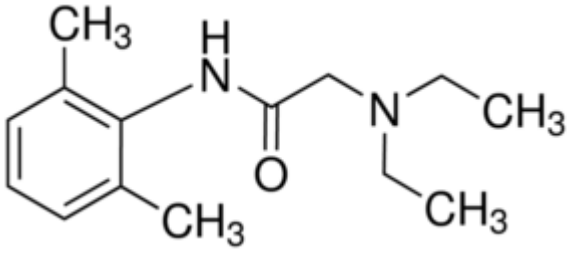
- an aromatic ring
- a connecting group which is either an ester or an amide
- an ionizable amino group



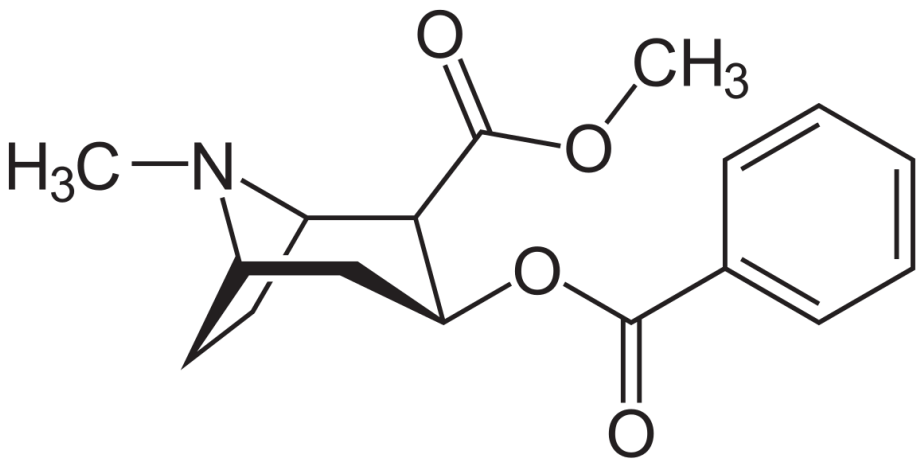
Chemical structures of prototypical ester and amide type local anesthetics in comparison with cocaine




**procaine/novocaine**




**lidocaine/xylocaine**



## Cocaine

Two important chemical properties of local anesthetic molecule that determine activity:

- **Lipid solubility:** it increases with extent of substitution of carbons on aromatic ring and/or amino group
- **Ionization constant (pK)** : it determines proportion of ionized and non-ionized forms of local anesthetic

Lipid solubility determines the potency, plasma protein binding and the duration of action of local anesthetics

| | Lipidsolubility | Relative potency | Plasma protein binding (%) | Duration (minutes) |
|---|---|---|---|---|
| Procaine | 1 | 1 | 6 | 60-90 |
| Lidocaine | 4 | 2 | 65 | 90-200 |
| Tetracaine | 80 | 8 | 80 | 180-600 |

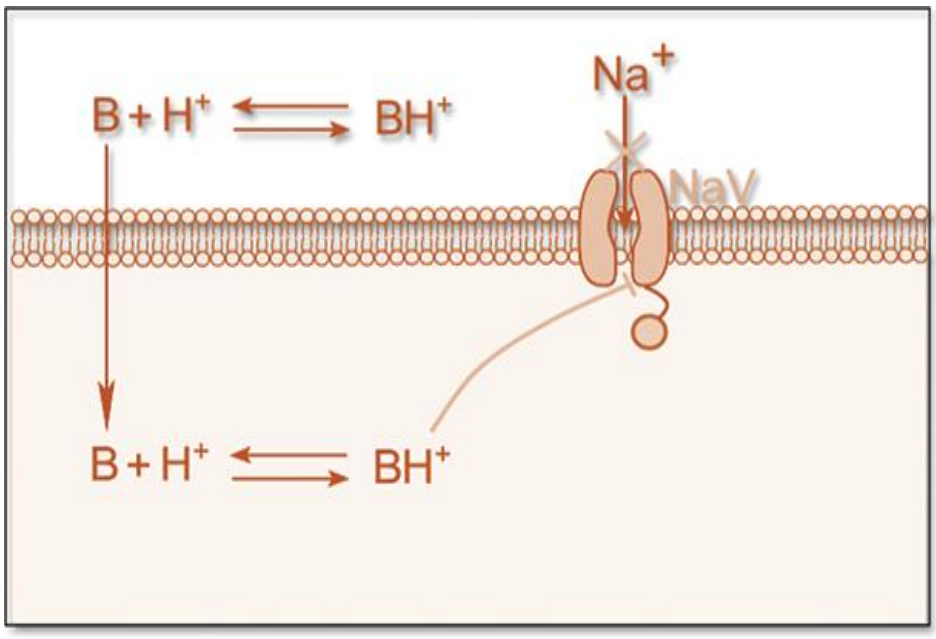
Local anesthetics are weak bases. The proportion of free base(R-NH2) and salt(R-NH3+) forms depends on pH and pK of amino group

pH = pK + log [base]/[salt]

(Henderson-Hasselbalch equation)

- Both the free base and ionized forms of local anestheticare necessary for the activity

- Local anesthetic enters the nerve fibre as a neutral free base and the cationic form blocks the conduction by interacting at the innersurface of the Na+channel

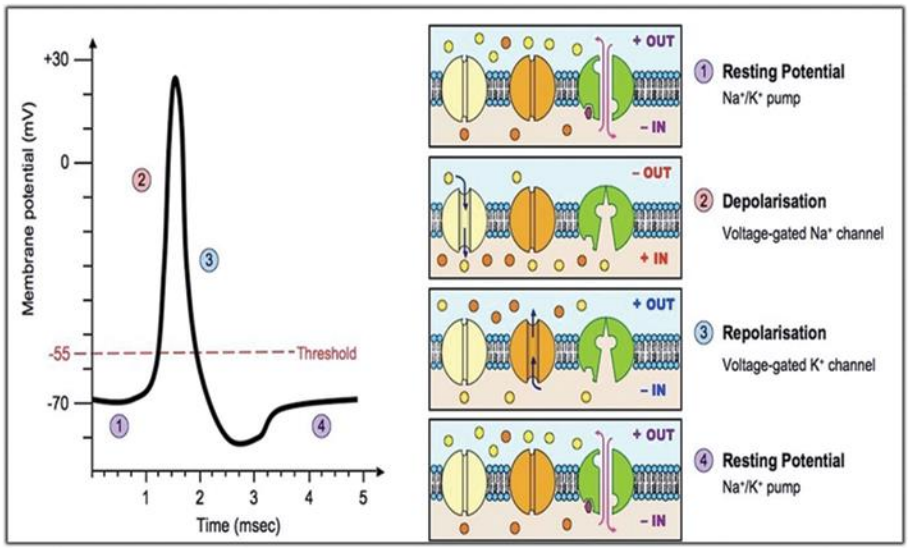



Local anesthetics with lower pK have a more rapid onset of action because more uncharged form causes more rapid diffusion to the cytoplasmic side of Na+channel.

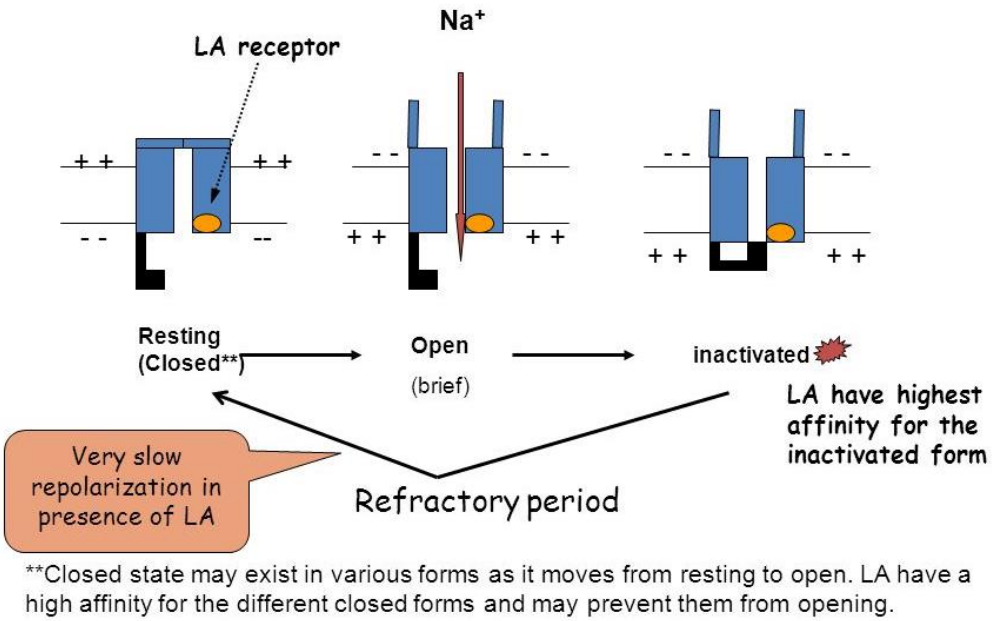
| | pK | % free base at pH 7.4 | Onset of anesthesia (min) |
|---|---|---|---|
| Lidocaine | 7.9 | 25 | 2-4 |
| Bupivacaine | 8.1 | 18 | 5-8 |
| Procaine | 9.1 | 2 | 14-18 |

## MECHANISM OF ACTION

- The Conduction of nerve impulses is mediated by generation of Action Potential along the axon
- The Cationic form of local anesthetic binds at inner surface of Na+channel preventing Na+influx and it rises the phase of membrane potential which in turn initiates the action potential and block the nerve impulses.

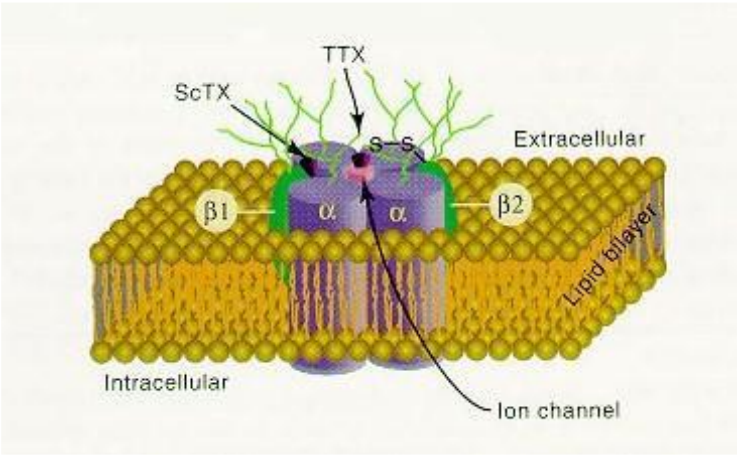



- Local anesthetics bind to the open form of the Na+channel from the **cytoplasmic side** of the neuronal membrane



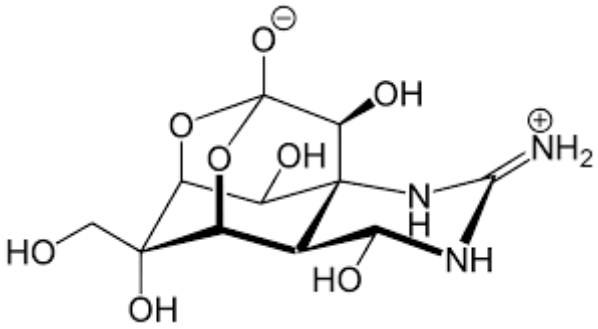

**Closed state may exist in various forms as it moves from resting to open. LA have a high affinity for the different closed forms and may prevent them from opening.

- In contrast, a number of highly polar toxins (e.g., tetrodotoxinand saxitoxin) block the Na+channel from the **outer surface** of the neuronal membrane

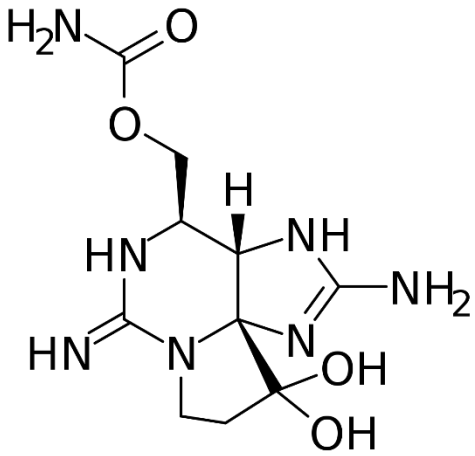



Schematic representation of a Na+channel showing binding sites for tetrodotoxin(TTX) and saxitoxin(ScTX)

Structures of two naturally occurring highly polar substances with powerful local anesthetic activity causing fatal paralysis –tetrodotoxin (puffer fish) and saxitoxin(shell fish)




**Tetrodotoxin**




**SAXITOXIN**

**Functional consequences of Na+channel blockade by local anesthetics**:

- **Nerves:** it decreases or abolishes the conduction
- **Vascular smooth muscle:** it produces vasodilatation
- **Heart:** it decreases the excitability due to reduced pacemaker activity and prolonging the duration of effective refractory period

- **Central Nervous System:** causes increased excitability, followed by generalized depression

**Effects of local anesthetics on Nerve Conduction**

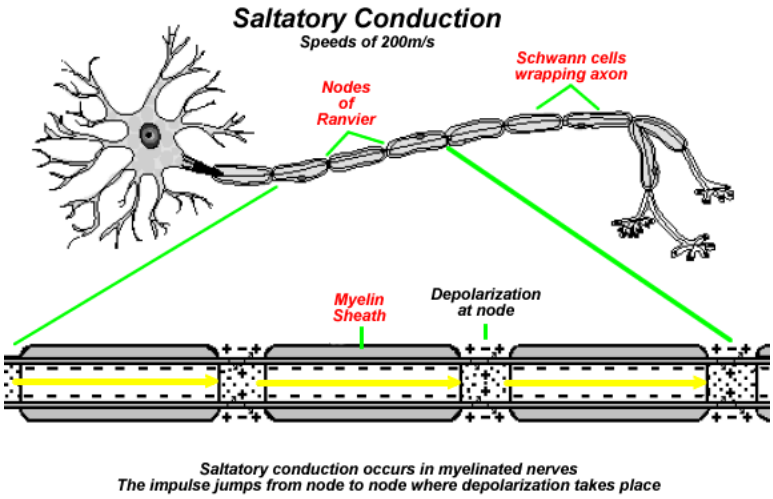
- Na+channels are present in all nerves. The local anesthetics, at sufficient concentrations, it completely block the action potential generation and there by conduction of nerve impulse
- "**Differential Nerve Blockade":** The nerve fibres differ markedly intheir susceptibility to conduction blockage by Local anesthetics. The small, non-myelinated neurons mediating pain are much more susceptible than large, myelinated fibres mediating motor functions

**Relative size and myelination and susceptibility to blockage by Local Anaesthetics**

| Fibre type | function | diameter (μm) | myelination | Susceptibility to LA block |
|---|---|---|---|---|
| Type A alpha | proprioception, motor | 12-20 | heavy | + |
| beta | touch, pressure | 5-12 | heavy | ++ |
| gamma | muscle spindles | 3-6 | heavy | ++ |
| delta | pain, temperature | 2-5 | heavy | +++ |
| Type B | preganglionic | <3 | light | ++++ |
| Type C dorsal root | pain | 0.4-1.2 | none | ++++ |

## Differential susceptibility of nerves to local anesthetics

- In neuronal conduction, depolarizing current moves along the nodes of Ranvier. Two to three successive nodes must be blocked to completely impair neuronal conduction




The Small fibres have smaller intermodal distances that is shorter length of the nerve fibre needs to be blocked to impair the conduction as compared to the larger nerve fibres

- Anesthetic blockade of Na+ channels exhibits **"use-dependence"**that is increased frequency of stimulation leads to increased level of blockade

High stimulation frequency increases the number of Na+ channels in the "open" form that preferentially local anesthetics bind.

Neurons with high rates of firing (e.g., pain fibres) or ectopic pacemakers in the myocardium will be highly susceptible to blockade by Local anesthetics

- In excitable tissues with longaction potentials, probability of Na+channels being in susceptible “open” form is increased leads to enhanced susceptibility to blockade by local anesthetics

  e.g., pain fibres have long action potentials (3 millisec) versusmotorfibres (0.5 millisec) so pain fibres are more susceptible to Local anaesthetics

The Cardiac muscle has prolonged Action potentials relative to other excitable tissues so the myocardium is highly susceptible to local anesthetics

**Effects of local anesthetics on vascular smooth muscle**

Blockade of Na+channels in vascular smooth muscle by local anesthetics produces vasodilatation

**Consequences of vasodilatation:**

- enhanced rate of removal of anesthetic from site of administration leads to decrease in duration of anesthetic actionand increases the risk of local anaesthetic toxicity
- Hypotension may be intensified by anesthetic-induced cardiodepression

Anesthetic-induced vasodilatation can be counteracted by the concomitant administration of a vasoconstrictor

**Consequences of including vasoconstrictor:**

- Prolongation of duration anestheticaction

- Decreases the risk of toxicity
- Decrease in bleeding from surgical manipulations

**Effects of vasoconstrictors on local anesthetic duration**

- Adrenalineis the conventional vasoconstrictor included in commercial Local anesthetic preparations
- The concentration of adrenaline in these preparations can vary and is expressed as grams/ml (e.g. 1:100,000 = 1 gram/100,000 ml)

| Local Anaesthetic | Adrenaline | Duration of Anaesthesia(min) |
|---|---|---|
| Lidocaine(2%) | - | 5-10 |
| Lidocaine(2%) | 1:100,000 | 60 |
| Lidocaine(2%) | 1:50,000 | 60 |

**Effects of Local Anaesthetics on Heart**

- Local Anaesthetics reduces the **myocardial excitability** and **pacemaker activity** and also prolong the duration of **refractory period** of myocardial tissue. This action of local anaesthetic is the basis of the **Antiarrhythmic** action.

- Local anesthetics induced **myocardial depression** (compounded by anesthetic-induced **hypotension**) can also be a manifestation of toxicity and can lead to **cardiovascular collapse** and even **death!**

## Effects of local anesthetics on CNS

- Local anaesthetics induces Central nervous system depression generally and at toxic doses it produces biphasic pattern of excitation followed by depression
- The excitatory phase likely reflects the preferential blockade of inhibitory neurons and effects can range from mild hyperactivity to convulsions
- The subsequent depressive phase can progress to cardiovascular collapse and even death if unmanaged.

## Applications of local anesthesia:

- **Nerve block:** injected locally to produce regional anesthesia(e.g., dental and other minor surgical procedures)
- **Topical application:** to skin for analgesia(e.g., benzocaine) or mucous membranes (for diagnostic procedures)
- **Spinal anesthesia:** injection into CSF to produce anesthesia for major abdominal surgeries

- **Local injection:** at end of surgery to produce long-lasting post-surgical analgesia and it reduces need for narcotics
- **i.v. infusion:** for control of cardiac arrhythmias (e.g., lidocaine for ventricular arrhythmias)

## LOCAL ANESTHETIC TOXICITY

**most common causes:**

- Inadvertent **intravascular injection** while inducing nerve block
- Rapid absorption following spraying of mucous membranes (e.g., respiratory tract) with local anesthetic prior to diagnostic or clinical procedures

**Manifestations of local anesthetic toxicity:** Allergic reactions, cardiovascular and CNS effects

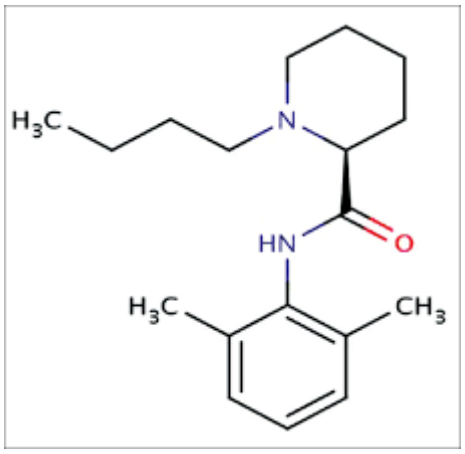
- **Allergic reaction**: restricted to esters–metabolized to allergenic p-amino benzoic acid (PABA)
- **Cardiovascular:**may be due to anesthetic(cardiodepression, hypotension) or vasoconstrictor(hypertension, tachycardia)
- **CNS:** excitability, agitation, increased talkativeness which may lead to convulsions followed by CNS depression

## PHARMACOLOGY OF LEVOBUPIVACAINE

Levobupivacaine is a long acting amide type local anesthetic that is the S(-) isomer of the racemic Bupivacaine.

### CHEMICAL STRUCTURE

Levobupivacaine ([2S]-1-butyl-N-[2,6-dimethylphenyl] piperidine-2-carboxamide) is an amino-amide local anesthetic drug belonging to the family of n-alkyl substitute pipecoloxylidide. Its chemical formula is C18H28N2 O




Chemical structure of levo-bupivacaine

### MECHANISM OF ACTION

Levobupivacaine exerts its pharmacological action through reversible blockade of neuronal sodium channels. Myelinated nerves are blocked through exposure at the nodes of Ranvier more readily than unmyelinated nerves and small nerves are blocked more easily than larger ones. In general, the progression of anaesthesia is related to the diameter, myelination and conduction velocity of the affected nerve fibers.

Specifically, the drug binds to the intracellular portion of sodium channels and blocks sodium influx into nerve cells, which prevents depolarization. It blocks nerve conduction in sensory and motor nerves mainly by interacting with voltage sensitive sodium channels on the cell membrane. It also interferes with impulse transmission and conduction in other tissues.

**PHARMACOKINETICS**

The dose as well as the route of administration of Levobupivacaine determines the plasma concentration following therapeutic administration and the absorption is dependent upon the vascularity of the tissue. After epidural administration of Levobupivacaine, the absorption is biphasic, with rapid absorption of a small quantity of drug into the circulation and slower absorption of the remainder of the drug. It has been observed that peak levels of Levobupivacaine in the blood reaches approximately 30 min after epidural administration and doses up to 150 mg had resulted in mean Cmax levels up to 1.2 µg/mL. The epidural absorption gets affected by age as the fraction absorbed decreases and the fast absorption phase is shorter in older (aged > 70 years) compared with the younger (aged 18-44 years) patients. The older patients also have a higher spread of analgesia by ~ 3 dermatomes. Therefore, in the elderly patients a lower dose of Levobupivacaine, according to their physical status is recommended. The volume of distribution is estimated at 66.91 ± 18.23 L (after intravenous administration of 40 mg). The pKa of levobupivacaine is 8.1, similar to the

pKa of the racemic bupivacaine. The half-life is 3.3hr. The rate of clearance is 39.06 ± 13.29 L/h.

Alpha1-glycoprotein is the main binding site for Levobupivacaine. Protein binding of Levobupivacaine is more (97%) than that of racemic Bupivacaine (95%). Less than 3% of the drug circulates free in plasma. The free proportion of the drug can have an action on the other tissues, causing unwanted side-effects and toxic manifestations. In newborns and in protein-deficient states like under nutrition and nephrotic syndrome, lesser amount of protein is available for binding, causing higher levels of free drug, resulting in toxic effects at lower doses. Levobupivacaine is extensively metabolized with no unchanged levobupivacaine detected in urine or feces. Cytochrome (CYP) CYP3A4 isoform and CYP1A2 isoform mediate the metabolism of levobupivacaine to inactive metabolites, desbutyllevobupivacaine and 3-hydroxy levobupivacaine, respectively. In vivo, the 3-hydroxy levobupivacaine appears to undergo further transformation to glucuronide and sulfate conjugates, which are excreted in urine. Metabolic inversion of Levobupivacaine to R (+)-Bupivacaine was notevident both in vitro and in vivo. Following intravenous administration, recovery of the radio-labeled dose of Levobupivacaine was essentially quantitative with a mean total of about 95% being recovered in urine and feces in 48 h. Of this 95%, about 71% was in urine while 24% was in feces.

## CLINICAL UTILITY

- Subarachnoid block
- Epidural anesthesia
- Post-operative analgesia
    - ❖ Epidural analgesia
    - ❖ Wound infiltration
- Peripheral Nerve Blocks
- Obstetric Anesthesia and Analgesia
    - ❖ Subarachnoid block for cesarean delivery
    - ❖ Labor analgesia

## LEVOBUPIVACAINE IN GERIATRIC ANAESTHESIA:

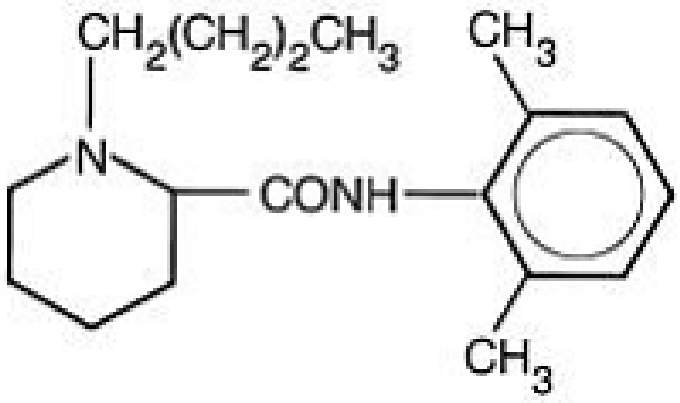
Elderly patients coming up for various surgeries including transurethral resection of the prostate or bladder tumour, orthopaedic trauma or joint replacement, cataract surgery, usually have some coexisting cardiac or pulmonary disease. Owing to its safer pharmacological profile, Levobupivacaine is considered to be a better local anesthetic than Bupivacaine when used for subarachnoid block in the geriatric population having co-morbid systemic diseases and undergoing prostatic resections. The addition of fentanyl can further reduce the side-effects by decreasing the effective dose of Levobupivacaine for adequate analgesia.

## ADVERSE EFFECTS

Levobupivacaine produces the same adverse effects as seen with racemic bupivacaine and other local anaesthetics. The most common adverse drug reaction reported is hypotension (31%) followed by nausea (21%),vomiting (14%), headache(9%), procedural pain (8%) and dizziness (6%). The cardiac toxicity, neurological injury after peripheral nerve block and unwanted CNS effects, may be lower than Bupivacaine. Allergic type reactions are rare and range in severity from urticaria to anaphylactoid-like reaction. During the administration of epidural anaesthesia, it is recommended that a test dose is administered initially and the effects monitored before the full dose is given. A test dose of a short-acting amide anaesthetic, such as three milliliters (3 mL) of lignocaine, is recommended to detect unintentional intrathecal administration. Accidental intrathecal injection during epidural blockade can produce high spinal anaesthesia with severe hypotension and loss of consciousness.

## PHARMACOLOGY OF BUPIVACAINE

Bupivacaine (MARCAINE, SENSORCAINE), is widely used amide local anesthetic; its structure is similar to that of lidocaine except that the amine-containing group is a butyl piperidine. Bupivacaine is an amino amide local anaesthetic with a slow onset. It is long acting and suitable for procedures lasting 2 – 2.5hrs. It was first synthesized by Ekenstam in 1957 and was used clinically in 1963.




It is available as hyperbaric solution in concentrations of 0.5% and 0.75% with dextrose 8.25%. Available Isobaric solutions are in concentrations of 0.5% and 0.75%.Maximum dose is 2mg/kg body weight.

**PHYSICO-CHEMICAL PROFILE.**

| | |
|---|---|
| Molecular weight(base) | 288 |
| pKa | 8.16 |
| Solubility in Alcohol | 1 in 8 |
| Solubility in Water | 1 in 25 |
| Octonol/water partition coefficient | High |
| Lipid solubility | 28 |
| Plasma protein binding | 95% |
| Anaesthetic index | 3.0-4.0 |

**PHARMACODYNAMICS**

Bupivacaine by virtue of its pharmacological effects, has a stabilizing action on all excitable membranes. In the central nervous system, stimulation can occur producing restlessness, tremors and convulsions in over dosage. Bupivacaine can also causes a reduction of automaticity in the heart.

PHARMACOKINETICS ABSORPTION

The absorption depends on:

- Site of injection(intercostals>caudal>epidural>brachial plexus > subcutaneous)

- ❖ Dose- the peak blood concentration increases with increase in dose.
- ❖ Presence of vasoconstrictors delays the absorption.

**DISTRIBUTION**

Bupivacaine is 95% protein bound to albumin and alpha-1 acid glycoprotein.

**METABOLISM**

Occurs in liver by N-dealkylation, primarily to pipecolyxylidine. N-desbutyl bupivacaine and 4-hydroxy bupivacaine are the other metabolites produced.

**EXCRETION**

Excretion is through urine(5% as pipecolyxylidine and 16% as unchanged form). The clearance is 0.47 l/min and elimination half life is 62 mins.

**EFFECTS IN CVS**

It has marked cardiotoxic properties. It can bind to myocardial proteins and thus decreases the rate of increase of phase 0 during the cardiac action potential. In higher concentration, the peripheral vascular resistance and myocardial contractility are reduced and this can lead to cardiovascular collapse.

## EFFECTS IN CNS

In CNS it causes reversible neural blockade. It has characteristic biphasic effect in CNS. Initial excitation is caused by inhibition of inhibitory interneuron pathways in cortex. In higher doses both facilitatory and inhibitory pathways are depressed.

## ADVERSE REACTIONS

### CNS

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

### CVS

Cardiotoxicity effects are due to high lipid solubility and high protein binding properties of the drug. Accidental intravenous injection causes dysrhythmias, atrioventricular block, ventricular tachycardia and ventricular fibrillation.

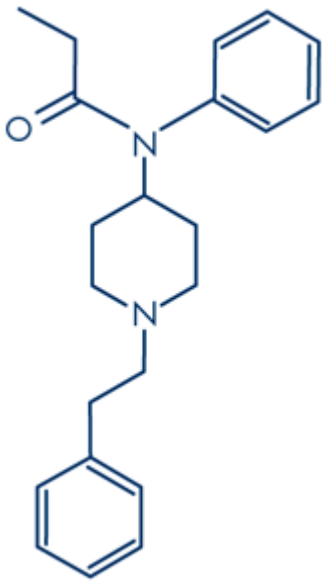
### ALLERGY

Allergy is extremely rare. It manifests as urticaria, pruritis, angioneurotic edema etc.

## PHARMACOLOGY OF FENTANYL

A tertiary amine which is a synthetic phenylpiperidine derivative. 4 anilinopiperidines that are structurally related to pethidines, It act at μ receptors as a agonist. 80-100 times more potent than Morphine.

## STRUCTURE




## PREPARATION

It is available as a clear solution for injection containing 50 micrograms/ml Fentanyl citrate.

## ROUTE OF ADMINISTRATION.

Oral, parenteral (iv, im), neuraxial (subarachnoid and epidural), transmucosal, transdermal.

## MECHANISM OF ACTION

It is a highly selective mu-agonist which specifically appears to be involved in the mediation of analgesia. Opioids appear to exert their effects by interacting with pre-synaptic Gi-protein receptors.

## PHARMACOLOGY OF SPINAL FENTANYL

- Dose 5-25 µg
- Onset 5-15 mins
- Duration 2-4 hrs.

## PHARMACOKINETICS METABOLISM

Fentanyl is extensively metabolized by N-demethylization producing Norfentanyl, which is structurally similar to Normeperidine. It is excreted by the kidneys.

| | |
|---|---|
| pKa | 8.4 |
| Molecular weight | 286 |
| Bound to plasma protein | 84% |
| T1/2µ | 1-2 mins |
| T1/2 α | 10-30 mins |
| T1/2β | 2-4 hrs |
| Clearance | 10-20ml/kg/min |
| Hepatic extraction ratio | 0.8-01. |
| Octanol-water partiant coefficient | 817 |

## CLINICAL PROPERTIES

- Minimal CSF spread.
- Rapid onset.
- Short duration.
- Low CSF solubility.
- Decreased side effects.
- Rapid analgesia.

## EFFECTS IN CVS:

Most significant effect is bradycardia caused by vagal stimulation. It does not affects cardiac output, mean arterial pressure, pulmonary capillary wedge pressure, pulmonary and systemic vascular resistance.

## EFFECTS IN RS:

Potent respiratory depressant. It decreases both respiratory rate and tidal volume. It also diminishes ventilator response to hypoxia and hypercapnia. Chest wall rigidity(wooden chest phenomenon) may occur.

## EFFECTS IN CNS

Analgesia, euphoria, sedation, hypnosis, miosis, nausea and vomiting.

**EFFECTS IN GI TRACT**

Delays gastric emptying, biliary colic.

**ENDOCRINE :** Attenuation of stress response.

**ADVERSE EFFECTS**

Pruritis, sedation, nausea, vomiting, apnea, urinary retention, seizures and chest wall rigidity may occur.

## ANAESTHETIC IMPLICATIONS IN GERIATRIC PATIENTS

Ageing is a normal physiological process, where the structure and functional capacity of organs and tissue progressively degenerates over the time. No ideal anaesthetic technique has been described in elderly population but if a thorough understanding of changes that occur in physiology and pharmacology is there, an optimal anaesthetic technique can be designed. Benign hypertrophy of prostate is common in elderly age group for which transurethral resection of prostate is required in symptomatic patients. This group of population has a greater anaesthetic risk because of the prevalence of coexisting cardiovascular and pulmonary disease. Spinal anaesthesia is technique of choice for TURP which besides providing surgical anaesthesia and postoperative analgesia, has added advantage of preserving cerebral function which in turn allows earliest recognition of unique complication related to Transurethral Resection of Prostate.

## Physiology and Pathophysiology of Ageing:

## Cardiovascular

Ageing alters both the pharmacokinetic and pharmacodynamics aspects of anaesthetic management. The functional capacity of organs declines and the co-existing diseases further contributes these changes. In terms of cardiac function, geriatric population have decreased beta-adrenergic responsiveness, so there is increased incidence of conduction abnormalities, bradyarrythmias and hypertension in these patients. Fibrotic infiltration of cardiac conduction pathway makes the elderly patients vulnerable to conduction delay and to atrial and ventricular ectopy. Elderly people also have an increased reliance on Frank-Starling mechanism for cardiac output. Therefore it is important to consider fluid administration carefully. In the non compliant older heart, small changes in venous return will produce large changes in ventricular preload and cardiac output. Due to diastolic dysfunction and decreased vascular compliance, the elderly patient compensates poorly for hypovolemia. Similarly, exaggerated transfusion is also poorly tolerated.

**DECREASED ARTERIAL ELASTICITY:**

- Elevated after load
- Elevated systolic blood pressure
- Left ventricular hypertrophy
- Decreased heart rate

- Decreased baroreceptor reflex
- Atherosclerosis
- Coronary artery disease
- Hypertension
- Congestive heart failure
- Cardiac arrhythmias
- Aortic stenosis

**Respiratory**

Chronic obstructive pulmonary disease (COPD), pneumonia, sleep apnea are very common among the elderly age group. The Closing volume increases with age, and FEV1 declines 8-10% per decade due to reduced pulmonary compliance. PaO2 decreases progressively with the age because of Ventilation perfusion(V/Q) mismatch and anatomical shunt. Thus, it is recommended that elderly patients are transferred to the PACU with oxygen via nasal cannula. Postoperatively respiratory complications are most common in geriatric patients. The most significant clinical predictor of adverse pulmonary outcome is the site of surgery, with thoracic and upper abdominal surgery having the highest pulmonary complication rate.

**Decreased compliance**

- Decreased alveolar surface
- Decreased residual volume
- Increased closing capacity
- V/Q mismatch
- Decreased PaO2

**Chest wall rigidity**

**Decreased muscle strength**

- Decreased cough
- Emphysema
- Chronic bronchitis
- Pneumonia
- Lung cancer

**Blunted response to hypercarbia and hypoxia**

**Renal function**

The Renal blood flow and the kidney mass decreases with age. Serum creatinine level remains stable due to reduction in muscle tissue. Impairment in sodium handling, concentrating ability and diluting capacity predisposes the elderly patients to dehydration and fluid overload. Reduced renal blood flow and decreased nephron mass increases the risk of acute renal failure in the postoperative period.

**Nervous system**

The nervous system is the target for virtually every anaesthetic drug, and the age related changes in nervous system function have compelling implications for anaesthetic management. Ageing results in decreases in nervous tissue mass, neuronal density and concentration of neurotransmitters, as well as norepinephrine and dopamine receptors .Dosage requirements for local and general anaesthetics are reduced. Administration of a given volume of epidural anaesthetic results in a more cephalic spread, having though a shorter duration of sensory and motor block. Elderly patients take more time to recover from general anesthesia especially if they were disoriented perioperatively.

Geriatric patients experience varying degrees of delirium. They are sensitive to centrally acting anticholinergic agents. The incidence of delirium is less with regional anaesthesia, provided that there is no additional sedation.

**Pharmacology**

The circulating level of albumin which is the main plasma binding protein for acidic drugs decreases with age. On the other hand, the level of α-1 acid glycoprotein the binding protein for basic drugs increases with age. The effect of ageing on pharmacokinetic depends upon the drug is used.

The decrease in total body water leads to a reduction in the central compartment and increased serum concentrations after a bolus administration of a drug. On the other hand, the increase in body fat results in a greater volume of distribution, thus prolonging drug action.Drug metabolism could probably be altered by the ageing effect on hepatic or renal function.

The elderly are more sensitive to anaesthetic agents and generally require smaller doses for the same clinical effect, and drug action is usually prolonged.

**Inhalation drugs:** Minimum alveolar anaesthetic concentration (MAC), decreases approximately 6% for every decade. There is altered activity of neuronal ion channels associated with acetylcholine, nicotinic and GABA receptors. Alterations in ion channels, synaptic activity and receptor sensitivity is probably responsible.

**Opioids:** The elderly require less doses for pain relief. Morphine clearance is decreased in the elderly. Sufentanil, alfentanil, and fentanyl are twice as potent in the elderly, due to an increase in brain sensitivity to opioids with age. There are changes in pharmacokinetics and pharmacodynamics of remifentanil, which is more potent in geriatric patients. Clearance and the volume of the central compartment decrease with age and the infusion rates should be titrated.

**Neuromuscular blockers:** The duration of drug action may beprolonged if their metabolism depends on renal or hepatic excretion. Cisatracurium undergoes Hofmann degradation and is unaffected by age.

**Peripheral nerve blocks**: The duration of analgesia may be prolonged with age depending on the baricity of the Bupivacaine solution. When using 0.75% Ropivacaine for nerve blocks, age is a major factor in determining the duration of motor and sensory block. When general anaesthesia carries great risk for the patient, administrating regional anaesthesia if possible could provide an excellent solution.

**Preoperative evaluation**

Common diseases in the elderly have a significant impact on anaesthesia and require special care. The risk from anaesthesia is more related with the presence of co-existing disease than with the age of the patient. Thus, it is more important to determine the patient's status and estimate the physiologic reserve in the preanaesthetic evaluation.

If the condition can be optimized before surgery this should be done without delay, because long delays increase the rate of morbidity.

Diabetes mellitus and cardiovascular disease are very common among geriatric patients. Pulmonary complications are one of the leading causes of postoperative morbidity in elderly patients. Pulmonary optimization is needed for these patients. Laboratory and diagnostic

studies, the history and physical examination are of great importance. Two more issues that must be always in mind in a geriatric patient is the significant possibility of depression, malnutrition, immobility and dehydration.

| Drug | Brain sensitivity | Pharmacokinetics | Dose |
|---|---|---|---|
| Inhaled agents | ↑ | | ↓ |
| Thiopental | ↔ | ↓ (↓ volume) | ↓ |
| Etomidate | ↔ | ↓ (↓ volume) | ↓ |
| Propofol | ↑ | ↓ (↓ clearance) | ↓ |
| Midazolam | ↑ | ↓ (↓ clearance) | ↓ |
| Morphine | ↑ | ↓ (↓ clearance) | ↓ |
| Remifentanil | ↑ | ↓ (↓ clearance) | ↓ |
| Atracurium | - | - | ↔ |
| Cis- atracurium | - | - | ↔ |

It is important to determine the cognitive status of an elderly patient. Cognitive deficits are associated with poor outcomes and higher perioperative morbidity. It is controversial whether general anesthesia accelerates the progression of senile dementia. Elderly patients require lower doses of premedication. Opioid premedication is valuable only if the preoperative condition of the patient involves severe pain. Anticholinergics are not required since salivary gland atrophy is usually present. However,

H2 antagonists are useful, to reduce the risk of aspiration. Metoclopramide could also be used to promote gastric emptying, although the risk of extrapyramidal effects is higher in elderly patients.

**Intraoperative care and anaesthetic management**

Advancing age is not a contraindiction for either general or regional anaesthesia. Some aspects of regional anaesthesia may provide benefit for the patient. It affects the coagulation system by preventing postoperative inhibition of fibrinolysis. Furthermore, it decreases the incidence of deep vein thrombosis after total hip arthroplasty.

The hemodynamic effects of regional anaesthesia may be associated with reduced blood loss in pelvic and lower extremity operations. More important, the patient maintains his airway and pulmonary function. Advanced age and general anesthesia are associated with hypothermia. Maintenance of normothermia is important as hypothermia is related to myocardial ischemia, and hypoxemia in the early postoperative period. In case of general anesthesia it is of major importance to titrate drug doses and it would be prudent to use short acting drugs.

The use of peripheral blocks in the elderly promises favourable outcomes without compromising the safety of the airway or risking major hemodynamic effects. However, it should always be kept in mind that there are some anatomic changes in geriatric patients and that peripheral

blocks have shown to last longer in these cases. The optimal physiological management is required to produce the best surgical outcome.

## POSTOPERATIVE CARE

Pulmonary problems are of major importance in the postoperative period. The need for shorter hospitalization cannot be overemphasized. Minimal-invasion surgery and regional over general anesthesia when possible, could probably lead to a more favorable outcome for geriatric patients

## COMMON CAUSES OF POSTOPERATIVE MORBIDITY

| | |
|---|---|
| Atelectasis<br>Pneumonia<br>Neurological disease<br>Myocardial infraction | Heart failure<br>Delirium<br>Acute bronchitis |

## CHOICE OF ANAESTHETIC TECHNIQUE FOR TRANSURETHRAL RESECTION OF PROSTATE

### SPINAL ANAESTHESIA:

Spinal anaesthesia offer several advantages over general anaesthesia. It is particularly useful for patients with significant respiratory disease. It confers good postoperative analgesia and may reduce the stress response to surgery. More importantly, spinal anaesthesia allows the anaesthetist to monitor the patient's level of consciousness, which makes it easier to detect the early signs of TURP syndrome. Early recognition of capsular tears and bladder perforation is also possible as the patient complains of periumbilical or shoulder pain provided the spinal level is limited to T10 a spinal block of T8 is required to eliminate the discomfort caused by bladder distension. Severe hypotension is uncommon with this level of blockade. The lithotomy position may compensate for sympathetic block by improving venous return. Treatment of hypotension with vasoconstrictors rather than rapid fluid is encouraged to reduce the risk of fluid overload.

### GENERAL ANAESTHESIA:

General anaesthesia is preferred when patient has a contraindication to spinal anaesthesia, unable to lie supine for any length of time, or has a persistent cough which make surgery, the choice of airway will depend on patient factors. The lithotomy position in combination with a head-down

tilt reduces the tidal volume and functional residual capacity, and increases the likelihood of gastric regurgitation. Tracheal intubation and positive pressure ventilation may counteract these problems. However, the use of laryngeal mask airway with spontaneous ventilation in selected patients is an acceptable alternative. Under light planes of general anaesthesia, penile erection may interfere with surgery. It can usually be managed by deepening anaesthesia.

**LOCAL ANAESTHESIA:**

Transurethral Resection of Prostate(TURP) in high risk patients has been performed using local infiltration of the perineum and the prostatic fossa. However, the quality of operative analgesia is inferior to a spinal anaesthetic and the prostate gland size should be less than 40g. If its more than 40g this technique cannot be recommended and alternative treatments should be explored.

## SURGICAL TECHNIQUE:

The operation is performed using a resectoscope, through which a diathermy loop is passed. The aim of the procedure is to resect the hyperplastic tissue while sparing the surgical capsule, although it does not form a well-defined plane with the surgical capsule. The prostatic tissue is resected in small strips under direct vision using the diathermy loop, which can both cut and coagulate. The bladder is continuously irrigated with fluid to allow direct vision and to wash away blood and debris. At the end of the procedure, a three-lumen catheter is inserted and irrigation is continued for up to 24hrs after operation. The procedure usually takes 30–90min, depending on the size of the prostate and the level of experience of the operator. It is performed in the lithotomy position, sometimes with head-down.

## POTENTIAL COMPLICATIONS DURING TURP

Potential problems during TURP

- Intraoperative

- TURP syndrome
- Haemorrhage
- Myocardial ischaemia
- Hypothermia
- Prostatic capsular perforation
- Bladder or urethral perforation
- Penile erection
- TURP syndrome
- Bladder spasm
- Ongoing bleeding
- Clot retention

- Deep venous thrombosis

- Myocardial ischaemia/infarction

- Postoperative cognitive impairment

Myocardial ischaemia may occur in up to 25% of the elderly patients undergoing Transurethral Resection of Prostate. Elderly patients are prone to hypothermia, particularly if the irrigating solution is at room temperature. Warmed irrigation fluids have not been shown to cause any increase in blood loss by local vasodilation and should be used in conjunction with active patient warming devices.

Sometimes, the surgeon may perforate the prostatic capsule, urethra, or bladder with the resectoscope. Most of the small perforations do not require further intervention. Prostatic capsular perforation may be associated with excessive bleeding, and require placement of a retroperitoneal drain. Intraperitoneal perforation may be diagnosed by shoulder-tip pain in patients with spinal anaesthesia.

Postoperative pain is not usually severe after either spinal or general anaesthesia, although discomfort from bladder spasm or from the urinary catheter may occur. It is unusual to require opioids after operation. Catheter pain may be treated with lidocaine gel.

Bladder spasm may be treated with muscarinic receptor antagonists (e.g. hyoscinebutylbromide, tolteridine, or oxybutynin), although there is an increased risk of precipitating delirium in elderly patients. Alternatives are benzodiazepines or a subhypnotic dose of ketamine (250 μg $kg^{-1}$) can be used.Clot retention may occur after operation, particularly if irrigation is inadequate, and may lead to bladder overdistension, which is painful and may precipitate severe bradycardia due to vagal stimulation. Mechanical measures such as flushing the bladder or milking the catheter may be successful, but occasionally the patient may need to be taken back to theatre for evacuation of a bladder haematoma.

This patient group is at particular risk from deep venous thrombosis. For low-risk patients with good mobility, compression stockings are usually adequate prophylaxis. Low-molecular-weight heparin should be considered in patients at higher risk (poor mobility, malignancy, intercurrent illness, and obesity). Postoperative cognitive impairment is also common in this patient group.

## HEMORRHAGE

Blood loss during TURP is inevitable and is typically in the region of 500 ml. It is difficult to quantify due to the large volume of irrigating solution used. Patients loses between 2.4 and 4.6 ml of blood per minute of resection whichever anaesthetic technique is used. In theory, blood loss can be estimated by assaying the haemoglobin concentration of the discarded irrigation fluid, by measuring the electrical conductivity of the discarded irrigation fluid, or in the laboratory by radioactive albumin or red-cell labelling techniques. Visual assessment of the colour of the discarded irrigation fluid is unreliable.

Factors associated with excessive bleeding include a large gland, extensive resection (>40–60 g of prostate chippings), coexisting infection, prolonged surgery (>1 h), and the presence of a preoperative urinary catheter. The histology of the gland is not associated with differences in bleeding. In practice, frequent measurement of the haemoglobin is the most useful investigation.

Urokinase released from raw prostate tissue may provoke systemic fibrinolysis which may worsen postoperative haemorrhage. Where blood loss is extensive, a bolus of tranexamic acid, e.g. 15–25 mg $kg^{-1}$, may reduce the volume of haemorrhage.

For patients with a normal preoperative haemoglobin, who undergo a small resection (<30 g), it is very unusual to require blood transfusion after operation.

**TURP SYNDROME**

The TURP syndrome is essentially a clinical diagnosis based upon a constellation of symptoms and signs associated with excessive absorption of irrigating fluid into the circulation. It comprises acute changes in intravascular volume, plasma solute concentrations, and osmolality, and direct effects of the irrigation fluid used (glycine and its metabolites in the UK, as glycine 1.5% is the most common irrigation fluid used). The effects are proportional to the volume of irrigating solution absorbed. The presentation is not always uniform, and milder cases may be unrecognized. Other types of endoscopic surgery that require the use of irrigation solution, e.g. hysteroscopy, may also give increase to the TURP syndrome.

Mild-to-moderate TURP syndrome may occur in 1–8% of patients. The overall mortality is 0.2–0.8%. It may present as early as 15 min after resection starts or as late as 24 h after operation. Severe TURP syndrome is now rare; however, it carries a mortality of up to 25%.

When glycine 1.5% is used as the irrigation fluid, early features of this syndrome include restlessness, headache, and tachypnoea, or a burning

sensation in the face and hands. Visual disturbance including transient blindness may be reported. Features of increasing severity include respiratory distress, hypoxia, pulmonary oedema, nausea, vomiting, confusion, convulsions, and coma. General anaesthesia may mask the early symptoms, and the only sign may be cardiovascular instability.

Irrigation fluid is absorbed at a rate of between 10 and 30 ml $min^{-1}$ of operating time. Five to 20% of patients will absorb >1 litre.[3] In some centres, ethanol 1% is added to the irrigation solution and the patient's breath is tested for ethanol every few minutes: a positive test indicates a significant quantity of fluid has been absorbed. This method is well evaluated and is practically easier than other methods involving either gravimetric weighing (patient placed on a bed scale and any increase in body weight equates to fluid absorption) or volumetric fluid balance (calculating the difference between the amount of irrigating fluid used and volume recovered).

A higher rate of absorption is produced by several factors.

1. The pressure of the irrigation fluid. The height of the bag should be kept as low as possible to achieve adequate flow of fluid. Seventy centimetres are usually satisfactory. However, the surgeon will

frequently stop and drain the bladder to remove chippings; during this time, the hydrostatic pressure within the bladder is low.

2. Low venous pressure, e.g. if the patient is hypovolaemic or hypotensive.
3. Prolonged surgery, especially >1 h, although this is now uncommon.
4. Large blood loss, implying a large number of open veins.
5. Capsular perforation, or bladder perforation, allowing a large volume of irrigation fluid into the peritoneal cavity, where it is rapidly absorbed.

Volume changes

Acute volume changes predominantly affect the cardiovascular system. The rapid absorption of a large volume of irrigation fluid can cause hypertension with reflex bradycardia, and can precipitate acute cardiac failure and pulmonary oedema. The magnitude of the hypertension is not related to the volume of fluid absorbed.

Rapid equilibration of hypotonic fluid with the extracellular fluid compartment may precipitate sudden hypotension in association with hypovolaemia. Hypotension and hypovolaemia may be compounded by the sympathetic block of spinal anaesthesia. This secondary phase at the end of the operation is often the first sign suggestive of the TURP syndrome.

**Solute changes**

Acute changes in plasma sodium concentration and osmolality predominantly affect the central nervous system (CNS). Acute hyponatraemia is produced initially by the dilutional effect of a large volume of absorbed irrigation fluid, but later is caused by natriuresis, and may cause headache, altered level of consciousness, nausea and vomiting, seizures, coma, and death. However, hypoosmolality is more important than hyponatraemia in CNS disturbance. The Nernst equation predicts that a moderate decrease in extracellular sodium concentration only minimally alters membrane excitability. Patients who are hyponatraemic but have a normal osmolality are likely to be asymptomatic. Rapid reduction in plasma osmolality overwhelms neuronal compensatory mechanisms. Free water is absorbed into the brain parenchyma, causing water intoxication, cerebral oedema, and raised intracranial pressure.

Serum sodium concentration should be measured in conjunction with serum osmolality. If the osmolality is normal or nearly so, no intervention is recommended to correct serum sodium if the patient is asymptomatic. Rapid correction of hyponatraemia may lead to central pontinemyelinolysis (CPM). The presence of symptoms has been described as the most important factor determining morbidity and mortality from

hyponatraemia. An acute decrease to <120mmol litre$^{-1}$ is invariably symptomatic and should be treated with hypertonic saline.

Dilutional hyponatraemia may prolong the action of non-depolarizing neuromuscular blocking agents, and may cause broadening of the QRS complex or T-wave inversion.

**Glycine and its metabolites**

Glycine is a major inhibitory neurotransmitter in the CNS and retina. Glycine toxicity may cause nausea, headache, malaise, and weakness, and also visual disturbances including transient blindness (sodium appears to play only a minor role in visual disturbances). Glycine may also directly depress the myocardium.

*N*-methyl D-aspartate (NMDA) receptor activity is potentiated by glycine, which paradoxically may precipitate encephalopathy and seizures. Magnesium (whose plasma level may also be reduced through dilution) exerts a negative control on the NMDA receptor and also having a membrane-stabilizing effect, and magnesium therapy should be considered as part of the therapy for seizures in TURP syndrome.

The liver and kidneys metabolize glycine by oxidative deamination to glyoxylic acid and ammonia. The redistribution half-life of glycine is 6 min. The terminal half-life of glycine is dose-dependent and varies from 40

min to several hours. The role of hyperammonaemia during TURP syndrome remains unclear, although ammonia is considered to be a cerebral depressant.

**Treatment**

If TURP syndrome is suspected, surgery must be abandoned as soon as possible and i.v. fluids stopped. Treatment should involve supporting respiration if necessary, with intubation and ventilation and the circulation. Bradycardia and hypotension should be treated with atropine, adrenergic drugs, and i.v. calcium. I.V. anticonvulsants (e.g. diazepam or lorazepam) should be used to control seizures and i.v. magnesium therapy considered, if seizures prove difficult to control. Blood should be obtained and checked for sodium, osmolality, and haemoglobin.

**Management of severe TURP syndrome.**

Diuretic therapy (e.g. i.v. furosemide 40 mg) is only recommended to treat acute pulmonary oedema caused by the transient hypervolaemia. Furosemide worsens hyponatraemia, but is effective at removing free water. Mannitol (e.g. 100 ml of 20%) causes less sodium loss than loop diuretics.

Hypertonic saline (3%) is indicated to correct severe hyponatraemia, if serum sodium <120 mmol litre$^{-1}$ or if severe symptoms develop, for

example, transient blindness, persistent nausea and vomiting, severe headaches, and pronounced hypotension (systolic pressure decrease >50 mm Hg). The rate of correction should be slow (not >1 mmol litre$^{-1}$ h$^{-1}$ in the first 24 h). Too rapid a correction may lead to hypervolaemia, cerebral oedema. Correction to normal is not indicated: the aim should be clinical improvement. Hypertonic saline should be given into a large vein.

**USE OF HYPERTONIC SALINE**

Calculate total body water as 0.6×body weight (kg), e.g. for a 70 kg man, TBW=42 litre

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2×TBW is the number of millilitres of NaCl 3% which will raise serum [Na] by 1 mmol litre$^{-1}$, e.g. 2×42=84 ml of NaCl 3% over 1 h will raise serum sodium by 1 mmol litre$^{-1}$

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Invasive monitoring of arterial and central venous pressures is very helpful in managing patients with large fluid shifts. Transferring the patient to a high-dependency or intensive care environment after operation is advised (TURP syndrome may worsen later as irrigation continues after operation and fluid may continue to be absorbed).

Visual disturbances caused by glycine typically resolve fully within 24 h and require no treatment. Patient reassurance is vital to allay anxiety.

## NEWER TECHNIQUES OF PROSTATIC RESECTION

Newer techniques of prostatic resection uses different types of energy like heat, laser, ultrasound, or microwave to vaporize prostatic tissue and coagulate surrounding blood vessels. These techniques are reported to cause less haemorrhage than the conventional Transurethral Resection of Prostate, but specimens for histology cannot be obtained. Since diathermy is not used, normal saline may be used as the irrigating solution, minimizing the risk of the TURP syndrome.

# REVIEW OF LITERATURE

Literature related to Levobupivaine , Bupivacaine, Anaesthetic management of TURP searched in google, pubmed, medknow and metascape search engines using keywords like levopubivacaine, bupivacaine, TURP from articles year 2007 to till date. The literature was searched and reviewed to seek for advantages and disadvantages of using levobupivacaine and bupivacaine in transurethral resection of prostate surgeries.

1. Shweta Mohan1 et al in 2013 conducted a study to compare the onset and duration of motor and sensory block and the duration of analgesia with levobupivacaine alone and in combination with fentanyl. A total of 80 patients between the age group of 50-70 years of ASA Grades II and III were divided into two groups of 40 each. Subarachnoid block in Group A received 0.5% levobupivacaine 2.5 ml (12.5 mg) + 0.9% Nacl 0.5 ml. Subarachnoid block in Group B received 0.5% levobupivacaine 2.5 ml (12.5 mg) + fentanyl 0.5 ml (25 µg). Baseline vitals, onset and duration of motor and sensory block and duration of analgesia were recorded. The onset and duration of sensory block were prolonged in fentanyl group. Onset of motor block was delayed, however, duration was prolonged in fentanyl group. The duration for first rescue analgesia was prolonged in the fentanyl group[(3)]

2. Belgin Akan et al in 2013 conducted a study to compare the efficacy and adverse effects of levobupivacaine alone and in combination with fentanyl and sufentanil during transurethral resection of the prostate (TURP) under spinal anesthesia.In this prospective, randomized, double-blind trial, 60 patients undergoing elective TURP under spinal anesthesia were randomized into three groups. Ten milligrams of 0.5% levobupivacaine in Group-I, 7.5 mg 0.5% levobupivacaine combined with 25 μg fentanyl in Group-II and 7.5 mg 0.5% levobupivacaine with 2.5 μgsufentanil in Group-III were administered intrathecally. The time for sensorial block to reach level T10 was 10.2 ± 2.0, 6.9 ± 1.7 and 7.0 ± 1.4 min in Group-I, II and III, respectively ($P < 0.001$). The maximum sensorial block level was T8 in all groups. The frequency of a complete motor block was higher in Group-I. The mean duration of motor block was shorter in Group-II and III than in Group-I ($P < 0.001$). There were no differences between groups regarding side effects ($P > 0.05$). The time for first analgesic request was shorter in Group-I than in the other two groups ($P < 0.05$). During the first postoperative 24-h period, 11 (58%) patients in Group-I, 9 (48%) patients in Group II and 9 (45%) patients in Group-III required an analgesic drug ($P > 0.05$).This study showed that combining lower dose levobupivacaine with fentanyl and sufentanil provides faster onset of

sensorial block, lower frequency and shorter duration of motor block, and longer analgesia time in TURP under spinal anesthesia[4]

3. ErkanYavuzAkcaboyet al conducted a study in 2011 to evaluate the clinical effectiveness and block quality of low dose levobupivacaine, and compare it with low dose bupivacaine when they are combined with fentanyl in Transurethral resection of prostate surgery.Forty nine patients undergoing transurethral prostate surgery were enrolled in this prospective, randomized and double blind study. Patients inlevobupivacaine group received 5 mg levobupivacaine + 25 μg fentanyland bupivacaine group received 5 mg bupivacaine + 25 μg fentanyl. Demographic data, surgery times, hemodynamic parameters, block qualities and patient and surgeon satisfactions were recorded and concluded that for transurethral prostate surgery 5 mg levobupivacaine with 25 μg fentanyl can provide stable hemodynamic profile, patient and surgeon satisfaction and effective sensorial blockade with less motor blockade in spinal anaesthesia; so it could be used at low doses as a good alternative to bupivacaine[1]

4. Deepak Choudhary et al in 2017 studied the effectiveness of intrathecal low dose isobaric levobupivacaine with fentanyl and compare it with low dose hyperbaric bupivacaine with fentanyl in transurethral resection of prostate. This prospective, randomized, double blinded

study was conducted in 60 ASA physical status I and II patients, aged between 50-80 years and posted for transurethral resection of prostate under subarachnoid block. Enrolled patients were divided into two groups of 30 each. Patients in Group B received 7.5mg, 0.5% hyperbaric bupivacaine with 25mcg fentanyl intrathecally while patients in Group L received 7.5mg, 0.5% isobaric levobupivacainewith 25mcg fentanyl intrathecally. Time to achieve sensory block to T10 level, max spread of sensory block, time to two-segment regression and time to S1 regression were recorded. Motor blockade was assessed at every 2 minute for 20 minute, at the end of the surgery and in recovery room. Onset time of motor block, maximum motor block and duration of motor block were also recorded. A total of 60 subjects were enrolled. Baseline parameters were comparable. Onset of sensory block was significantly faster in group B compared to group L. The mean time of onset in Group B was 4.75±0.79 min. and in Group L was 6.60±0.61 min. Both group had statistically significant difference in onset and duration of motor block. The mean time of onset of motor block in Group B was 6.4±1.6 min and in Group L was 9.9±2.3 min. The mean duration of motor block in Group B was 164.17±22.8min and in Group L was 138.27±23.5min. Group B had statistically significant dense block compared to group L. The median Modified bromage scale in Group B was 1(95% C.I. 1.18-1.68) and in Group L was 2 (95% CI

2.13-2.86). In group B, 20 patients had complete motor block while in group L number of patient with complete motor block was only 4. Their results suggested that subarachnoid low-dose isobaric levobupivacaine fentanyl provides lesser degree of motor block & for short duration when compared with heavy bupivacaine[7]

5. Rosa Herrera et al conducted a descriptive, observational pilot study to assess the hemodynamic impact of subarachnoid anesthesia with isobaric levobupivacaine versus hyperbaric bupivacaine for hip fracture surgery. Hundred twenty ASA status I-IV patients aged 65 and older undergoing hip fracture surgery were enrolled. The primary objective of our study was to compare hemodynamic effects based on systolic blood pressure (SBP) and diastolic blood pressure (DBP) values, heart rate (HR) and hemoglobin (Hb) and respiratory effects based on partial oxygen saturation ($SpO_2$%) values. The secondary objective was to assess potential adverse events with the use of levobupivacaine versus bupivacaine. Assessments were performed preoperatively, at 30 minutes into surgery, at the end of anesthesia and at 48 hours and 6 months after surgery.Among intraoperative events, the incidence of hypotension was statistically significantly higher ($p$ <0.05) in group BUPI (38.3%) compared to group LEVO (13.3%). There was a decrease ($p$ <0.05) in systolic blood pressure (SBP) and diastolic blood

pressure (DBP) at 30 minutes intraoperatively (19% in group BUPI versus 17% in group LEVO). $SpO_2$% increased at 30 minutes after anesthesia onset (1% in group BUPI versus 1.5% in group LEVO). Heart rate (HR) decreased at 30 minutes after anesthesia onset (5% in group BUPI versus 9% in group L). Hemoglobin (Hb) decreased from time of operating room (OR) admission to the end of anesthesia (9.3% in group BUPI versus 12.5% in group LEVO). The incidence of red blood cell (RBC) transfusion was 13.3% in group BUPI versus 31.7% in group LEVO, this difference was statistically significant. Among postoperative events, the incidence of congestive heart failure (CHF) was significantly higher in group BUPI (8,3%). At 6 months after anesthesia, no differences were found.Given the hemodynamic stability and lower incidence of intraoperative hypotension observed, levobupivacaine could be the agent of choice for subarachnoid anesthesia in elderly patients.[20]

6. Erdil F et al to compare the block durations and haemodynamic effects associated with intrathecallevobupivacaine or bupivacaine in elderly patients undergoing transurethral prostate surgery. Eighty patients were prospectively randomised to receive plain 1.5 μg) for spinal anaesthesia. The time to reach T10 and peak sensory block level, and to maximum motor block were significantly shorter in group bupivacaine

compared to group levobupivacaine (p ml (15 ml plain bupivacaine 0.5% (group bupivacaine) in combination with fentanyl 0.3 ml levobupivacaine 0.5% (group levobupivacaine) or 1.5 to compare the block durations and haemodynamic effects associated with intrathecallevobupivacaine or bupivacaine in elderly patients undergoing transurethral prostate surgery. Eighty patients were prospectively randomised to receive plain 1.5< min after injection (p min until 30 0.05). Peak sensory block level was also significantly higher in group bupivacaine. In group bupivacaine, mean arterial pressure was significantly lower than group levobupivacaine, starting from 10 < 0.05). Hypotension and nausea were less common in group levobupivacaine than group bupivacaine (p <0.05). Because of the better haemodynamic stability and fewer side-effects associated with levobupivacaine, it may be preferred for spinal anaesthesia in elderly patients[25]

7. Susmita Bhattacharyya et al To compare the hemodynamic changes and adequate surgical condition between saddle block and subarachnoid block for TURP. Ninety patients of aged between 50 to 70 years of ASA-PS I, II scheduled for TURP were randomly allocated into 2 groups of 45 in each group. Group A patients were received spinal (2 ml of hyperbaric bupivacaine) and Group B were received saddle block (2 ml of hyperbaric bupivacaine). Baseline systolic, diastolic and mean

arterial pressure, heart rate, oxygen saturation were recorded and measured subsequently. The height of block was noted in both groups. Hypotension was corrected by administration of phenylephrine 50 mcg bolus and total requirement of vasopressor was noted. Complications (volume overload, TURP syndrome etc.) were noted. Incidence of hypotension and vasopressor requirement was less ($P < 0.01$) in Gr B patients.Adequate surgical condition was achieved in both groups. There was no incidence of volume overload, TURP syndrome, and bladder perforation and concluded thatTURP can be safely performed under saddle block without hypotension and less vasopressor requirement.[5]

8. Kararmaz A et al evaluated the effect of low-dose bupivacaine plus fentanyl administered intrathecally in elderly patients undergoing transurethral prostatectomy. Patients were randomly assigned to one of two groups. Group F received plain bupivacaine 4 mg with 25 micro g of fentanyl and sterile water to a total of 1.5 ml, and Group B received only 0.5% plain bupivacaine 7.5 mg for spinal anaesthesia. Sensory block was adequate for surgery in all patients. The mean level of motor block was higher and the duration of motor block was longer in Group B ($p < 0.0001$). Hypotension and shivering were significantly more common in Group B ($p < 0.05$). The addition of fentanyl 25 micro g to plain bupivacaine 4 mg provides adequate analgesia for transurethral

prostatectomy with fewer side-effects in elderly patients when compared with the conventional dose of bupivacaine[30]

9. Prajapati J et al conducted a study to evaluate the efficacy of addition of fentanyl 25 µg intra thecally to bupivacaine 5 mg.The patients were randomly allocated into 2 groups, each having 30 patients. Group-A: Inj. Bupivacaine 5 mg (0.5%) (1ml) Bupivacaine 7.5 mg (0.5%) (1.5 ml). A standard L4 Space in sitting / lateral position with 22G/23G BD spinal under all aseptic and antiseptic precautions after local infiltration of 2 cc 2 % lignocaine. were injected after checking of free flow of CSF and selected. All the observations were recorded and all the results were analyzed statistically. e of onset sensory blockade was significantly shorter in group A than group B. Group A took less time to reach the peak sensory level (3.57 min) as compared to group B (5.8 min). Onset of motor blockade was delayed in group B as compared to group-A, and t statistically significant. Changes in pulse rate of all groups are statically not significant and comparable. The incidence of hypotension and shivering was significantly higher in group B as that intra thecal bupivacaine 5 mg combined with fentanyl 25 provided adequate anesthesia for TURP in elderly patients and is associated with lower incidence of hypotension and shivering than a conventional dose of bupivacaine[2]

## MATERIAL AMD METHODS:

This is a Single centre Prospective, Randomized, Single Blinded Study was conducted at urology theatre, Department of Anaesthesia, Tirunelveli Medical College and Hospital from January 2018 to July 2019.

This study was done in 60(sample size) patients who undergone Transurethral Resection of Prostate of ASA physical statusI and II. Ethical committee approval and informed written consent from patients involved in this study are obtained before starting this study.

**INCLUSION CRITERIA:**

Patients in the age group of 65-75yrs with physical status ASA I & ASA II posted for elective TURP

**EXCLUSION CRITERIA:**

- History of allergy to any drugs
- Any contraindications to regional anaesthesia
- Abnormal coagulation profiles
- Spinal Abnormalities
- Patient with heart disease, respiratory disease, hepatic and renal disease, seizure disorder

**RANDOMIZATION:**

Patients will be allocated into two groups by simple randomization into group A and group B by computer generated random number sequence.

**ALLOCATION AND INTERVENTION:**

**Group A** – will receive 0.5% Levobupivacaine 7.5mg + inj fentanyl 25mcg

**Group B** – will receive 0.5% Bubivacaine 7.5mg + inj fentanyl 25mcg

**MATERIALS:**

25 guage Quincke needle, Inj Levobupivacaine, Inj Bupivacaine, Inj Fentanyl

**STUDY METHODS**:

- Preoperative assessment will be done
- Anaesthetic machine is checked before starting the procedure
- Ensure the availability of working laryngoscope, oral airway, laryngeal mask airway and endotracheal tube of various sizes
- Make sure that the essential emergency drugs are available
- Ensuring the operating table tilts are corrected
- In operating room routine monitoring including ECG, NIBP, pulse oximeter will be attached and baseline vital parmeters will be recorded
- Intravenous access will be secured with 18G venflon and ringer lactate solution will be started
- Under strict aseptic precaution, lumbar puncture is to be performed at L3 and L4 interspace using 25 guage Quincke needle in sitting a

position and the study drug will be injected after confirming the free flow of CSF

- Immediately after performing intrathecal injection patient will be placed in supine position and time will be noted
- Block characterstics will be assessed every 2min till the end of the surgery
- Sensory block was assessed by pin prick in the mid-clavicular line in each dermatome on both sides with a blunt 25G needle at three point scale –0-sharp pain, 1-dull pain (analgesia),2-no pain (anaesthesia)
- Maximum height of the block and time taken to achieve maximum height also recorded
- Motor blockade was assessed based on a Modified Bromage Scale at six point scale, 1- complete block(unable to move feet or knees), 2-almost complete block(able to move feet only), 3-partial block(just able to move knees), 4-detectable weakness of hip flexion while supine(full flexion of knees), 5-no detectable weakness of hip flexion while supine, 6-able to perform partial knee bend
- Onset of sensory blockade was defined as the time taken from the completion of the injection of study drug til the patient did not feel the pinprick at T10 level

- Onset of motor blockade was defined astheinterval between intrathecal administration of drug and impairment in motor power on movement
- ECG, SPO2 AND NIBP will be monitered every 2min till the end of the surgery
- Common side effects observed after subarachnoid block are hypotension and bradycardia. Hypotension is defined as drop insystolic blood pressure of more than 20% percent from baseline and its managed with inj Ephedrine intravenously in increments of 6mg if necessary and Bradycardia is defined as heart rate of less than 60 and its managed with inj Atrophine 0.6mg
- Supplementary 5 l/ min O2 was given to all patients via face mask
- At the end of surgery patient shifted to postoperative ward
- In postoperative ward block characteristic was done at every hour till complete motor recovery
- For sensory block, time to two-segment regression and time to regression to S1 dermatome was recorded
- Duration of sensory block was taken as the time from the onset of sensory block to regression of sensory block up to S1 dermatome

- The duration of motor blockade was defined as interval from intrathecal administration to the point at which patient was able to move his limbs

# METHODOLOGY

## STATISTICAL TESTS USED:

Data was entered into Microsoft Excel (Windows 7; Version 2007) and analyses was done using the Statistical Package for Social Sciences (SPSS) for Windows software (trial version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical variables. Comparison between groups was analysed using Chi-square test of independence and Fischers test (when appropriate) for categorical variables and Unpaired t test or Non-parametric test analogous to t test was used to compare quantitative variables depending on normality of distribution. Line chart was used for visual representation of the analysed data. Level of significance was set at 0.05.

# RESULTS

## TABLE 1: PATIENT DEMOGRAPHICS IN BOTH GROUPB B AND L:

| Variable | Group B<br>Mean ± SD | Group L<br>Mean ± SD | P Value |
|---|---|---|---|
| Age (years) | 68.9 ± 2.5 | 68.13 ± 1.6 | 0.167 |
| Height (cm) | 169.17 ± 2.8 | 167.93 ± 3.6 | 0.147 |
| Weight (kgs) | 65.5 ± 3.5 | 64.83 ± 3.6 | 0.477 |
| ASA (I:II) | 16:14 | 18:12 | 0.602 |
| Duration of surgery (mins) | 50.5 ± 2.5 | 51.83 ± 2.8 | 0.060 |

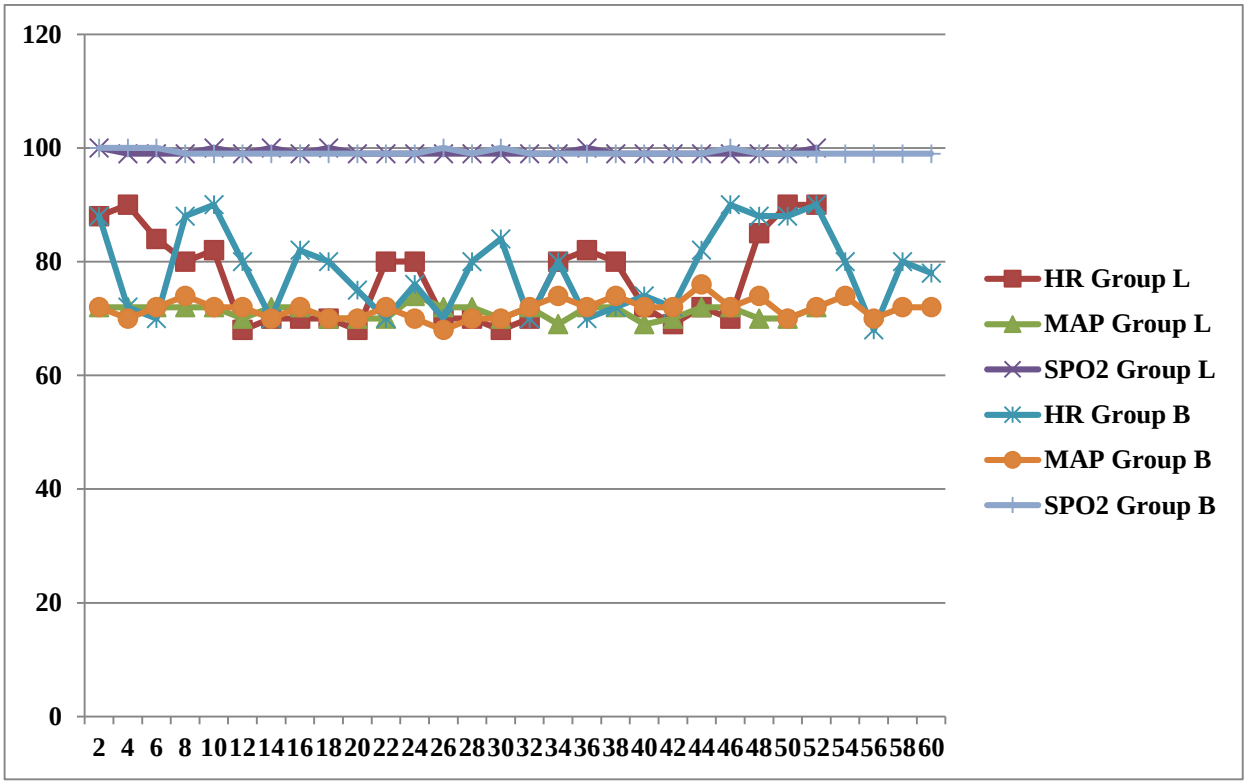
There was no significant difference in the patient demographics of both groups B and L. The duration of surgery and ASA grade distribution also did not differ significantly in both groups. At baseline both groups were comparable in terms of the above parameters (Table 1).

**TABLE 2: HAEMODYNAMIC PARAMETERS DURING SURGERY:**

| Variable | Group B<br>Mean ± SD | Group L<br>Mean ± SD | P Value |
|---|---|---|---|
| Heart rate (beat/min) | 78.5 ± 7.2 | 77.1 ± 7.8 | 0.456 |
| Mean arterial pressure (mmhg) | 71.7 ± 1.7 | 71.2 ± 1.2 | 0.171 |
| SPO2 (%) | 99.2 ± 0.40 | 99.2 ± 0.43 | 0.759 |

The baseline haemodynamic parameter heart rate, Mean arterial pressure and SPO2 did not vary significantly in both groups (P>0.05)

**FIGURE 1: TRENDS OF HAEMODYNAMIC PARAMETER IN GROUP B AND GROUP L:**




The trends in the haemodynamic parameter also did not vary in both groups (figure 1). So both the groups were comparable in terms of haemodynamic parameters.

## TABLE 3: CHARACTERISTICS OF BLOCK IN BOTH GROUPS

## BAND L:

| Variable | Group B Mean ± SD | Group L Mean ± SD | P Value |
|---|---|---|---|
| Time of onset of sensory block (min) | 6.43 ± 7.8 | 7 ± 0.0 | 0.694 |
| Time of onset of motor block (min) | 7 ± 0.525 | 11 ± 0.643 | <0.001 |
| Maximum sensory level achieved (Thoracic dermatome) | 6.9 ± 0.89 | 8 ± 0.40 | <0.001 |
| Time to two segmental regression (min) | 84.3 ± 3.6 | 88.3 ± 1.9 | <0.001 |
| Time to S1 segment regression (min) | 193.8 ± 8.9 | 183.8 ± 3.1 | <0.001 |
| Duration of sensory block (min) | 226.4 ± 4.5 | 227.1 ± 6.2 | 0.673 |
| Duration of motor block (min) | 176.8 ± 5.4 | 150.1 ± 4.9 | <0.001 |

The mean time of onset of sensory block in group L (Mean (SD) - 7±0.0) was half a minute longer than group B (Mean (SD) – 6.4±7.8) but it was not statistically significant (P > 0.05). Hence the mean duration of sensory block in group B (Mean (SD) – 226.4±4.5) was also not statistically different from group L (Mean (SD) – 227.1±6.2).

The mean time of onset of motor block in group L (Mean (SD) - 11±0.64) was 4 minute longer than group B (Mean (SD) - 7±0.52) and was statistically significant (P<0.001). The mean duration of motor block in group L (Mean (SD) - 150±4.9) was 26 minutes less than that of group B (Mean (SD) - 176±5.4) and it was significant (P<0.001).

The mean maximum sensory level achieved in group L was more (Mean (SD) – 8±0.40) than group B (Mean (SD) – 6.9±0.89) and it was statistically significant (P<0.001). Mean time taken to two segment regression was lower in group B (Mean (SD) – 84.3±3.6) than group L (Mean (SD) – 88.3±1.9) and was significant (P<0.001). But mean time taken for S1 segment regression was more for group B (Mean (SD) - 193±8.9) compared to group L (Mean (SD) – 183.8±3.1) and was statistically significant (P<0.001)

**TABLE 4: DISTRIBUTION OF MAXIMUM MODIFIED BROMAGE SCALE ACHIEVED:**

| MBS | Group B | Group L |
|---|---|---|
| 1 | 24 (80%) | 1 (3.3%) |
| 2 | 6 (20%) | 21 (70%) |
| 3 | 0 | 8 (26.7%) |
| **P value** | <0.001 | |

The median MBS in group L is 2 [95% CI (2.1 – 2.3)] and in group B the median MBS is 1 [95% CI (0.4 – 1.60] which was significant difference (p <0.001). The maximum spread of sensory block was T8 in group B and T9 in group L.

**TABLE 5: DISTRIBUTION OF SIDE EFFECTS IN BOTHY GROUPS B AND L:**

| Side effects | Group B Number of patients (%) | Group L Number of patients (%) |
|---|---|---|
| Nausea | 2 (6.7%) | 1 (3.3%) |
| Shivering | 7 (23.3%) | 6 (20%) |
| Pruritis | 0 (0.0%) | 0 (0.0%) |
| Bradycardia | 0 (0.0%) | 0 (0.0%) |
| Hypotension | 0 (0.0%) | 0 (0.0%) |
| Respiratory depression | 0 (0.0%) | 0 (0.0%) |
| **P value** | <0.001 | |

The most common side effect in both groups were shivering which was found in around 20% of the patients. The next common is side effect is nausea . There was no significant difference among the distribution of side effects in both groups. The other threatening complications like bradycardia, hypotension and respiratory depression were not found in any of the parameters. The stable haemodynamic parameters in both groups can be the reason for this.

## DISCUSSION

Geriatric group of population are always challenging for anaesthetist as advancing age, co-morbidities, altered pharmacokinetics and pharmacodynamics properties of drugs increases the morbidity and mortality in these age group of patients[13,14].

Bibulet et al[15] reported that in elderly population intrathecal administration of Bupivacaine was associated with 40% increase in incidence of hypotension compared to young population. There is no ideal anaesthetic technique has been described in elderly population. If a thorough understanding of changes that occurs in physiology and pharmacology is there, an optimal anaesthetic technique can be designed. Spinal anaesthesia is the most commonly used anaesthetic technique for Transurethral Resection of Prostate surgery. Levobupivacaine, the pure S enantiomer of racemic Bupivacaine, is a long-acting local anaesthetic that has been recently introduced in the clinical routine. Levobupivacaine is proving increasingly popular to replace Bupivacaine because of its similar efficacy and fewer cardiovascular and CNS side effects[16]. In our study also we demonstrated that Levobupivacaine provides similar efficacy compared to Bupivacaine administered intrathecally. Its pharmacokinetic properties are similar to those of racemic Bupivacaine. In most of the studies where the same doses of Levobupivacaine and Bupivacaine were

used, sensory and motor block characteristics were found to be similar [17-19]. Various studies suggested that intrathecal hyperbaric Bupivacaine is associated with higher incidence of hypotension and bradycardia intraoperatively.

Rosa Herrera et al[20] studied hemodynamic impact of isobaric Levobupivacaine versus hyperbaric Bupivacaine for subarachnoid anesthesia in patients aged 65 and older undergoing hip surgery and found that Levobupivacaine group had lower incidence of intraoperative hypotension.

Fattorini et al[19] reported that better cardiovascular stability in the Levobupivacaine group compared to Bupivacaine in orthopeadic surgery. Our study didn't found any significant difference in hemodynamic stability. It was possible probably because of dose of local anesthetic (LA) used was too small to produce any significant cardiovascular effect. Addition of fentanyl further helped in reducing the dose of local anaesthetics.

Ben David et al[21] compared Bupivacaine alone and fentanyl added as adjuvant to Bupivacaine and found that Bupivacaine alone is associated with higher incident of hypotension. Our results showed that intrathecal hyperbaric Bupivacaine is associated with early onset of sensory & motor block as compared to isobaric Levobupivacaine. Hyperbaricity of

Bupivacaine may be attributed to it as it helped in early cephalic spread of local anaesthetics. Our results are in line of other studies where both agents were compared intrathecally[22].

D'Souza et al[23] compared intrathecal hyperbaric 0.5% Bupivacaine and isobaric 0.5% Levobupivacaine for lower abdominal surgeries and proved that hyperbaric Bupivacaine produces clinically and statistically significant earlier onset of sensory and motor block as compared to isobaric Levobupivacaine.

Sari et al[24] Erdil et al[25] and Erbay et al[26] found that onset of motor block & progression of block to T4 was significantly fast in Bupivacaine group when compared with Levobupivacaine in spinal anaesthesia. Our study results show that hyperbaric Bupivacaine produces dense motor block for prolonged duration compared to isobaric Levobupivacaine. This result is well supported by various previous studies[26]. The mean Maximum Modified Bromage scale achieved in Group B was significantly higher compared to Levobupivacaine. In bupivacaine group 20 patients had complete block while in Levobupivacaine group only 4 patients had complete motor block.

Acboy et al[27] compared intrathecal administration of Bupivacaine with fentanyl and levobupivacaine with fentanyl and found that

bupivacaine produces higher degree of motor block compared to levobupivacaine.

Gulen Guler et al[28] compared Levobupivacaine and hyperbaric Bupivacaine for cesarean sections in spinal anesthesia and concluded that the combination of Levobupivacaine with fentanyl can be a good alternative in cesarean sections as duration of motor block is short compared to Bupivacaine.

Gautier et al[29] compared the same doses of Levobupivacaine and Bupivacaine during spinal anesthesia for caesarean delivery, and reported that duration of motor block and analgesia was shorter in the levobupivacaine. Addition of opiods further decreases duration of motor block.

Kararmaz et al[30] studied that addition of fentanyl to Levobupivaine significantly shortens duration of motor block. The max sensory level achieved, two segment regression time and regression time to S1 dermatome didn't had significant difference among both group. There was no significant difference regarding adverse reactions.

# CONCLUSION

We concluded from this study that intrathecal administration of low dose 0.5% Levobupivacaine(7.5mg) plus fentanyl in elderly patients undergoing Transurethral Resection of Prostate was as safe as the administraton of low dose hyperbaric Bupivacaine(7.5mg) plus fentanyl. Our result shows that there is no significant differences in hemodynamic stability and maximum sensory level between two groups since we used low dose of bupivacaine. Low-dose bupivacaine and levobupivacaine use in TURP surgeries should be prompted in view of reduced incidence of hemodynamic adverse effects in the geriatric population. Our results, also suggest that intrathecal low-dose of isobaric Levobupivacaine fentanyl provides lesser degree of motor block and for short duration when compared with heavy Bupivacaine. Although onset is delayed with Levobupivacaine, it can be considered as suitable alternative of Bupivacaine early ambulatory surgeries which requires less motor blockage. Various studies proved that, using isobaric levobupivacaine in combination with fentanyl elicits effective sensorial blockade and less motor blockade with stable haemodynamic effects than hyperbaric bupivacaine in combination with fentanyl in various abdominal surgeries and orthopaedic surgeries to achieve a reliable sensory block with earlier ambulation. We have done this research to throw light on effect of low

dose Levobupivacaine especially in elderly patients who is undergoing various surgeries under spinal anaesthesia because of better hemodynamic stability and fewer side-effects.