REVIEW
OF LITERATURE
REVIEW OF LITERATURE

Ophthalmic surgery has been performed since the time of Greeks, Egyptians and Arabs much before the advent of any form of anaesthesia. Lid surgery by cauterization for ectropion and entropion was one of the earliest ophthalmic surgeries. Cataract operations were done by a process known as ‘reclination’, more commonly known as couching.

In the year 1800, Humphrey Davy described the anaesthetic properties of nitrous oxide and suggested its use for surgical procedures. In 1846 Morton successfully demonstrated the use of ether for anaesthetic purposes.

Early Local Anaesthetics:

The early Egyptians are said to have rubbed the powdered skin or fat of crocodile upon the patients skin to produce local anaesthesia, but without much success (Atkinson, 1943).

Cocaine:

Gaedeke in 1855 was the first to discover the alkaloid of coca leaves and called it Erythroxylin. (Atkinson, 1943).

The use of cocaine for ophthalmic purpose was demonstrated in 1884, for the first time by a young Austrian resident in ophthalmology – Carl Koller. Koller prepared aqueous solutions of cocaine and proved its anaesthetic potency in animal and human eyes (Feibel, 1989).

Nerve block and discovery of procaine:

The infiltration of cocaine near or into nerve was reported by Hall and Halsted in 1884 and yet it was not until thirty years after this report that ‘Van Lint’ in 1914 thought of blocking the facial nerve to produce akinesia of orbicularis.

In 1899, the discovery of the chemical composition of cocaine and its atomic groups by ‘Einhorn’ made its synthetic preparation possible. This lead to discovery of procaine by Einhoxin in 1905.

Epinephrine:

In 1901, Tikamine isolated the active salts of the suprarenal gland and named them as epinephrine. The contribution increased greatly the efficacy of local anaesthesia and facilitated operative procedures in which considerable bleeding is encountered (Atkinson, 1943).

The year 1940 saw the start of the next major advance. Working in Stockholm on the structure of the alkaloid gramine, Erdtman – an organic chemist, tasted one of the substances that had been produced as a precursor of gramine. The significance of ensuing numbness was appreciated immediately and the search for a chemically useful derivative was started by Erdtman and continued by Lofgren who synthesized lignocaine in 1943. Lofgren in 1948 laid the foundation of subsequent studies of local anaesthetic drugs.
Ophthalmic Anaesthesia:

In 1884, Herman Knapp of New York was the first one to describe retrobulbar anaesthesia in enucleation surgery (Atkinson, 1943; Feibel, 1989; Friedberg, 1989).

Van Lint in 1914 popularized the use of procaine for facial block but only in 1930’s did the use of procaine for retrobulbar anaesthesia became widespread (Atkinson, 1943).

Atkinson in 1949, in his preliminary report on the use of hyaluronidase with local anaesthesia in ophthalmology reported that with hyaluronidase added to the anaesthetic solution, there is less ballooning of the tissues, due to rapid diffusion, and not as much procaine solution is required to produce the anesthesia.

Atkinson (1943) advocated the use of a 22 gage needle, 3.5 cm long for deeper injections, such as retrobulbar injection within the muscle cone and blocking of the lid.

Retrobulbar anaesthesia, a common form of anaesthesia, has numerous complications associated with it. These include central retinal artery occlusion (Klein et al, 1982), perforation of the globe(Duker et al, 1991), contralateral amaurosis (Friedberg et al, 1986), direct needle injury to posterior ciliary arteries, ophthalmic artery or optic nerve (Ellis, 1974; Edward B. Mclean, 1975).

Davis and Mandel in 1986, introduced the peribulbar anaesthesia which eliminates the serious side effects of retrobulbar block.
Various pharmacological as well as technical advances are still advocated to increase the efficacy, duration, safety and reduce complications of regional ocular anaesthesia.

Ritchie and Greengard (1965) suggested that it is the lipid soluble moiety of the local anaesthetic agent which is more concerned with the penetration of tissue barriers and that the electrically charged cation form is probably the active agent that finally engages at the charged surface of an excitable membrane.

Bromage P.R. et al (1967) demonstrated improved quality of block when carbon dioxide enriched local anaesthetic was injected epidurally, and concluded that this was not due to greater concentration of anaesthetic cation at the nerve axon but due to direct stabilizing effect of carbon dioxide on excitable tissues.

Bromage P.R. et al (1972) sought for the latency and duration of supraclavicular brachial block in 183 patients using carbonated lignocaine and bupivacaine hydrochloride. He found that carbonated lignocaine had the shortest latency and duration. Bupivacaine had longest latency and duration, while mixture of both carbonated lignocaine and bupivacaine hydrochloride produced rapid onset with moderately longer duration.

Gary Strichartz (1976) concluded that local anaesthetics block nerve conduction by preventing the increase in membrane permeability to sodium ions and it is the cationic protonated form that appears to be more active than the neutral form.
Alon, P. Winnie, Cheng – Hin Tay et al (1977) described a new model for the study of pharmacokinetics of local anaesthetics which allows the separate determination of onset and recovery of sensory and motor block in peripheral (mantle) and central (core) bundles within the nerve trunks. In his study he concluded that motor fibres located peripherally blocked first and were last to recover in comparison to sensory fibres situated centrally.

Daniel C. Moore (1981) reported the pH values of the commonly used, commercially prepared local anaesthetic agent with and without epinephrine 1 : 200,000 as well as additives that they contain by the Beckman model 3560 digital pH meter. With the exception of chlorprocaine, all solutions of the local anaesthetic drugs without epinephrine had pH values of 4 or greater and solution with epinephrine had pH values less than 4. In his study he specified that 2% lignocaine without epinephrine has pH of 6.32, while commercially prepared 2% lignocaine with epinephrine has a pH of 3.86.

Hilger M. (1985) in a double blind study compared 0.5% bupivacaine with epinephrine 1:200,000 (pH 3.9) with an alkalinized solution of bupivacaine with epinephrine 1:200,000 (pH 6.4) when used for brachial plexus block. He reported that alkalinization of bupivacaine solution increased the onset and prolonged duration of sensory block.

Radha Sukhani and Alon P. Winnie (1987) experimented in fifty healthy patients undergoing upper extremity surgery by
subclavian perivascular technique. They compared carbonated lignocaine and lignocaine hydrochloride and found that the carbonated lignocaine reduced the latency of anaesthesia by 45% as compared with its hydrochloride salt, producing complete motor block in almost as many as twice patients. The duration of anaesthesia provided by the two agents was virtually identical as was duration of motor block. They concluded this due to the liberation of carbon dioxide from the carbonated solution which diffuses very rapidly across a nerve membrane causing a fall in the intracellular pH, and the production of cationic trap which results in marked increase in the amount of active cation available at the receptor sites on the sodium channels inside the nerve membrane. Furthermore carbon dioxide may also have a direct stabilizing effect on the nerve membranes.

Zahl K. et al (1989) undertook a prospective, double masked, randomized study to see if a pH adjusted mixture of lidocaine, bupivacaine and hyaluronidase had faster and more complete onset of neural blockade, when used for peribulbar anaesthesia. Eighty patients were randomly assigned to four groups and received a peribulbar block with one of four mixture: group 1 (L) = 2% lidocaine, group 2 (LPH) = 2% lidocaine with 0.06 meq/ml sodium bicarbonate, group 3 (LE) = 2% lidocaine with 1 : 100,000 epinephrine (commercially prepared), or group 4 (LEPH) = 2% lidocaine with 1 : 100,000 epinephrine with 0.06 meq / ml sodium bicarbonate. To 5ml of each of the preceding groups, 5ml of 0.75% bupivacaine and 150 units of hyaluronidase was added. After each block, extraocular muscle movement was followed in each quadrant until akinesia developed. In the event of incomplete akinesia, blocks were supplemented at 20
minutes. The LPH group had the fastest onset to complete akinesia (7.0 ± 2.0 minutes, mean ± SEM) when compared with the onset time of all other groups (group 1 = 11.5 ± 1.9 minutes, group 4 = 13.1 ± 1.4 minutes, and group 3 = 16 ± 1.8 minutes, significance greater than 95% by analysis of variance). Further move, when compared with group 3 by analysis of variance, group 4 had a faster onset time. The authors concluded that pH adjustment of solutions of lidocaine / bupivacaine / hyaluronidase, with or without epinephrine improved the onset time of peribulbar anaesthesia.

Scott G. Eccarius et al (1990) conducted a double – masked, randomized clinical trial to determine if subcutaneous eyelid injections of a bicarbonate – buffered lidocaine – epinephrine – hyaluronidase mixture were less painful than unbuffered injections. Twenty-one patients received both buffered (pH = 7.4) and unbuffered (pH = 4.6) injections. After each injection, patients recorded pain on a scale of 0, "no pain," to 10, "severe pain". Mean pain score for buffered injection was 2.0 versus 4.1 for unbuffered injections (P = 0.0003). Seventeen (81%) of 21 patients ranked the buffered injection less painful. They concluded that use of a buffered (pH = 7.4) mixture is effective in making ophthalmic anaesthesia less painful.

Lewis P. et al (1992) carried out a random comparison of plain with pH – adjusted bupivacaine with hyaluronidase for peribulbar block. 50 patients scheduled for cataract surgery received either plain (pH 5.4) or pH – adjusted (pH 6.8 range 6.7 – 6.9) 0.75% bupivacaine. Hyaluronidase was added to both solutions prior to peribulbar block. The time of onset of akinesia of the globe and the need for supplementary injections were recorded by an independent observer.
Patients who returned for surgery to the second eye received the alternative local anaesthetic solution for the second peribulbar block. The relative efficacy for the different anaesthetic solutions was compared in patients who underwent unilateral surgery (Group A, n = 50). In 12 patients (Group B) who underwent bilateral surgery, direct comparisons between eyes in the same patient were possible.

In both groups of patients, eyes receiving peribulbar block with the pH – adjusted solution showed a shorter time to partial akinesia of the globe (P < 0.05) (Group A : 5.7 ± 1.76 minutes for 23 patients who received pH – adjusted solution against 6.9 ± 1.98 minutes for 24 patients who received plain bupivacaïne solution). However, there was no difference between the solutions in the time to complete akinesia of the globe (Group A : 10.7 ± 4.8 min for 17 patients who received plain bupivacaïne solution against 8.5 ± 2.7 minutes for 18 patients who received pH – adjusted solution), but the number of supplementary injections required for an effective block with pH – adjusted solution was increased (9 out of 26 in the plain versus 13 out 24 in the pH – adjusted solution). Onset time to akinesia of the lateral and superior rectus muscles was shortened in patients receiving the pH – adjusted solution but there was minimal effects on the medial and inferior recti.

Roberts JE, Macleod BA and Holands RH (1993) carried out a double blind study to determine the effect of pH and the addition of hyaluronidase to a mixture of lignocaine and bupivacaïne on the efficacy of peribulbar anaesthesia. One hundred patients were assigned to one of five groups. All group received a solution of two parts bupivacaïne (0.75%) and one part lidocaine (2%) (with 1: 100,000 adrenaline) as the base components of their anaesthesia. Group 1 received only the bupivacaïne – lidocaine mixture, pH 3.9. Group 2 received a solution supplemented with
hyaluronidase (ten units. ml\(^{-1}\)) pH of 5.1. Group 3 received the bupivacaine – lidocaine mixture alkalinized with sodium bicarbonate to a pH of 5.1, the same as solution 2. Group 4 received the mixture with hyaluronidase alkalinized to pH of 6.7. Group 5 received the bupivacaine-lidocaine mixture alkalinized to a pH of 6.7. Efficacy of each block was graded according to the degree of residual movement 30 minutes following injection as described by House et al. The solution containing hyaluronidase and pH adjusted to 6.7 was found to be the most effective (P < 0.025) (2 out of 20 failed blocks against 9 out of 20 in Group 3 and 11 out 20 in Group 1, 2 and 5.). No differences were found in the incidence of failed blocks among the other groups. Similarly, group 4 had a lower mean motor score (P < 0.05) than the other groups, but no difference existed among the other groups. Thus presence of hyaluronidase without alkalinization did not improve the efficacy and similarly, alkalinization in the absence of hyaluronidase was ineffective.

Martin Zehetmayer, et al (1997) compared the efficacy of a sodium-bicarbonate adjusted preparation of lidocaine 4% (pH = 7.2) and standard lidocaine (pH = 5.2) for topical anaesthesia in clear corneal cataract surgery. They included 44 eyes of 34 patients in this study. In 22 eyes, pH – adjusted lidocaine 4% was administered; in the other 22, standard lidocaine 4%. Aqueous and serum concentrations of lidocaine were measured by high – performance liquid chromatography and ultraviolet detection. Subjective pain was assessed using a visual analog scale of no pain (0%) to worst imaginable pain (100%). On the first postoperative day, visual acuity, IOP and corneal staining with fluorescein were examined. In the pH – adjusted lidocaine group, significantly higher lidocaine concentrations were found in the aqueous humor (15.06µg/ml ± 8.2 versus 4.75 ±
3.5μg/ml; P < 0.0001). In all samples (n = 8), serum lidocaine concentration were below a minimum detectable level of 0.02μg/ml. Subjective pain ratings were similar in the pH- adjusted and standard lidocaine groups (mean 9.73 ± 10.4% and 10.0 ± 15.4% respectively).

In their study, they concluded that pH – adjusted lidocaine 4% was a safe, effective topical anaesthetic for clear corneal surgery and has minimal local and systemic toxicity. Admininistration of pH adjusted lidocaine 4% resulted in significantly higher aqueous humor lidocaine concentration than administration of standard lidocaine 4%.

Mack YH Chow, Alex TH Sia, CK Koay and YW Chan (1998) assessed the onset of sensory and motor block as well as the distribution of sensory block after axillary brachial plexus block. 1.5% lignocaine hydrochloride containing adrenaline (1:200,000) with and without sodium bicarbonate was given in 38 patients and they found that alkalinization of lignocaine did not offer a significant clinical advantage in axillary brachial plexus block.

Ririe DG, Walker FO, James RL, and Butterworth J (2000) performed median nerve blocks in 10 volunteers in a randomized, double blind cross over study to compare the effects of 1% plain lignocaine with 1% lignocaine mixed with sodium bicarbonate 0.1 mmol/liter. Sensations of hot, cold, pin prick, light touch and motor sensations were assessed at two minute intervals. pH was 6.4 ± 0.1 for plain lignocaine and 7.7 ± 0.2 for alkalinized lignocaine. The final data suggested that addition of bicarbonate to lignocaine for median
nerve block significantly increased the rate of motor block without changing the onset or extent of sensory block.

**Aim Of Local Anaesthesia In Ophthalmic Surgery**

The aim of anaesthesia in ophthalmology is to provide pain relief, akinesia and hypotony, aside from considerations of morbidity and mortality.

The eye should be motionless during surgery to prevent inadvertent rise of intraocular pressure and to provide stability to the surgeon. Any procedure should not be painful for the patient as this will result in sudden movement of his head, disrupting the surgeons stability and concentration.

The feeling of pressure by various manipulations on the eye is unavoidable and this should be explained to the patient.

Any movement of the eyelids should not be present as squeezing of the lids will result in rise of IOP.

Most important is to maintain an IOP at or below normal levels for safe surgery; achieved by applying pressure on the eyeball by one of the various available methods.

The field of surgery should be bloodless. This is achieved by addition of adrenaline.
The patient should be comfortable at all times, preoperatively, during surgery and postoperatively.

**THE IDEAL LOCAL ANAESTHETIC**

The criteria for an ideal local anaesthetic are: It should be –

- Non – irritating
- Non – pain producing
- No – neurotoxicity
- No toxicity to any of the peripheral organs of the body
- Dissoluble in a sterile and soluble solution.

In this regard the present amide local anaesthetic come close in ophthalmology because of the smaller amounts of local anaesthetic required to render the operative field pain-free and immobile. No clinically useful commercial concentrations of local anaesthetics have been found that produce painless injection. Therefore, the use of a painless dilute solution of local anaesthetic is required to anaesthetize the patient without producing pain; pH adjustment and slow injection alleviate much pain.

**PHARMACOLOGY OF LOCAL ANAESTHETIC DRUGS**

A local anaesthetic is a drug which reversibly blocks the transmission of peripheral nerve impulses. The agents conform to a common structural arrangement consisting of a benzene ring attached to an amine group by an intermediate chain, which includes either an ester or an amide linkage.
Aromatic Group  Intermediate Chain  Amine Group

**Mechanism of Action**

During the resting phase the interior of a peripheral nerve axon has a potential difference of about $-70$ mv relative to the outside. The resting potential exists because there are more anions than cations within the cell. In the present context the most important ions are sodium and potassium. The high extracellular sodium concentration is maintained because at rest the membrane is impermeable to sodium. However it is freely permeable to potassium ions, which diffuse out of the cell until the negative intracellular electrochemical potential created by their loss balances the concentration gradient.

Depolarization of the fibre is the result of a sudden increase in membrane permeability to sodium. Nerve stimulation causes changes in the configuration of large protein molecules present in the cell membrane resulting in “channels” in these proteins to open and it is through these channels that sodium ions enter the axoplasm. Entry of the positively charged sodium ions raises the membrane potential to about $+20$ mv, at this point the electrochemical and concentration gradients for sodium balances one another and the channels close. Both concentration and electrochemical gradients then favour movement of potassium out through the membrane until the resting potential is restored. The impulse generated is transmitted along the axon because a local current flows between the depolarized segment of nerve and the next segment. The voltage change associated with
this current opens the sodium channels in the next section, so that the action potential is propagated along the nerve.

Local anaesthetic drugs prevent the development of the action potential in a nerve by preventing sodium ion movement through the sodium channels.

It is the lipid soluble un-dissolved base form of the drug that penetrates the neuronal membrane to reach the interior of the axoplasm. But the blockade of conduction is produced by the water-soluble dissociated cationic form. The degree of dissociation is dependent on the drug’s dissociation constant (pKa). This is the pH at which the drug is present in half undissociated and half dissociated form. The pKa of commonly used local anaesthetics is between 7.6 and 8.9. Most commercial preparations of local anaesthetics are quite acidic to improve stability of the drug and thus prolong its shelf life. At this range of pH less drug is available in the undissociated base form, which is required for transfer of the drug across the perineural sheath and neural membrane. After penetration, the drug re-equilibrate in the axoplasm of the nerve with the charged cationic form. Cationic form of the drug then enters the sodium channel from the intracellular side of the nerve membrane and binds to an anionic site within the sodium channel producing conformational changes in the channel structure. The physical presence of ions and the conformational change in the channel structure block sodium ion movement and prevent depolarization. Agents influencing the degree
of dissociation should therefore have an effect on the onset and degree of neural blockade.

**CARBONATED LOCAL ANAESTHETIC SALTS**

It has been known for a long time that the hydrogen ion concentration is an important factor in the uptake of local analgesic agents. Begnon in 1892 mentioned cocaine with alkali added, and in 1910 Gross suggested how alkalinized solutions worked. The theory of carbonated local analgesics has been aptly put forward by Bromage in 1965.

The theory behind the idea of alkalinizing lignocaine is that like most local anaesthetics, lignocaine is a weak base with a pKa of 7.9. Despite being a weak base it is commercially available as an acidic solution. This is done to increase its stability and shelf-life. The acidic solution has more drug in the ionized form. When used in nerve block, the anaesthetic solution has to cross the perineural sheath and nerve membrane. The non-ionized or the base form of the local anaesthetic is permeable to these structures, thereby the alkalinized solution has a faster onset of action.

Dissociation of lignocaine (pKa = 7.9)

<table>
<thead>
<tr>
<th>pH</th>
<th>Non-ionized (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.45</td>
<td>&lt; 5%</td>
</tr>
<tr>
<td>6.5</td>
<td>≈ 10%</td>
</tr>
<tr>
<td>7.4</td>
<td>≈ 24%</td>
</tr>
</tbody>
</table>
A solution with a pH more close to the pKa of the drug contains more drug in the non-ionized permeable form, hence a faster onset time.

**Lignocaine Hydrochloride With Adrenaline**

To prevent oxidation of adrenaline most commercially available local anaesthetic solutions containing adrenaline are supplied at a lower pH than their counterparts without adrenaline. In our study, the premixed lignocaine adrenaline solution used was supplied at a mean pH of approximately 3.45. Adrenaline counteracts the vasodilating effects of local anaesthetics and prolongs postoperative analgesia with lignocaine.

**HYALURONIDASE**

The discovery of hyaluronidase dates back to 1949 when Atkinson reported that larger injections of local anaesthetic for cataract surgery were feasible with hyaluronidase.

Hyaluronidase is an enzyme which depolymerizes the mucopolysaccharide hyaluronic acid, a component of the mucoprotein ground substance or tissue cement of the tissue spaces. It decreases the viscosity of the intercellular ground substance and helps quick dispersion of fluids infused subcutaneously. The depolymerizing effect is of short duration and reversible.

It is prepared from the testes and semen of mammals and purified so as to remove most of the inert material, sterilized and freeze dried.
Hyaluronidase is packed as a phosphate buffer and has maximal activity in the pH range 6.4 – 7.2; thus success increases with alkalinized lignocaine hyaluronidase mixture. Hyaluronidase also maintains anaesthetic solubility during alkalinization.

Due to its high activity and absence of untoward effects the quantity of hyaluronidase used is not critical. Usually 1 vial i.e. 1500 International Units (I.U.) is added to a 30 ml vial of lignocaine.

Hyaluronidase is virtually a non-toxic preparation. Allergy to hyaluronidase has been reported, but the report occurred many years ago when the process of purification was not at its current level.

**CLASSIFICATION OF LOCAL ANAESTHETIC AGENT:**

**ESTERS**
- Cocaine
- Benzocaine
- Procaine
- Amethocaine
- Chloroprocaine

**AMIDES**
- Cinchocaine
- Lignocaine
- Mepivacaine
- Prilocaine
- Bupivacaine
- Etidocaine
- Ropivacaine

**LIGNOCAINEx**

Lignocaine was synthesized in 1943 by Lafgren and Landquist and was first introduced in the clinical practice by Gورد in 1948. It is now one of the most widely used local anaesthetic agent. Its chemical name is Diethylamino – 2, 6 – aceto – xylidine.

It belongs to the Anilide group of amide local anaesthetics.
Structure of Lignocaine

Physiochemical Properties:

Lignocaine hydrochloride is an odourless, white crystalline powder. Its partition co-efficient is 2.9, pKa is 7.9, molecular weight 234 and protein binding 64%.

Solubility:

It is freely soluble in water.

Stability:

Very stable, the stability of lignocaine is absolute within a wide range of temperature and pH.

Sterilization:

Vials containing lignocaine solution can be sterilized by boiling or autoclaving. Lignocaine crystals can be autoclaved for 6 hours or subjected to multiple autoclaving without loss of potency.

Absorption, Metabolism and Excretion:

Lignocaine is absorbed rapidly from the gastrointestinal and respiratory tracts even after parenteral administration.
Although it is effective when used without any vasoconstrictor, in the presence of epinephrine the rate of absorption and toxicity is decreased, and the duration of action is usually prolonged.

The highest concentration of the drug is found in kidney after systemic absorption. Appreciable levels are found in lungs, spleen, heart and brain, low levels are found in the liver.

It has a high affinity for the fatty tissues. It has a half life of 1.6 hours. Most of the drug is metabolized by biotransformation into free and conjugated phenol. The ring structure is hydroxylated. It is metabolized in the liver by the enzyme oxidase to monoethylglycine and xylidine. The latter compound retains significant local anaesthetic and toxic activity. In man about 75% xylidide is excreted in the urine as 4 - hydroxy 2 - 6 diethyl aniline and less than 3% is excreted unchanged in urine.

**Anaesthetic Properties:**

Lignocaine is useful for ophthalmic blocks. It is effective topically when instilled into the conjunctival sac. Lignocaine is commonly made up with adrenaline in an attempt to delay the rate of absorption from the site of injection by producing local vasoconstriction. Lignocaine 2% is commonly used for ophthalmic blocks.

Lignocaine has a fast onset, but short duration. Three ml of a 1% concentration placed 5 to 7 mm behind the hind surface of the globe at the opening of the muscle cone will usually provide dilatation
of the pupil indicating block of the ciliary nerves within 10 or 15 seconds. Onset of corneal anaesthesia occurs within a minute, and a minor effect on motor activity of the extraocular muscles in 90% of patients, but a significant motor block in 10%; 1% lignocaine will last from 20 minutes to an hour.

2% lignocaine will block the ciliary ganglion in approximately the same period of time and provide complete block of the extraocular muscles in 5 to 10 minutes in 75% of patients and will last for 45 minutes to 2 hours; 4% lignocaine will produce complete akinesia in 5 minutes in 75% and in 90% by 10 minutes but produce little or so akinesia in the remaining 10% of patients and will last from 1 to 3 hours.

Duration is quite variable with lignocaine. It is not uncommon for 4% to wear off in 30 to 45 minutes in persons with high levels of anxiety; this effect is probably due to blood flow or some other phenomenon, as yet incompletely understood in anxious people.

Local anaesthesia tend to wear off much more rapidly in people who use excessive alcohol, nicotine and barbiturates. Epinephrine is essential to adequate blocks in such people. Epinephrine extends the analgesia and akinesia time of lignocaine hereby providing a much more pleasant post-operative course.

**Dosages:**

Basically it should be remembered that smallest dose producing desired result should be given. Dosage for debilitated and aged
patients should be appropriately reduced. The suggested maximum
dose of lignocaine with adrenaline is 7mg/kg body weight and without
adrenaline is 3 mg/kg body weight.

**Systemic Effects:**

a) **Effect on central nervous system**: Lignocaine causes initial
sleepiness in many patients. It has also been used as an
anticonvulsant in the treatment of status epilepticus.

b) **Effect on the cardiovascular System**: Lignocaine is a useful
drug in the treatment of cardiac dysrhythmias. It stabilizes
membrane of damaged and excitable cells tending to suppress
ectopic foci. In therapeutic doses it causes no consistent change
in the heart rate and does not depress conduction in purkinje

There is usually no myocardial depression, instead
improvement in the cardiac output and blood pressure has been
observed when used in cardiac dysrhythmias (Harrison DC et
al, 1963). The greatest value of lignocaine is in the acute
treatment of ventricular dysrhythmias after myocardial
infarction or cardiac surgery.

c) **Neuromuscular function and ganglionic synapse**: Local
anaesthetics also affect transmission at the neuromuscular
junction. Similar effect occurs at autonomic ganglia. These
effects are due to the block of the ion channel of acetylcholine receptors. (Neher and Steinbach 1978).

LOCAL ANAESTHETIC TOXICITY

Toxic reactions are generally caused by –
1. Relative overdose
2. Accidental intravascular injection leading to high plasma concentration.
3. Susceptibility of the individuals.
4. Various predisposing factors like liver disease, extremes of ages, pyrexia, shock, renal disease.

SYSTEMIC TOXICITY

Local anaesthetic toxicity is a function of plasma free drug concentration and is influenced by the drug, the dose and the injection site. The spectrum of toxicity extends from mild and non-threatening to cardio-respiratory collapse and death.

The early symptoms of toxicity are numbness of the tongue and circumoral region. Light headedness and tinnitus are encountered most frequently in patients on IV antiarrhythmic therapy. They appear at plasma lignocaine concentration of about 5 μg/ml. Further progression of toxic manifestations beyond mild central nervous system symptoms, like drowsiness, visual disturbances and muscular twitching occur at lignocaine concentration of 5 – 10 μg/ml. Above 10 μg/ml convulsions, coma and respiratory arrest are likely.
Profound CNS effect can occur with rapid injection of local anaesthetic into the head or neck because of retrograde flow into the brain from either arteries or veins. This bizarre, potentially lethal complication can only be prevented by slow injection.

**Prevention and Management of Systemic Toxicity:**

Prevention of local anaesthetic toxicity is a matter of minimizing blood concentration. Reducing blood concentration can be accomplished by slow injection, slow pick-up of anaesthetic from the tissue in which it has been deposited, and avoiding intravascular injection of the local anaesthetic drug.

High injection rate in an orbital vein can cause retrograde flow back into the brain with onset of convulsions, even though the concentration measured in the venous blood may be inconsequential. The actual concentration in the brain will be the major determinant.

Local anaesthetic injected in the sheath of the optic nerve can move subdurally or in the subarachnoid space along the optic chiasm into the subarachnoid space of the other eye or into the midbrain causing apnea, sympathetic blockade, or vagal blockade with varying cardiovascular effects. Brainstem anaesthesia is thus induced. However, this is not the only route by which brainstem anaesthesia can happen. Transfer across the intact dura, and hydraulic dissection along the dural cleavage zone of the attachment of the dura to the skull at the orbital apex are other mechanisms. Zahl has reported the latter for peribulbar anaesthesia.
ALLERGY

The treatment of acute allergic response is a major emergency. It is fortunate that allergy to the amide local anaesthetics is an extremely rare event.

Many so-called allergic reactions to these drugs are reactions to their additives and preservatives and not to the local anaesthetics—methylparaben, a preservative, and sodium metabisulphite, an antioxidant, are the most common offender.

Reaction to ester drugs are more common.

APPLIED ANATOMY OF THE ORBIT

The orbit is a four-sided pyramid with its base pointing anteriorly and its apex posteromedially. The medial walls of the right and left orbits are parallel to each other. The mean distance from the inferior orbital margin to the apex is 55 mm. This has important implications when injections are made into the orbit. The deeper the injections, the narrower is the space, and the greater the chance of causing damage to the structures within. The inferotemporal quadrant is relatively avascular and is probably the safest approach for orbital injections.
**Fig. 1** The right superior orbital fissure  
* (Batterbury & Bowling - 1999)*

**Fig. 2** The nerves and muscles of the orbit  
* (Batterbury & Bowling - 1999)*
Squeezing and closing of the eyelids are controlled by the zygomatic branch of the facial nerve (VII), which supplies the motor innervation to the orbicularis oculi muscle. This nerve emerges from the foramen spinosum at the base of the skull, anterior to the mastoid and behind the earlobe. It passes through the parotid gland before crossing the condyle of the mandible, then passes superficial to the zygoma and malar bone before its terminal fibres ramify to supply the deep surface of the orbicularis oculi. The facial nerve also supplies secretomotor parasympathetic fibres to the lacrimal glands, and glands of the nasal and palatine mucosa.

Movement of the globe is controlled by the six extraocular muscles. The motor nerves which control these muscles emerge from the skull through the superior orbital fissure. The common tendinous ring forms the fibrous origin of the four rectus muscles at the apex of the orbital cone. The trochlear nerve (IV) emerges through the superior orbital fissure outside the common tendinous ring and supplies the superior oblique muscle. All the other motor nerves to the extraocular muscles pass inside the common tendinous ring and are situated inside the cone. The ophthalmic division of the oculomotor nerve (III) divides into superior and inferior branches before emerging from the superior orbital fissure. The superior branch supplies the superior rectus and the levator palpebrae superioris muscles. The inferior branch divides into three to supply the medial rectus, the inferior rectus and the inferior oblique muscles. The abducent nerve (VI) emerges from the superior orbital fissure beneath
the inferior branch of the oculomotor nerve to supply the lateral rectus muscle (Figure 1).

Sensation to the eyeball is supplied through the ophthalmic division of the trigeminal nerve (V). Just before entering the orbit, it divides into three branches: lacrimal, frontal and nasociliary. The nasociliary nerve is sensory to the entire eyeball. It emerges through the superior orbital fissure between the superior and inferior branches of the oculomotor nerve and passes through the common tendinous ring. Two long ciliary nerve give branches to the ciliary ganglion and, with the short ciliary nerves, transmit sensation from the cornea, iris and ciliary muscle. Some sensation from the lateral conjunctiva is transmitted through the lacrimal nerve and from the upper palpebral conjunctiva via the frontal nerve. Both nerve are outside the cone (Figure 2).

The cone is the area between the four rectus muscles and the posterior surface of the globe. The muscles arise from a fibrous ring which bridges over the superior orbital fissure. Through this common tendinous ring pass the optic nerve, the ophthalmic artery, the two divisions of the oculomotor nerve, the nasociliary nerve and the abducent nerve. The superior and inferior ophthalmic veins may also pass through the ring. Tenon's capsule or bulbar fascia is a thin membrane that envelops the eyeball from the optic nerve to the sclerocorneal junction, separating it from the orbital fat and forming a socket in which it moves. The sheaths of the rectus muscles interconnect in the perimysium in a complex and variable manner and form the walls of the cone.
ANAESTHESIA TECHNIQUES FOR INTRAOCULAR SURGERY

Ophthalmic regional anaesthesia should provide conditions appropriate for the surgeon's needs and planned surgery.

Topical anaesthesia with 1% tetracaine, 0.4% oxybuprocaine eyedrops or other topical anaesthetic may be used for minor surgery to the conjunctiva if akinesia of the globe is not necessary.

Many different techniques and ingredients may be used to achieve the aims of akinesia, analgesia and a soft eyeball.

Three different methods are practiced:

- Extraconal (peribulbar)
- Intracanal (retrobulbar)
- Sub-Tenon's anaesthesia

![Diagram](Fig 3: Techniques for ocular anaesthesia: P = Peribulbar, R = Retrobulbar)

Intracanal anaesthesia places the injectate in the fatty compartment which surrounds the nerve to be blocked, whereas extraconal techniques rely on variable diffusion across connective tissue septa (Fig 3). Extraconal techniques were introduced more
recently in the expectation that the incidence of complications would be reduced. Sub-Tenon's injections involve a minor surgical procedure, and although avoiding some of the complication of the two other techniques, have their own problems.

All orbital blocks should be performed with the patient looking straight ahead in the primary gaze position. This ensures that the optic nerve is slack and out of the direct line of approaching needles.

The gauge of the needle should be the finest that can be used comfortably. In practice, this would be a 24 or 27 gauge needle, as finer needles are difficult to manipulate and larger needles may cause more pain and damage. Sharp needles are used because blunt needles are painful to insert and cause vasovagal syncope.

Following orbital injection, gentle digital pressure and massage help to dispense the anaesthetic agent and reduce IOP.

**Extraconal (Peribulbar) Anaesthesia:**

The techniques rely on the placement of relatively large volumes and high concentrations of local anaesthetic outside the cone. The anaesthetic mixture takes time to diffuse through the connective tissue layers of the cone. Spread of the anaesthetic superficially ensures that the terminal fibres of the facial nerve are blocked as they enter the orbicularis oculi. Most peribulbar methods require two initial injections. The volume injected depends on the shape of the orbit. The infertemporal injection should be made to a depth of no more than 30 mm from the infraorbital margin. The safest sites for
injection are in the inferotemporal quadrant and just medially to the medial canthus. The supersonal quadrant should be avoided, as injection at this site may damage the trochlear apparatus or cause haemorrhage.

COMPLICATIONS OF LOCAL ANAESTHESIA

Haemorrhage

This is a serious complication of both intraconal and extracanal injection with a frequency between 0.1 and 3%. Haemorrhage may be either arterial or venous in origin and may be concealed or revealed. Extravasation of blood into the periorbital tissues increased the tissue volume and pressure. This is transmitted to the globe, raising the intraocular tension and creating difficult and dangerous conditions for intraocular surgery.

Prevention of Haemorrhage

Patients with hypertension are more likely to bleed and optimal control of arterial pressure should be achieved before surgery is attempted. The fewer injections that are made into the orbit, the less is the chance of damaging a blood vessel. Cutting and slicing movements at the needle tip should be avoided. Fine needles are less traumatic than thicker ones. Deep intraorbital injections are more likely to cause haemorrhage than are shallow injections. The inferotemporal quadrant has fewer blood vessels and is less hazardous. The addition of epinephrine to the injectate may reduce the incidence of haemorrhage. It is advisable to apply firm digital pressure to the
orbit as soon as the needle is withdrawn after an intraorbital injection, as this reduces any tendency to ooze.

**Central Spread:**

**Mechanism**

The cerebral dura mater provides a tubular sheath for the optic nerve as it passes through the optic foramen. This sheath fuses to the epineurium of the optic nerve and is continuous with the sclera, providing a potential conduit for local anaesthetic to pass subdurally to the brain. Central spread occurs if the needle tip has perforated the optic nerve sheath and injection is made. Even a tiny volume injected under the optic nerve sheath may pass to the central nervous system and/or cross the optic chiasma to the opposite eye and may cause life threatening sequelae. The time of onset of symptoms is variable, but any major sequelae develop usually in the first 15 minutes after the injection. It is therefore advisable that the patients face is not covered up on the operating table for at least this interval after the block has been inserted.

**Signs and Symptoms of Central Spread:**

The symptomatology of central spread is varied and depends upon which part of the central nervous system is affected by the local anaesthetic. As a result of the anatomical proximity of the optic nerve to the midbrain it is usual for this area to be involved. A range of different signs and symptoms has been described, involving the cardiovascular and respiratory systems, temperature regulation,
vomiting, temporary hemiplegia, aphasia and generalized convulsions. Palsy of the contralateral oculomotor and trochlear nerves with amaurosis is pathognomonic of CNS spread and should be sought in any patient whose response to questions following block are not as crisp as they were beforehand.

**Treatment of Central Spread:**

The treatment is symptomatic throughout the duration of effect of the local anaesthetic drug. With longer acting local anaesthetic agents, treatment must be required for 60 – 90 minutes. The patient must be monitored intensively.

**Prevention of Central Spread:**

Intraconal or extraconal injections should always be made with the patient looking strength ahead in the primary gaze position. The optic nerve is then slack and out of the way of the advancing needle. If the needle encounters the optic nerve in this position, it is unlikely to damage or perforate its sheath, as slackness in the structure allows the nerve to be pushed aside. If the eyeball is directed away from the primary gaze position in any other extreme direction, the optic nerve is stretched; the nerve cannot be easily pushed aside.

**Puncture of the eyeball**

Global puncture is a serious complication of local anaesthesia for eye surgery. It has been reported following both intraconal and extraconal injections.
Puncture of the eyeball is most likely to occur in patients with high myopia, previous retinal banding, posterior staphyloma or a deep sunken eye with a narrow orbit.

Global puncture is often a double puncture of the posterior segment of the eyeball. Puncture is usually recognized at the time of surgery and presents as an exceptionally soft eye. Timely management of posterior segment injury is a must because the needle track through the vitreous will eventually form a band of scar tissue. If this is not excised, it contracts and detaches the retina, sometimes causing sudden total blindness in the affected eye.

**Optic Nerve Damage:**

Fortunately, this is a rare complication which results from obstruction of the central retinal artery. This artery is the first and smallest branch of the ophthalmic artery, arising from the vessel as it lies below the optic nerve. It runs for a short distance within the dural sheath of the optic nerve and about 35mm from the orbital margin, pierces the nerve and runs forward in the centre of the nerve to the retina. Damage to the artery may cause bleeding into the confined space of the optic nerve sheath, compressing and obstructing blood flow. If the complication is recognized soon enough, it maybe possible to perform surgical decompression of the optic nerve.

**Myopathy of the Extraocular Muscles:**

The inadvertent injection of a long acting local anaesthetic into any extraocular muscle body may result in prolonged weakness of the
muscle. An injection site some distance away from these muscles should be selected.

**Vasovagal Syncope:**

This is more likely to occur in young and anxious patients when eye blocks are administered. Painful injection with a blunt Atkinson needle may cause this response. It is important that a vein is cannulated before any block is given. Treatment is symptomatic and should include administration of oxygen, intravenous injection of an anticholinergic agent and appropriate positioning. Differentiation from central spread should be made by testing vision and extraocular movements in the opposite eye.