

REQUIREMENTS OF AN IDEAL LOCAL ANESTHETIC

The ideal local anaesthetic would possess many desirable properties. It should produce available paralysis of the sensory nerves but not of other tissues

1. The agent should have non-addictive properties.
2. It should be readily soluble and stable in water.
3. The local anaesthetic should possess a pH neutrality and be nonirritating to the tissues.
4. It should possess a minimum of systemic local, toxicity, as evidenced by absence of tissue damage at the injection site
5. The local anesthetic should be absorbed slowly to minimize danger of systemic, toxicity and to prolong the effect at the site of injection.
6. After systemic absorption the compound should be readily and promptly detoxified.
7. It should be compatible with adrenaline so that it anaesthetic vasoconstrictor
8. There should be no hyperaesthesia following the recovery of sensation by the tissues.
9. The local anaesthetic should withstand heat sterilization and be relatively inexpensive.

Mechanism of Action:

Local anaesthetics are generally water soluble acid salts. When these salts are injected into the slightly alkaline body tissues they appear to hydrolyze slowly releasing the alkaloidal base, which then acts upon the nerve tissue.

Generally, local anaesthetics prevent the generation and conduction of nerve pulses. Their site of action is the cell membrane and the block they produce is the result of interference with changes in membrane permeability to potassium and sodium ions and possibly calcium ions. These permeability changes are responsible for the rising and falling phases of the action potential and they follow depolarization of the membrane. In the presence of a local anaesthetic, the electrical excitability of the tissue gradually decreases until eventually, complete block ensues.

How local anaesthetics affect the transient changes in ion permeability as unknown but the potency of these compounds is matched by their ability to increase the surface pressure of monomolecular lipid films. It has been suggested that the anaesthetic “squeezes” the lipid molecules closer together. In the lipid membrane layers of nerves this could have the effect of

closing membrane “pores” so reducing ionic permeability. This would have the effect of stabilizing the membrane and reducing its excitability.

Pharmacological Actions

In addition to their action in blocking conduction in nervous tissue, the local anaesthetics interfere with the function of all organs in which the transmission of electrical impulses occurs. The most important effects are on the CNS and heart.

Central Nervous system – Most local anaesthetics stimulate the CNS and overdose may lead to tremors, restlessness, and convulsions. Central depression may occur later and death may result from respiratory depression. The stimulant action may be the result of a block in vulnerable central inhibitory pathways. Although all local anaesthetics cause stimulation, cocaine is unique in having a powerful effect on the central cortex and it may be this which makes cocaine addictive, synthetic local anaesthetics have less stimulant action on higher centres and do not cause addiction.

Cardiovascular system – If given systemically, local anaesthetics have quinidine-like action on the myocardium and reduce its excitability and force of contraction: they also prolong the refractory period and slow conduction. These effects cannot easily be taken advantage of because the drugs are rapidly destroyed and their CNS effects usually predominate. All local anaesthetics except lignocaine and cocaine produce vasodilatation by a direct action on the arterioles.

Fate and Metabolism of local anesthetics

All local anesthetics are broken down in the liver to non-toxic products and procaine is also inactivated in the plasma by circulating cholinesterase. Local anaesthetics can be divided into two general groups: those detoxified rapidly (e.g. procaine) and those detoxified slowly (e.g. cocaine). From a practical stand point, the toxicity of a local anaesthetics determined by the ratio between the rate of absorption and the rate of destruction.

Chemistry of local Anaesthetics

The very large numbers of local anaesthetics available have many actions in common and their chemical structural show many similarities. The very large numbers of local anaesthetics available have many actions in common and their chemical structural show many similarities. The very large number of local anaesthetics available has many actions in common and their

chemical structural show many similarities. They are all water soluble salts of lipid-soluble alkaloids and consist basically of three parts, an amino group, a connecting group with which an ester or amide, and an amino alcohol residue in which the amino group may be substituted by alkyl groups or form part of an alicyclic ring. Alterations in all three parts of the molecule give compounds of varying potency and toxicity. Local anaesthetics may be divided into three main groups

1. Cocaine, a naturally occurring alkaloid and the first local anaesthetics to be used.
2. Para-aminobenzoic acid derivatives/(procaine, amethocaine etc)
3. Agents including lignocaine, cinchocaine, benzocaine many of which chemically resemble the AARA drugs.

The Administration of Local Anaesthetics

Local anaesthetics may be administered in a number of ways:

1. As a cream, ointment, spray, solution or powder to mucous membranes or to damaged skin around wounds.
2. By infiltration. The drugs may be injected locally into subcutaneous tissue to block sensation for the performance of minor superficial surgery.
3. By injection into the subarachnoid space of the spinal cord to produce block of motor and sensory roots and autonomic fibres. This is known as spinal anaesthesia and will block the sensation of pain from the regions of body innervated by the affected segments of the spinal cord.
4. By injection near a major nerve trunk to block sensation from the truncated region of the body e.g. brachial plexus block.

Potentiation of effects of L.A.

Effects of local anaesthetics may be potentiated by the use of vasoconstrictors such as adrenaline and by hyaluronidase. Addition of adrenaline HCL or other vasoconstrictors to a solution of the drug will prolong the action of local anaesthetics. Cocaine is the only exception it has a clear vasoconstrictor effect. The sterile 1:1000 solution of adrenaline is added to a local anaesthetics solution following sterilization and shortly before use. A concentration of one part of adrenaline in 50,000 parts of L.A. solution should not be exceeded and 1 in 100,000 is preferred. Vasoconstrictors also decrease the toxicity of a L.A. by delaying absorption and preventing high blood concentrations since slower absorption provides more fibre destruction of a local

anaesthetics by the tissues of the body. Hyaluronidase, a mycolytic enzyme, hydrolyses by a hyaluronic acid and increases diffusion of injected substances. It may be added to local anaesthetics solutions to injected S.C. to promote tissue diffusion and thereby to increase the duration of anaesthesia may be due to extensive absorption of L.A. Hyaluronidase has two shortcomings:

1. It may enhance absorption and toxicity of L.A.
2. It has expensive and these two has its wide application in veterinary practice.

Local Anaesthetic Agents.

Procaine HCL – Procaine HCl is a white crystalline powder dissolving in an equal weight of water. Solutions of procaine HCl can be sterilized repeatedly by boiling w/o loss of anaesthetic potency but the boiling should not be done as metal vessels or glass that contain alkalis. A distinct should be discarded.

Pharmacological Action

Procaine was synthesized after cocaine was discovered to be habit forming and relatively toxic. Procaine HCl as the most widely used and the most satisfactory of all the LAs. A large number of LA comps have been studied toxicity associated with an increased anaesthetic efficiency. Procaine is not as active as cocaine. However, it is considerably less toxic than cocaine and most other commonly used local anaesthetics. The solution of HCL is nonirritant and promptly effective when injected subcutaneously. Anesthetic is relatively brief because the drug is absorbed rapidly and destroyed quickly by the liver. Anesthesia with procaine is commonly prolonged by the addition of a vasoconstrictor to the solution to delay absorption of the local anesthetic from the site of injection.

Metabolism:

Procaine is hydrolyzed primarily in the liver and, tissues of the body. In the cat the livers is the responsible for up to 40% of the procaine metabolism. An-enzyme hydrolyzes procaine to PABA and diethyl aminoethanist. The enzyme procaine esterase is the same as plasma cholinesterase. The kidneys play no significant part in the reduction of procaine blood levels. But they excrete PABA rapidly and to a considerable extent. PABA exhibit no local anesthetic action Diethyl amino ethanol possesses only a part of the full anesthetic activity of procaine.

Toxicity

A rapid i.v injection of procaine (45mg/ kg) from the cat or rabbit produces a lethal effect; if the drug is administered slowly or by s.c route, the dose required to produced death as about 10 times greater. The greatest difference between the toxicities of procaine HCL and a potent local anesthetic such as cocaine HCL is the rate of metabolism. Cocaine is slowly metabolized whereas procaine is rapidly detoxified.

The use of procaine when the ambient temperature is high may lead to increased absorption from s.c infiltration sites to the extent that CNS stimulation or convulsions occur. Vasoconstrictor agents should be employed into the L.A to reduce or prevent this problem. If convulsions occur the use of the ultra short- acting barbiturates i.v. are indicated.

Clinical use.

Local anesthetic by tissue infiltration with a procaine HCL solution is a routine clinical technique employed for the relieve of pain. The majority of these clinical applications are to relieve pain of the skin. Anaesthesia is produce by anaesthetizing a major nerve supply of specific areas, such as perineural injection of the mandibular nerve for a dental operation in the dog, of the corneal nerve for dehorning in the goat or cow and of the last thoracic and first two lumbar nerves on the left side for rumenotomy or caesarean section in the cow. Procaine is also used to reduce or anaesthesia or anesthesia for tail docking in the lamb. Or dog, for nerve blocks in the foot and for enucleation of the surgical removal of the eye ball from its socket or shelling out of a tumour or origin from its capsule of the eye in cattle referred to as peterson eye block. In the recent years procaine has been used intravenously to produce retrograde regional anesthesia of the ruminants. In cattle, procaine is used epidurally to produce anesthesia for obstetrical procedures and perineal operations. The use in small animals has not been as frequent because of the problem with restraint of the animal during surgery.

Procaine hydrochloride is used as veterinary medicine for infiltration, conduction and epidural anaesthesia. For infiltration in small animals, a concentration of 1% is generally employed, whereas as larger animals 2% is preferable. About 2-5ml of a 2% solutions are used for nerve block or conduction anaesthesia in small animals. In large animals, 5-10ml of a 4% solutions are most commonly employed for this purpose. Adrenaline hydrochloride solution may be added to give a concentration of 1:100,000, i.e. 1ml of adrenaline HCL solution (1:1000) to each 99ml of anaesthetic solution.

For surface anaesthesia, procaine HCL is not as effective as other L.A. as it is rarely used.

I. V. Injection – In dogs and humans, i.v. injection of procaine HCL depresses cardiac irritability induced by general anaesthetic and thereby decreases the incidence of cardiac arrhythmias and ventricular fibrillation. This effect of procaine led to the development of procainamide HCL, which is used prophylactically and therapeutically for treatment of cardiac arrhythmias occurring in heart disease or from general anaesthesia/. I.V. procaine HCL has been used as a treatment of spasmodic colic in horses and is suited to this type (i.e. “spasmodic”) of colic.

Stimulant Action

The horse seems to be more sensitive to the CNS stimulation of procaine HCL than other species of domestic animals. Stimulation produced in the horse by procaine resemble that of opiate doping. Central stimulation of cow using procaine need a considerable larger dose, whereas, the pig falls intermediately between the horse and the cow. Due to its CNS stimulant and analgesic actions, procaine has been used illegally in race animals to improve performance and/or to mask lamelessness in track and racing events.

LIGNOCAINE

Lignocaine (Lidocaine) as a white or slightly yellow powder with a characteristic odour, it is relatively stable but nearly insoluble in water.

Metabolism and fate:

Lignocaine is metabolized primarily in liver at a rate nearly as rapid as that of procaine. The unchanged form is excreted in the urine of the dog in a concentration of 10% - 20%. A large amount of lignocaine is conjugated with sulphate and excreted in this form. Following the i. v. administration of lignocaine (10mg/kg) in pregnant guinea pigs, it rapidly crosses the placenta. High concentrations are found in the fetal liver, heart, and brain. The kinetics and oral absorption rate of lignocaine have been determined in the dog, 78% of the administered dose of lignocaine reaches the general circulation. Emesis occurs regularly at 2.5hours after the administration of lignocaine.

Pharmacological Action:

Lignocaine HCL isa water soluble, local anaesthetic that produces more prompt, potent, and extensive anaesthesia than an equal concentration of procaine HCL in fact, the anaesthetic potency and area of anaesthesia are about twice those of procaine HCL.

Lignocaine is used for infiltration, nerve conduction, epidermal topical anaesthesia,. Depending on the concentration of solution and the procedure, the onset of mucosal anaesthesia appear in about 5 minutes and the effect persists for 30minutes or more. Lignocaine HCL is effective at about one half of the concentration of procaine.

For infiltration anaesthesia, 0.5% is normally used in small animals of Adrenaline HCL. For conduction anaesthesia, a concentration of 1% in large animals and 2% -3% in large animals is used usually with a vasoconstrictor. In the horse, 50 and 30ml of a 2% solution are effective in blocking the thoracic and pelvic limbs respectively. A concentration of 1%-2% lignocaine HCL is suggested for epidermal injections.

Clinical Use

In dogs and cats: The epidural use of lignocaine HCL (1ml of a 2% solution per 4/5kg or 20mg/4.5kg) will block cranially to lumbar vertebra I (L₁) and 1ml of a 2% solution per 3.4kg will block to thoracic vertebrae 5 (T₅) in the average dog or cat. The onset of epidural analgesia with lignocaine is relatively rapid. 3-12minutes and the duration of action is 45-90minutes. In the treatment of cardiac arrhythmia, lidocaine is used intravenously at the rate of 2mg/kg every 20-30minutes.

In pigs, Goats and Sheep: In the pit dosage of lidocaine required to produce epidural anaesthesia to T₁₀ to permit a laparotomy has been determined by the length (in cm) of the animal measured from the external occipital protuberance to the first coccygeal vertebrae. The recommended dose of 2% lignocaine up to 40cm in length is 1ml, after this an additional 1.5ml are administered for every 10cm increase in the vertebra column of the pig. The dose/length relationship also applies to the dog.

Lignocaine HCl (1% or 2%) has been used in cornual nerve block of the goat; 2ml of the L.A are injected at each site to block the lacriminal and infratrochlear branches of the corneal nerve. In adult sheep lignocane (2%) has been used for epidural anesthesia. About 10 minutes prior to the epidural injection a phenothiazine tranquilizer such as chlorpromazine HCl (25-50mg) is admin. 1m . the dose of lignocaine varies from 8to 12ml: onset of anesthesia occurs 2-10 minutes after the injections. The analgesia produced by lignocaine in sheep it preceded by a short period of muscular twitching, which is followed by profound relaxation.

For use as spinal (intrathecal) anesthetic, a 2% lignocaine solution (5ml) is injected into the cumbosacral space of sheep. Anesthesia last on average for more than on have.

In cattle: In cattle, lignocaine is preferred for a number of surgical procedures in conjunction with tranquilizers. For low epidural analgesia 4ml of a 2% solution has been used w/o & with 1:80,000 Adrenaline. In cattle where high epidural analgesia was produced, 60ml of a 2% lignocaine hydrochloride solution were used, this dose produced recumbency in all animals. Analgesia lasted 220-360 minutes. For anesthesia with lignocaine involving the lower portion of the limbs of cattle, a tourniquet is placed around the limb just below or above a hock. Then 10-20ml of 2% lignocaine hydrochloride are injected into any superficial vein below the tourniquet. Rapid anesthesia develops and normal sensation and limb movements return 5 minutes after release of the tourniquet.

In Horses: Lignocaine is probably the most commonly used local anesthetic for nerve blocks in the equine. 10 to 20 ml of 2% lignocaine blocks the mandibular nerve and desensitizes the mandible, lower molars, incisors and lower lips. Blockage of other major nerves usually does not require as great a volume of anesthetic

Toxicity: when injected w/o adrenaline sufficient lignocaine is absorbed from the site of a nerve block or regional anesthesia to depress the CNS, producing a general drowsiness. Local irritate is rare. Over dosage will cause muscular twitching, hypertension, nausea.