Local Anaesthetics

Local Anaesthetics

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- Susceptibility of nerve fibres
- Classification
- Mechanism of action
- Effect of pH on LA action

Local Anaesthetics

- Prolongation of action by vasoconstrictors
- Pharmacokinetics
- Uses
- Adverse effects
- Drug interactions

Local Anaesthetics (LAs)

- reversible loss of sensory perception, especially of pain
- block generation and conduction of nerve impulse

CHEMISTRY

- weak bases .
- A hydrophilic secondary or tertiary amine on one side (basic amine side chain) and a lipophilic (aromatic part) on the other are joined by an alkyl chain through an ester or amide linkage.
- Cocaine, procaine, chloroprocaine, tetracaine, benzocaine.

Amide-linked LAs

- **Longer acting**
  - bupivacaine, Levo-bupivacaine, ropivacaine, dibucaine
- **Intermediate acting**
  - Lignocaine (lidocaine), mepivacaine, prilocaine, articaine

Ester-linked LAs

- **Longer acting**
  - Tetracaine
- **Intermediate acting**
  - Cocaine
- **Short acting**
  - Procaine,
  - Chloroprocaine, Benzocaine(mucopain), Proparacaine(proxymetacaine)

Miscellaneous

- Pramocaine
- Dyclocaine
- Oxetacaine (mucain)

Amide Versus Ester

- More intense and longer duration
- Bind to α_1 acid glycoprotein in plasma
- Not hydrolysed by plasma esterases
- Rarely cause hypersensitivity reactions;
- no cross sensitivity with ester LAs
- Because of their short duration, less intense analgesia and higher risk of hypersensitivity, the **ester-linked** LAs are rarely used for infiltration or nerve block,
- but are still used topically on mucous membranes.

Dosage and Administration

- Anaesthetic procedure
- Area to be anaesthetised
- Vascularity of the tissues
- Duration of the anaesthesia
- Individual tolerance
- Physical condition of the patient
- Vasoconstrictor agent

Lignocaine

Mechanism of Action:

- inhibiting Sodium influx required for the initiation and conduction of impulses.

Onset and Duration of Anesthesia:

- less than 2 minutes for 2% lignocaine.
- Duration of nerve block 60 to 120 min
- average duration ~90 to 180 min for 2% lignocaine with epinephrine 1:200,000

Pharmacokinetics

- 95% metabolized (dealkylated) in the liver mainly by CYP3A4
- pharmacologically active metabolites monoethylglycinexylidide (MEGX) and
- then subsequently to the inactive glycine xylidide.
- MEGX has a **longer** half life than lidocaine, but also is a less **potent** sodium channel blocker.
- About 60-80% circulates bound to the protein alpha$_1$ acid glycoprotein.

Pharmacokinetics

- elimination half-life of is biphasic and around 90–120 minutes.
- may be prolonged in hepatic impairment (average 343 min) or congestive heart failure (average 136 min).
- Renal dysfunction does not affect kinetics but may increase the accumulation of metabolites.
- acidosis and the use of CNS stimulants and depressants affect the CNS levels of lignocaine
- excreted in the urine (90% as metabolites and 10% as unchanged drug).

Lignocaine

PRODUCT IDENTIFICATION			FORMULA		
Concentration %	Lignocaine (mg/mL)	Epinephrine (mg/mL)	Methyl Paraben (mg/mL)	Sodium Chloride (mg/mL)	Sodium Metabisulfite (mg/mL)
2% with Epinephrine	20	1:200,000 (5mcg/mL)	1	6	0.5
2% plain	20	----	1	6	---

Precautions

- To minimize intravascular injection, aspiration should be performed.
- If blood is aspirated, the needle must be repositioned.
- Absence of blood in the syringe does not assure intravascular injection.
- Inject slowly and take care not to exceed the maximum safe dose, especially in children.

Drug interactions

- Propranolol (probably other β blockers also) may reduce metabolism by reducing hepatic blood flow.
- Vasoconstrictor (adrenaline) containing LA should be avoided for patients with IHD, PVD, cardiac arrhythmia, thyrotoxicosis, uncontrolled hypertension, and those receiving β blockers or TCA
- during administration of general anesthetic, since cardiac arrhythmias may occur under such conditions.

Drug interactions

- Haloperodol causes hypotension
- Alcohol needs higher dose

ADR of Lignocaine

- Allergic reactions are characterized by cutaneous lesions, urticaria, edema or anaphylaxis reactions.
- Allergic reactions as a result of sensitivity to lidocaine are extremely rare
- The detection of sensitivity by skin testing is of doubtful value.

Toxicity of Lignocaine

- Central Nervous System: Restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors,
- Cardiovascular System: bradycardia, hypotension, and cardiovascular collapse, which may lead to cardiac arrest.

Management of Emergencies

- The first consideration is **prevention**, by careful and constant monitoring of cardiovascular and respiratory vital signs
- the patient's state of consciousness after each local anesthetic injection.
- Resuscitative equipment, oxygen, and other resuscitative drugs should be available for immediate use.
- At the first sign, oxygen should be administered.

Maximum Recommended Dosages

- Adult: lidocaine with epinephrine - below 500 mg and should not exceed **7** mg/kg.
- When used without epinephrine -below 300 mg and should not exceed **4.4** mg/kg

Lignocaine 2% Epinephrine 1:80,000

Adrenalin

- **Dosage Forms And Strengths**
- Adrenalin 1 mg/mL (1:1000) 1 mL
- **Adults and Children >30 kg :** 0.3 to 0.5 mg (0.3 mL to 0.5 mL) I.M.
- maximum of 0.5 mg (0.5 mL) per injection, repeated every 5 to 10 minutes as necessary.
- **Children < 30 kg :** 0.01 mg/kg (0.01 mL/kg) of maximum of 0.3 mg (0.3 mL)

Adrenaline (epinephrine) dosages chart

Age (years)	Weight (kg)	Vol. adrenaline 1:1000	Adrenaline autoinjector
<1	5-10	0.05-0.1 mL	
1-2	10	0.1 mL	10-20 kg (~1-5yrs) 0.15mg (green labelled device)
2-3	15	0.15 mL	
4-6	20	0.2 mL	
7-10	30	0.3 mL	>20kg (~>5yrs) 0.3mg (yellow labelled device)
10-12	40	0.4 mL	
>12 and adults*	>50	0.5 mL	

Ropivacaine

- long-acting, pure *S*-enantiomer , amide local anaesthetic.
- less cardiotoxic than racemic bupivacaine but more than lignocaine.
- adverse event profile similar to that of bupivacaine

Ropivacaine

- Several cases of CNS toxicity have been reported after intravascular administration
- But very less cardiovascular toxicity has been reported .
- The outcome of intravascular administrations is favourable
- preferred because of its reduced CNS and cardio toxic potential

Ropivacaine

- 2 mg/mL-- 10 mL and 20 mL vials,
- 7.5 mg/mL--10 mL and 20 mL vials,
- 10 mg/mL--10 mL and 20 mL vials,
- Maximum recommended dose 3 mg/kg

Levobupivacaine

- amino-amide group. It is the S-enantiomer of bupivacaine.
- less vasodilation and longer duration as Compared to bupivacaine
- less potent than racemic bupivacaine
- ADRs rare when it is administered correctly

Levobupivacaine

- Systemic exposure to excessive quantities mainly results in CNS and CVS effects.
- CNS effects usually occur at lower blood plasma concentrations
- CVS effects present at higher concentrations,

Levobupivacaine

Presentation

0.25% Injection:

Each ml contains Levobupivacaine Hydrochloride 2.5mg.

0.5% Injection:

Each ml contains Levobupivacaine Hydrochloride 5mg

Levobupivacaine

Local Infiltration :

Adults 0.25% Maximum recommended dose 2mg/kg

Local Infiltration :

Children < 12 yrs

0.25% 0.25 - 0.50 ml/kg (1.25 - 2.5mg/kg)

Safety of ROP and LBUP

- larger doses and blood concentrations of ropivacaine (ROP) and lignocaine will be tolerated better as compared with levobupivacaine (LBUP).
- Lignocaine intoxication results in myocardial depression from which resuscitation is successful but will require continuous drug support.
- After LBUP, or ROP, resuscitation is not always successful, and the administration of epinephrine may lead to severe arrhythmias.