Local Anesthetics Pharmacology

Dr. Rajesh Choudhary
M. Pharm. (Pharmacology), Ph. D.

www.youtube.com/pharmacologyconceptsbyrajeshchoudhary

www.pharmacyconcepts.com

Disclaimers: Content of the slide is taken from various books, online contents and google images for the education purpose only.

Content of the Lectures

- Definitions
- Classification of the Las
- Chemistry
- Pharmacology

Introduction

- Local anesthetics (LAs) are drugs which used either topical of local injection for the anesthesia in the applied area.
- They cause reversible loss of sensory perception, especially of pain, in a restricted area of the body.
- They block generation and conduction of nerve impulse within the neurons, without causing any structural damage.
- They interrupted both sensory as well as motor impulse, resulting in muscular paralysis and loss of autonomic control as well.

Introduction

- The first clinical uses of a local anesthetic agent occurred in 1884, when **cocaine** was employed as a topical agent for eye surgery and to produce a nerve block.

General Anesthesia vs Local Anesthesia

	General anaesthesia	*Local anaesthesia*
1. Site of action	CNS	Peripheral nerves
2. Area of body involved	Whole body	Restricted area
3. Consciousness	Lost	Unaltered
4. Care of vital functions	Essential	Usually not needed
5. Physiological trespass	High	Low
6. Poor health patient	Risky	Safer
7. Use in non-cooperative patient	Possible	Not possible
8. Major surgery	Preferred	Cannot be used
9. Minor surgery	Not preferred	Preferred

Classification of LAs

A. Injectable LAs

1. Low potency, short duration: Procaine Chloroprocaine
2. Intermediate potency and duration: Lidocaine (Lignocaine), Prilocaine
3. High potency, long duration: Tetracaine (Amethocaine), Bupivacaine, Ropivacaine, Dibucaine (Cinchocaine)

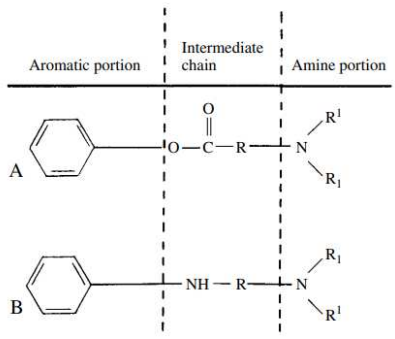
B. Surface Las

1. Soluble: Cocain, Lidocaine, Tetracaine
2. Insoluble: Benzocaine, Butyl-amino-benzoate, Oxethazaine

*Some other drugs, e.g. **propranolol, chlorpromazine, H1 antihistaminics, quinine have significant LA activity**, but are not used for this purpose because of local irritancy or other prominent systemic activity.

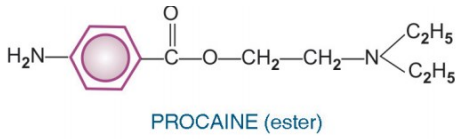
Chemistry of LAs

- The clinically useful LAs are weak bases with amphiphilic property
- The basic components in the structure of local anesthetics are the lipophilic aromatic portion (a benzene ring), an intermediate chain [either ester linkage (combination of an aromatic acid and an amino alcohol)or amide linkage(combination of an aromatic amine and an amino acid)], and the hydrophilic amine portion

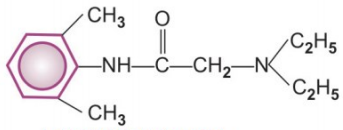


Chemistry of LAs

- **Ester-linked LAs:** Cocaine, procaine, chloroprocaine, tetracaine, benzocaine.
- **Amide-linked Las:** Lidocaine, bupivacaine, dibucaine, prilocaine, ropivacaine.
- **Features of Amide Las over Ester LAs**
  - Produce more intense and longer lasting anaesthesia
  - Bind to alfa 1 acid glycoprotein in plasma
  - Not hydrolysed by plasma esterases
  - Rarely cause hypersensitivity reactions; no cross sensitivity with ester LAs



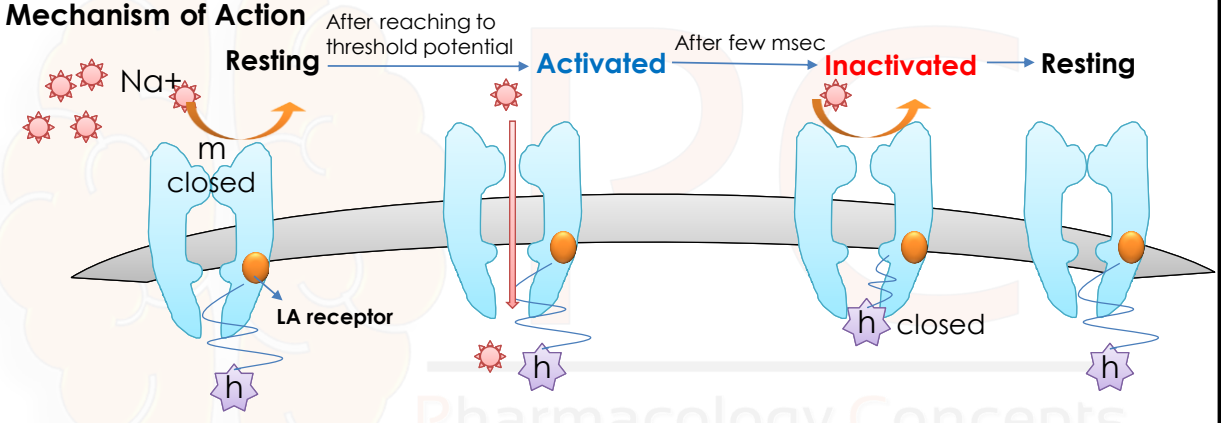
PROCAINE (ester)



LIDOCAINE (amide)

Pharmacology of LAs

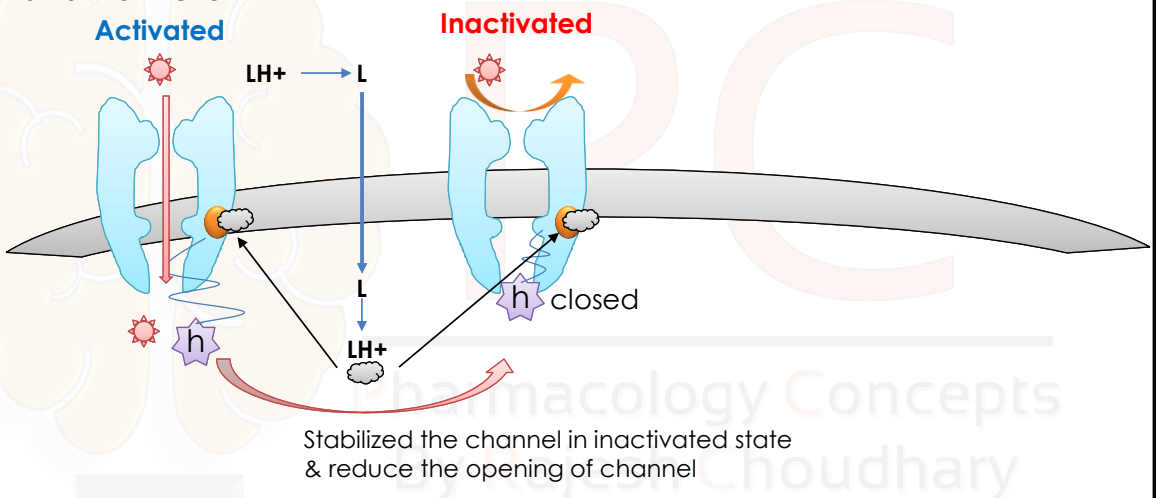
Mechanism of Action



m= make or m gate (Activation gate);
h = halt or h gate (Inactivation gate)

Pharmacology of LAs

Mechanism of Action



Pharmacology of LAs

Mode of Action:

- The LAs bind with the LA receptor located at **Voltage gated Na+ Channel** and stabilize the channel or prolongation in inactivated state and increase the threshold of channel opening.
- The LAs block nerve conduction by decreasing the entry of Na+ ions during upstroke of action potential (AP).
- As the concentration of the LA is increased, the rate of rise of AP and maximum depolarization decreases causing slowing of conduction.
- Finally, local depolarization fails to reach the threshold potential and conduction block ensues

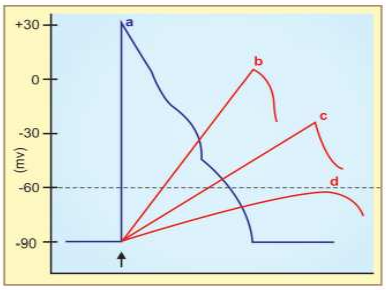


Fig. 26.1: Effect of progressively increasing concentrations (b,c,d) of a local anaesthetic on the generation of an action potential in a nerve fibre, (a) Untreated nerve fibre

Pharmacology of LAs

LOCAL ACTION:

- Block sensory nerve endings, nerve trunks, neuromuscular junction, ganglionic synapse and receptors at locally
- It also reduce the release the **Ach** from motor nerve endings.
- The LA often fails to afford adequate pain control in inflamed tissues (like infected tooth). The likely reasons are:
- a. Inflammation lowers pH of the tissue— greater fraction of the LA is in the ionized form hindering diffusion into the axolemma.
- b. Blood flow to the inflamed area is increased—the LA is removed more rapidly from the site.
- c. Effectiveness of Adr injected with the LA is reduced at the inflamed site.
- d. Inflammatory products may oppose LA action

Pharmacology of LAs

Systemic Action:

1. CNS:

- All LAs are capable of producing a sequence of stimulation followed by depression.
- **Cocaine** is a powerful CNS stimulant causing in sequence euphoria—excitement—mental confusion— restlessness—tremor and twitching of muscles— convulsions—unconsciousness—respiratory depression—death, in a dose-dependent manner
- Procaine and other synthetic LAs are much less potent in this regard. At safe clinical doses,

Pharmacology of LAs

Systemic Action:

2. CVS:

A. Heart:

- LAs are cardiac depressants at high dose
- decrease automaticity, excitability, contractility, conductivity and prolong effective refractory period (ERP).
- It shows quinidine like like antiarrhythmic action
- Amide derivative of procaine, procainamide is a class IA antiarrhythmic

Pharmacology of LAs

Systemic Action:

B. Blood Vessels:

- LAs tend to produce fall in BP. This is primarily due to sympathetic blockade,
- but high concentrations it causes vasodilatory effects.
- Toxic doses of LAs produce cardiovascular collapse. Cocaine has sympathomimetic property; increases sympathetic tone, causes local vasoconstriction, marked rise in BP and tachycardia.

3. Others: Procaine and related drugs have weak anticholinergic, antihistaminic, ganglion blocking, neuromuscular blocking and smooth muscle relaxant properties, but these are clinically insignificant.

Pharmacology of LAs

ADR: Systemic Toxic effects

- CNS effects are light-headedness, dizziness, auditory and visual disturbances, mental confusion, disorientation, shivering, twitchings, involuntary movements, finally convulsions and respiratory arrest. **This can be prevented and treated by diazepam**
- Cardiovascular toxicity of LAs is manifested as bradycardia, hypotension, cardiac arrhythmias and vascular collapse
- Injection of LAs may be painful, but local tissue toxicity of LAs is low
- Hypersensitivity reactions like rashes, angioedema, dermatitis, contact sensitization, asthma and rarely anaphylaxis occur

Pharmacology of LAs

Precautions & Interaction

- Before injecting the LA, aspirate lightly to avoid intravascular injection.
- Inject the LA slowly and take care not to exceed the maximum safe dose
- Propranolol (probably other β blockers also) may reduce metabolism of lidocaine and other amide LAs by reducing hepatic blood flow.
- Vasoconstrictor (adrenaline) containing LA should be avoided for patients with ischaemic heart disease, cardiac arrhythmia, thyrotoxicosis, uncontrolled hypertension, and those receiving β blockers (rise in BP can occur due to unopposed a action) or tricyclic antidepressants (uptake blockade and potentiation of Adr).

Pharmacology of LAs

Clinical Uses

- **Surface anesthesia**
- **Infiltration anesthesia**
- **Conduction block**
- **Spinal anesthesia**

PC
Pharmacology Concepts By Rajesh Choudhary

Thanks for Watching

Subscribe my YouTube Channel