* Feature of amide LAs compared to ester LAs
* produce more intense and longer lasting anaesthesia
* bind to α1 acid glycoprotein in plasma
* Not hydrolysed by plasma esterases
* Rarely cause hypersensitivity reactions, no cross sensitivity with ester LAs...

26-07-2018

LOCAL ANAESTHETIC

Local anaesthetic prevent or relief pain by interupting nerve conduction

They bind to the specific receptor within the pore of Na^+-ion channels that block the flow the flow of Na^+-ion from these channels

Local anaesthetic —X→ Na^+-channel

The main advantage of this drug is

* effect in specific region
* effect is reversible

Local anaesthetics are administered by variety of route including

- Topical
- Regional IV

Nerve or field block anaesthesia is it relieves pain

* Chemistry and History

First local anaesthetic was cocaine because of its toxicity and addictive properties Da re search for cocaine substitute has started

In 1905 a derivative of this compound was discovered that is procaine

Procaine is prototype of all local

anaesthetic.
like lidocaine, benzocaine

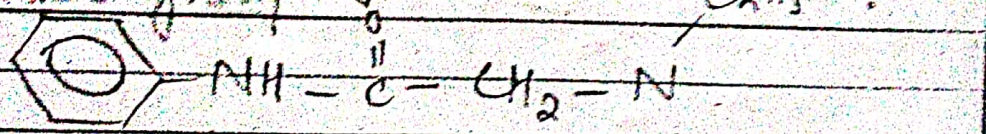
Chemistry

Chemically local anaesthetic contain hydrophilic and hydrophobic group

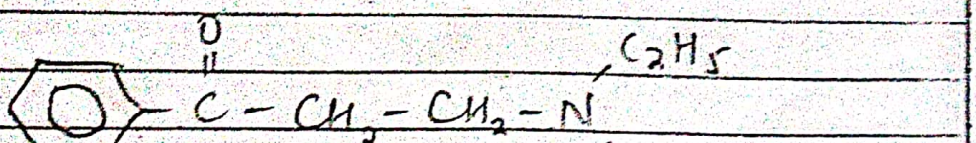
Hydrophilic and hydrophobic are linked either by ester linkage or by amide linkage

Hydrophilic group is either secondary amine or Tertiary amine and hydrophobic portion is an aromatic ring.

Amide group



Ester linkage



Hydrophobic group is responsible for potency and duration of action of local anaesthetic actually The receptor site on Na^+ ion channel is hydrophobic in nature. So the hydrophobic portion easily binds

with the hydrophobic site of Na^+ ion channel As a result it increase the duration of action of local anaesthetic

local anaesthetics are weak bask drugs. So these drugs are mixed with HCl, that convert these drug into salt form So the salt form of local anaesthetic increases

* - solubility
* - Stability

The physiochemical properties (PKa) of local anaesthetic and pH of physiological medium influence the stability of local anaesthetics.

The PKa of local anaesthetic equals to the pH of physiological medium

If there is 50% of charged form and 50% of uncharged form of local anaesthetic.

$$pKa = pH + \log \frac{\text{charged}}{\text{uncharged}}$$

Extracellulary local anaesthetic gain equilibrium with charged and uncharged form. So uncharged form cross the plasma membrane.

Intracellularly again equilibrium is established & intracellularly charged form is responsible to bind with the Na^+-channels.

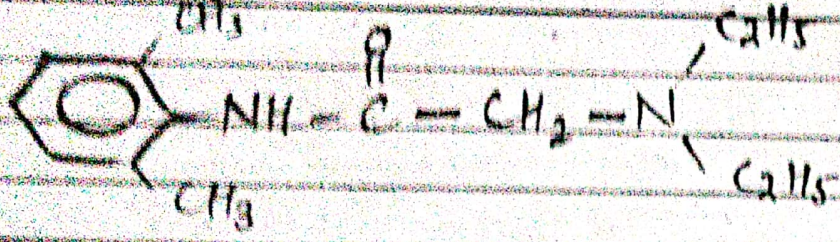
28-02-2018

LOCAL ANAESTHETIC

- Esters
  - Long acting
    - Tetracaine
  - Short acting
    - Procaine
  - Surface acting
    - Benzocaine
- Amide
  - Long acting
    - Ropivacaine
    - Bupivacaine
  - Medium acting
    - Lidocaine
    - Xylocaine
    - Lignocaine

Lidocaine

Lidocaine is introduced in 1948.
It is Aminoethyl amide.
It is prototype of amide class of local anaesthetics.
It produce more intense and extensive anaesthesia similar to procaine.
Its general structure is;



Lidocaine

Procaine is the prototype of ester type.

Lidocaine is needed at that time when local anaesthesia of medium action is required.

* Iontophoretic
Spray on the surface of skin by electrophoresis and ion formed cross the membrane gradient.

Pharmacokinetics

Lidocaine is completely absorbed after parenteral administration. In addition to the preparation for injection and Iontophoretic needle free drug delivery system of Lidocaine and Epinephrine solution is available.

also used for Local anaesthetic This procedure is used for dermal surgery and provide anaesthesia to the depth of 10mm.

Lidocaine is metabolized by microsomal enzyme into the monoethyl glycine xylidide and Glycine xylidide.

Both metabolites have also anaesthetic property. These metabolites further metabolized into mono-ethylene and glycine xylidide that are eliminated through urine.

Pharmacodynamics

These drugs block the conduction of Nerve impulse.

These drugs decrease / prevent the increase in permeability of excitable membrane to Na^+-ions. As a result conduction of Nerve impulse is blocked.

As a drug binds with the receptor, anaesthetic action progressively develop and nerve conduction is blocked

The degree of blockage depends upon how the nerve is stimulated. The resting membrane is less responsive to the Na^+-ion blocker as compared to the membrane that is highly stimulated. Local anaesthetic also targets some anatomical fibres. For example small unmyelinated C-fibres that mediates;

* - pain sensation

and small myelinated A sigma fibre that mediates

* - pain and Temperature sensation

are blocked more rapidly than long-myelinated $A\alpha$, $A\beta$, $A\gamma$ that also mediates;

* - pain, Temperature and touch sensation

so This hypothesis that small fibres are more responsive to local anaesthetic than large fibres

Adverse Effects

This cause dose-dependant adverse effects

For example

- Drowsiness
- Tinnitus (ear ringing)

At higher dose it also cause

- Coma
- Convulsion
- and respiratory depression

Lidocaine is also used as an anti-arrhythmic drug.

PROCAINE

- introduced in 1905
- It is aminoester
- general structure is