Aleksandar Rašković

LOCAL ANAESTHETICS

Local anaesthetics

chemistry – have specific structural features!

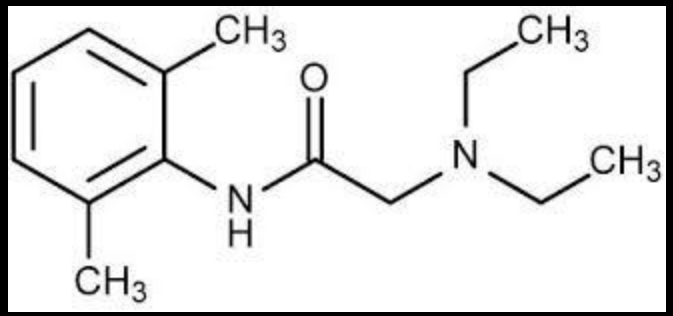
1. lipophilic part - aromatic nucleus
2. this part is joined by an amide or ester linkage to alkyl chian (second part)
3. hydrophilic amino terminus

=> lipophilicity of the aromatic group facilities penetration into the neuronal membrane

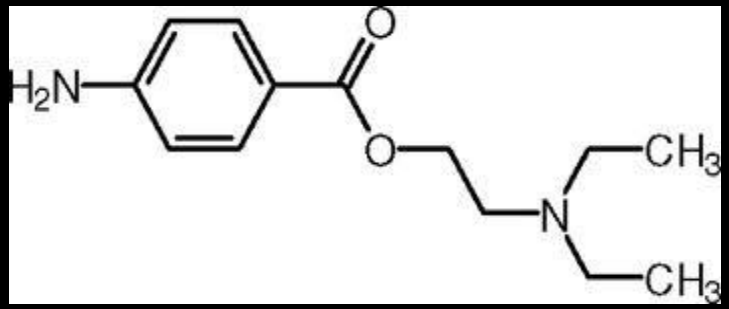
=> because of the amino terminus, local anaesthetics are weak basis

Local anaesthetics

lidocaine (amide)



procaine (ester)



Local anaesthetics

Mechanism of action

1. reversible, dose-dependent reduction in the rate of rise and height of the action potential
2. Non-ionized drug crosses into axoplasma!
3. binding of the ionized drug on the inner surface of the Na channel
4. reduce conductance of Na into the cell

pH has the effect on anaesthetic activity of local anaesthetics

they are more effective at pH 7.0 than at pH 8

in case of low pH, local anasthetic will be ionized, and cannot penetrate to the Na channel!

Local anaesthetics

Anaesthetic action is increased by repeated stimulation of the nerve fibre – frequency dependent block:

Sensitive nerves are more affected with local anaesthetics than motoric!

The result of this is a differential sequence of onset of analgesia:

Pain sensation is affected earliest, followed by temperature, tuoch, proprpioception and finally motor function

First are affected A-δ and C fibers – conduct pain sensation

Local anaesthetics

types of local anaesthesia

Topical – anaesthetic is applied to the surface of the skin, burns, or mucous membrane (lidocaine, not procaine)

Infiltration – drug is injected directly into or around an area to be treated (for minor surgical procedure)

Regional nerve block – drug is injected in close proximity to the nerve (dental procedure)

Local anaesthetics

- Spinal – cerebrospinal fluid in the lumbal subarachnoid space to reach the roots of the spinal nerves – for surgery on the lower limbs, pelvis, obstetrics
- Epidural – extradural space through which the nerve roots pass
- Uses are the same as for spinal anaesthesia, but advantage is that anaesthetic agent is less likely to rise accidentally to a higher segment of the spinal cord
- Intravenous – for surgery on a limb
- Sympathetic nerve block – intractable pain of carcinoma

Local anaesthetics

Diffusion from site of administration is the major factor in determining duration of action

Vasodilating properties differ among the agents

Procaine, lidocaine – strong dilating effect

Bupivacaine – weaker

Cocaine – vasoconstriction

Highly protein-bound agents as bupivacaine and ropivacaine have an extended duration of action

Reduced transfer across the placenta

Local anaesthetics

Amids are metabolised exclusively by the liver (except prilocain – plasma and kidneys)

Esters undergo hydrolysis by plasma esterases

Active metabolites:

Lidocaine – *monoethylglycine xylidide* responsible for toxicity (sedation)

Prilocaine – ortho-toulidine – methemoglobinemia

t ½ of amide-type agents range from 90 to 160 min

Reduced hepatic function predispose toxicity of amide-type agents!

Local anaesthetics

Adverse effects and toxicity

In general, toxicity manifests in the 1. CNS and 2. cardivascular system

CNS – both, excitatory and inhibitory phenomena

confusion, desorientation, tremor, seizures

Respiratory and cardiovascular arrest

CV toxicity – decreased cardiac output, hypotension, collapse

Decreased myocardial conduction – lidocain and procain are anti-arrhythmic agents

Local anaesthetics

In general, the incidence of toxicity of local anaesthetics is very low

Recommendation for maximum doses are given!

A true allergy to an amide local anaesthetic is rare

Esters are more allergenic

Allergy to adiuvans is more probably (methylparaben, antioxidant metabisulfite)

Local anaesthetics

Other indications

Anti-arrhythmic agents

Lidocaine – I b

Procaine-amide – I a

In combination with antibiotics:

Procain benzyl penicillin – procain slows rate of absorption of penicillin

Lidocaine + ceftriaxone – relief the pain after i.m. injection

Local anaesthetics

To prevent vasodilating effect and to prolong duration of action, adrenaline/noradrenaline is administered

Arrhythmia

Diabetes mellitus

Local anaesthetics

Commonly used local anaesthetics

Esters

Cocaine – too toxic for any use than topical

application to oropharyngeal or nasal mucous membrane prior to local surgical procedures

Procaine – slow onset, short duration of action, weak potency (not efficient topically)

More allergenic than the amides

Tetracaine – 10 times as potent as procaine

Slow onset, long duration; spinal anaesthesia – rapid onset!

Local anaesthetics

Lidocaine – most commonly used local anaesthetic agent

Rapid onset; intermediate duration of action

Prominent vasodilating properties (+ adrenaline)

Prilocaine – less vasodialtion than lidocaine, methemoglobinemia

Mepivacaine – similar to lodocaine; not effective as a topical agent

Not used in obstetric anaesthesia (biotransformation is prolonged in fetus)

Local anaesthetics

Bupivacaine

Onset of action is slower than of lidocaine

Long duration of action

Good separation of sensory and motor blockade

Greater toxicity than lidocaine, in particular, greater cardiotoxicity

% of protein binding is higher!

Ropivacaine – S enantiomer of bupivacaine – less cardiotoxic than bupivacaine

Local anaesthetics

Pregnancy

Although animal studies have revealed no evidence of harm to the foetus, lidocaine crosses the placenta and should not be administered during early pregnancy unless the benefits are considered to outweigh the risks.

Lidocaine given by local perineal infiltration prior to delivery crosses rapidly into the foetal circulation. Elevated lidocaine levels may persist in the newborn for at least 48 hours after delivery. Foetal or neonatal bradycardia, hypotonia or respiratory depression may occur.

Local anaesthetics

Dental anaesthesia

lidocaine

mepivacaine

articaine

Obese patient – dose should be calculated on the basis of ideal body-weight