Local anesthetics

Definition :-

- ✓ Local anesthetics are drugs that cause reversible loss of sensition in a local area
- ✓ Without loss of consciousness .

Chemistry :

Weak bases.

Classification :

They can be Amides or Esters

E.g. :

Properties of estesrs and amides		Duration of action	Note
Esters	Pro**cain**	Short	procain is not effective as topical anesth.
	Co**cain**	Medium	produce **VC**
	Benzo**cain**	Medium	only for surface
	Tetra**cain**	Long	
Amides	L**i**do**cain**(l**i**goncain).	Medium	Effective surface .anesthetic
All contain **i** other than the one which is presenting the suffix - cain	Mep**i**v**acin**	Medium	Not effective as a topical anesthetic
	Pr**i**lo**cain**	Medium	Methemoglobinemia
	Bup**i**va**cain**	Long	is more cardiotoxic
	Et**i**do**cain**	Long	
	Levobup**i**va**caine**	Long	
	Rop**i**va**caine**	Long	

Amides act for longer duration ofaction than esters .

❖ Pharmacokinetics in general :

➲ Absorption:

- Systemic absorption of LA affected by :-
- Dosage
- Drug tissue binding
- Site os injection
- Vasoconstrictor drug .
- Physicochemical properties of the drug .

➲Distribution :

- Widely distributed
  - ① To highly perfused organ
    - ✘ Brain
    - ✘ liver
    - ✘ Kidney
    - ✘ Heart
  - ② To moderately perfused organs
    - ✘ GI
    - ✘ Muscle
  - Esters have a short T½

➲ Metabolism: T and F

- LA are converted in the liver or in plasma to more water-soluble metabolites and then excreted in the urine .

1- **Esters** :

- ✓ Are hydrolyzed very mainly and rapidly in the blood by pseudocholinesterase (butyrylcholinestrase). They can be metabolized in the liver too . however, they can't be metabolized by acetylcholinesterase→ so short plasma T½ .
- ✓ Plasma cholinesterase activity is reduced in :
  - ✘ New born
  - ✘ Pregnancy
  - ✘ Genetic variation

2- **amide**:

- ✓ in the liver by chy P450
- ✓ factrs affecet their metabolism :-
  - ✘ liver diz .
  - ✘ enzyme enducers &inhibitors
  - ✘ hepatic blood flow.

➲ Excretion :

- Main rout of excretion urine
- Acidity → excretion (because amides & estres r alkaline substances)

➲ Mechanism of action:

- Primarily → block voltage gated Na^+ channels .
- Prevent initiation (generation) and propagation (conduction) of nerve impulse (action potential). (Remember: this effect is reversible)

Differential sensitivity of nerve local anesthetics :

- Smaller fibers are susptible to the action of local anesthesia than larger fibers
- Sensory fibers are paralyzed before motor fibers .
- The order of sensation loss :
  1. Pain
  2. followed by cold ,warm ,touch
  3. Deep pressure

Effects of pH on the activity of local anesthesia :

- Local anesthetics are influenced by changes in PH .their activity increase with rise PH -more alkalinity – since more "unionized " drugs will be available ,this form penetrates through the lipid layer .lowering PH –acidity- to their activity since more ionized form will be available .

⇒ That's why local anesthetics are much less effective when injected into infected tissue

Types of L .N

According to methods of producing local ans ,: MCQ all except

1) Surface (topical) ans.
2) Infiltration ans .
3) Field block ans .
4) Nerve block ans .
5) I.V regional ans (bier block).
6) Spinal ans (sub arachnoids / intrathecal block)
7) Epidural ans (extradural),(peridural)

N.B : in case ja Q y8ol (by inhalation) Rong ✕ Rong

❶Surface (topical) ans

A) Skin &mucous membrane
B) mucous membrane.

A) mucous membrane

- ✕ Eyes
- ✕ Nose
- ✕ Mouth
- ✕ Throat
- ✕ tracheobronchial tree
- ✕ esophagus
- ✕ GIT.

- ✓ D**i**bucaine &L**i**docaine(amide)
- ✓ Tatracain & benzocaine (esters)
- ✓ N.B: procain is not effective as topical

B) Skin & mucous membrane

- ✓ Dibucain
- ✓ skin →EMLA(lignocain + prilocaine)
- ✓ benzocain →only for surface
- ✓ cocain → also has surface anesthetic action .

❷ infiltration :

- ✓ Direct injection into tissue to reach nerve branches & terminals .
- ✓ Most of the drugs E.g:
- ✓ L**i**docain, procain, bup**i**vacaine.

❸ field:

- ✓ Local anasethetic injected S.C to anaesthetize the region distal to the injection
- ✓ The same drugs used for infiltration as anesthesia .

❹nerve block :

- ✓ Injection close to nerve trunk e.g :
- ✓ Brachial plexus ,intercostals or dental nerve .
- ✓ Drugs : lidocain ,procaine ,bupivacain

❺intravenous : Bier block

- ✓ Injected I.V distal to pressure cuff to arrest blood flow
- ✓ Used in limb surgery .
- ✓ Most of the drug E.g :

Lidocain ,procaine ,bupivacain

❻spinal(sub arachnoids**) ,(**intrathecal **).**

- ✓ Injected into subarachinoid space (containing CSF) to acts on spinal roots and spinal cord .

◈Used for:-

- abdomen ,pelvis ,leg .
- Mainly when general anesthesia can not be used

◈Drug: lidocine

⟐Adverse effects :

1) 1-bradychardia ,hypotension→ due to sympathetic block .
2) respiratory depression → due to effect on pherenic nerve or respiratory center.
3) urinary retention → effect on pelvic anatomic (parasympathetic nerve)
4) paraplesia
5) meningitis .

❼Epidural (extradural).:

- ✓ Injected into epidural space to acts on spinal roots

⟐uses :

- ✓ **Same as spinal** :-
- ✓ Widely used in **obstetrics** (as for painless child birth).

⟐Drugs:

lodicaine & bupivacaine

⟐Advers effects : -

- ✶ Like spinal but **<u>less</u>**
- ✶ avoid potentially serious hazards of **<u>putting foreign substance into CSF</u>** .

Adverse effect of L.A:

1. Hypersensitivity: MCQ

- Dermatitis, asthma, rash, edema, anaphylaxis.
- Almost exclusively with esters due to metabolite PABA, so usually derivatives of PABA e.g.: procaine, tetracaine. (PABA= para amide benzoic acid)

2. CNS:

- Most important in **IV** route.
- Sleepiness, light headedness, visual & auditory disturbances & restlessness.
- **Circum oral & tongue numbness** (this is **the first sign** of CNS **toxicity) & metallic taste**.
- Nystagmus & muscular twitching.
- Tonic-clonic convulsions
- Stimulation followed by depression.
- Prevention by Benzodiazepines.
- Treatment by:
  - ✓ **oxygen**, tracheal intubation, mechanical ventilation for respiratory depression.
  - ✓ **Benzodiazepines** (midazolam, diazepam).
  - ✓ **Succinylcholine** for muscle manifestations of seizures.

3. Skeletal muscle:

(NMJ = neuromuscular junction) & autonomic ganglia block.

4. CVS: T and F

- ♥ (Direct **&** indirect) effect **on** cardiac **&** smooth muscles & (indirect) **on** autonomic nerves.
- ♥ **Bupivacaine** →is **more cardiotoxic** than others:-
  - Myocardium → ↓excitability, ↓conducyion rate,↓ force of contraction

    causing→ ↑arrhythmia (ventecular arrhythmia), widened QRS complex,
  - cardiac arrest.
- ♥ Mostly arteriolar dilatation → ↓BP (except **cocaine** which produce **VC**).
- ♥ Cardiovascular collapse & death.
- ♥ **Cocaine** block nor-adrenaline uptake → **VC** → **hypertension**
  - precipitate arrhythmia,
  - cerebral hemorrhage,
  - myocardial infarction.

5. Smooth muscles: depress →GI, vascular ,bronchial, uterine smooth muscles.

6. Methemoglobinemia: **prilocaine** due to metabolite **toluidine,** treatment by: **IV methylene blue** Or **Ascorbic acid.**

Factors affecting L.A action: T and F

1) **Diameter of nerve fiber**: smaller the diameter faster the block.

2) **Myelination**: myelenated nerves block before the unmyelated nerves of the same diameter.

3) **High firing rate** (frequency of depolarization)→more block (pain fibers)

4) **Long AP** (action potential) duration →more block (pain fibers).

5) **Infection** →↓action due to →↓ in pH.

6) **Hypercalcaemia**→ partially antagonize the action of L.A.

7) **Hyperkalaemia** →enhances the effect.

8) **Tachyphylaxis** (repeated injection result in loss of effectiveness due to extracellular acidosis).

9) **Fiber position** in the nerve bundle: in large nerve trunks, **motor nerves** are located in the outer portion so they are the **first** to be exposed to the drug when given by injection into the surrounding tissues.

Some L.A:

Benzocaine

(Ethyle 4-aminobenzoate)

- ✓ Lack terminal hydrophilic amino group.
- ✓ Only slightly soluble in water.so it is useless for injection . it is applied topically assurface anesthetic in the form of ointment or powder .
- ✓ Slowly absorbed.
- ✓ Used only for surface anesthesia.

Mepivacaine

- Not effective as a topical anesthetic.

Bupivacaine:

- More cardiotoxic than other L.A drugs.

Procaine:

- Metabolized by psuedocholinesterase.
- Onset of action is slow.
- Duration of action is short.
- Potency is less.
- Not effective as surface anesthetic.

Lignocaine:

(lidocaine,xylocaine)

- Amide.
- Metabolized by hepatic microsomal enzymes.
- Onset of action is rapid.
- Duration of action is intermediate.
- Potency is more.
- Effective surface anesthetic.

Adrenaline:

- Catecholamine.
- Stimulate α_1, α_2, β_1, β_2 receptors.
- Causes **vasoconstriction** by stimulating α1 receptors:
  ↓ Absorption, ↑ duration, ↓ dose, ↓ side effects.
- Precaution: end arteries, so should not be used in **fingers**, **toes**, **ear**, **penis**.

☑مقارنة مع محاضرة السنة الماضية تعتبر اقصر شوي لكن كافية بإذن المولى

☑المحاضرة ابد مو ناقصه عن سلايدات الدكتورة يعني لو تقارنون النقط والفواصل بتلقوانها نفسها

المحاضرة تعتبر محاضرة من ضمن المنهج يعني تندرس، مو خاصه بالاب بس

وكل عام وانتم بالف خير وصحه وسلامه ♥

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