**Local Anesthesia**

**Lec. # 2**

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🌢 LA raise threshold of action potential and stop it

🌢 LA receptor found in Na+ channel

**✓Today lecture is about LA pharmacology .**

*Outline :-*

✓-pharmacokintics

✓-absorption

✓-systemic action of LA

**PHARMACOKINTICS**

Is the study of the movement of the drug in the body which involve :absorption (up take ) , distribution , metabolism ,excretion

🖐 LA is dividing in to 2 big categories:-

1. Ester

2. Amide (most used nowadays)

🌢 the most common use LA in dentistry = procaine (Novocain )

🌢 Others common : lidocain, articain, mepivacin, bupivacine, prilocaine

🌢cocaine, very addictive

🌢one of the draw backs of ester LA is that they are very rapidly hydrolysable by pseudocholinesterase

🡪 what is the difference btw LA and all other drug from pharmacokinetics point of view ??

LA start to work as soon as you deposit it in the tissue ,other drugs like antibiotics start to work after they reach the tissue ; they need to be absorbed then distributed to start the effect unlike LA which if absorbed and distributed will lose its effect .

**🖐 ABSORPTION**

✓ It depend on method of administration

✓method of administration :- 1.Topical 2.injection (subcutaneous, IM, IV) 3. Oral

*(IN DENTISTRY IT’S SUBCOTANOUS)*

**A: INJECTION :**

✓Absorption depend on

1. vascularity of site (as it increase the absorption will increase also)

2. vasoactivity of the agent

✓Usually LA agent is vasodilator, except cocaine (addictive drug )

✓Vasodilator will increase absorption

✓ you have to ask if the pt’s has used any recreational drug in past 24 hours (especially cocaine ) ,because he will have a high blood pressure and if by accident you give him LA (i.v) or excessive LA with vasoconstrictor this will lead to hypertensive crisis

✓most potent vasodilator among LA = procaine , it can be used as vasodilator when an accidental injection of vasoconstrictor happen in certain body part like finger ,toe , …

✓ How we can counter the effect of vasodilatation in LA ? by using vasoconstrictor

**B:ORALLY**

✓We don’t use them because:

1. Very poorly absorbed except, cocaine

2. High hepatic first pass effect (70% metabolism in liver)

🌢 almost all are used as antiarrhythmic drug in emergency situation to control cardiac arrhythmias

**C: TOPICAL**

*1. Skin*

✓Poorly absorbed when applied on intact skin, but in case of non –intact skin ex. Sunburn it is well absorbed

✓also if it made in mixture with material that facilitate the absorption, it could be absorb through intact skin

2. Muocus membrane

🌢 it’s highly absorbed

🌢 absorption is variable : 1.trachea is 100% absorption 2. Pharyngeal 3.esophageal

**🖐DISTRIBUTION**

✓once it’s in the blood , it’s distributed to the all organ in the body . highly perfuse organ will get the highest level of LA

✓ organ with the highest perfusion are : 1. Kidney 2.GIT 3.skeletal muscles 4. Brain

✓ toxic effect of LA obviously depend on the plasma concentration (increase conc.= increase toxic effect)

✓plasma conc. Depend on: 1. Rate of absorption 2. Rate of distribution 3.rate of elimination

✓all the LA cross the BBB ,placenta and they are found in the blood of fetus

🌢 *half life* :- the time need to get rid of half the conc.

🌢 we need 5-6 half life to get rid of 97-98% of any drug

**🖐METABOLISM**

**ESTER**

✓ Metabolized mainly in the plasma by pseudocholinesterase (which is also involve in the metabolism of Ach – neurotransmitters )

✓pt’s who have deficiency in this enzyme ,the LA will accumulate in his blood ,so they are more prone to the toxic effect of ester LA

✓IT’S have relative contraindication, especially when it is given with other muscle relaxant like succinylcholine which also depend on this enzyme for metabolism

✓ one of the metabolite of ester LA is PABA (an allergic agent for some ppl)

**AMID**

🌢 metabolism in the liver

🌢 liver : lidocaine ,methodicain , ethodicain ,bupivicaine

🌢lung : prilocaine

🌢 blood and liver : articaine (have ring like ester ,so some of them can be metabolized in the blood )

**🖐EXCERETION**

✓primary in the kidney

✓some excreted without change and other break down in to metabolites

✓relative contraindication in pt’s with renal insufficiency (limit the dose)

✓usually a patient with CVD , we give him up to 2 carpules of LA because Of the amount of vasoconstrictor

✓healthy pt’s can be give up to 8-9 carpules ,but what we worry about is the accumulation of LA agent .

✓usually what limit number of cartilages at first is the vasoconstrictor but later on is the LA

✓usually the LA blocks the action potential in all excitable membrane ,that’s why we expect the most effects of LA is on CNS and muscle (cardiac and smooth muscle that control blood vessels ).so , most toxic effect of LA IS on CNS and CVS .

***🡪Effect of LA in CNS:***

♥ Low therapeutic non –toxic doses ,no significant effect but once you cross certain level of LA conc. In the plasma the effect on CNS start to appear

♥ Initial effect of LA in the CNS is depressive ,because it limit Action Potential threshold. As you increase the dose you turn it into convulsive phase

(Depression >>>convulsion >>>more depression )

***¥ Anticonvulsive properties* :**

✓in certain conc. LA have depressive effect ,so it has some anticonvulsive properties and has been used to terminate or decrease the duration of seizures (grand mal or petit mal seizures )

✓ Lidocain , procain ,mepivecain have been used

✓how do they work ? pt’s with seizures have centers in the cortex of brain that are hyper excited , LA depress this center

✓ low blood level 0.5 -4 microgram /ml (anti convulsion level )

✓ as the dose increase ( more than 7 microgram /ml ) we enter in other zone which is pre-convulsion sign and symptom

✓ and other increase we enter in tonic – clonic convulsion phase .

✓in pre – convulsive phase LA cause sign and symptoms related to CNS except **numbness of tongue** (this is due to direct action of LA ) because of high level of LA in the blood that reach this tissue and cause direct action

✓ As the conc. goes higher we go to the convulsive phase ,usually seizures is self limiting because the activity of the heart is not affected ,so the circulation is continuous and the re-distribution and elimination of LA is keeping on ,as a result the conc. will become less

✓Seizures activity itself causes metabolite acidosis this result in higher percentage of LA free base in the blood , which lead to another seizure phase .

✓As conclusion, there is 2 factors that cause this fluctuation btw convulsive phase and recover phase :

(انه المريض بدخل في مرحلة convulsion وبرجع يطلع منها )

1. The circulation is not interrupted and as time goes ,the conc. Of LA become less and stop the seizures phase .

2. As the blood flow to the brain , the metabolic acidosis occur and this cause potentiation to the convulsive phase a gain .

*(LA conc. Goes up and down )*

✓Again, the most imp. Effect of LA in the CNS

1. Depressive

2. Convulsive

3. Depression to the CNS

4. Analgesic effect

Procaine has been shown it increase pain threshold, it was been used in the management of arthiritis and the painful condition (chronic pain ) .put ,it has narrow safety margin so you might put the pnt in the risk of the toxic effect of LA and that’s why they don’t use it anymore .

5. Mod elevation

✓cocaine is very effective, causes uphoria and improves the mood ,but the disadvantage Is that it’s very addictive

✓the father of medical cocaine was very addictive

✓procaine , in some people they believe it improve the mood but this is not proven yet

**🡪Effect of LA on CVS:**

♥ CVS is more resistant , need higher level of LA to be affected

♥ Usually the effect is on :

1. Myocardium

2.vasculuture

***Myocardium:***

🌢 the main feature it causes myocardium depression that’s why LA is used as anti-arrhythmic drug

🌢What does the anti-arrhythmic affect the myocardium?

1. Excitability 2.conduction rate 3. Contraction force

🌢most important procaine and lidocaine (IV) are usually given to the pt’s with ACLS ( advanced cardiac life support ) especially those with dangerous arrhythmias

🌢 As the levels goes up we have 1. Reduced contractility 2.reduced cardiac output which ends up with circulatory collapse ( decrease Cardiac Output lead to hypotension in addition to the effect of LA in vascular (dilution)

***Vasculutre:***

✓all have vasodilator effect expect cocaine so, they lead to hypotension as they start from toxic dose

***🡪 Effect of LA locally :***

local tissue toxicity in the skeletal muscles , in general any deposition of fluid with the muscle tissue could cause tissue damage and tissue trauma which take awhile but usually its reversible in 2 weeks (this can occur when you mistake when giving the ID in medial pterygoid especially ) we can manage this by warm compress and muscle relaxant.

***🡪effect on respiratory system :***

\* they relax bronchial smooth muscle (bronchial dilation) , because it have depressive effect .

\* in any high toxic dose we have respiratory arrests due to the effect on CNS

***🡪effect on neuromuscular tissue :***

✓it’s very slight ,but it’s significant if it’s in conjunction with other muscle relaxant (ex. Succinylcholine ;depolarizing or non-depolarizing muscle relaxants )

**¥drug interaction:**

🌢 when you administer LA in pt’s who taken CNS depressant (like , benzodiazpam , barbiturates ) . this will potentiate the effect of CNS depressant

🌢 procaine + succinylcholine in pt’s who have cholinesterase deficiency and pt’s who have taken barbiturates which induce hepatic metabolism so we have reduced effect on LA

🌢 Malignant hyperthermia, it was believed that it’s caused by amid LA but there have never been a report of malignant hyperthermia

*REFERANCE: handbook of LA , 6th edition*

NO MATTER HOW TOU FEEL, GET UP, DRESS UP, SHOW UP AND NEVER GIVE UP.

Best Wishes All ^^

Khitam Hamad ☺