Local Anesthetic Drugs

Pharmacokinetics of local anesthetics

This lecture will be talking about local anesthetic drugs that are found in the book and SHOULD be memorized by heart.

Anesthetic drugs are classified as we all know into:

1- Ester Group: it is recently not much clinically used as it causes allergy but in very small category. Some patients have allergy from the amide anesthetics and in these cases we refer to the ester group.
2- Amide Group.

If the patient has allergy to both ester and amide anesthetics, they should undergo General Anesthesia. Example on that, a patient in the 80s who had to extract her tooth and had allergy to both ester and amide anesthetics drugs -without the knowledge of the dentist-, was given local anesthesia and went into anaphylactic shock. Anaphylactic shock in the first time is manageable and is not severe and starts gradual but if it comes in the second time it might be very quick and fatal! This happens due to antigen reaction that was recognized by the body in the previous attack. We should always be careful.

As we know, general anesthesia is not given until a written consent is taken from the patient. Written consents should involve the risk factors such as dying on the dental chair during procedure, time of exposure to anesthesia, the amount will be given and other instructions post-surgical.

Anesthetic agents exert pharmacological action on blood vessels. With the exception of cocaine that causes vasoconstriction, all other anesthetic drugs are vasodilators. Vasodilation decreases the duration of action. The blood flow will be high. This causes more uptake of the drug and thus less duration. Being that Procaine is the most potent vasodilator and the least one is Mepvicaine meaning that it has a longest duration of action.

Metabolism (Biotransformation):

- **Amide local anesthetics**: they are hydrolyzed in the liver. We should be careful with patients who have liver diseases as they cannot bio transform those drugs.
- **Ester local anesthetics**: they are hydrolyzed in the plasma by pseudo cholinesterase.
The most important consideration in local anesthetics is their Toxicity. It depends on the rate of absorption from the injection site to the blood stream until it is metabolized. Toxicity depends on the dose and the metabolism. As the dose increases, the toxicity increases. And as the metabolism increases, the toxicity decreases.

- Chloroprocaine: it is hydrolyzed very quickly and thus has the least toxicity.
- Tetracaine: has the greatest toxicity (16 times slower than Chloroprocaine).

The duration of pulpal and soft tissue anesthesia:
- **Pulpal**: gives the duration of the field work and fades quickly 1-2 hours after procedure.
- **Soft tissue**: it stays longer. The patients still feel their lips and we have to make sure to tell them that they don’t bite their lips.

Factors affecting depth and duration of pulpal and soft tissue anesthesia:
- **Accuracy in deposition**: it is where we place the local anesthetic drug. ID block is the most difficult to give.
- **Status of tissues**: it the tissue is:
  - Normal: normal uptake of anesthesia.
  - Infected: if there is hyperactive area or acidic media that will delay the reach of anesthesia, the onset of action will be longer.
- **Anatomical variations**: We can give ID block accurately but the patient may have some variation that still cause pain during procedure. Such patients may have two ID nerves.
- **Type of injection**.
- **Protein binding**.
- **Lipid solubility**.
- **Individual response to drugs**: Bell-shaped curve.

**Bell-Shaped curve**:

It represents the area of our procedure. It starts with a little increase in the amount of anesthetic drug after 2-3 min after injection until reaching the top of the curve that represents the

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maximum amount and then it starts to drop gradually and that is the area where the action of local anesthetic fades away due to metabolism in the blood stream and each group is hydrolyzed in different ways as we know.

A) Ester Local Anesthesia: they are metabolized in the plasma.

1) Procaine (novocaine):
- It is the first synthetic injectable local anesthetic used.
- It is hydrolyzed into its major metabolite PABA (ParaAminoBenzoic Acid). And PABA is excreted unchanged in the urine. The allergic reaction towards esters is not due to the parent compound (Procaine) itself. It is due to the presence of PABA.
- 1:3000 people have the Atypical form of pseudo cholinesterase causing the inability to hydrolyze ester LA and other chemically-related drugs such as Succinyl Choline that has a similar structure to ester group.

Succinyl choline is a short-acting muscle relaxant that is metabolized in the same way as esters are. It is used in major surgery and general anesthesia. So patients will take longer time to recover from anesthesia due to the competition of ester group and Succinyl choline to metabolism. This has dangerous effect on the patient as the local anesthetic will stay longer and will have the risk of being toxic.

Succinyl choline produces apnea (suspension of external breathing) that lasts for 2-3 minutes. And this is our fear if Succinyl choline increases in the blood due to the inability of metabolism in the recommended rate. We care about the amount of oxygen reaching the brain as not to decreases causing apnea.

People with Atypical pseudo cholinesterase that is a hereditary condition are unable to hydrolyze Succinyl and thus apnea is prolonged.
- Excreted in the urine
- Potency= 1
- Toxicity= 1
- Effective dental concentration is present in 2-4% with adrenaline 1:80,000
- Long onset of action= 10 min (you should wait 10 min to start your procedure)
- Used for patients with proven allergy for amide groups
- Used to treat arteriospasm as it is an excellent vasodilator. It is specifically used in medical emergency cases.
- Has allergy effect higher than amide
- Pulpal anesthesia: 5 min (very short)
- Soft tissue anesthesia: 30 min
- Maximum dose = 60 mg/Kg

2) **Propoxycaine:**
- It has rapid onset = 2-3 min
- Potency = 7
- Toxicity = 7 (very toxic)
- It is best given in combination with Procaine that will give a great duration of action (modifies the potency from 1 into 7) and to patients with amide allergy.

B) **Amide LA: they are metabolized in the liver.**

Examples on amide LA are Lidocaine, Mepvicaine, Articaine, Etidocaine, buvipcaine, and prilocaine.

Excretion: small percentage is excreted unchanged in the kidney.

1) **Ligocaine: (lidocaine, xylocaine)**
- The most commonly used agent (the Father Agent)
- Metabolized in the liver
- Excreted via the kidney (80% as metabolites and 10% unchanged)
- Potency = 2
- Toxicity = 2
- Most common vasodilator (less than procaine and more than prilocaine or Mepvicaine)
- Possess more rapid onset (2-3 min). This makes it a preferable agent to be used.
- Non-existent allergy (except in very minor cases)
- Produces more profound anesthesia, longer duration of action
- Has a half-life = 1.6 hours
- Forms of administration:
  - The most common injectable form found
  - If found topical (4%), it is used for children before the injectable form
  - Can be found as sprays (10%), it is used in endoscopy but has many disadvantages as it stimulates cough receptors
  - It can be found as gel (2%). Used only on dry surfaces not preferred orally
• And can be found as ointment (5%). Used in moist surfaces as Oral Cavity

  - Available in different formulations:
  • 2% without vasoconstrictor (it has a very limited pulpal anesthesia)
    
    It is used in patients with:
    1- Heart problems
    2- Hypertension
    3- Hyperthyroidism only in cases with advanced levels of thyrotoxicosis. We don’t want to increase their pressure because these patients already come to clinic feeling anxiety and fear
  • 2% with vasoconstrictor (Epinephrine 1:50,000)
  • 2% with vasoconstrictor (Epinephrine 1:80,000)
    
    - Pulpal anesthesia: 45-60 min.
    - Soft tissues anesthesia: 3-5 hours.
    - Concentration given in 2% plain Lidocaine = 36 mg.
    - Maximum dose without vasoconstrictor= 4.4 mg/Kg = 8 cartridges –providing patient is healthy-. Doses should not be given haphazardly!
  ** If 10 cartridges are given and the patient still didn’t response, abort the patient and don’t give more doses to prevent going into toxicity level.

2) **Prilocaine (Citanest), (a very powerful substitute for Lidocaine):**

  - Potency= 2
  - Toxicity= 1 (40% less than lidocaine)
  - Metabolized in the liver to OrthoToluidine. It is important as it is transformed into methemoglobinemia. This metabolite leads to cyanosis. And thus it is contraindicated with people having sickle cell anemia.
  - It has some biotransformation in the lung (a specific feature)
  - Excreted in the urine
  - Plain solution= 4%
  - Vasoconstrictor= 3% Prilocaine + 0.03 IU/ml Felypressin. –IU: International Unit- Felypressin is given to patients with hypertension as it doesn’t increases the blood pressure.
  
  This combination is given to provide similar action to lidocaine.

  Felypressin has systemic factors:
  *provides coronary artery vasoconstriction
*has oxytocic action on uterus
- It is mainly used when adrenaline is best avoided.
- Slightly slower onset than lidocaine (4 min)
- Maximum recommended dose = 4% = 72 mg = 6 mg/Kg = 6 cartridges
- Pulpal anesthesia: 60 min
- Soft tissue: 3-5 hours

3) Mepivicaine:
- Potency = 2
- Toxicity = 2
- Metabolized in liver
- Excreted in kidney
- Available as 3% plain solution
- 2% with adrenaline 1:80,000
- Rapid onset = 1-2 min
- The least vasodilator: this will increase the duration of action
- Plain longer pulpal anesthesia: 30 min
- Plain Soft tissue anesthesia: 2-3 hours
- Recommended for:
  X: Pediatrics (only plain, we don’t like using vasoconstrictor)
  X: Geriatrics
  X: Dental procedure not requiring long pulpal anesthesia
- 4.4 mg/Kg = 4.5 cartridges, if adult dose=2.2 ml

➢ In our clinics, we use 1.8 ml adult does

4) Articaine (Carticaine):
- Potency = 1.5 of lidocaine and 1.9 of procaine
- It is a vasodilator (similar to that of lidocaine)
- Onset = 1-2 min
- It has a lipophilic part that is called the Thiophene Ring that can be transformed into methemoglobinemia that gives it the contraindication to use in patients with sickle-cell anemia
- It is contraindicated in patients with sulfur allergy.
WE SHOULD ALWAYS ASK THE PATIENT ABOUT HISTORY OF ALLERGY

5) **Bupicaine (Marcaine):**
- Long duration of action
- Potency= 4 times of lidocaine and prilocaine. This means increases toxicity as well.
- Toxicity= 4 times more than lidocaine
- Long onset of action= 6-10 min
- It has a half-life= 2.7 hours
- Metabolized in the liver
- Excreted in the kidney
- 0.75% with adrenaline in 1:200,000
- 0.5% with adrenaline in 1:200,000
- Maximum dose is the least= 1.3 mg/Kg = 10 cartridges
- Mainly used in Oral Surgery: in long dental procedure (90 min pulpal anesthesia)
- Not recommended for young or disabled patients

6) **Etidocaine:**
- Potency= 4 times that of lidocaine
- Toxicity= 2-4 that of lidocaine and thus should be comparable
- Onset of action= 1-3 min
- Long acting local anesthetic drug

- Two long duration local anesthetic drugs are Etidocaine and Bupicaine.

C) **Topical Anesthesia:**
- Longer duration of action as it has to penetrate intact mucus membranes
- Limited depth= 2-3 mm of surface
- The most commonly used formulas is the EMLA preparation
- Most common used orally is Lidocaine (Benzocaine)
- Not effective on palatal surfaces or attached gingiva

*Wishing you all the best of luck ^_^*

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