***-Clinical Action of specific Agents –***

**Local Anesthesia**   
Sheet no.5 - 1/11/2015



Doctor : Omar karadsheh

Written by : saja Al- garalleh & corrected by : Aseel Al-Majali .

ـــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــــ

Local anesthetic Agents are classified to :   
  
A\* ( according to their chemical linkage ).

1. **Ester-linked LA agents :**   
-firstly discovered .  
- are really hydrolyzed in aqueous solutions.  
- Example : Procaine .  
2. **Amide-linked LA agents :  
-** are relatively resistant to hydrolysis.   
- Examples : Lidocaine , Articaine “lastly discovered” .   
  
B\* ( according to their duration ) :

1. **Short duration** **pulpal anesthesia** :  
-about 30 min , used in pediatric dentistry mainly .   
*Mepivcaine HCL 3%* by infiltration *.  
Prilocaine HCL 4%* by infiltration .  
2.**Intermediate duration pulpal anesthesia** :   
- about 60 min   
*Articaine HCL 4% + epinephrine 1:100000  
Lidocaine HCL 2% + epinephrine 1:100000  
Prilocaine HCL 4% + epinephrine 1:200000***3. Long duration pulpal anesthesia :**- 90 min or more .  
*Bupivacaine HCL 0.5% + epinephrine 1:200000* By nerve block   
\* indicated when the ptn needs RCT , full mouth implants or full mouth restorations   
 **\*\* Depth and duration of LA agents** :

- Duration of pulpal ( hard tissue ) and soft tissue anesthesia for each drug affected by many factors :

1**. individual response to the drug** ( the bell-shaped curve) :   
-variation in individual response to a drug is common and expected “ most ptns will respond in a predictable manner to drug’s action for (40 – 60 min) on average ; however , some ptns will have shorter or longer duration of anesthesia “   
- people are calssified according to their respond to LA agents to :

*\* normo-responders : 70%  
\* hyper-responder : 17%  
\* hypo-responder : 15%*

2. **Accuracy in deposition of the LA agents**.

3. **The status of the tissues into which a LA is deposit** :   
- normal healthy tissue : good duration of LA   
- area of inflammation or infection (acute\chronic) : usually decrease depth and duration of LA.  
- Increased vascularity of the site of drug deposition results in more rapid absorption of LA and less duration .   
\*\* Buffered LA promise to overcome the negative effect of inflammation and infection .

4. **Anatomical variations** :

- Infiltration in maxilla will not be effective in case the ptn has short maxilla or the zygomatic arch close to the root of 6 .   
- palatal root of maxillary molars may not be adequate anesthetized even in the presence of normal thickness when the root flares greatly towards midline of the palate

- block in mandible will not be effective in increased thickness of cortical plate of bone , the width of ramus and the height of the mandibular foramen will affect the depth of LA agents .   
   
5. **Type of injection ( infiltration \ nerve block) .**

**\* Maximum Doses of LA agents :**   
-doses of LA drugs are presented in terms of mg per unit of body weight; ( mg/kg ) or (mg/pound) .  
- Administration of maximum dose based on body weight produces a local anesthetic blood level below usual threshold for an overdose ( toxic).   
-maximum doses are unlikely to be reached in most patients , especially adults of normal body weight for most dental procedures .  
- some groups of patients represent potentially increased risk from high local anesthetic blood levels : “ light body weight children or debilitated elderly individuals” .   
  
- changes in liver function , plasma protein binding , blood volume and other important physiology functions influence the manner in which LA agents are distributed and transformed in the body : net result of these changes is increased plasma blood levels of drug associated with increase relative risk of overdose reaction .  
  
***- symptoms of overdose ( toxicity ) of LA agents :***  
CNS over stimulation ( seizures , tremor ) followed by depression ( Drowsiness ) .

- Toxicity affected by dose “amount of LA agent” and Time of administration “ 3 hrs better than a short time” .   
  
***\*\* calculation of maximum dose ( MRD) : “calculate how many cartridge we can give the patient “***for Articaine 4% ??!   
- how mg in one cartridge :  
4\100 \* 1000 = 40 mg/ml   
volume of one cartridge = 1.8 ml   
so ; 1.8 \* 40 = 72 mg / cartridge   
MRD for articaine and lidocaine = weight of the body \* **7mg/kg** .  
number of cartridge = MRD / how mg in one cartridge .  
**Examples :**  
>> **40 years old healthy male ptn , 90 kg**LA= articaine 4% HCL + Epinephrine 1:200000 .  
🡺 firstly calculate how mg in 1 cartridge ?  
4/100 \* 1000 = 40 mg\ml   
40\* 1.8 = **72 mg /cartridge** .   
🡺 Maximum dose of Articaine in mg : 7mg/kg \* body weight  
 7mg/kg \* 90 = **630 mg  
🡺how many cartridges we can give the ptn ? = (630 mg) / (72mg/cartridge)   
 = 9 cartridges .**

**>> 6 years old healthy child , 20 kg .**

LA= Mepivacaine 3% HCL , no vasoconstrictor . (MRD = 6.6 \*body weight) .  
🡺 3\100 \* 1000 = 30 mg\ml   
30 \* 1.8 = 54 mg/cartridge .   
🡺MRD= 6.6 \* 20   
 = 132 mg   
🡺 # of cartridge = (132 mg )/ (54mg/cartridge)   
 = 2.5 cartridge  
  
\*\* if the ptn was given more than one cartridge and he/she is not anesthetized ( anesthesia is not adequate ) and another LA agent was also given ! :  
MRD must be calculated for each LA agent , MRD shouldn’t exceed the lower concentration from the tow different types . then substrate how much mg’s does the ptn receive from lowest MRD value to calculate how much cartridge the ptn can receive from the second LA agent .

**Example :**  
>> female ptn , 45 kg , healthy   
received 2 cartridges of LA = *mepivacaine 2% + levonodefrin 1:200000*

🡺 (2\100\*1000) \* 1.8 = 36 mg/ cartridge   
🡺 MRD = 6.6 \* 45   
 = 297 mg   
🡺 ptn given 2 cartridges ; ( 2\* 36 = 72 mg )   
but Anesthesia is inadequate ! , *so Atricaine 4% + epinephrine 1:100000* was given to the same ptn .  
how much Articaine can this patient receive?   
Articaine 4%= (4/100 \* 1000) \*1.8   
 = 72 mg/cartridge .   
🡺 MRD= 7mg/kg \* 45   
 = 315 mg   
\*\* the dose of both LA agents shouldn’t exceed the lower value of the tow calculated doses which is 279 mg .   
- ptn already recived 72 mg .   
🡺 297 -72 = 225 mg ( how much Articaine can the ptn tolerate before reaching the max dose ) .   
🡺 num of cartridge = 225 mg / ( 72 mg/cartridge)   
 = 3 cartridges .

**A\* Ester-type LA agents :   
  
Procaine :  
  
-**metabolism : hydrolyzed rapidly in plasma by pseudocholinestrase enzyme .   
- Execration : more than 2% uncharged in the urine .  
- potency =1 , Toxicity = 1 .  
- The greatest vasodilator of all currently used LA agents .  
- onset of action = 6-10 min ( we mix it with propoxyine ) .  
- Effective dental concentration = 2% to 4 % .  
- Indication: ptn with vasoconstriction in blood vessels .  
-Not clinically used as topical anesthesia .   
  
**Propoxycaine :**  
- potency = 7-8 , Toxicity = 7-8 .  
- metabolism ; hydrolyzed in both plasma and liver .  
- Excretion : Kidney .  
- onset of action : rapid ( 2-3 min ) .   
-Effective dental dose = .4%  
-Not clinically used as topical anesthesia.  
\*\* propoxycaine was combined with procaine in solutions to provide more rapid onset and more profound and longer-lasting anesthesia than could obtain with procaine alone . --propoxycaine isn’t available alone because of it’s higher toxicity ( 7-8 ) .  
  
 **B\* Amide –Type LA agents :**

**Lidocaine HCL :**- Metabolism : in the liver .  
- Excretion : in the kidney .  
- potency = 2 , Toxicity = 2 .  
- strong vasodilator .  
- onset of action = 3-5 min ( rapid) .  
-Effective Dental dose= 2 %   
- used as topical anesthesia ( 5%) .  
-safe during injection .  
- pregnancy classification = B

|  |  |  |  |
| --- | --- | --- | --- |
| % | Vasocontictor | Duration ( pulpal ) | Duration (soft tissues) |
| 2 | Epi 1:50000 | 60 | 180-300 |
| 2 | Epi 1:100000 | 60 | 180-300 |

-

-lidocaine HCL has 2 formulations with epinephrine 1:50000 , 1:100000 . Both are the same duration on pulpal and soft tissues , the difference between them is the haemostatic action for the 1:50000 concentration 🡺 leads to decrease bleeding in the area of drug administration . caused by alpha stimulating action of epinephrine.

- After LA administration there will be rebound vasodilatation :  
Epi stimulate both alpha and beta receptors , firstly cause vasoconstriction by stimulating of alpha receptor then the core of Epi decrease , so beta receptors will be stimulated .   
( after stop working , bleeding increase ) ! .

**Mepivacaine HCL :**- Metabolism : in the liver .  
- Excretion : in the kidney .  
- potency = 2 , Toxicity = 1.5-2 .  
-not used as topical anesthesia .  
- onset of action = 3-5 min ( rapid) .  
-Effective Dental dose= 3 % without vasoconstrictor.   
 2% with vasoconstrictor . .  
- pregnancy classification = C   
-milder vasodilation property of mepivacaine leads to longer duration of pulpal anesthesia than observed with other LA when administered without vasoconstrictor .

|  |  |  |  |
| --- | --- | --- | --- |
| % | Vasocontictor | Duration ( pulpal ) | Duration (soft tissues) |
| 3 | No vasoconstrictor | 20-40 min | 2-3 hours |
| 2 | With vasoconstrictor | 60 min | 3-5 hours |

-

**Prilocaine HCL :**- Metabolism : hydrolyzed by hepatic amidase into orthotoluidine which can induce formation of methemoglobin ( producing methemoglobinemia ) that reduces blood’s oxygen carrying capacity leading to cyanosis.   
 - Excretion : in the kidney .  
- potency = 2 , Toxicity = 1 ( 40% less toxic than lidocaine ) ..  
- onset of action =slower than lidocaine .  
- pregnancy classification = B.   
  
  
**Articaine HCL :**- Hybrid molecule have both Ester and Amide characteristics .   
- Excretion : in the kidney .  
- potency = 1.5 times of lidocaine , Toxicity = 1.9 times of Procaine .  
- onset of action = Articaine 1:200000 🡺 infiltration ( 1-2 min ) , block ( 2-3 min ).  
 Articaine 1:100000 🡺 infiltration ( 2-3 min ) , block ( 2-2.5 min ).   
- not used as topical anesthesia .  
- pregnancy classification = C .   
  
  
**Bupivacaine HCL :**- Metabolism : in the liver .  
- Excretion : in the kidney .  
- potency = 4 times of lidocaine and Prilocaine , Toxicity = more than 4 times of lidocaine .  
-not used as topical anesthesia .  
- onset of action = 6-10 min ( slow ) .  
- pregnancy classification = C .   
- used mainly in lengthy dental procedures for which pulpal anesthesia in excess of 90 min .  
|- management of post operative pain (surgical , post implant )   
  
\*\****FDA Pregnancy categories :****-category A :* no evidence of risk in first trimester .   
*-category B :* animal reproduction studies have failed to demonstrate a risk to fetus and no risk in pregnant women .   
  
*-category C :*  animal reproduction studies have shown an adverse effect on fetus and no adequate and well controlled studies in humans .   
*-category D :* positive evidence of human fetal risk .  
*-category X:* studies in animals or humans have demonstrate fetal abnormalities , positive evidence of human fetal risk .   
  
 \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*  
  
\*\***Topical Anesthesia:**- conventional topical anesthesia are unable to penetrate intact skin but do diffuse through any mucous membrane .   
- concentration of LA applied topically is greater than that of the same LA administered by injection .  
- topical anesthesia formulation don’t contain vasoconstrictor .

- poor solubility in water .  
- when concentration increases , the effectiveness increases but can lesd to toxicity .  
- poor absorption into CVS .  
- as a general rule , topical anesthesia are effective only on surface tissue ( 2-3 mm ) .   
- Benzocaine , Lidocaine , Tetracaine .   
- spray not commonly used , because it’s widely distributed to large area of tissue .   
  
\*\***Cocaine :**- the only LA agent used as a vasoconstrictor ( no bleeding ) .  
-onset of action quite rapid ( 1 min ) , duration as long as 2 hours .   
- used exclusively via topical application , injection is contraindicated because of toxicity .  
- absorbed rapidly but eliminate slowly .  
  
\*\***ELMA : ( Eutectic Mixture of local anesthesia )**- ELMA cream : ( lidocaine 2.5% + prilocaine 2.5 % )   
- placed on the skin for an hour until penetrate the skin “ must apply 1 hour before the procedure , reach maximum effect after 2-3 hours ) .   
- mainly used as topical anesthesia on skin in case of ulcers .  
- not recommended to use on mucous membrane ( in the oral cavity )   
- supplied as : 5g or 30 g tube / ELMA disk(white , round cellulose disc ) .   
  
 ***\*\*Brand names of lidocaine 🡺 lingnospan , octocaine , xylocaine .   
 Articaine 🡺 orubloc , lorcaine .***

**BEST OF LUCK ☺ .**