Local Anesthetic drugs

Pharmacology
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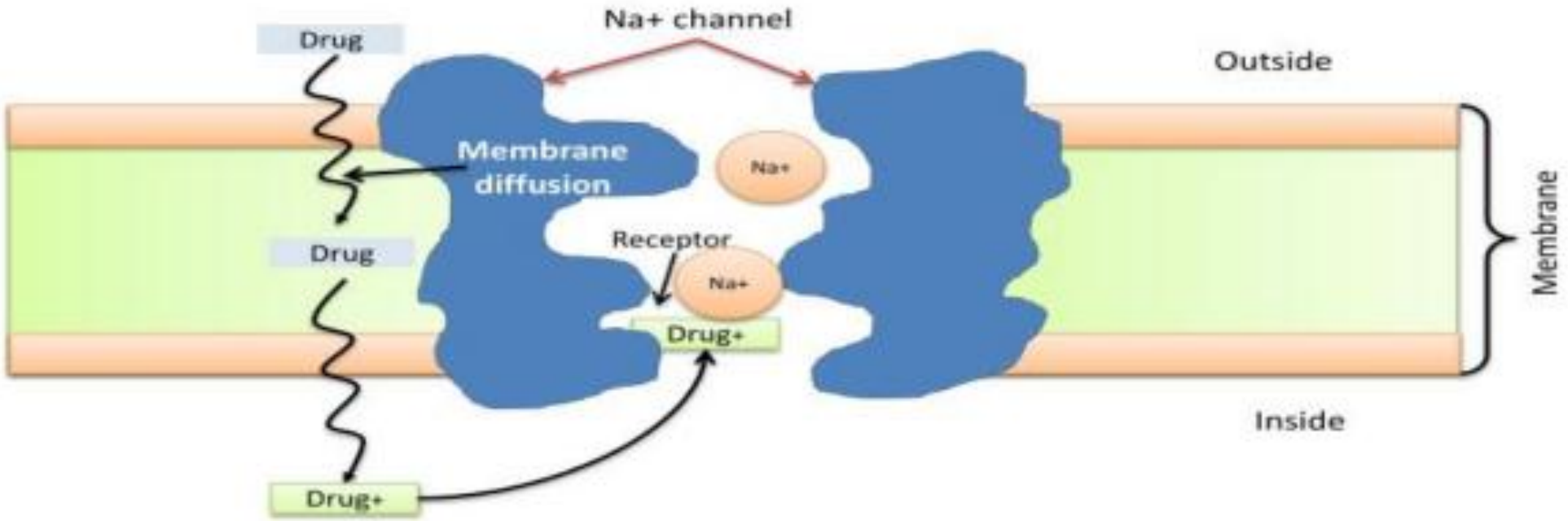
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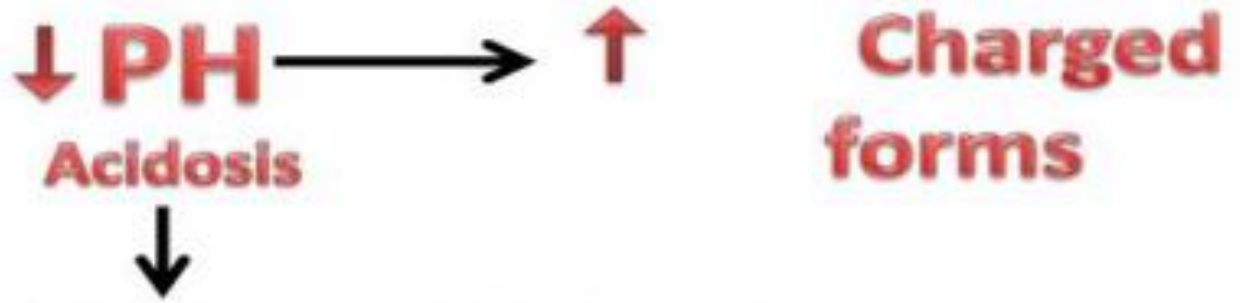


Acidosis such as caused by inflammation at a wound partly reduces the action of LAs. This is partly because most of the anesthetic is ionized and therefore unable to cross the cell membrane.

Local anesthetic drugs (agents)

- Local anesthetic are drug which upon topical application or local injection cause reversible loss of sensory perception , especially of pain in a restricted area of the body , it provides pain control during dental therapy , it interrupts propagation of impulse preventing it from reaching the brain.

Uses of Local anesthetics

- **Local anesthetics uses include:**
- **Surface anesthesia** is the application of an local anesthetic spray, solution, or cream to the skin or a mucous membrane; the effect is short lasting and is limited to the area of contact.
- **Infiltration anesthesia** is infiltration of local anesthetic into the tissue to be anesthetized; surface and infiltration anesthesia are collectively topical anesthesia
- **Field block** is subcutaneous injection of an local anesthetic in an area bordering on the field to be anesthetized.
- **Peripheral nerve block** is injection of local anesthetic in the vicinity of a peripheral nerve to anesthetize that nerve's area of innervation.

Uses of Local anesthetics. cont

- **Plexus anesthesia** is injection of local anesthetic in the vicinity of a nerve plexus, often inside a tissue compartment that limits the diffusion of the drug away from the intended site of action. The anesthetic effect extends to the innervation areas of several or all nerves stemming from the plexus.

- **Epidural anesthesia** is an local anesthetic injected into the epidural space, where it acts primarily on the spinal nerve roots; depending on the site of injection and the volume injected, the anesthetized area varies from limited areas of the abdomen or chest to large regions of the body.

- **Spinal anesthesia** is an local anesthetic injected into the cerebrospinal fluid, usually at the lumbar spine (in the lower back), where it acts on spinal nerve roots and part of the spinal cord; the resulting anesthesia usually extends from the legs to the abdomen or chest.

Uses of Local anesthetics. cont

- **Intravenous regional anesthesia (Bier's block)** is when blood circulation of a limb is interrupted using a tourniquet (a device similar to a blood-pressure cuff), then a large volume of local anesthetic is injected into a peripheral vein. The drug fills the limb's venous system and diffuses into tissues, where peripheral nerves and nerve endings are anesthetized. The anesthetic effect is limited to the area that is excluded from blood circulation and resolves quickly once circulation is restored.

- **Local anesthesia** of body cavities includes intrapleural anesthesia and intra-articular anesthesia.

- **Transincision (or transwound) catheter anesthesia** uses a multilumen catheter inserted through an insicion or wound and aligned across it on the inside as the incision or wound is closed, providing continuous administration of local anesthetic along the incision or wound.

Local anesthetics – Formulation

Biologically active substances are frequently administered as very dilute solutions which can be expressed as *parts of active drug per 100 parts of solution (grams percent)*

- Ex.: 2% solution =
- $\frac{2 \text{ grams}}{100 \text{ cc's}} = \frac{2000 \text{ mg}}{100 \text{ cc's}} = \frac{20 \text{ mg}}{1 \text{ cc}}$

- Maximum Recommended Dosage

Table 2. Maximum Recommended Dosage of Local Anesthetic Agents

Anesthetic	Maximum Dosage		Maximum total dosage	mg/carpule
	mg/kg	mg/lb		
Lidocaine 2% 1:000,000 epi	4.4	2.0	300mg	36mg
Mepivacaine 3% plain	4.4	2.0	300mg	54mg
Articaine 4% 1:100,000 epi	7.0	3.2	500mg	72mg
Prilocaine 4% plain	6.0	2.7	400mg	72mg
Bupivacaine 0.5% 1:200,000 epi	1.3	0.6	90 mg	9mg

Adapted from Stanley Malamed, Handbook of Local Anesthesia, Fifth Edition

A)To calculate the maximum amount of Lidocaine 2% with 1:100,000 epinephrine and the number of carpules that can be safely administered to a 30 pound patient

Maximum Dosage (mg/lbs) X weight (lbs) = Maximum Total Dosage (mg)
2.0 X 30 = 60 mgs

Maximum Total Dosage (mg) ÷ mg/carpule = Maximum # carpules
60 ÷ 36 = 1.67 carpules

B)To calculate the maximum amount of Mepivacaine 3% plain and the number of carpules that can be administered to a 30 pound patient the clinician would perform the following calculations.

Maximum Dosage (mg/lbs) X weight (lbs) = Maximum Total Dosage (mg)
2.0 X 30 = 60 mgs

Maximum Total Dosage (mg) ÷ mg/carpule = Maximum # carpules
60 ÷ 54 mg = 1.1 carpules

Dilution of local anesthetics

- The dilution of L.A. agent as **2 %** means that there is **two grams** (2000 mg) of the L.A. agent in **100 ml** of the solution

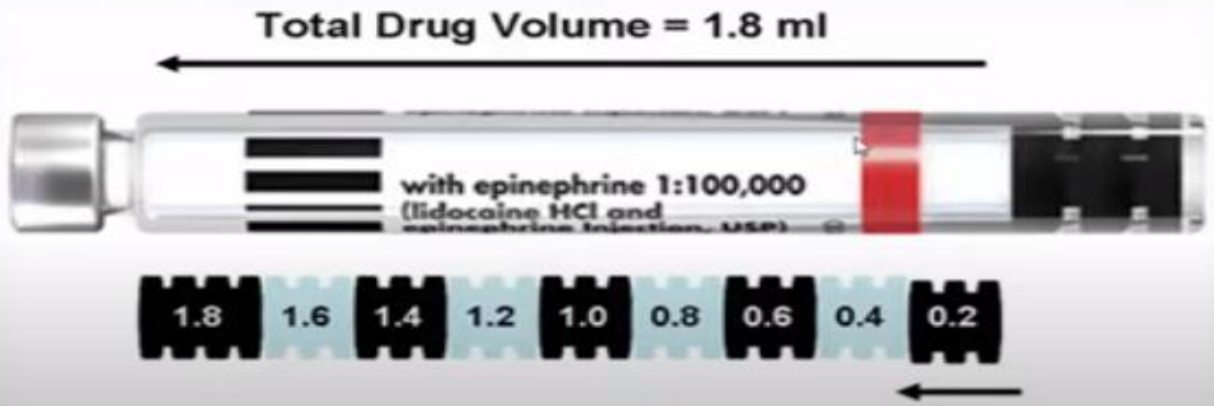
- 2 % means 2 g / 100 ml
- 2 % means 2000 mg / 100 ml

- 2000 mg – 100 ml
- ? mg - 1.8 ml
- ? = 1.8 x 2000 / 100 = 36 mg
- Therefore carpule of 1.8 ml contains 36 mg solution

What is a "stopperful"?

- The anesthetic cartridge has a rubber "stopper" in it
- Each time you express enough solution to move the stopper one time its own width, you have given 0.2 ml of solution (i.e. **one stopper = 0.2 ml**)
- **Multiply the # of stoppers given by 0.2 ml**. That will be how much solution you have administered
- Example: You give 3 "stoppersful" of solution – 3 X .02 ml = 0.6 ml of solution

Another good tip to know



¼ cartridge of 3% mepivacaine

- Volume of drug given
  - 1.8 ml ÷ ¼ = 0.45 ml
  - ¼ cartridge = 0.45 ml
- 3% solution means 30 mg/ml
- Multiply total ml given by amount of mg in 1 ml(mg/ml)
  - 0.45 ml X 30 mg/ml = 13.5 mg
- This patient was given 13.5 mg (0.45 ml) of 3% mepivacaine

Dilution of V.C.

Dilution of V.C. *Cont.*

The dilution of V.C. 1: 1000 means that there is one gram (1000 mg) of the V.C. in 1000 ml (1 liter) of the solution, or in other words 1.0 mg/ml of the solution

How to calculate mg/ml

- Epinephrine 1 : 100,000 used as an example
- Ratio of 1 : 100,000 means:
  - 1 gram of epi in 100,000 ml of solution
  - Reduce this to find mg/ml

$$\frac{1\text{ gram}}{100{,}000\text{ml}} = \frac{1000\text{ mg}}{100{,}000\text{ ml}} = \frac{1\text{ mg}}{100\text{ ml}}$$

- How much epi is in **1 ml** of solution?

Divide 100 ml into 1 mg = 0.01 mg/ml

- How much epi is in one cartridge?

0.01 mg/ml X 1.8 ml = 0.018 mg epi/cartridge

Maximum Recommended Dose

- Maximum amount recommended to be given to avoid toxicity
- Dentistry uses several different drugs
  - Some come in differing concentrations
- ALL have a maximum recommended dose (MRD)
  - Can be based on patient weight (mg/lb of weight)
  - Can be an **absolute** maximum
- Must be able to compute mg of drug given to avoid reaching MRD

Determining Absolute MRD

- 4% prilocaine absolute MRD 600 mg
- Divide absolute MRD by # of mg in a cartridge
  - 600 mg divided by 72 mg/cartridge = 8.3 cartridges
  - Note how much more this is than the MRD for a 100 lb patient!
- Look what happens to a pt. weighing 167 lb
  - 167 lb patient X 3.6 mg/lb = 601.2 mg
- All weights 166 lb or >can only receive 8.3 cartridges

Determining MRD by weight

- 4% Prilocaine: 3.6 mg/lb; not to exceed 600 mg
- Multiply pt weight by MRD mg/lb
  - 100 lb patient X 3.6 mg/lb = 360 mg MRD
- Determine mg/cartridge for 4% prilocaine
  - 4% = 40 mg/ml X 1.8 ml = 72 mg/cartridge
- Divide the MRD (in mg/lb) by mg in one cartridge
  - 360 mg divided by 72 mg/cartridge = 5 cartridges
- This says a 100 lb pt should not receive more than 5 cartridges or 360 mg of 4% prilocaine

Vasoconstrictors

- Dosage of vasoconstrictor given also must be calculated
- Amounts are expressed as a concentration ratio
- Ratios used in dentistry:
  - 1: 20,000
  - 1: 50,000
  - 1: 100,000
  - 1: 200,000
- REMEMBER: the bigger the number, the less concentrated the solution

How to calculate mg/ml

- Epinephrine 1 : 100,000 used as an example
- Ratio of 1 : 100,000 means:
  - 1 gram of epi in 100,000 ml of solution
  - Reduce this to find mg/ml

1 gram	=	1000 mg	=	1 mg
100,000ml		100,000 ml		100 ml

- How much epi is in **1 ml** of solution?

Divide 100 ml into 1 mg = 0.01 mg/ml

- How much epi is in one cartridge?

0.01 mg/ml X 1.8 ml = 0.018 mg epi/cartridge

Table 3. Maximum dosages allowable for the administration of infiltrative local anesthesia.

	Maximum Dose (Plain)	Duration of Action (Plain)	Maximum Dose (with Epinephrine)	Duration of Action (with Epinephrine)
Esters				
Procaine	5mg/kg	20 to 30 minutes	7mg/kg	30 minutes
Chloroprocaine	11mg/kg	15 to 30 minutes	14mg/kg	30 minutes
Amides				
Lidocaine	4mg/kg	30 minutes to 2 hours	7mg/kg	Up to 3 hours
Mepivacaine*	4mg/kg	1.5 to 3 hours	7mg/kg	Approximately 20-30% longer
Prilocaine	7mg/kg	30 minutes to 1.5 hours	8mg/kg	Up to 2 hours
Bupivacaine**	2mg/kg	2 to 4 hours	3mg/kg	3 to 4 hours
Ropivacaine	5mg/kg	2 to 6 hours	N/A	N/A

* Avoid in pregnancy. ** Avoid in pregnancy until term.

Friends of Locals

- • Epinephrine
- • Added to provide longer duration of anesthesia, promote hemostasis, & slow systemic absorption
- • May increase pain of injection by lowering pH
- • Avoid in “end-arterial fields” (digits, nose, ears, penis); if trouble arises, apply nitro paste or inject intravascular phentolamine (Phentolamine is an alpha adrenergic antagonist used to reverse soft tissue anesthesia).
- • Sodium Bicarbonate
- • Mix with lidocaine (9 mL lido 1% to 1 mL bicarb 8.4%)
- • Increases pH, thus faster diffusion into nerve & faster onset of action

Lignocaine(Lidocaine)

- Lidocaine, also known as lignocaine and sold under the brand name Xylocaine . It is also used to treat ventricular tachycardia

- Lignocaine Classified under - Amide
- 2-diethylamino 2,6 acetoxylidide hcl
- Metabolised- Liver by microsomal fixed function oxidases to monoethyl glycerine and xylidide

- Excretion -<10% unchanged, >80%-metabolised
- Vasodilaton ->Procaine, <Mepivacaine

Lignocaine

- Pka -7.9 , ph(plain)-6.5, ph(with V C)5 - 5.5, Onset of action 2-3 min,
- Anesthetic half life 1.6hrs.
- Topical anesthetic -yes
- Recommended dose - 7mg/kg not>500mg with VC • 4.4mg/kg not>300mg
- For children with VC 3.2 mg/kg.
- It is non allergic available in three formulations
- Ligno2% with out VC.
- Ligno2% with VC 1:80,000
- Ligno2% with VC 1:100,000
- Adverse reactions- CNS stimulation then Depression, Overdose causes unconsciousness and respiratory arrest.

Bupivacaine

- Bupivacaine Classified under amide
- 1-butyl 2,6 pipecoloxylidide
- Toxicity <4 times - Lignocaine, Mepivacaine
- Metabolism - Liver by Amidases
- Excretion by kidney (16% unchanged)
- Vasodilation- relatively significant
- Pka-8.1,ph(plain)- 4.5-6, ph(vc)- 3-4.5
- Onset of action –6-10 min, Anesthetic half life-2.7hrs,
- Dose 1.3mg/kg ,Maximum dose-not >40mg,Absolute maximum dose-not> 90mg

Bupivacaine

Available as 0.5% soln 1:2,00,000 (vc)

- Indicaton- pulpal anesthesia.
- management of post op pain.
- Duration –Pulpal- 90- 180 min • Soft tissue-4-12 hrs
- Contra indication- burning sensation at site of injecton, in children-anticipating self trauma

Procaine

- Procaine
- Classified under -Esters.
- 2Diethylamino ethyl 4aminobenzoate HCL.
- Metabolised-in Plasma by plasma pseudocholine esterases
- Excretion >2%unchanged, 90% -PABA,8% diethyl aminoethanol in urine.
- Pka-9.1,High degree of vasodilation, 2% procaine 15-30min soft tissue LA

Mepivacine

- Mepivacine
- Classified -amide type
- 1 methyl 2,6 pipecoloxylidide hcl
- Metabolism-microsomal fixed funcn oxidasea in liver.
- Maximum dose 4.4 mg/kg , absolute max dose-300mg.
- Excretion-1-10% unchanged urine.
- Pka-7.6,anesthetic half life-90min,
- Mild vasodilator, 3% mepivacaine used in patients with vc contraindicaton. Low reported cases-allergy. Over dose CNS stimulation followed by depression.

Articaine

- Articaine Classified- amide
- 2 carboxymethoxy 4 methylthiophene HCL.
- Metabolised- liver.
- Excretion - kidney 10% - unchanged.
- Pka 7.8, anesthetic half life-1.2-2 hrs,
- dose - 1mg/kg , absolute maximum dose - 500mg

VASOCONSTRICTORS

- Vasoconstrictors are the drugs that constricts the blood vessels and thereby control tissue perfusion.
- They are added to local anaesthesia to oppose the vasodilatory action of local anesthetic agent.

- What happens if you don't use a vasoconstrictor?
- Plain local anesthetics are vasodilators by nature.
- 1) Blood vessels in the area dilate.
- 2) Increase absorption of the local anesthetic into the cardiovascular system (redistribution)
- 3) Higher plasma levels ➡ increased risk of toxicity
- 4) Decreased depth and duration of anesthesia ➡ diffusion from site.
- 5) Increased bleeding due to increased blood perfusion to the area.
- 6) Patient is simply not as numb.
- 7) More anesthetic goes into the circulation.

Vasoconstrictors

- Vasoconstrictors resemble adrenergic drugs and are called sympathomimetic, or adrenergic drugs

- 1) Constrict blood vessels ➡ decrease blood flow to the surgical site.
- 2) Cardiovascular absorption is slowed ➡ lower anesthetic blood levels.
- 3) Local anesthetic blood levels are lowered ➡ lower risk of toxicity
- 4) Local anesthetic remains around the nerve for longer periods ➡ increased duration of anesthesia.
- 5) Decreases bleeding.

Contraindication

- Vasoconstrictors should not be used in the following locations (why????)
- Fingers
- Toes
- Nose
- Ear lobes

Vasoconstrictors

- Catecholamine
  - Norepinephrine
  - Levonordefrin
  - Isoproterenol
  - Dopamine
- Non catecholamine
  - Amphetamine
  - Methamphetamine
  - Ephedrine
  - Hydroxyamphetamine
  - Metaraminol
  - Methoxamine
  - Phenylephrine

Local anesthetic cartridge and vials

- It contains primary the Local anesthetic agent and also the other ingredients which are as follows :
  1. Local anesthetic drug .
  2. Vasoconstrictor drug .
  3. Preservative for the Vasoconstrictor .
  4. Ringers solution .
  5. Distilled water .
  6. General Preservative .

Cartridge

- The cartridge contains the anesthetic solution.
- In the U.S. it contains 1.8ml (cc) of anesthetic solution. This amount may vary in other countries.
- Its components consist of a cylindrical glass tube, rubber stopper, aluminum cap and diaphragm.
- The glass cylinder is surrounded by thin plastic label that describes the contents and protects the patient if the cartridge cracks.
- The stopper is located at the end of the cartridge that receives the syringe harpoon. It is no longer color coded to the type of anesthetic used so the practitioner should double-check the contents of the cartridge before administrating the anesthetic solution to the patient. The stopper is slightly indented from the lip of the glass cylinder and the cartridge should not be used if it is flush.