Tikrit University
College of Veterinary Medicine

Pharmacology

Subject name: **Local Anesthesia**

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Lecturers link

Local Anesthesia

A drug induce state in which the central nervous system is altered to produce varying degree of pain relief ,depression of consciousness, skeletal muscle relaxation and diminished or absent reflexes.

General anesthetics;- a gent that induce the state of anesthesia, they affect the whole body with loss of consciousness being one of those effects.

Local anesthetics:- agents that render a specific portion of the body insensitive to pain without affecting consciousness also called regional anesthetics.

Topical anesthetics a class of anesthetics that are applied directly to the skin and mucous membrane they consist of solution, ointment ,gels cream, powder ophthalmic drops and suppositories.

Epidural:-the anesthetics agents is injected via a small catheter into the epidural space ,which is just outside the dura mater of the spinal cord.

Infiltration:- small amounts of anesthetics solution are injected into the tissue that operative site, this approach to anesthesia is commonly used for such procedures as suturing wound or dental surgery. Often agents that cause constriction of local blood vessels .

Nerve block:-

Anesthetics solution is injected at the site where a nerve innervates a specific area such as a tissue. This allows large amounts of anesthetic agents to be delivered to a very specific area without affecting the whole body. It is often reserved of more difficult to treat pain syndromes such as patients diagnosed with various cancers and chronic orthopedic pain.

Spinal:-

Anesthetic solution is injected into the epidural space or the subarachnoid space that surrounds the spinal cord ,used obstetric procedures.

Pharmacological effects:-

Local anesthetics attach themselves to specific receptors in the nerve membrane. After combining with receptor the local anesthetics block conduction of nerve impulses by

decreasing the permeability of the nerve cell membrane to sodium ions. This then decrease the rate of depolarization of the nerve membrane (↑ excitability),

-is reversible blockage of peripheral nerve conduction

-inhibit the movement of the nerve impulse along the fibers, at sensory ending

-they affect the myelinated fiber only at the nodes of Ranvier

The losses of nerve function are in the following order:-

1- autonomic

2-cold

3-warmth

4-pain

5-touch

6-pressur

7-motor

Chemistry

--Local anesthetics are weak bases and are usually made available clinically as salts to increase solubility and stability.

--Most local anesthetic agents consist of a lipophilic group (eg, an aromatic ring) connected by an intermediate chain via an (ester or amide) to an ionizable group ,and then Amino group(hydrophilic ,water soluble).

A. The aromatic ring is the lipophilic (base) portion of the molecule and is what penetrates the nerve, and determines the anesthetic potency.

B. The intermediate chain determines if the local anesthetic is an ester or an amide

C. The terminal amine is the hydrophilic (acid) portion of the molecule it is the active form in the cartridge and binds to the receptor sites on the nerve membrane. In order to bind to the receptor sites,

---ester links are more prone to hydrolysis than amide links, esters usually have a shorter duration of action.

----In the body, they exist either as the uncharged base or as a cation. The relative proportions of these two forms is governed by their pK_a and the pH of the body fluids

according to the Henderson-Hasselbalch equation:

Because the pK_a of most local anesthetics is in the range of 8.0-9.0, the larger percentage in body fluids at physiologic pH will be the charged, cationic form.

--The cationic form(salt) is the most active form at the receptor site because it cannot readily exit from closed channels.

---, the uncharged form(free base) is important for rapid penetration of biologic membranes and producing a clinical effect,

. Therefore, local anesthetics are much less effective when they are injected into infected tissues because a smaller percentage of the local anesthetic is nonionized and not available for diffusion across the membrane in an environment with a low extracellular pH.

Local anaesthetics can also be classified into two categories based on their chemical structure:
a. Ester linked local anaesthetics e.g. cocaine, procaine, tetracaine, benzocaine, chloroprocaine.
b. Amide linked local anaesthetics e.g. lidocaine, bupivacaine, dibucaine, prilocaine, ropivacaine.

Rate of Onset:-

- **Potency**
  - **Correlates closely with lipophilicity, with more lipophilic local anesthetics being more potent**
- **Dose**
  - **Increased dose, either by increasing volume or increasing concentration, accelerates the rate of onset**
- **Un-ionized fraction**
  - **accelerates the rate of onset**
- **Epinephrine**
  - **Reduces the rate at which the drug washes away**
- **Elimination pharmacokinetics**
  - **Rapidly eliminated drugs demonstrate rapid onset, because they are given in relatively higher doses**

Duration of Action;-

- **Rate of systemic absorption**

- **Tissue vascularity**
- **Use of epinephrine**

- **Rate of elimination**
  - **Particularly for esters, which are metabolized locally**
- **Dose**
- **Potency**
- **General groups:**
  - **Short: Procaine, chloroprocaine**
  - **Intermediate: lidocaine, mepivicaine, prilocaine**
  - **Long acting: Tetracaine, bupivacaine, etidocaine, ropivacaine, levobupivacaine**

Pharmacokinetics

A. ABSORPTION

Systemic absorption:-depend on:-

- Vascularity
- pH
  - Slower absorption if solution is alkaline, because more is bound into the tissues.
- Lipophilicity
  - Slower absorption for more lipophilic drugs, again because more is bound in the tissues
- Epinephrine

Decreases local blood flow, decreasing absorption . This is important for drugs with intermediate or short durations of action such as procaine, lidocaine, and mepivacaine (but not prilocaine).

B. DISTRIBUTION

The amide local anesthetics are widely distributed after intravenous.

- can occur in lipophilic storage sites (eg, fat). After an initial rapid distribution phase, which consists of uptake into highly perfuse organs such as the brain, liver, kidney, and heart,

-a slower distribution phase occurs with uptake into moderately well-perfused tissues, such as muscle and the gastrointestinal tract.

C. METABOLISM AND EXCRETION

The local anesthetics are converted in the liver (**amide type**) or in plasma (**ester type**) to more water-soluble metabolites and then excreted in the urine

Ester-type local anesthetics are hydrolyzed very rapidly in the blood by circulating butyrylcholinesterase (pseudocholinesterase) to inactive metabolites. Therefore, procaine and chloroprocaine have very short plasma half-lives (1 minute).

The type amide local anesthetics is hydrolyzed by liver microsomal cytochrome P450 isozymes. There is considerable variation in the rate of liver metabolism of individual

Not As a result, toxicity from amide-type local anesthetics is more likely to occur in patients with hepatic disease.

Toxicity

A. CENTRAL NERVOUS SYSTEM

1. All local anesthetics At low concentrations, all local anesthetics have the ability to produce sleepiness, light-headedness, visual and auditory disturbances, and restlessness.
Convulsions due to excessive blood levels

B. CARDIOVASCULAR SYSTEM

local anesthetics block cardiac sodium channels and thus depress abnormal cardiac pacemaker activity, excitability, and conduction. At extremely high concentrations, local anesthetics can also block calcium channels.

D. HEMATOLOGIC EFFECTS

The administration of large doses (10 mg/kg) of prilocaine during regional anesthesia may lead to accumulation agent capable of converting hemoglobin to methemoglobin.

E. ALLERGIC REACTIONS

The ester-type local anesthetics are metabolized to *p*-aminobenzoic acid derivatives. These metabolites are responsible for allergic

Amides :-

Lidocain:-

Is one of the most commonly used local anesthetics ,is an amide derivative of xylidine it has a rapid onset ,lidocain 2% with vasoconstriction provides profound anesthesia of medium duration.(ointment ,injection,)

Adverse reaction:-hypotension,headach,

LIGNOCAINE

Lignocaine is completely absorbed following parenteral administration, its rate of absorption depending upon various factors such as site of administration and the presence or absence of vasoconstrictor agent.
Lignocaine is metabolised rapidly by the liver and metabolites and unchanged drug are excreted by the kidneys.
The elimination half-life of lignocaine following an intravenous bolus injection is 1.5 to 2.0 hours.
Adverse Effects
CNS

BUPIVACAINE(t1\2 3h)
It is a potent and long acting local anaesthetic used for spinal, infiltration, epidural anaesthesia and nerve block.

Side effects include cardiac arrest, cardiac arrhythmias and respiratory failure.

Bupivacaine (0.5%) with adrenaline is less frequently used in dentistry because of its poor penetration into bone

Ester group

BENZOCAINE
It is a local anaesthetic belonging to the ester group. It inhibits conduction of nerve impulses from sensory nerves. This action is a result of alteration of cell membrane permeability to ions. It is poorly absorbed from the intact epidermis.

Cocaine:-as a surface anesthesia ,cocaine prevent the uptake of catecholamine (noradrenaline)into sympathetic nerve ending

Procaine:- is used as antiarrhythmic agent (procainamide), and is used with penicillin

General anesthetics

A drug induce state in which the central nervous system is altered to produce varying degree of pain relief ,depression of consciousness, skeletal muscle relaxation and diminished or absent reflexes

:. **general Anesthesia involves three main changes**

Unconsciousness

Loss of response to pain

Loss of motor reflexes

Stage of anesthesia:-

Stage 1

Stage 1 anaesthesia, also known as the "induction", is the period between the initial administration of the induction agents and loss of consciousness. During this stage, the patient progresses from analgesia without amnesia to analgesia with amnesia. Patients can carry on a conversation .at this time

Stage 2

Stage 2 anaesthesia, also known as the "excitement stage", is the period following loss of consciousness and marked by excited and delirious activity. During this stage, respirations and heart rate may become irregular. In addition, there may be uncontrolled movements, vomiting, breath holding, and pupillary dilation. rapidly acting drugs are used to minimize time in this stage and reach stage 3 as fast as possible

Stage 3

Stage 3, "surgical anaesthesia". During this stage, the skeletal muscles relax, vomiting stops, and respiratory depression occurs . Eye movements slow, then stop, the patient is unconscious and ready for surgery. It has been :divided into 4 planes

1-eyes initially rolling, then becoming fixed

2-loss of corneal and laryngeal reflexes

3-pupils dilate and loss of light reflex

4-intercostal paralysis, shallow abdominal respiration

Stage 4

Stage 4 anaesthesia, also known as "overdose", is the stage where too much medication has been given relative to the amount of surgical stimulation and the patient has severe brain stem or medullary depression. This results in a cessation of respiration and potential cardiovascular collapse. This stage is lethal without cardiovascular and respiratory support

:Two main theories interaction with either

-the lipid membrane bilayer or

-with hydrophobic binding sites on protein molecules

Action on specific receptors

Barbiturates and benzodiazepines promote the actions of the inhibitory neurotransmitter GABA

Opioids act on their own specific receptors

Ketamine activates kappa opioid receptors

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Classification of general anesthetic drugs :-

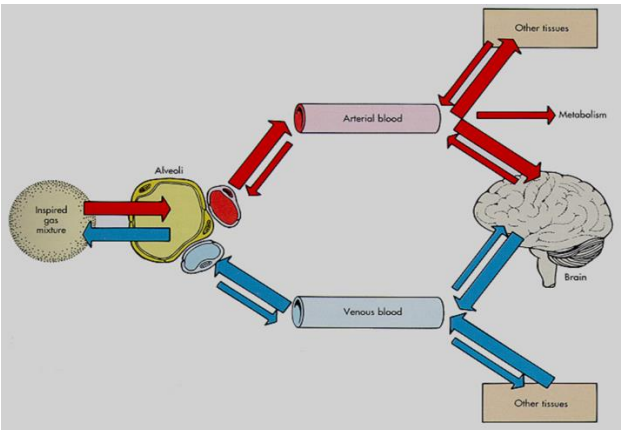
1-inhalation drugs

Liquid : halthone,chloroform, diethylethes

Gases:-cyclopropan ,ethylene, nitro oxide

MAC(minimum alveolar concentration

A measure of potency of inhaled anesthetics



Pharmacokinetics of Inhaled Anesthetics

1-Amount that reaches the brain

(Indicated by oil:gas ratio (lipid solubility

2-Solubility of gas into blood

The lower the blood:gas ratio, the more anesthetics will arrive at the brain

General Actions of Inhaled Anesthetics

1-Respiration

Depressed respiration and response to CO2

2-Kidney

Depression of renal blood flow and urine output

3-Muscle

High enough concentrations will relax skeletal muscle

4-Cardiovascular System

Generalized reduction in arterial pressure and peripheral vascular .resistance

Isoflurane maintains CO and coronary function better than other agents

5-Central Nervous System

Increased cerebral blood flow and decreased cerebral metabolism

Nitrous Oxide

widely used

Potent analgesic

Produce a light anesthesia

Do not depress the respiration/vasomotor center

Used adjunct to supplement other inhalationals

2-intervenouse:-

Barbiturate(thiopental)

Non-barbaturate(ketamine)

Organ Effects

Most decrease cerebral metabolism and intracranial pressure

Most cause respiratory depression

May cause apnea after induction of anesthesia

Cardiovascular Effects

Barbiturates, benzodiazepines and propofol cause cardiovascular depression

Thiopental sodium

Side effects

Hypotension 

apnoea

airway obstruction

Drugs give pre-operative:-

-narcotic analgesic

-muscle relaxante

-sedative ,anxiolytic

-anti-muscarinic