

Mechanism of Relieving Pains

SALICYLATE

Aspirin, a salicylate is also known as acetylsalicylic acid.

1. Relief of pains.
2. Reduction of fever (antipyrexia).
3. Anti inflammatory
4. Reduction of platelet aggregation.

Mechanism of action.

- Inhibition of cyclooxygenase which is responsible for synthesis of prostaglandin.
- It diminishes prostaglandin

Clinical Use:

1. Used in all *spp*.
2. Relief of mild to moderate pain resulting from musculoskeletal conditions such as arthritis or hip dysplasia.
3. Post adulticide treatment of heart worm disease
4. Analgesic.
5. Treatment of cardiomyopathy
6. Treatment of edotoxic shock.

Adverse effect

- Gastric users (irritation).
- Cats are susceptible to overdose

Dosage – 10-25mg/kg P.O. in dogs and 10mg/kg in cats.

PHENYBUTAZONE PYRAZOLONE DERIVATES NSAID

1. Analgesia for mild to moderate pain.
2. Anti inflammatory action.
3. Anti pyrexia.

Clinical Uses

- Relief from musculoskeletal conditions in horses and dogs.
- Used in treatment of lameness.
- In dogs, cattle used as analgesia and antipyretic effect.

Adverse effect

Gastro intestinal bleeding and bone marrow suppression

Dosage:

Dogs 22mg/kg P. O. initial dose

15mg/kg I.V. T. D.

Cats 15mg/kg I.V. T. D.

10-14 – mg/kg POBID

ACETAMINOPHEN

- It has an analgesic
- Limited antipyretic and anti inflammatory activity.

Clinical Uses.

The uses are limited in vet medicine because of its risk of potential toxicity and other substitutes.

Dosage in dogs: 15mg/kg P.O. Q.D. is needed.

Adverse effect

- Methemoglobinemia
- Cyanosis
- Anaemia
- Liver damage.

PROPIONIC ACID DERIVATIVES

CARPROFEN

- Approved for oral and injectable used in dogs and cats. $t_{1/2}$ 8hrs.

Mechanism of action

- It works by inhibiting cyclooxygenase

Clinical Use

- Used for postoperative pain from soft tissue and orthopedic pain.

Adverse effect

- Git ulceration
- Bleeding

Dosage

4mg/kg in dogs and cats STD or TID

KETOPROFEN

- Analgesic
- Antipyretic
- Anti inflammatory activity

Clinical Uses

- Mostly used in horses.
- It is also used in dogs and cats.
- Used in treatment of pain and inflammation. Associated with musculoskeletal disorders.
- It is used in post operative and chronic pain in dogs.

Adverse effect

- Git bleeding or ulceration.
- Renal dysfunction.
- Generalized bleeding.

IBUPROFEN

Reported side effects in dogs.

MECLOFENAMIC ACID

Used for treatment of acute or chronic inflammatory disease in horses.

Dog – 2.2mg/kg P.O. BID

Cat – 2.2mg/kg P.O. BID

NEUROMUSCULAR BLOCKING AGENTS

Drugs

The drugs acting to bring about muscle relaxation do these at the following sites:

- Peripherally at the neuromuscular junction
- Centrally in the cerebrospinal axis either directly on the muscle fibre itself to reduce skeletal tone or bring about paralysis or complete relaxation

Indication for the use of Neuromuscular Blockers

- In orthopaedic or intra thoracic surgical procedures to cause relaxation of skeletal. Muscle for easier access.
- In reduction of joint dislocation or bone fractures
- They facilitate endotracheal intubation
- Endoscopy
- Artificial respiration with adequate relaxation of abdominal and thoracic muscles including the diaphragm.

Caution: These drugs should only be used when facilities for resuscitation are available.

Peripherally acting Muscle relaxants

- They are classified as non depolarizing type or antagonists: act as analogues of Ach
- Agonists (depolarizing) type

Mechanism of action: The peripherally acting neuromuscular blockers are structurally similar to Ach (acetylcholine) thus, they are analogues, these drugs are non depolarizing agents at the neuromuscular junction.

Tubocurarine: It is a prototype of a non-depolarizing muscle relaxants.

Constituent: An alkaloid curare

Sources: Various specie of *Strychnos toxifera*, *Condrodendron tementosum*

Other uses: hunting the South American Indian use the crude extract “*ourari*” as arrow poison.

Drugs that interact with tubocurarine: aminoglycoside, gentamicin, neomycin inhibits Ach release from the cholinergic nerves by competing with calcium.

Alcuronium: Is a synthetic derivative of the alkaloid toxiferine obtained from *calabash curare*. It has relatively long duration of action of about 70 minutes. Its advantage is it has

minimal cardiovascular and histamine releasing side effects due to their virtue of being antagonism to acetylcholine combine with nicotinic receptor and prevent binding of Ach or could cause depolarizing effect and are hence called agonists.

Non depolarizing Muscle relaxants: These drugs prevent depolarization of the muscle membrane and inhibit muscle contraction, thus bring about flaccid paralysis. Because they compete with the Ach they are termed competitive blockers.

Classes:

- Long acting (90-180 minutes)- (1) D-tubocurarine (2) Metocurine (3) dexcurium (4) Pipecuronium (5) Gallamine.
- Intermediate acting(20-40 minutes)- Vecuronium, atracurium
- Short acting (10-20 minutes) Mivacurium

Newer agents of intermediate duration 30-40 minutes example *Rocuronium*

It is excreted unchanged by the kidney

Dose Mg/Kg,lv	Initial	Dosage increment
Horse	0.05	0.01
Dog	0.1	0.02

Atracurium has minimal vagolytic or sympatholytic properties

Advantage: It could be administered to animals with hepatic or renal failure.

Dose, Mg/Kg	Initial	Dosage increment
Slow 1v	0.15	0.06
Horse		
Sheep, dog, Cat	0.5	0.2

Reading Assignment

Vecuronium

Gallamine triethiodide

NOTE: The action of the peripheral acting muscle relaxants could be counteracted by neostigmin, endophonium.

Pancuronium: Is a synthetic steroidal compound that is free from hormonal activity it is about five times are potent as D-tubocurarine but has slow onset of and longer duration of action (120-180 minutes).

Advantages: It does not induce histamine release or significant changes in blood pressure.

Side effects: It has side-effects such as tachycardia in dogs and cats due to vagolytic action.

Pharmacokinetics: Injected by I.v reaches steady state and metabolized by the liver and excreted by the kidney.

Depolarizing Muscle relaxants.

Example: Decamethonium, Succinylcholine or (suxamethonium).

The clinical application of these group drugs is limited because its action cannot be reversed and should not be use except there is provision for artificial respiration facility.

This drug should not be used in conscious animal.

Succinylcholine consists of two Ach molecules linked by their acetyl groups. It is normally broken down rapidly by plasma.

Psuedocholinestrases: It has a rapid onset of action (1-2 minutes) and short duration of action of up to 5 minutes in horses and 25 minutes in the dog. In some species such as cattle, sheep have low plasma levels of the Metabolizing enzymes and thus the action of the drug is greatly prolonged in these species.

Drug interaction: Neostigmine prolongs the duration of action of succinylcholine *antihelminthics* inhibits cholinesterases and thus prolong the duration of action of succinylcholine. *Nifedipine* a calcium blocker also prolong the effect and increases ion muscle relaxing effect.

Uses: With anesthetic agents it is used in obtaining a muscle relaxing effect in all surgery.

- Casting
- Restraining horses
- In dart guns to capture wild animal

Adverse effect: Succinylcholine is associated with depolarization and consists of uncoordinated muscular contraction, salivation and sometimes bradycardia.

Succinylcholine is contra-indicated in cattle

CENTRALLY- ACTING MUSCLE RELAXANT

Centrally acting muscle relaxant (or spasmolytic) reduce skeletal tone by selective action in the cerebrospinal axis. They probably act as the GABA receptors in the C.N.S

Examples include: Mephensin, baclofen, guaiacol glycerol, ether, chlorodiazepoxide and diazepam they do not alter consciousness but reduces skeletal spasticity in a variety of neurologic conditions such as cerebral palsy multiple sclerosis, stroke, spinal cord injury and flexor spasms.

Mephenesin:

Chemistry: A propanediol derivative, it inhibits polysynaptic excitation of motor neurons in the spinal cord to produce flaccid muscle paralysis. It is no longer in use because it cause thrombophlebitis.

Guaiacol Glycerol Ether (GGE)

It mephensin like compound that inhibits polysynaptic spinal reflexes and is currently used as adjunct in induction of anaesthesia in horses and cattle. 10% solution (in water or 5% dextrose) is administered to effect until the animal becomes ataxic. A bolus dose of general anaesthetic agent such as thiopentone or other would produce recumbency. The dose of thiopentone recommended is (1gm/180kg) is half the normal dose of GGE it is excreted in urine.

Indications:

(1) In surgery (2) Antitussive (3) decongestant

Benzodiazepines

- Chlordiazepoxide
- Diazepam

They have anxiolytic and sedative properties but only diazepam appears to be widely used in veterinary anaesthesia

Uses: used in taming of wild animal

- Sedation
- Skeletal muscle relaxation
- Anti convulsant in status epilepticus

- It is used in combination with ketamine, opioids

The dose in all species is up to 1mg/kg or 1mg/kg-1 commonly administered as injection.

DIRECT ACTING MUSCLE RELAXANTS

Dantrolene is a hydantoin derivative

- It has a direct action on the muscle fibre
- It reduces the amount of calcium release from its stores in the Sarcoplasmic

reticulum and hence prevents the excitation –contraction coupling in the skeletal muscle.

Neuromuscular transmission is not affected.

Dantrolene has been used specifically in the treatment of anaesthetic

- induced malignant hyperthermia

Dose Mg/Kg, I.v

Horse, dog up to 2

Pig up to 5

Drugs used for acute local muscle spasm are as follows:

Carisoprodal, Chlorophenesin, Chlorzoxazone Cyclobenzaprine, Metaxalone.