DISSOCIATIVE ANESTHESIA

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Dissociative anesthesia implies dissociation from the surrounding with only superficial sleep mediated by interruption of neuronal transmission from unconscious to conscious parts of the brain.

- During dissociative anesthesia, the animal maintains its pharyngeal, laryngeal, corneal, palpebral, and swallowing reflexes. The eyes also remain open.
- Dissociative anesthetic agents increase muscle tone, spontaneous involuntary muscle movement (occasionally seizures are seen in some species)
- Salivation, lacrimation are also increased.
- Somatic analgesia is good.
- Ketamine and tiletamine (combined with zolazepam in Telazol®) are the two dissociative anesthetics currently available in veterinary practice.

Dissociatives(Phencycline derivatives): Ketamine and Tiletamine

KETAMINE HYDROCHLORIDE

- Clear, colourless and odorless powder soluble in water.
- Because of low pH the compound is irritating to tissues.

The Mechanism of action of ketamine has not been established. It appears that ketamine exerts its effects via antagonism of CNS muscarinic receptors and by agonism of opioid receptors. It is thought to be specific antagonist of N-methyl, D-aspartate glutamate receptrors (NMDA). NMDA is a principal excitatory receptor system in the mammalian brain

<u>Anesthetic action and effect on CNS</u>

1. The drug produces a loss of sensory perception or response and a state of unconsciousness.
2. The anesthesia is referred to as cateleptoid anaesthesia.
3. Eyes remain open with corneal and light reflexes.
4. It produces seizures which is more in dogs, horses and less in cats.
5. Ketamine rapidly enters the brain and to brain\plasma concentration ratio becomes constant in less than one minute after rapid I/V administration.
6. It is rapidly metabolized in liver.
7. Alters reactivity of the CNS to sensory impulses without blocking sensory input at spinal or brain stem levels. These impulses may reach cortical areas but fail to be perceived because of depression of the association areas during anesthesia. Thus the term dissociative anesthetic is often used.

Effect on cardiovascular system

Cardiovascular effects of dissociatives are dose dependent. At clinical doses, ketamine (and tiletamine) centrally stimulate the sympathetic system resulting in tachycardia, increased blood pressure and increased cardiac output. Large doses of ketamine depress the myocardium directly and may produce hypotension.

Since ketamine increases blood pressure and intracranial pressure it should not be used in head injuries or intraocular surgery.

Effect on respiratory system

Ketamine and Telazol® produce less respiratory depression than other intravenous anesthetic agents (propofol, etomidate, barbiturates); however, clinically effective dose of ketamine or Telazol® may induce apnea in some susceptible animals.

1. Respiratory rate increases
2. Tidal volume decreases
3. Apneustic pattern of breathing
4. Laryngeal and pharyngeal reflexes are mildly abolished.

Hepatic responses

In most species, ketamine and Telazol® are metabolized by the liver. In cats, a significant amount (50%) of ketamine is excreted unchanged by the kidney. This difference may account for differing responses seen in dogs and cats receiving dissociatives. Dogs tend to have slow and stormy recoveries (head shaking, salivating, muscle rigidity, vocalization, defecation) from ketamine and Telazol®, while cats tend to have faster and smoother recoveries.

1. Ketamine is metabolized by the body with a distribution of drug not only to organs, but to body fat, liver and kidneys.
2. So animals with hepatic and renal disease do not metabolize the drug properly and thus have prolonged sleeping time.

Clinical applications of ketamine

- Ketamine should be used cautiously in patients at increased seizure risk.
- Ketamine possesses better somatic analgesia than visceral analgesia.
- Its analgesic effect is partly mediated by N-methyl-D-aspartate (an excitatory neurotransmitter) antagonistic activity.
- In dogs and horses, ketamine should be used in combination with or after premedication (xylazine, detomidine, medetomidine, diazepam, midazolam, and acepromazine) with a

sedative or a tranquilizer - violent involuntary movements (muscle rigidity and/or seizures) will occur if ketamine is given alone.

- o In dogs, ketamine is often combined with diazepam, midazolam, or medetomidine, whereas as in horses, xylazine or detomidine is used.
- o Ketamine has been used in combination with guaifenesin as an induction agent in large animals (horses, cattle).
- o Eyes remain wide open with nystagmus at times, and, therefore protective eye lubrication is indicated to protect the damage of the eye during anesthesia.
- o Emergence hallucination and delirium can be prevented with concurrent use of sedatives/tranquillizers.
- o Increased muscle rigidity is counteracted by use of sedative possessing good muscle relaxant effect (e.g. benzodiazepines)
- o Both hypothermia and hyperthermia is observed. Hypothermia is due to its effect on thermoregulatory centers, and hyperthermia on increased muscle activity or hyperactive behavioral change.

Use of ketamine in obstetrics:

Ketamine has been shown to cross the placental barrier. It is better induction agent than thiopentone. The fetus may be depressed, but the claimed advantage of using ketamine in some cesarean sections is the short half-life. However, this is only useful where ketamine can be used as an intravenous induction agent and not for maintenance of anesthesia

Is a useful drug for

1. Chemical restraint
2. Induction of anesthesia
3. Production of surgical anesthesia.
4. Concurrent medications of preketamine medication in cats have resulted in better muscle relaxation, reduction in salivation, more complete analgesia and fewer undesirable reactions during the recovery.

   e.g – For smoother induction and improved muscle relaxation and fewer complications in recovery.it is combined with acepromazine or xylazine.

- To reduce salivation it is combined with glycopyrolate and atropine.
- In combination with inhalant it is very effective in cats.

Combinations for clinical usage

For Dogs

First combination

Atropine - 0.04 mg/kg S/C

after 15-20 minutes

Xylazine - 2mg/kg body weight in a single syringe I/M + Ketamine – 10 mg/Kg body weight, in a single syringe I/M and maintenance mostly by ketamine using I/V route.

Second combination

Atropine –0.04 mg/kg S/C

After 15 minutes

Diazepam – 0.4 mg/kg + Ketamine – 6-12 mg/kg in a single syringe I/V and maintenance mostly by ketamine using I/V route.Duration of anaesthesia is 5-15 minutes.

Third combiantion

Atropine – 0/04 mg/kg S/C

After 15 minutes

Acepromazine –0.04 mg/kg I/V

After 10-15 minutes

Ketamine – 10 mg/kg I/V

Duration of anaesthesia is 10-20 minutes.

For cats

For good sedation

Atropine – 0.04 mg/kg S/C

After 15 minutes

Acepromazine – 0.1 mg/kg S/C

After 10-15 minutes

Ketamine 2-8 mg/kg I/M or I/V

Duration of anaesthesia 5-10 min I/V, 15-20 min I/M.

For anesthesia

Atropine – 0.04 mg/kg S/C

After 15 minutes

Acepromazine – 0.1 mg/kg S/C and after 10 minutes

Ketamine – 11 mg/kg I/V

Duration of anesthesia is10 min, redosing if necessary can be done with ketamine “to effect”.

For Cattle

Calves:

1. IM Xylazine 0.1 - 0.2 mg/kg
   Ketamine 5.0 - 10.0 mg/kg
   Or
2. IV Xylazine 0.1 mg/kg
   Ketamine 2.0 mg/kg

Ketamine can be expensive to use in adult cattle, but is used IV as in calf.

For Horses

Ketamine is used only by the intravenous route in the horse, and only after the administration of sedatives usually in conjunction with xylazine. The addition of diazepam (0.02 mg/kg) between xylazine and ketamine gives a smoother induction. Can be expensive compared to thiopental induction, but induction and recovery is smoother. Occasionally a horse can become excited, this is usually due to poor sedation, noisy surroundings or inadvertant intra-carotid injection (use catheters).

Dose:

Xylazine 1 - 1.25 mg/kg IV.

When horse is properly sedated (2-3 minutes) then ketamine is administered IV. (Diazepam at 0.02 mg/kg IV can be given 2 minutes after Xylazine) Ketamine 2 - 2.25 mg/kg IV.

Onset of action is slow taking about 50-60 seconds following administration of the ketamine. The horse sits on its haunches and then rolls quietly over to one side. Analgesia lasts for 10 to 15 minutes. Recumbency is for 15 to 20 minutes.

- The horse gives no warning of recovery but rolls quietly into sternal recumbency and remains in that position until able to rise.
- Anesthesia may be prolonged by additional doses of 1/4 to 1/2 of the original dose of ketamine, or of both ketamine and xylazine.

Tiletamine (in Telazol®)

- Telazol® consists of equal parts (weight to weight) of tiletamine, a dissociative anesthetic and zolazepam, a benzodiazepine derivative. The pharmacologic actions of these two drugs are complementary with tiletamine providing analgesia and immobilization and zolazepam providing muscle relaxation and tranquilization.
- Telazol® comes as a powder and needs to be re-constituted with 5 ml solution of sterile water or other liquid solution of choice (e.g., ketamine, xylazine). Following reconstitution with

sterile water, each ml of solution contains 100 mg of Telazol® (50 mg of tiletamine and 50 mg of zolazepam) per ml.

- Telazol® is a product similar to ketamine and diazepam (Ket-Val) combination.
- In the dog, the plasma half life of zolazepam is 1 hour and that of tiletamine is 1.2 hours. Therefore, the effect of tiletamine outlasts that of zolazepam, and may result in emergence delirium associated with dissociative anesthesia recovery.
- On the other hand, in the cat, the plasma half life of zolazepam is 4.5 hours and that of tiletamine is 2.5 hours. This longer lasting effect of zolazepam over tiletamine may partly explain the smoother recovery characteristics in this species compared to that in the dog.
- Telazol® has been used extensively in exotic large animal (large cats, pigs, and hoof-stock) as a darting agent for immobilization.