PREANAESTHETICS -ANTICHOLINERGICS, SEDATIVES, TRANQUILIZERS

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PREMEDICATION (Preanesthetics):

A. General use

1. Sedation of intractable animals for routine diagnostic procedures, examination, trailering etc.
2. Sedation for minor surgical procedures in conjunction with local anaesthesia.
3. Preanesthetic medication:
   a. Reduces anxiety and improves induction quality.
   b. Decreases amount of induction agent needed.
   c. Lengthens and promotes smoother recovery from anaesthesia.
   d. Decreases the minimum alveolar concentration for inhalation agents
   e. Decrease salivary and bronchial secretions
   f. Block vagal reflexes, which can cause bradyarrhythmias.
   g. Provide pre-, intra-, and immediate post-operative analgesia.

Administration of premedicant drugs:

a) They are usually given IM 30-40 minutes before induction. (The time will depend on the drugs used.)

b) They can be given intravenously to quieten patients. This may be faster acting and have a more profound effect.

c) Occasionally, the drugs are given orally. The patient may be extremely difficult to handle (drug is hidden in food or water) or the drug may be better absorbed by this route.

d) The patient must be left quiet for the drugs to have their full effect.

PREMEDICANT DRUGS:

A) Anticholinergic Agents :

- `Drying' agents which also block vagal tone

1) Naturally found. e.g. atropine.

2) Synthetic. e.g. glycopyrrolate.

B) Tranquilizers, or Neuroleptics

- These are calming agents which reduce stress.
- The animal can arouse from sedation
- These drugs have no analgesic properties

I). Phenothiazine derivatives. e.g. acepromazine

II). Butyrophenones. e.g. droperidol, azaperone.

III). Benzodiazepines. e.g. diazepam, midazolam.

C) Sedatives

I). Alpha-2 agonists. e.g. xylazine, detomidine.

II). Chloral hydrate

D) Opioid Analgesic Agents

These drugs produce analgesia and sedation.

1) Agonists. e.g. meperidine, morphine, oxymorphone.

2) Agonist/Antagonists. e.g. pentazocine, butorphanol.

A} ANTICHOLINERGIC AGENTS:

Mechanism of Action

Competitive antagonists of acetyl-choline (ACh) thereby attenuating physiologic responses to parasympathetic nerve impulses. Since this is a competitive antagonism, large doses of ACh or other cholinomimetic drugs will overcome this block. They act immediately distal to postganglionic nerve endings. However, the block is not equally effective throughout the body. For example salivary glands respond to very low doses of atropine whereas somewhat larger doses would be required for effects on the heart.

1.Atropine:

A. Plant derived alkaloid with parasympatholytic activity.(Atropa belladona)

B. General effects:

1. Stimulates the medulla and higher cerebral centres.
2. Paralyzes the ciliary body and causes mydriasis
3. Inhibits nasal, oral and bronchial secretions
4. Dilates bronchioles causing a decrease in airway resistance.
5. Increases heart rate.
6. Decrease gastric secretions, smooth muscle tone and peristalsis.

C. Excretion:

1. Rapidly distributed throughout the body.
2. Destroyed by enzyme degradation and a portion is excreted by kidney.

D. Indications:

1. Inhibition of salivary and bronchial secretions.
2. Protection against reflex cardiac dysrrythmia eg. Vago-vagal, oculocardiac etc and bradycardia caused by increased vagal tone due to anaesthetic agents, intubation, and manipulation of ocular and visceral structures.
3. Atropine crosses blood brain barrier and can stimulate the vagus nerve before blocking them.Rarely, bradycardia and partial heart block will occur before heart rate increases.

E. It is contraindicated for use in treatment of abdominal pain in horse and most other animals because it can cause ileus.

F. Dose:

1. Equine : 0.0165-0.022 mg/kg I/V or I/M. If atropine is to be used as a preanesthetic medicant, 0.5-1.0 gallon of mineral oil can be given approximately 6 hours prior anaesthesia. This will help prevent fermentation of ingesta and gas accumulation in the intestinal tract due to atropine induced ileus. However it is not to be used routinely in equines since salivary secretions are not a problem in equine anesthesia and bradycardia, when encountered can be treated intraoperatively. It is used in horses that have either partial AV block or partial sinoatrial heart block when auscultated just prior to induction of anaesthesia.
2. Bovine, ovine, caprine : 0.02-0.04 mg/kg I/V or I/M. It can be given at 0.13 mg/kg I/M or 0.066 mg/kg I/V if desired. Atropine is not very effective in reducing oral secretions in ruminants. Some authors argue that it decreases the volume and increases the consistency of the secretions, making it more difficult for the cilia to remove pulmonary secretions, and increases the incidence of bloat in ruminants.
3. Swine : 0.066-0.088 mg/kg I/M
4. Small animals : 0.022-0.044 mg/kg S/C

II.GLYCOPYROLATE

A. Synthetic anticholinergic compound

B. General effects:
    1. Causing reversibly with muscarinic cholinergic receptors blocking the effect of acetycholine.
    2. It is poorly lipid soluble and does not penetrate blood brain barrier (BBB) or placental barrier (PB) as readily as atropine does.
    3. Rapid absorption following I/M administration, rapid clearance from the body
    4. Decreases salivary and gastrointestinal secretions

5. Increases heart rate
6. Produces smooth muscle relaxation
7. Dilates bronchioles, causing a decrease in airway resistance.

C. Most (60%) is rapidly excreted unchanged in the urine.

D. Indications:

1. Indications and contraindications are the same as those stated for atropine.
2. It may decrease gastric acidity more than atropine and therefore be more protective if regurgitation and aspiration of stomach contents occurs in horse and swine.

E. Doses:

1. Equine, swine: 0.005 mg/kg, I/V, I/M or S/C.
2. Bovine, caprine, ovine: 0.005-0.01 mg/kg, I/V, I/M or S/C.
3. Small animals: 0.011 mg/kg, S/C

Atropine vs Glycopyrrolate

l. Tachycardias not as extreme with glycopyrrolate.

2. Glycopyrrolate reduces volume and acidity of gastric secretions at therapeutic doses.

3. Little or no CNS effects with glycopyrrolate.

4. Onset of action IM, IV

Atropine 15-20 min 0.5-2 min

Glycopyrrolate 35-45 min 2-5 min

5. Duration of action of vagal blocking effect of glycopyrrolate is 2-3 hours and probably no more than 1.5 hours with atropine. Antisialogue effects last much longer.

SEDATIVES AND TRANQUILIZERS

1. Tranquilizers are either given slow I/V or I/M or by oral route.
2. As tranquilization develops the animal relaxes and hangs its head, the ears may droop. In cattle and horses the penis is relaxed and partially extruded. The dog may lie down, the eyes are glazed.

A. PHENOTHIAZINE DERIVATIVES :

M of Action: The principle central activity is the blockade of excitatory dopaminergic receptors, which are primarily in the basal ganglia. A deficiency of dopamine within the basal ganglia has been shown to be associated with a definite dysfunction of this system, such as Parkinson's Disease syndrome in humans, and catalepsy in experimental animals.

B. General effects

1. Causes depression of brain stem, which depresses alertness.
2. Potentiate analgesic agents and general anaesthetic agents.
3. Moderate anti-acetylecholine, anti-histamine and anti-cholinesterase effects.
4. Dose dependent alpha-adrenergic blockade causing vasodilation and hypotension.
5. Can cause hypothermia.
6. The sedative effects of these tranquilizers can be overridden and cause them to have little or no effect when given to excited animals.
7. Usually increasing the dose of these agents will not improve sedation.
8. Have an anti arrhythmic effect.
9. Lower the seizure threshold.

C. Excretion

1. Detoxified in the liver
2. Excreted through the kidney

D. Contra-indications

1. Do not use in cases of organophosphate poisoning or after recent treatment with organophosphate type anthelmintics.
2. Use with extreme caution, or not at all, in cases of hypovolemic or endotoxic shock.
3. Do not use epinephrine to counteract hypotension due to phenothiazine type tranquilizers, because it will potentiate hypotension (reversal effect). Alpha-receptor stimulation (vasoconstriction) provided by epinephrine will be partially blocked by the tranquilizer, allowing the beta effect (vasodilation) to prevail. Expansion of blood volume with fluids should be instituted. Norepinephrine, phenylephrine, or other agents that cause alpha stimulation could also be used.
4. Should not be used in animals with phenothiazine sensitivity.
5. Intracarotid injection of tranquilizers must be avoided as it will precipitate seizures and can cause death.
6. Coccygeal arterial injections in cattle can result in sloughing of the tail distal to the injection site.
7. Do not use for sedation in animals with diseases of the male external genitalia, especially in horse.
8. Has been implicated as a cause of permanent paraphimosis in stallions known as priapism.

D. Agents

1. Chlorpromazine hydrochloride (Largectil)
   a. Limited use in large animal anesthesia.
   b. General effects
      -Strongly hypertensive
      -Produces hyperthermia
   c. Dose:

   1.Equine – 1.1-2.2 mg/kg I/V or I/M. Given I/V, full depression occurs in approximately 5-15 minutes, lasting approximately 5-8 hours. Given I/M, depression occurs in 45-60 minutes and lasts 12-18 hours.

   2.Cattle – 0.2-1.1 mg/kg I/V or 1.1-2.2 mg/kg I/M.

   3.Sheep and goats – 0.55-4.4 mg/kg I/V or 2.2-6.6 mg/kg I/M.

   4.Swine – 1.1 mg/kg (0.5 mg/lb) I/M

   5.Dog/Cat – 0.5-1.0 mg/kg I/M or I/V

2. Trifluprомazine hydrochloride (siquil)
   1. 2-3 times as potent as chlorpromazine
   2. May cause transitory stimulation of the animal

   Dose:
   1. Equine - 0.22-0.44 mg/kg I/V or I/M
   2. Cattle – 0.11 mg/kg I/V
   3. Sheep and goats – 1.0 mg/kg I/V
   4. Dog -

3. Acepromazine maleate (Acepril)
   1. Most potent phenothiazine derivative.

   2 .In horses, it produces an insignificant decrease in heart and Cardiac output, a significant decrease in central venous pressure, MAP and respiratory rate and no changes in arterial blood gas analysis and is a potent vasodilator.

   3. Most of action occur within 15-20 minutes following I/V administration and last approximately 2 hours.

   4. Contraindicated for sedation during skin testing for allergy due to its antihistaminic effect.

   5. May cause permanent penile paralysis especially in cases of disease of external genitalia.

   6. May cause transitory stimulation of the animal.

7. Poor analgesic.

Dose:

Equine – 0.044-0.088 mg/kg I/V or I/M

Bovine – 0.01-0.02 mg/kg I/V or 0.03-0.1 mg/kg I/M

Caprine and ovine - <50kg- 0.1-0.2 mg/kg I/V, >50kg – 0.05-0.1 mg/kg I/V

Dogs – 0.03-0.05 mg/kg I/V or I/M.

Cats – 0.03-0.05 I/V.

Other phenothiazines are

1. Propiopromazine hydrochloride
2. Piperacetazine
3. Ethyl isobutazine

Advantages of Acepromazine :

Sedation

Antiarrythmogenic

Antiemetic

Potentiate other anaesthetics.

CAUTION

- Fairly long acting tranquilizer - some dogs still a bit ataxic or sedate 24 hr. after administration, especially geriatrics.
- **Caution** in young puppies (<2 months) - can get extreme sedation even with the lower doses.
- Lower doses in Boxer dogs ? Boxers are prone to vagal syncope so an anticholinergic should be used and/or low doses of phenothiazines. Rare, but may cause asystole.
- **Contraindicated** in breeding **stallions.** Risk 1:10,000 of priapism

B. BENZODIAZIPINE DERVATIVES

1. Diazepam is the most commonly used benzodiazipine in veterinary practice (Calmpose)
2. It is used primarily to treat seizures as is given prophylactically to prevent the anticipated seizure activity of other drugs such as ketamine hydrochloride.

Other benzodiazipines are

1. Zolazepam
2. Midazolam

Zolazepam is used with tiletamine (Dissociative Anaesthetic) in the name of TELAZOL

a) Diazepam (Calmpose 5mg/ml)

Actions on nervous system:

- The effect is produced because of CNS depression.
- Diazepam can be given orally, IV or IM (with unreliable absorption).
- Benzodiazipine receptor sites have been found within the CNS. It is hypothesized that benzodiazipine protagonism of these receptors potentiates the action of GABA which is generally an inhibitory neurotransmitter.
- Administration to normal dogs and cats is often associated with a dramatic increase in excitability during premedication.
- Diazepam is an effective appetite stimulant. It has been used intramuscularly and orally at doses ranging from 0.05 mg/kg to 0.4 mg/kg to treat anorexic cats.
- It causes mutual potentiation when used with barbiturates.
- The CNS actions of narcotic analgesics are potentiated.
- Dissociative anaesthetics like tiletamine or ketamine produces poor muscle relaxation and when used along with diazepam produces good muscle relaxation.
- Diazepam (0.36 mg/kg) and ketamine (3.6 mg/kg) given together intravenously after a parasympatholytic premedication.
- Diazepam (0.27 mg/kg) ketamine (5.5 mg/kg) I/V together can be used in cats.
- Muscle relaxation produced by diazepam is probably central in origin although some of this action is attributable to direct activity at neuromuscular junction.

Cardiovascular effects:

- The cardiovascular depressant effects of the benzodiazipines are not usually important at low doses.
- Diazepam decreases catacholamine release and this accounts for some antidysrythmic properties that have proven useful in treating certain kind of myocardial hyperexcitability.
- Most injectable preparations of diazepam contains propylene glycol which causes dysrhythmias and cardiovascular depression.
- It also increases the coronary blood flow.
- When used with narcotic analgesic (fentanyl) it has supra-additive or synergistic effect decreasing cardiac output, peripheral resistance and arterial blood pressure.

Other effects:

The respiratory effect of diazepam is very less.

Doses:

Dogs – 0.1-0.5 mg/kg I/V, p.3-0.5 mg/kg I/M

Cats – 0.1-0.5 mg/kg I/V, 0.3-1.0 mg/kg I/M

Horses – 0.02-0.1 mg/kg I/V

For prevention of seizures in adults 0.1-0.15 mg/kg I/V

For prevention of seizers in neonatal foals 0.11-0.44 mg/kg I/V

Bovine – 0.4 mg/kg I/V

Full recovery occurs in 45-60 minutes

Ovine and caprine – 0.11 mg/kg I/V as a preanesthetic agent just prior to ketamine and 0.25-0.5 mg/kg I/V for sedation.

b) Midazolam (Versad 5 mg/mL**)**

1. A water soluble benzodiazepine with greater potency than diazepam in humans and with a shorter half-life.

2. It may cause excitement if given alone in small animals, particularly in high doses. There seem to be more problems of excitation in cats than in dogs.

3. It works well as an intramuscular sedative in pigs but it is expensive.

4. It is a very potent hypnotic in humans and high doses can produce light anesthesia. This is not true for animals.

5. It is absorbed well from IM sites.

6. Midazolam is often used with an opioid analgesic to induce anesthesia in dogs. Occasionally there is excitement therefore it is probably best used in patients which are already depressed. Better to give the opioid first and follow up with the midazolam when some sedation seen.

8. Doses are similar to the lower range for diazepam.

c) Zolazepam

This drug is used with **tiletamine** (a cyclohexamine) in the combination **`Telazol'**. Trials are still being carried out in various species although it is available in mainland Europe and the U.S.A.

In 1981 a specific benzodiazepine antagonist was discovered. The generic name is flumazenil. In early literature it was referred to as RO 15-1788.

DISADVANTAGES / CONTRAINDICATIONS OF BENZODIAZIPINES ARE,

1. Highly protein bound 99%.
2. Calmpose carrier is propylene glycol.

3. Concentration in fetus may cause teratogenic effects during 1st week of development.
4. Paradoxical anxiety or fear.

C. BUTYROPHENONE DERIVATIVES

Mechanism of Action

1. Block the central actions of dopamine and norepinephrine.
2. May mimic GABA in extrapyramidal system

Examples are Azaperone ,Droperidol ,Haloperidol and Lenperone

General effects:

1. Produces hallucinations, restlessness, mental agitation and even feeling of aggression. (These symptoms appear when the animal is in recovery phase).
2. Produce hypertension due to alpha-adrenergic blockade.
3. Potent antiemetics

B) Pharmacological Properties

1**. Nervous System**

a. Sedation. Long action.

b. Extrapyramidal signs such as rigidity or tremors are seen more often with Butyrophenones than with phenothiazines.

c. Antiemetic

d. Decrease motor activity

e. Behavioral changes common.

f. Ataxia at higher doses.

2. Cardiovascular System

Vasodilation due to alpha-1 receptor blockade, but hypotension is not as severe as with phenothiazines.

C) Clinical Use

Droperidol, azaperone and, to a much lesser extent, lenperone are the only Butyrophenones used in veterinary anesthesia in North America.

Fluanisone is used in the U.K.

1. Droperidol

d. Not used alone in veterinary anesthesia but rather **combined** with fentanyl in the commercial product **Innovar-Vet.**

e. When used alone in dogs, usually prefer to stand or half sit. Decreases voluntary motor activity. Look "stoned".

f. A fairly long acting drug and its combination with fentanyl (lasts 20 minutes) doesn't seem particularly rational.

g. May see behavioral changes even after apparent recovery from the drug especially in Doberman Pinschers which often develop fine muscle twitching over the face and head. Avoid the use of the drug in this breed.

Dose: Dogs – 0.7-1.7 mg/kg I/V, 2.2-2.9 mg/kg I/M

2. Azaperone (Stresnil, Suicalm)

a. Used almost exclusively in **pigs** for sedation, as a premedication or to decrease aggression.

b. Duration of action 2-3 hours.

c. Vasodilation and decrease in pressure. May see cutaneous flushing.

d Attenuates malignant hyperthermia response to halothane.

e Dose in Pigs:

Low dose: 0.4-1.2 mg/kg IM. For transportation.

Medium dose: 2 mg/kg IM. Sedation and premedication.

High dose: 4 mg/kg IM. Recumbency. Not often used.

3. Lenperone

a. United States approved use in dogs and cats in l981.

b. Lower potency in blockade of alpha-1 receptors.

c. Shorter duration?

4. Fluanisone

a. Available in the U.K. combined with fentanyl as commercial preparation - `Hypnorm'. Used in a similar fashion to Innovar-vet.

4. Haloperidol: (Serinase)

Cattle – 0.5 mg/kg I/V

Dog – 0.5-1.0 mg/kg I/V

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SEDATIVES

ALPHA-2 AGONISTS

Often referred to as **sedative analgesics.** The compounds in this group used for sedating animals: **Xylazine, detomidine, medetomidine** and **romifidine.** These are all Thiazine derivatives.

a) Mechanism of Action

1. Activation of central [[alpha]]2 receptors

2. Alpha-2 receptors are located both presynaptically and postsynaptically in the peripheral and central nervous systems.

3. Presynaptic [[alpha]]2 receptors regulate the release of transmitter from the sympathetic nerve endings, i.e. the release of norepinephrine or dopamine is inhibited.

4. Alpha receptors are also found in the spinal cord and probably mediate the profound analgesia caused by this drug.

5. Emetic action which is not prevented by dopaminergic blockers.

6. Centrally acting muscle relaxant.

b) Pharmacological Properties

1. Nervous System and Muscle Relaxation

a. Sedation

b. Analgesia

c. Centrally-mediated muscle relaxation.

d. Emetic action in carnivores.

2. Cardiovascular System

a. Initial rise in blood pressure due to action on post-synaptic alpha-2 receptors and resultant vasoconstriction.

b. Within 2-5 minutes after an intravenous injection the arterial pressure will begin to decrease. This is due to the central alpha-2 adrenergic action which depresses normal sympathetic outflow from medullary pressor centres. *c.* Activation of alpha-2 receptors ultimately cause depolarization of the excitatory neurons of the dorsal motor-nucleus of the vagus and leads to an increased vagal tone and resultant bradycardia. Second degree A-V block is very common for the first few minutes post IV injection. Bradycardia is also a reflex response to the initial hypertension.

d. Decreased cardiac contractility and decreased cardiac output.

e. Bradycardias can be severe in small animals.

f. Ventricular arrhythmias are common in small animals.

g. Increased sensitivity to epinephrine induced arrhythmias, especially with xylazine.

3. Respiration

In clinical doses, very little change. In horses and dogs, rate may decrease but arterial carbon dioxide levels do not rise significantly, although arterial O2 tension can decrease. In combination with other respiratory depressants the final effect can be profound. In cattle there is an increase in respiratory rate with rapid, shallow breathing

4. Other

a. Depresses gastrointestinal and rumenal motility.

b. Hypoinsulinemia with subsequent hyperglycemia and glycosuria.

c. Increased intrauterine pressure in cattle with potential problem for abortion in the last trimester with xylazine.

d. Depressed thermoregulation in cats, dogs and cattle has been reported.

e. Local anesthetic action in *vitro*.

c) Pharmacokinetics

1. Undergoes rapid metabolism with several metabolites. (20 minutes in rats)

2. Half-life of elimination after IV administration of a single dose is 45.5 minutes in the horse, 36.5 minutes in cattle, 23 minutes in sheep, and 30 minutes in dogs.

d) Clinical Use of Xylazine (xylazil (100mg/ml), xylaxin (20mg/ml), izine (20mg/ml)

1. Equine

a. While the heart rate does decrease, severe bradycardia is not the problem that it is in small animal and does not warrant the routine use of an anticholinergic. heart rate rises after 3 - 5 minutes.

b. Contraindicated in animals with hypotension or arrhythmias.

c. Can usually be used safely in horses with second-degree A-V block provided the block is one which resolves upon excitement or exercise. Give slowly if IV and use lower dose range.

d. One of the best analgesics for visceral pain.

e. **Dose :0.25-1.1 mg/kg IV.** Use low doses in draught horses. Xylazine is also used for analgesia by the **epidural** route as **0.17 mg/kg in 10 mL of saline**

2. Canine

a. Best never use without an anticholinergic (controversial because of AV blockade).

b. Because of the problems of ventricular arrhythmias and decreased cardiovascular function, particularly when combined with ketamine, it is not recommended for use as a premedicant for inhalation anesthesia.

c. Emesis occurs after IM administration.

d. **Contraindicated** in intestinal obstruction and in respiratory obstruction e.g. brachycephalics.

e Not reliable in aggressive dogs.

f. **Dose: 0.5-1.0 mg/kg IV, IM, SC.**

Duration: 30 min IV, 2 hours IM.

If used, be aware of the cardiovascular depression. Use O_2, avoid in sick, pediatric and geriatric patients.

3. Feline

a. As in dogs, ventricular arrhythmias can be a problem, however if used in very low doses with ketamine and atropine it is fairly safe. It is contraindicated in cats with cardiopulmonary disease or animals with metabolic derangements that may affect cardio-vascular function.

b. Emesis is a side effect.

c. **Dose: 0.25-1.0 mg/kg IM, SC.**

4. Ruminants

a. Require a much lower dose than other species. Become recumbent with higher doses.

b. Causes decreased rumen motility. Monitor carefully for bloat. Cattle salivate profusely and bellow. Local analgesic techniques can be used with sedation provided by xylazine. Do not leave cattle unattended until there is full neck tone.

c. Use **very low doses in young goats.** (0.02 mg/kg)

d. If animal is sick, depressed, hypovolemic etc. be extremely cautious with its use. Avoid its use in the last trimester of pregnancy.

e. Generally do not require the use of an anticholinergic.

***f.* Dose: 0.05-0.08 mg/kg IM.** Standing sedation. Recovery 2-3 hr.

0.2-0.30 mg/kg IM. Recumbent. prolonged effects, recovery in 5-6 hours.

0.1-0.2 mg/kg IV. Recumbent in 2-5 minutes if kept quiet. Can give in the coccygeal vein, useful for bulls.

0.07 mg/kg in 5.0 - 7.0 mL sterile saline by epidural Injection. Gives analgesia for castration or laparotomy.

5. Pigs

a. Variable response. Expensive.

b. **Dose: 2 mg/kg IV, 4 mg/kg IM**

e) Clinical Use of Detomidine (Dormosedan ,Norden))

Licensed for use in horses.

Presentation: 10 mL, 10 mg/mL.

1. Greater potency and longer duration than xylazine. Ataxia in 80% cases and local muscle tremors possible with high doses. About 30% of animals exhibit piloerection and sweating.

2 Reports of sudden deaths in horses given activated sulfonamides alongside detomidine.

3 Other mortality reports: at the present its use as a premedication agent in horses before halothane anesthesia is not recommended due to some unexplained deaths. There is some difference of opinion on the validity of this stance.

4. Also used as a premedicant prior to ketamine anesthesia

5. Effective as a sedative/analgesic together with butorphanol +/- local anesthesia for minor surgery or standing laparotomies.

6. Dose:

Horses:

10-30 µg/kg IV, 20-50 µg/kg IM. The head droops and the animal plants its feet. The lower dose is usually adequate for most procedures. Further analgesia can be produced by using butorphanol once sedation from the detomidine has set in.

Cattle:

Similar dose range. Tend to remain standing.

f) Clinical Use of Medetomidine

For **small animals.** Available in the U.K. as Domitor. Used in a similar way to xylazine, but has the same disadvantages. It is marketed with a specific antagonist, **atipamezole (Antisedan)** which has remarkable arousal effects within a minute of administration. The dextro-rotatory form **(Dexmedetomidine)** is more potent and this may be marketed in the future instead of the racemic mixture now available.

Dose: Dogs 10-80 µg/kg IM:

Cats 50-150 µg/kg IM

Dexmedetomidine has been used for epidural analgesia in cats and dogs and as a capture agent for wildlife. Investigation into its use are continuing.

g) Clinical Use of Romifidine (Sedivet)

Now licensed for use in horses. It is claimed to produce less ataxia than xylazine. Romifidine's effects are longer lasting than xylazine.

Equivalent dose to 1 mg/kg of xylazine is 100 µg/kg romifidine.

Alpha 2 Antagonists.

1. Xylazine sedation was originally "antagonized" by **doxapram** which is a general CNS stimulant not a true antagonist. This is still occasionally used in ruminants

2. 4-aminopyridine

3. Yohimbine (Antagozil)- general stimulant. Give slow IV, or tachycardia.

Dose: Cattle 0.125 mg/kg IV. Not very good results.

Horse 0.075 mg/kg IV.

Dogs 0.1 mg/kg IV.

Cats 0.5 mg/kg IV.

4. Tolazoline. Works better in cattle than yohimbine. The better antagonist for all species.

Dose: Cattle 1.0 mg/kg IV. ,Sheep 2.0 mg/kg IV.

Dogs 2.0 mg/kg IV ,Cats 2.0 mg/kg IV.

5. Idazoxan.

Dose :All species: 0.05-0.1 mg/kg

6. **Atipamezole (Antisedan).**

Specific antagonist for medetomidine. Give equal volume to medetomidine used. Attempts are often made to reverse alpha-2 / ketamine combinations using alpha-2 antagonists. It should be realized that complete reversal cannot be expected if the ketamine is still active.