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Chemical Immobilisation of Indian Mammals in Captivity

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Editor's Note: This is a paper written for the Post-graduate course in Wildlife diseases and management, Zoological Society of London. The paper was to be a written essay on an aspect of wildlife disease or capture relative to the trainee's own country. Navin Kumar has selected Chemical Immobilisation of Indian Mammal as his topic. We are proud to publish this excellent paper and feel that it will be of use to veterinarians in India.

Abstract:

During the last two decades a number of drugs have become available which, when used separately or when combined with another, have facilitated the handling and movement of nervous and aggressive animals. These drugs are usually grouped according to their principal properties into Narcotics such as Etorphine and Fentanyl and sedatives such as Azaperone and Xylazine and anaesthetics such as Phencyclidine and Alphaxalone.

Knowledge of the clinical pathology of these drugs and of the different responses found amongst the various mammals is necessary if the effect required is to be accurately and safely obtained. Narcotics, for instance, are contraindicated in the felidae on account of their severe excitatory side effects but in some carnivorous families the milder side effects can be overcome by combining the narcotics with a sedative.

This paper sets out to describe these different effects and to show that an understanding of them is important when selecting the appropriate drug for a particular case.

Introduction

Veterinarians working in zoos are becoming more involved in the care of wild animals kept in the zoos and wild parks. The concept of this paper is to share the experience with Veterinarians working in various zoos in India. A decade back there was no captive equipment and drugs hence various physical restraints were adopted, in the process a few animals died due to capture stress, injuries, fractures and so forth. The safest means of capture is to immobilise chemically which facilitates the veterinarians to attend to clinical diagnosis, surgery and translocation of captive animals. In recent years immobilising agents were developed.

Drugs used to tranquilise and immobilise wild animals vary from species to species. These drugs and their combinations act at various sites within the brain to produce tranquillisation, sedation, analgesia, anaesthesia. The chemical immobilisation may vary depending on factors such as drug molecular size, pH and ionic change, route of administration, tissue change and leakage, amount of drug per body weight (dosage) and other variables such as species of animal, age, sex, season, time of day, animal behaviour and pathologic condition.

The most useful and safe dosage is that which rapidly immobilises an animal without causing adverse side effects. The immobilising agent should preferably be reversible and rapidly eliminated.

During the course of the study at Whipsnade Wild Animal Park during 1991-92 a few immobilisations were done with immobilsation drugs and in combinations on a few species. The most common drugs used were Immobilon, Etorphine, Xylazine, Ketamine, Telezol, Medetomidine. Data listed in the table are based on practical experience during the course study of Wildlife Diseases and Management offered by the Zoological Society of London to veterinarians during 1991-92. The animals listed are limited to common species in Indian zoos.

Etorphine hydrochloride (M-99):

Pharmacology: Etorphine hydrochloride was described as a synthetic morphine-related derivative. Etorphine can shortly be described as a potent analgesic and narcotic. In ungulates it produces excitation followed by analgesia, alleviation of the feeling of fear, loss of aggressiveness, depression of respiration, stiffness of the muscles of neck and limbs, inhibition of gastrointestinal and ruminal motility and lowering of the body temperature. At low doses animals will remain on their feet but ataxia and a certain amount of excitement will dominate the condition. Injected animals walk away with a typical mincing gait. At higher doses the animals will stop in a cataleptic state or lay down in sternal recumbancy. Excitement is covered by deep analgesia and areflexia. The consciousness is depressed but not totally lost.

Following intramuscular injection the first signs of action are seen after 4-5 minutes and the duration is a few hours. The action of Etorphine may be reversed through competitive antagonism by the morphine antagonists Diprenorphine (Revivon) M-50.

In elephants, rhinoceros and wild horses and wild ass, Etorphine also produces a tranquilising effect and Etorphine given alone usually at very low dosage gives sufficient immobilisation. In most other ungulates, especially in nervous species in the wild, the excitement may cause injuries to the animals. Higher doses of Etorphine will immobilise even these animals after an initial state of excitement, but muscle relaxation is poor. Etorphine mixed with a suitable tranquilizer may completely eliminate the excitement and potentiate the effect of Etorphine thus allowing the dose of Etorphine to be lowered. Etorphine is commercially available as Immobilon and contains 2.45mg/ml Etorphine hydrochloride and 10mg/ml

Acepromazine. It is also available as Etorphine hydrochloride alone.

Antagonist
Diprenorphine (M-50) is a specific antidote developed for Etorphine. When given intra-venously it displaces Etorphine from the brain in from 30 seconds to 2 minutes. During that time the animal will awake and be capable of full defences. Etorphine and Diprenorphine are the bare derivatives and chemically related to morphine.

Pharmacology of M-50
Diprenorphine is a narcotic antagonist used to reverse the effects of Etorphine (M-99).

Indications
Diprenorphine acts as a depressant on the central nervous system and if used in excessive dosage may complicate recovery.

Administration
Diprenorphine is injected I/v, if possible, otherwise I/m. The recommended dose is twice the milligrams of the injected dose of Etorphine. When injected I/v reversal usually occurs in 1-4 minutes. I/m injection requires 15-25 minutes for reversal effect.

Side-Effects
No side effects should be noticed unless an overdose is given. An overdose will cause narcosis similiar to low doses of Etorphine.

Xylazine (Rompun) - Pharmacology
Xylazine is a non-narcotic sedative, analgesic and muscle relaxant. It acts in the central nervous system, stimulating norepinephrine release at Alpha-2 adrenergic receptor sites causing animals to appear sleepy. Stimulation during the induction stage may prevent optimum sedation. When approached suddenly a sedated animal may rouse explosively with reflexive defense mechanisms like kicking, biting may not be abolished.

Indications
Xylazine is used as a mild sedative and at higher doses for immobilisation. It can be used singly or in combination with other drugs for a wide variety of species. The primary role in wildlife immobilisation is in combination with narcotic and dissociative agents where it markedly enhances their effect and can improve reversibility of the condition. It is very effective in captive or tame animals rather than in excited or free-ranging wildlife. Xylzine has been used alone to capture various species of deer, but prolonged induction times and other side effects severely limit situations in which it is a drug of choice. Xylazine may be given intravenously or intramuscularly. There is a wide species variation in the optimum dosage. Immobilisation occurs within 3-5 minutes following I/v or 15-30 minutes after I/m. Analgesia lasts from 15-30 minutes by sleep like state is maintained for 1-2 hours. Duration of action may be quite long, often in excess of 5 hours.

Side-Effects and Precautions
Occasionally muscle tremors, bradycardia and partial A-V block occur with normal doses. Atorphine should be given if necessary to prevent cardiac effect. Xylazine also causes relaxation of the distal oesophagus, rumen and intestinal stasis, which can result in reflex or regurgitation and aspiration or rumen contents, bloat and other gastro-intestinal problems. Xylazine produces an additive effect when combined with tranquilizers and barbituates. The analgesic effect is variable. The depth of analgesia should be ascertained before clinical diagnosis or surgical procedures are begun.

Antidote
Yohimbine hydrochloride (Antagonil): Yohimbine hydrochloride causes rapid and often complete recovery from xylazine sedation. Other reversal agents are available for Rompun: Antisedan, RXB2002A, Colx.

Ketamine hydrochloride - Pharmacology
Ketamine is a non-barbituate dissociative anaesthetic agent. The animal usually retains normal pharyngeal-laryngeal reflexes. This desirable effect minimizes inhalation of ingesta near the glotis. Ketamine does not produce skeletal muscle relaxation. Nystagmus may be noted during induction. Profound analgesia is rapidly produced. Excessive salivation can be alleviated with Atrophine. Ketamine is detoxified in the liver. Metabolites are excreted via the urine. Ketamine produces a fixed expression in the eyes. The eyelids are dilated and stay open yet the cornea usually remain moist. Peripheral reflexes persist. Because swallowing reflexes are usually unaffected, excessive saliva is swallowed as usual. Induction is characterised by ataxia. This ataxia can be a problem in some species if no tranquilizer administered concurrently. The animal lies down. The animal becomes insensitive to external stimulation. Lateral nystagmus appear, then disappear with increased depth of anaesthesia. Ketamine may be safely and effectively used for anaesthesia of numerous other species of wild animals. It is particularly effective in wild carnivores, reptiles and birds but not suitable for most ungulates with the addition of a sedative or tranquilizer. The duration of effect varies with the species and dosage administered. Recovery is usually smooth in carnivores and furbearers. In ungulates, recovery may be stormy so Ketamine is usually combined with a tranquilizer to balance its anaesthetic effects, allow lower doses of Ketamine, smooth recovery and improve the recovery time.

Side-Effects and Precautions
Ketamine causes tonic clonic convulsions in few wild felids. Other carnivores are similiarly affected. Primates are less commonly effected. Convulsive effects can be obviated by administering Diazepam with a Ketamine antidote. There is no known clinical antidote for Ketamine.

Medetomidine - Pharmacology
This is a potent sedative and specific full agonist of both pre- and postsynaptic Alpha-2-adrenoceptors. The Alpha-2/Alpha selectivity ratio of Medetomidine is 1620 as compared with 160 for Xylazine. Medetomidine is a racemic mixture, the active isomer is predominantly the D-enanticimer (discamedetamidine). Medetomidine acts by modulating noradrenaline release

on adrenalinergic nerve terminals and is devoid of affinity for beta-1, beta-2, H1, H2, 5-HT, 5HT2 muscarine, dopamine, tryptamine, GABA, my- and delta-type opiate and benzodiazepime receptors. Characteristic effects of medetomidine in animals include sedation, analgesia, relief of anxiety, bradycardia, hypotension and hypothermia. At high doses medetomidine has hypnotic or anaesthetic effects. Medetomidine is metabolised in liver and metabolites are excreted mainly in the urine.

Antidote: Atipamezole is a reversal agent for medetomidine (and xylazine).

Tiletamine hydrochloride and Zolazepam hydrochloride (Telazol) - Pharmacology: Tiletamine hydrochloride is a cyclohexanone dissociative agent related to Ketamine hydrochloride and Phencyclidine hydrochloride. Zolazepam hydrochloride is a non-phenothiarzine pyrazalodiazepinone tranquilizer. Zolazepam effects include sedation, muscle relaxation, but no bradycardia. The combination capitalizes on the desirable characteristics of each while minimizing the side effects. Combined Tiletamine hydrochloride-Zolazepam hydrochloride is used for chemical immobilization and surgical anaesthesia in a wide variety of carnivores, artidactylids, birds, reptiles and amphibians. Onset occurs within 5-12 minutes after intramuscular injection. Recovery is prolonged.

Antidote
There is no specific antidote for Telazal. There is no a reversal agent called Benzodiazipinis sychas zylazepam.

Acepromazine Maleate - Pharmacology: Acepromazine maleate is a phenothiazine derivative and has been used in veterinary practice in most countries for a long time. Acepromazine is a nervous system depressant which, used on its own, produces sedation in most animals at low dosage. It will trigger anticonvulsant, hypotensive and weak analgesic action and potentiate the effect of analgesics and barbituates. As other phenothiozine derivatives it is an adrenalytic and should not be used on exhausted and excited animals. Disturbances of the heat regulatory mechanism in shade-loving antelopes has been observed under field condition. This can be quite significant.

Indications
Acepromazine is rarely used alone for immobilisation purposes but rather in combination with Etorphine, Ketamine. Its muscle relaxation characteristic is of particular value when used with Ketamine and Phencyclidine.

Side-Effects
Acepromazine in combination with other hypotensive agents occasionally , instead of producing central nervous system depression, acts as a stimulant and hyper-excitability ensues.

Drug Combinations

"Hellabrunn" Mix
The mix is prepared by dissolving 500mg Xylazine dry powder in 4ml of 100mg/ml Ketamine solution. The combination has a 45-60 minute duration of action and can be used in a wide variety of mammals, birds and reptiles. To increase the duration of effect, Ketamine should be given i/v or i/m. The mix gives good muscle relaxation in mammals, birds and reptiles unlike Ketamine alone, which produces muscle rigidity and tremors. Due to the high level of Xylazine in the mix, if ruminants are not fasted for 24 hours there is a risk of ruminal tympanic developing. In antelope, relaxation of the tongue and pharynx leads to a risk of asphyxiation in these species, therefore it becomes necessary to intubate antelope by giving Hellabrunn mix and place them in sternal recumbency for the duration of the immobilisation. The mix has a very slimey emetic effect in all carnivores, particularly big cats which can be prevented with administration of 1-2mg Atrophine prior to the mix. Elephants are also sensitive; 1-3ml is adequate for elephants for minor procedure.

Combination of Etorphine and Xylazine
Etophine alone produces muscle tremors which are abolished if combined with Xylazine. The duration of action of the combination is approximately 45 minutes (though can be much longer) and has the advantages of being reversible with the use of Revivon. The authors recommend Revivon should be administered at twice the Immobilon dose. The animal should be observed for 10 hours after immobilisation due to the risk of renarcotisation. Side-effects, especially in equids, include tachycardia and sweating.

In antelope and horses, disturbances of blood pressure may also be seen and occasionally these may lead to spontaneous heart failure. The combination if contraindicated in cats and primate and as such is extremely dangerous to the operator and reversal agents should be on hand in the event of accidental injury. Literature review and field trial at Whipsnade with this combination has recorded that time to onset of immobilisation was shorter than with use of Etorphine alone. Excellent muscle relaxation for almost any surgical procedure; no problems with reversal of effect using anatagonist, M50 and Yohimbine. This combination offers the advantage of excellent muscle relaxation and opportunity for rapid reversal of drug action.

Combination of Xylazine and Ketamine
In ruminants this combination provided quick immobilising action and good muscle relaxation. Because Ketamine is metabolised more rapidly than Xylazine, recovery is more rapid than when anaesthesia is induced with Xylazine alone.

Combination of Medetomidine and Ketamine
This combination can be used to induce complete immobilisation. In trials on captive leopards, Medetomidine has been found to have a potency up to 30 times that of Xylazine, allowing a 3/4 reduction in Ketamine doses required for immobilisation, a reduction time to onset of deep sedation, improved myorelaxation during immobilisation and an improved reversal with a reduction in the degree and duration. These effects are entirely due to the increased Alpha-2 effect. The same would be seen if more Xylazine were used though the volume would be increased. The combination of Medetomidine and Ketamine provides good immobilisation for a

variety of minor surgical procedures in exotic felid and canines. The recommended dosages: 233mg/kg Medetomidine; 2.33mg/kg Ketamine - though it is preferred to use less Medetomidine and more Ketamine because of the cardiac depression of Medetomidine.

Discussion

Quite a lot of mammalian species were immobilised during the course study of Wildlife Diseases and Management offered by the Zoological Society of London at Whipsnade Wild Animal Park, out of which a few Indian mammals immobilised can be of great interest for vets working in captive conditions where they can adapt the procedures of immobilisation with confidence. These animals were immobilised for various reasons like clinical, surgical, haematology and translocations. The dosages of immobilising drugs best suited is given in table 3 and in all care was taken especially in herbivores to see that there was no regurgitation. Monitoring the depth of immobilisation like respiration, pulse, temperature right from induction time to recovery is very important with regular intervals of 5-10 minutes. This helps to know the depth of anaesthesia. One of the most recent developments noticed was dependent upon the type of operational procedures required on the animal.

It was interesting to observe that endotracheal tube and inhalation anaesthesia were applied. Augumented anaesthesia or increasing the depth of anaesthesia was used in animals previously immobilised by injectable agents. They are the major general anaesthetic agents in balanced techniques because they can be quickly installed or removed from animals through the respiratory system and the depth of anaesthesia can be precisely controlled during the cause of a prolonged surgical procedure. One advantage in placing an endotracheal tube in an animal is the availability of a means for support of pulmonary ventilation. Intubation facilitates treatment of atelectasis with pailitive premire and prevention or treatment of abnormalities in arterial carbondioscids by increasing or decreasing minute volume.

It is an advantage to be able to supply increased concentrations of oxygen to the alveoli and in a limited way to provide a potential means for evaluating the health of respiratory function. This is accomplished with an anaesthetic machine that can run in a closed configuration. For all species inhalation anaesthesia follows the quantal dose response concept, which states that the incidence of effect increases as the dose increases, that is, inhalation agents are predictable which is not true with injectable agents which tend to be unpredictable and idiosyncratic from one animal to the next and from one species to another. Some of the effective inhalation anaesthetics used were Halothane, Isoflane. The combination of immobilising drugs in practice at Whipsnade Wild Animal Park also did give good response and excellent results especially the combination of Immobilon and Xylazine.

Conclusion

Ketamine hydrochloride on primates in recommended doses is a good immobilising drug, has good induction, sedation and restraint, fair muscle relaxation. It is good for short procedures such as translocation, TB testing, blood collection and radiography but causes slight salivation. In ruminants the combination of Etorphine and Xylazine gave a shorter time to onset of immobilisation than with the use of Etorphine alone. Excellent muscle relaxation is produced for almost any surgical procedure and there are no problems with reversal of effect using antagonist.

The combination of M50 and Yohimibine offers the advantages of excellent muscle relaxation and opportunity for rapid reversal of drug action.

The combination of Xylazine and Ketamine in ruminants provides quick immobilisation action and good muscle relaxation. Because Ketamine is metabolised more rapidly than Xylazine, recovery is more rapid than when anaesthesia is induced with Xylazine alone. This combination in Felidae is best for immobilisation, good analgesia, good muscle relaxation, good safety margin, and the best oral anaesthetic for wild carnivores.

Ketamine alone is a good analgesic and gives good immobilisation for surgery with some muscle twitching. In Canidae, Ketamine alone is a good analgesic and gives good immobilisation but with convulsions and seizures. Combination with Xylazine is the best immobilisation, good analgesia, good muscle relaxation, good safety margin and is the best overall general anaesthetic for wild canines.

Miscellaneous Considerations

Immobilising drugs are potent and dangerous. In India except for Ketamine hydrochloride, none are available. Xylazine is now being imported and marketed by one or two firms and is very expensive. Since Etorphine is a narcotic, so far no clearance has been given by the Drug Enforcement Department hence import of Etorphine into the country needs lots of excise and formalities to be cleared. Drug companies are unable to justify the expense in importing and carry out extensive testing necessary to licence a drug for use in wild animals. However, immobilising agents must be used by the zoo veterinarians if proper health care is to be given. There is a decided advantage in using combinations that allow dosage reduction. Skill and experience are prerequisites to the successful combination of immobilising agents.

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Table 1.
List of Common Immobilising Drugs

Name	Trade-Name	Class of Agent
Etorphine	M-99	Narcotic
Ketamine-Hydrochloride	Vetlar/Ketlar	Cyclohexamine (Dissociative)
Xylazine	Rompun	Sedative/Tranquillizer
Tiletamine- Zolazepam	Telazol	Cyclohexamine (Dissociative)
Meditomidine	Dormitor	Alpha2 Antagonist

Table 2
Drugs Used to Modify Effects of Immobilising Agent

Name	Trade-Name	Class of Agent
Diprenorphine	M-50	Narcotic Antagonist
Diazepam	Valium	Benzodiazepine
Yohimbine-Hydrochloride	Antogonil	Xylazine Antagonist
Acepromazine-Maleate	Acepromazine	Phenothiszine Tranquillizer
Atropine-Sulphate	Atropine	Parasympatholytic
Atipamezole HCL	Antisedon	–
RX821002A	–	Alpha2 Antagonsist

Table 3
Recommended Immobilising Drugs and Dosages

Species	Drug 1	Dosage (mg/kg)	Drug 2	Dosage (mg/kg)	Drug 3	Dosage (mg/kg)
Primates	Ketamine	8-10				
	Telazol	2-6				
Cervidae	M99		Xylazine	Tilazol		
Hog Deer	M99	1.5-3mg	Xylazine	3-4mg/kg		
Barasinga	M99	3-5mg				
Axis Deer	M99	3-6mg	Xylazine	3-4mg/kg		
Sika Deer	M99	2-4mg	Xylazine	3-4mg/kg	Tilazol	4.5-5mg/kg
Bovidae			Xylzine		Tilazol	
Nilgai	M99	4-6mg	Xylazine	3mg/kg	Tilazol	6-8mg/kg
Yak	M99	3-8mg	Xylazine	0.6-1mg/kg		
Gazelle	M99	2-3mg			Tilazol	2.5-15mg/kg
Black Buck	M99	2-3mg	Xylazine	3mg/kg	Tilazol	4.5-10mg/kg
4-horned Antelope	M99	2-3mg	Xylazine	3mg/kg		
Mouflon	M99	1-2mg				
Gaur	M99	5mg				
Felidae	Ketamine	5-10mg/kg				
	Telazol	1.5-5mg/kg				
	Ketamine & Xylazine	10mg/kg of Ketamine & 2mg/kg Xylazine				
Canidae	Ketamine & Xylazine	10mg/kg Ketamine & 2mg/kg Xylazine				