TRANQUILIZING EFFECTS ON DIFFERENT SPECIES OF ANIMALS BASED ON AGE, DOSE LEVEL, ONSET AND DURATION OF ANESTHESIA

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ABSTRACT

The effects of xylazine administration on arterial blood pressure, arterial blood pH, blood gases, rectal temperature, and heart and respiratory rates were recorded in healthy dog, cat, goat, cattle, sheep etc.based on age, dose level, onset, and duration of anesthesia. Xylazine (0.2 mg/kg, i/m) was administered. All baseline measurements were taken before the xylazine administration and were repeated at 5, 15-, 30-, 45-, and 60-min intervals. It was found that heart rate decreased at 15 to 60 min and rectal temperature decreased significantly at 30 to 60 min., but respiratory rate did not change significantly. Mean arterial blood pressure declined significantly at 15 to 60 min after anesthesia. In conclusion, reversal with the antagonist atipamezole is advised whenever serious cardiorespiratory problems arise. Medetomidine sedation also causes vomiting, increased urine production, alterations in uterine and endocrine activity, decreased intestinal motility, and lower intraocular pressure.

Keywords: Sedation, cardiovascular, tranquilizer, xylazine.

CHAPTER I

INTRODUCTION

A tranquilizer or sedative is a substance that induces sedation by reducing irritability or excitement. They are CNS depressants and interact with the brain actively, causing deceleration. Most of them have effects on gamma aminobutyric acid. To make tranquil or calm to relieve of mental tension and anxiety by means of drugs.

Tranquilization: Tranquilization is a state of calmness and quiet, but the patient is relaxed and indifferent to their surroundings.

Sedation: Sedation is a mild degree of CNS depression where a patient is awake but unaware of their surroundings.

Anesthesia: Anesthesia is a state of controlled temporary loss of sensation or awareness that is induced for medical purpose, it may include some or all of analgesia, paralysis, amnesia an unconsciousness.

Two basic classes of local anesthetics exist that aminoamides and the amino esters. Aminoamides have and amide link between the intermediate chain and the aromatic end.
Common sedatives include barbiturates, benzodiazepines, gamma-hydroxybutyrate (GHB), opioids and sleep-inducing drugs such as zolpidem (Ambien) and eszopiclone (Lunesta). Sedatives are central nervous system depressants and vary widely in their potency. They are usually in the form of a pill or liquid.

Major tranquilizers: Major tranquilizers, which are also known as antipsychotic agents, or neuroleptics, are so called because they are used to treat major states of mental disturbance in schizophrenics and other psychotic patients.
Antipsychotic medications that are used for some types of mental distress or disorder - mainly schizophrenia and manic depression (bipolar disorder). They can also be used to help severe anxiety or depression.
They all affect the action of a few chemicals in the brain called neurotransmitters – chemicals which brain cells need to communicate with each other.

Dopamine is the main neurotransmitter affected by these medications. It is involved in how we feel: It is also involved in the control of muscle movements.
If parts of the dopamine system become overactive, they seem to play a part in producing hallucinations, delusions and thought disorder. The basic aim is to help feel better, without making one feel slowed down or drowsy.

Minor tranquilizers: Minor tranquilizers, which are also known as anti-anxiety agents, or anxiolytics, are used to treat milder states of anxiety and tension in healthy individuals or people with less serious mental disorders.
The principal minor tranquilizers are the benzodiazepines, among which are diazepam (Valium), chlordiazepoxide (Librium), and alprazolam (Xanax). These drugs have a calming effect and eliminate both the physical and psychological effects of anxiety or fear.
Benzodiazepines' mechanism of action is enhancing the action of the neurotransmitter gamma-aminobutyric acid (GABA), which inhibits anxiety by reducing certain nerve-impulse transmissions within the brain. Other, less commonly used minor tranquilizers include meprobamate (Equanil,Miltown) and buspirone (BuSpar).

Objectives of the study:

The main objectives are to find optimum dose, onset and duration of anesthesia for dog, sheep, cattle and goat and the goal of this study was to explore effects on physiology of different organ and organ systems.

CHAPTER II

MATERIALS AND METHODS

2.1 Tranquilization Gun

In this experiment, the JM standard Dan-Inject rifle (Dan-Inject ApS, Kolding, Denmark), one of the popular injection guns, was used to deliver the dart. According to the manufacture's information, the length of the gun is 105 cm, weighing 2.9 kg, with an 11 mm bore barrel, using CO_2 as the gas pressure. The telescopic sight is 1.5-4.5×32 mm, and the effective range is 1-40m. The target is pointed with a crossed hair type telescope. The maximum pressure of this dart gun is 16 bar. In this study, the maximum gun pressure used was 11 bar, and the dart size was 3 mm.

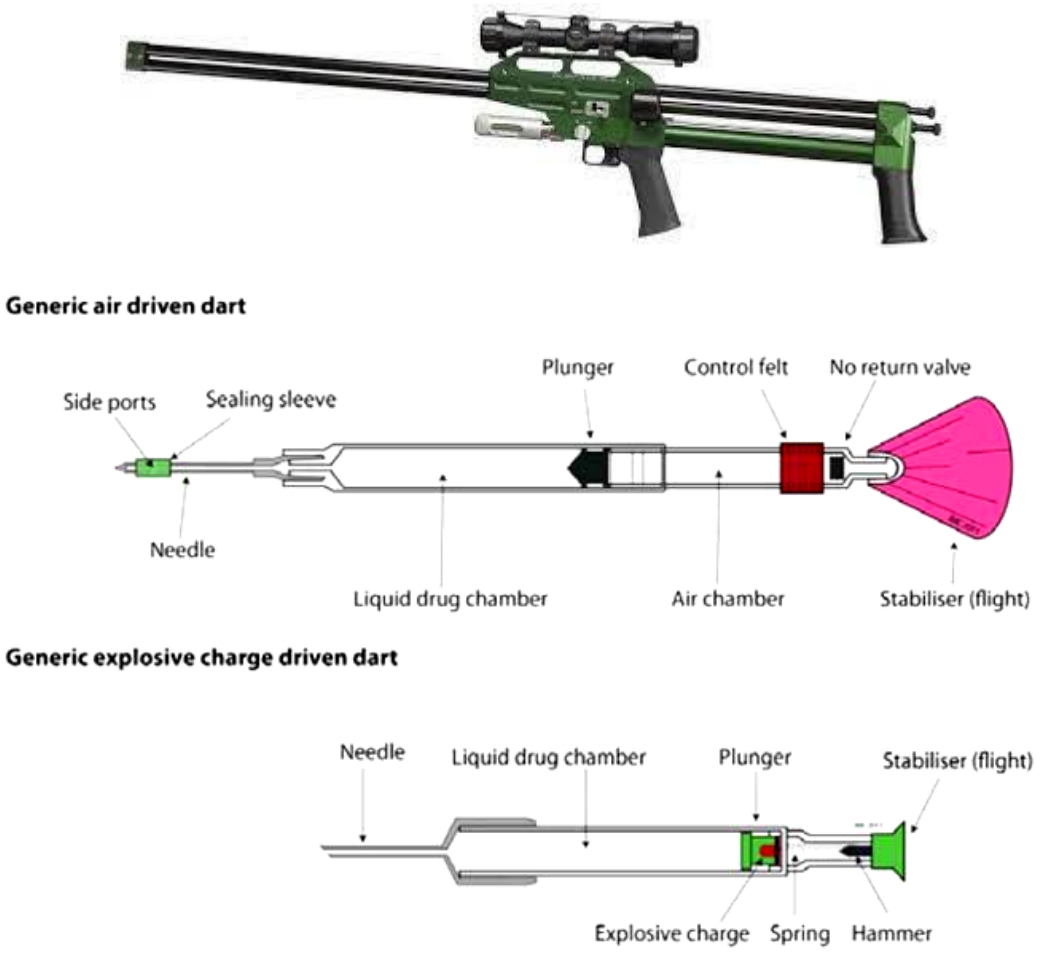

Figure 1: Tranquilizing gun with darts description.

2.2 Target

The target was constructed from A4 paper with a cross mark attached to a polypropylene board and ethylene-vinyl acetate foam. The shooting stage was fixed to minimize human effects. The target distance (shot range) was 5-20m.

2.3 Experimental Design

To minimize the variation between individuals, only one person administered the shot. For each shot, a gun was positioned on the stage. According to the manufacturer's advice (for single-dart injection), the gun's pressure was changed to determine the best pressure for each distance (Table 1). To test the accuracy of the pistol at each distance, a single dart was fired once to the target point (control), and then three times for each experimental scenario. The experiment was done in the field with.

Table1: Distance of target (shot range) and the gun pressure

Distance(meter)	**Pressure Setting(bar)**						
5	1	2	3*	4	5	6	7
10	2	3	4*	5	6	7	8
15	3	4	5*	6	7	8	9
20	5	6	7*	8	9	10	11

*Company’s recommendation for single dart injection

2.4 Criteria

The inclusion criteria were that two darts must hit the target and not penetrate the target animal deeply. For exclusion criteria: (1) A scenario of “too-low impact,” one or two darts did not hit the target; (2) a scenario of “too-high impact,” the dart deeply penetrated the target board; and (3) the two darts pierced away from each other by more than 15 cm which could be a miss shot in shooting large animals up to deer size.

PHOTO GALLERY

Fig 2.1: Shooting on Dog with Tranquilizer Gun

Fig 2.2: Seduced Dog

Fig 2.3: Measuring respiration rate of seduced Dog

Fig 2.4: Measuring heart rate of seduced Goat

CHAPTER III

RESULTS AND DISCUSSION

3.1 Tranquilization Effect

The goal of anesthesia is to give the patient reversible forgetfulness, analgesia, unconsciousness, and immobility with the least amount of risk to them. However, the homeostasis of the patient may be compromised by anesthetic medicines and adjuvants at unknown times and in unpredictable ways. Xylazine is a useful sedative in cattle, sheep, goats, horses, cats and primates. It may also be a valuable (but relatively short acting) analgesic in sheep and goats (Grant and Upton, 2004). Xylazine, medetomidine and dexmedetomidine should be used with caution in sheep, since they can produce severe hypoxia (Kästner, 2006; Kästner et al., 2007).

Table 2. Tranquilizing effects of Xylazine on different species of animal based on age, dose level, onset, and duration of anesthesia.

Species	**Drug used**	**Body weight (kg)**	**Dose (mg/kg)**	**Onset (Minute)**	**Duration of Anesthesia (minute)**
Dog1	Xylazine	22	2	50	50
Dog2	Xylazine	26	1	10	45
Sheep1	Xylazine	23	0.2	35	13
Sheep2	Xylazine	20	0.2	33	12
Cattle1	Xylazine	330	0.2	25	45
Cattle2	Xylazine	280	0.2	18	18
Goat1	Xylazine	22	0.2	15	65
Goat2	Xylazine	20	0.2	12	60

The major use of xylazine in laboratory animal anaesthesia is in combination with ketamine to produce surgical anaesthesia. Xylazine has been reported to cause pronounced hyperglycaemia (Saha et al., 2005) and a marked diuresis (Greene and Thurmon, 1988).

In this study xylazine was given in dog at 1-2 mg/kg body weight. The onset of tranquilizer effect was about 10-50 minutes. And the duration of sedation was about 50 minutes. As well as xylazine was given in cattle, sheep and goat at 0.2mg/kg body weight. The onset of tranquilizer effect in cattle, sheep and goat was about 18-25, 33-35 and 12-15 minutes respectively. And the duration of sedation in cattle, sheep and goat was about 18-45, 12-13 and 60-65 minutes respectively.

During sedation there was found marked salivation in sheep and goat. The other side effects were lower the temperature, heart rate and respiration rate in every different animals. For delivering consistent amounts of analgesia, low dose continuous infusion strategies may be preferable. Additional research is needed to better understand the dose-related cardiovascular effects of α2-agonists in veterinary anesthesia to reach their full potential.

3.2 Effects on Respiratory System

The respiratory rate decreases under sedation with 2-agonists for varied lengths of time. Even at sublethal doses, the respiratory depression caused by 2-agonists alone is less severe than that caused by other sedatives. Respiratory depression results after the CNS depression caused by 2-adrenoreceptor activation. Medetomidine significantly decreased respiratory rate in dogs at dosages between 20 and 60 g/kg BW. When medetomidine was delivered alone, there were no discernible decreases in arterial oxygen tensions. These outcomes are in line with trials in which dogs received doses of ranitidine of 40 and 120 mg/kg BW, respectively, and showed a decrease in respiratory rate without appreciable changes in arterial blood gases. Dexmedetomidine alone did not lower respiratory rate in cats, and medetomidine alone did not significantly change arterial blood gas readings. It's crucial to understand that when a 2-agonist is administered alongside other sedatives, the severity and relevance of the respiratory depression it causes will rise. In dogs premedicated with medetomidine and induced with propofol, hypoxemia, cyanosis, increased arterial carbon dioxide tension, and decreased respiratory rate have all been seen. Medetomidine (30 g/kg BW, IM) and butorphanol

(0.2 mg/kg BW, IM) significantly reduced the respiratory rate in dogs as compared to medetomidine (30 g/kg BW, IM) alone or medetomidine and ketamine (3 mg/kg BW, IM) alone) (Sinclair, 2003).

3.2.1 Respiratory Rate

Holding the hand in front of the nostrils allowed researchers to measure the patient's respiratory rate prior to the induction of anesthesia, after 5 minutes, and then every 15 minutes for the next 120 minutes (Ullah, 2017). The central and peripheral chemoreceptors' sensitivity to CO2 and oxygen is altered by anesthetics and a few perianesthetic medications in a dose-dependent way. Regarding preserving homeostasis during the perioperative period, this has significant clinical ramifications. In animals that have been hypercarbic or hypoxemic while under anesthesia, outward indications will likewise lessen. Unsedated animals typically show evident tachypnea and a rise in VT or respiratory effort in reaction to severe hypoxemia or hypercapnia, but in anesthetized animals, these outward indicators of an imminent crisis may be absent or much attenuated (Tranquilli et al., 2007). The phenothiazine and benzodiazepine sedatives often reduce the respiratory rate, especially if an animal is somewhat excited prior to administration, but they do not appreciably alter arterial blood- gas tensions (Turner et al., 1974).

3.3 Body Temperature

With a clinical thermometer, the patient's body temperature was measured in the rectum prior to anesthesia induction, after five minutes, and then every fifteen minutes for the next 120 minutes (Ullah, 2017). Opioid medication also has an impact on the hypothalamus thermoregulatory system. The most frequent reaction is typically hypothermia, especially when opioids are administered in conjunction with other CNS-depressants during the perioperative period (Moore, 2005). Opioid medication does, however, occasionally result in hyperthermia in cats, horses, pigs, and ruminants. An increase in muscular activity linked to CNS stimulation in these species may be partly responsible for this rise in body temperature; however, a particular central hypothalamic mechanism has also been suggested, albeit it is yet unclear how it works (Tremblay, 1990). Panting is seen commonly after opioid administration, most often in dogs, but this effect tends to decrease with the onset of hypothermia.

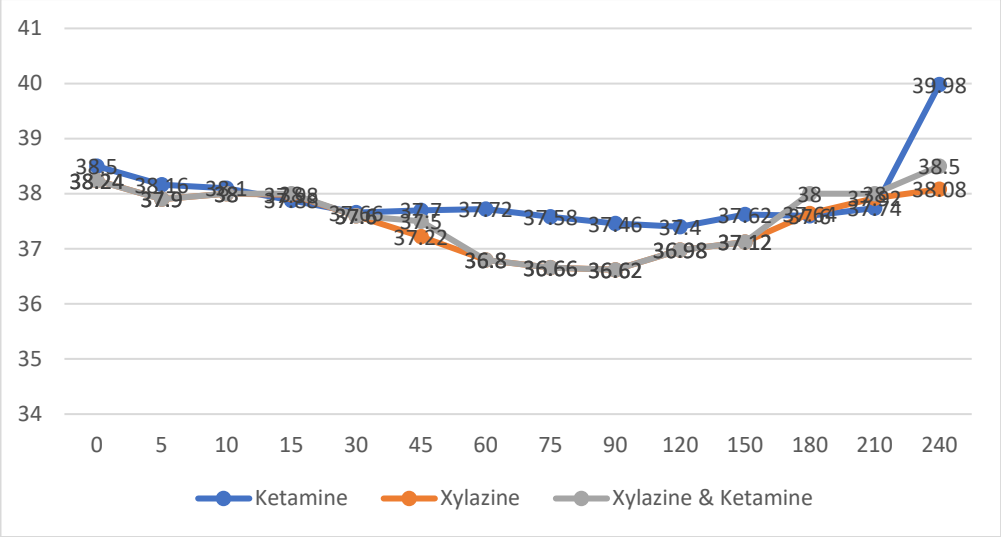

Figure 3: Temporal change in mean rectal temperature (^{o}C) following administration of ketamine, xylazine and their combination in dogs.

3.4 Effects on Cardiovascular System

Many humoral variables are jointly responsible for maintaining the integrity of the circulation. Although the effects of anesthetics and chemical restraints (barbiturates, butyrophenones, phenothiazines, and inhalation anesthetics) on clotting time and bleeding time in most animals are not fully understood, they are widely thought to be significant. Animals with thrombocytopenia or inherited coagulation-factor deficits (von Willebrand's disease) are especially susceptible to exacerbating bleeding issues. Numerous medications prevent platelet aggregation, which often makes a considerable contribution to hemostasis (Barr et al., 1992).

3.4.1 Pulse Rate

With the aid of a stethoscope, the heart's pulse was heard before anesthesia was induced, after five minutes, and then every fifteen minutes for the next 120 minutes (Ullah, 2017).

3.4.2 Hemodynamic Effects

The haemodynamic effects of α2-agonists in the dog have typically been described as a biphasic blood pressure response with decreased heart rate and cardiac index. This study found that medetomidine caused qualitatively similar changes, irrespective of dose between 1 and 20 kg IV.

3.4.3 Cardiac Output

Cardiac output decreases following a2-agonist administration in dogs (Bloor et al., 1992). The precise mechanism is unknown although several mechanisms have been suggested, including: (i) direct myocardial depressant effect; (ii) decreased function in response to α_2-agonist-mediated increase in after load; and (iii) myocardial hypoxia and dysfunction in response to coronary vasoconstriction (Murrell and Hellebrekers, 2005).

3.5 Muscle Relaxation

It has long been understood that 2-agonists induce analgesia and muscular relaxation. Inhibition at 2-adrenoreceptors at the interneuron level of the spinal cord underlies the accompanying muscle relaxant effect, which is a useful characteristic of 2-agonists in veterinary medicine (Cullen, 1996).

3.6 Analgesia

Alpha2 and opioid receptors can be found on some of the same neurons and in similar areas of the brain. Beyond just being receptors, these molecules have shared machinery. The same signal transduction systems (membrane associated G proteins) are activated by the binding of either 2-agonists or opioid agonists to their receptors, and this causes a series of events that cause potassium channels in the neuronal membrane to open. The pain route is effectively severed when potassium channels in the postsynaptic neuron are activated, as this causes the cell to become hyperpolarized and ultimately render it resistant to excitatory input. As a result, analgesia is produced by 2-agonists and opioid agonists (Sinclair, 2003).

3.7 Other Effects

3.7.1 Hypothermia

In contrast to the consistent drops in body temperature reported with the use of other anesthetic agents that induce vasodilation, alpha2-agonists may enable better maintenance of body temperature due to peripheral vasoconstriction and central redistribution of blood, with a subsequent reduction in cutaneous heat losses. Small animals should still have their body temperatures checked, and appropriate measures should be taken to maintain body heat and avoid sharp drops (Sinclair, 2003).

3.7.2 Endocrine

According to reports, alpha2-agonists, most often xylazine, cause an increase in serum glucose by inhibiting the release of insulin, promoting the release of glucagon, or doing both in the and cells of the pancreas (Angel and Langer, 1988).

3.7.3 Urinary Activity

Drugs that stimulate α-adrenoreceptors make the uterus more contractile in both pregnant and non-pregnant women (Nicolás barceló et al., 2021). Due to anecdotal instances of early labor and abortions, anesthesia textbooks advise against using xylazine in severely pregnant cows because it promotes contraction of the bovine uterus (Tranquilli et al., 2007). Small doses of detomidine given to pregnant cows and clinical doses of medetomidine given to pregnant dogs, respectively, cause a decrease in myometrial contractility (Galbete et al., 2017).

3.7.4 Vomiting

Typically, α 2-agonists cause vomiting in small animals by activating the chemoreceptor trigger zone, which is located close to the locus coeruleus in the brain (Jarolmasjed and Kolahian, 2010). After using xylazine, up to 50% of dogs and 90% of cats have early drowsiness that is accompanied by vomiting. Vomiting was seen in up to 90% of cats and 8% to 20% of dogs during medetomidine sedation (Tranquilli et al., 2007).

3.7.5 Gastrointestinal Motility

The activation or inhibition of α2-adrenoreceptors situated both presynaptically and postsynaptically appears to be the key determinant of the adrenergic regulation of gastrointestinal secretions and motility. In general, α2-agonists suppress reticuloruminal contractions and colonic motility in sheep, cattle, and horses, decrease gastric acid secretion (Bloor et al., 1992), extend intestinal transit time (Morrell et al., 1991), and prolong intestinal transit time (Bloor et al., 1992). The dose and specificity of the α2-agonist alter the gastro-intestinal suppression. It has been shown that medetomidine significantly reduces the motility of the colon in dogs as well as the electrical activity of the small intestine. The α2-adrenergic antagonist atipamezole totally blocked these effects, demonstrating that the influence on gastrointestinal motility is mediated via α2-adrenoreceptors (Sinclair, 2003).

3.7.6 Tear Production

When used separately, xylazine and ketamine HCl significantly reduce and increase tear production, respectively, but when combined, the effect is not severe enough to have a negative impact on the surface of the eye. It is desirable that xylazine and ketamine be administered simultaneously, or at the very least, in the same syringe without a pause in between. Furthermore, for satisfactory outcomes, the dose of xylazine should be less than 1 mg/kg. When xylazine alone or in combination with ketamine is administered to dogs, the authors advised using ocular lubricants or artificial tears (Sehgal et al., 2018).

CHAPTER IV

CONCLUSION

In this study, the anesthetic regimen had no significant influence on respiratory rate, but showed significant changes at 15, 30 and 60 minutes after xylazine administration in mentioned animals. The effects of xylazine on the arterial blood pressure depend on the relative effects of the central and peripheral stimulation. This study has shown that xylazine administration in goats depresses the cardiovascular system and care must be taken in minimizing any depression which may result from anesthesia. On the other hand, the decline in body temperature may affect other physiologic parameters, therefore monitoring of body temperature is essential for anaesthetized patient. Xylazine, an adrenoceptor agonist, has the potential to cause tachypnea. Furthermore, for satisfactory outcomes, the dose of xylazine should be less than 1 mg/kg. It is advised that the xylazine anesthetic regimen be utilized in the above-mentioned animals for the safe induction and maintenance of anesthesia at the prescribed dose based on the data gathered from the current investigation. During the procedure, it is important to pay attention to your breathing and heart rate.

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BIOGRAPHY

This is **Mahiun Talib Emon**, the second child of **Md. Habibul Islam** and **Sultana Rajia**, doing his graduation on Doctor of Veterinary Medicine (DVM) at Chattogram Veterinary and Animal Sciences University under Faculty of Veterinary Medicine. He passed the Secondary School Certificate Examination (SSC) in 2014 from Ideal Preparatory High School, Sherpur Distric and got GPA 5.00 and then Higher Secondary Certificate Examination (HSC) in 2016 from Sherpur Govt. College, Sherpur Distric and got GPA 5.00 out of 5.00. Currently he is doing his yearlong internship. He has a great enthusiasm in his study area to develop day one skills and gain more practical knowledge to be prepared for the modern era of science.