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Short Communication

Evaluating the Efficacy of Xylazine, Ketamine, and Atropine in Sheep for Veterinary Pharmacology Instruction

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The current research was conducted with the objective of developing a practical laboratory of Veterinary Pharmacology course, specifically for the purpose of evolving a practical part of the theory in the chapter of general anesthetics. The practice of the evaluation of drugs acting on the central nervous system in this discipline has difficulty with the choice of experimental model, because sometimes there are no laboratory animals such as rats, mice or rabbits; however, it is possible to use larger animals such as sheep. In this paper, we demonstrated that sheep is a suitable experimental model for demonstrating the action of drugs that produce sedation and anesthesia. The effects by the action of xylazine, ketamine and atropine can be produced in about 60 min which corresponds to time allotted in a teaching practice. Therefore, the authors recommended other sister colleges in Ethiopia and elsewhere in the world to use sheep as experimental model for demonstration of general anesthesia for their students.

Key words: Anesthetics, drugs, central nervous system, sheep.

INTRODUCTION

The key to successful surgery and a successful practice is working toward better implementation of anesthesia, from drug delivery to monitoring. Safe and effective anesthesia provides an opportunity for better surgery, and faster and more comfortable recovery (Grubb et al., 2010). Veterinary Pharmacology is delivered for third year students in College of Veterinary Medicine, Mekelle University. The course has got both theory and practical parts. One of those practical parts is demonstration of general anesthesia in laboratory animals so as to prepare the students for the upcoming courses like Veterinary Surgery. However, the assessment of drugs acting on the central nervous system in this discipline has difficulty with the choice of experimental model, because there are no laboratory animals such as rats, mice or rabbits; nevertheless, it is possible to use larger animals such as sheep.

The sheep can be an experimental model for the evaluation of drugs that act on the central nervous system during the available time for laboratory practice. The objective of this paper is to develop adequate anesthetic technique that can fit with the allotted time for laboratory

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practice in our college using sheep as experimental model.

MATERIALS AND METHODS

Study area

The present study was conducted in Veterinary Pharmacology Laboratory at College of Veterinary Medicine, Mekelle University, Kelamino Campus. Kelamino is located in Mekelle city. Mekelle is situated approximately 783 km north of Addis Ababa at an altitude of 2,000 meter above sea level. The mean annual rainfall of the study area is 628.8 mm. The annual minimum and maximum temperatures are 11.8 and 29.94°C, respectively (Bureau of Planning and Economic Development (BoPED), 1998).

Drugs and instruments used for the study

Drugs and instruments used in the current study were the following. Xylazine: bulbs (1 ml equivalent to 23.32 mg); Ketamine: bulbs (1 ml equivalent to 50 mg); atropine ampoules (1 ml equivalent to 1 mg), Digital Thermometer (range 32 to 42°C), endotracheal tubes, stethoscope (YUYUE), 1 ml syringes, cotton and disinfectant: iodine tincture (2%).

Experimental animals

The experimental animals were male sheep. The animals were identified by their numbers: Sheep No.1, 2, 3 and 4. The body weights of the animals ranged from 17 to 23 kg.

Administration of drugs

The drugs were administered in the inside of the inner thigh intramuscularly based on their body weight. The injection site was disinfected by 2% tincture of iodine and the drugs were administered as follows: Sheep No. 1 and 2 received xylazine at the dose rate of 0.3 mg/kg. Sheep No. 3 and 4 received xylazine at the dose rate of 0.3 mg/kg, atropine 0.2 mg/kg and after 15 min, ketamine at the dose rate of 15 mg/kg was administered. Atropine was used for the reduction of salivary and bronchial secretions (Walter et al., 2008). Sheep No.3 and 4 were intubated using endotrachial tubes so as to avoid potential obstruction of the upper airway (Taylor, 1991).

Measurement of parameters

The sheep were controlled all the time before and after the administration of the drugs. The actions of the drugs on the central nerves system such as sedation, cutaneous insensibility and unconsciousness were recorded after the administration of the drugs. The Ramsay sedation scale was used to assess the level of sedation after administration of the drugs (Ramsay et al., 1974). Heart rates, respiratory rates, rectal temperatures and rumen motility were recorded before and after the application of the drugs (Grubb et al., 2010). Heart rate and respiratory rate were determined with the help of stethoscope and stop watch in the left and right lateral sides of the thoracic cavity, respectively. Rectal temperature was recorded using a digital thermometer. Ruminal motility was recorded by placing hand firmly behind the last rib in the depression of paralumbar fossa in the left side for 2 min.

RESULTS

In sheep No. 1 and 2, symptoms like sedation, motor in coordination with visible muscle relaxation, cutaneous insensibility and increase salivary secretion were observed after 15 min of drug administration. These symptoms disappeared in 45 to 60 min. In sheep No. 3 and 4, sedation followed by drowsiness, ataxia, relaxation of the limbs and unconsciousness with slight salivation were observed in less than 3 min after the administration of the drugs. After 60 min, the animals recovered from unconsciousness but maintained some degree of cutaneous insensibility and ataxia, and muscle relaxation with difficulty for walk. All animals at the end of the experiment recovered; any case of complication or death was not present. Table 1 depicts the physiological parameters results obtained in the experimental sheep before and after administration of the drugs.

DISCUSSION

Sheep No. 1 and 2 showed physiological parameters in normal range for the species prior to the administration of xylazine (Mendoza et al., 2010). However, there was decrease in body temperature after the administration of the drug and this could be explained by blocking of the hypothalamic thermoregulatory center by xylazine (Walter, 2008). The decrease in heart rate could be attributed to inhibition of the release of the neurotransmitter noradrenalin. The increase in respiratory rate could also be attributed to the activation of alpha 2 adrenergic receptors and their implication for the relaxation of the bronchial smooth muscles (Schwartz and Clark, 1998; Kastner, 2006; Walter, 2008). After application of the drug, sheep No. 1 and 2 exhibited effects of xylazine action like sedation, analgesia and muscle relaxation. Xylazine is an alpha 2 adrenergic receptor agonist. Alpha-2 agonists inhibit noradrenalin release and P nociceptive release. The locus ceruleus is particularly rich in alpha-2 receptors, and is involved in the sedation. Muscle relaxation might be attributed to the action of xylazine and inhibition of transmission of nerve impulses in intraneuronal level. Inhibition of motility of rumen could be explained due to the inhibition of release of the neurotransmitter acetylcholine exerted by xylazine (Schwartz and Clark, 1998; Johnston, 2005; Kastner, 2006; Walter, 2008).

Similarly, sheep No. 3 and 4 showed physiological parameters in normal range for the species before administration of xylazine, atropine and ketamine (Mendoza et al., 2010). The decrease in temperature, heart rate, the increase in respiratory rate and inhibition of ruminal motility

Table 1. Recorded physiological parameters in the four experimental sheep before and after administration of the drugs.

Parameter	Sheep No. 1 and 2		Sheep No. 3 and 4	
	Before inj.	After Inj.	Before Inj.	After Inj.
Ave temp (°C)	39	38	39.5	38.5
Ave. RR (per min)	14	24	18	26
Ave. HR (per min)	75	60	76	70
Ave. RM (per 2 min)	2	NP	2	NP

Ave. Tem = average temperature, Ave. HR = average heart rate, Ave. RM = average runimanl motility, Ave. RR = average respiratory rate, Before inj. = before injection, After inj. = after injection, NP= not perceptible for more than 2 min.

could be explained similar to sheep No. 1 and 2. The result obtained from sheep No. 3 and 4 showed synergism between xylazine and ketamine. Atropine action decreased the salivary secretion when compared to sheep treated only with xylazine.

In addition, ketamine produced a dissociative anesthesia due to inhibition of excitatory neurotransmitter acetylcholine and excitatory neurotransmitter glutamate (Edmonds et al., 1995). Ketamine also exerted agonist action on Mu and gamma opioid receptors (Sarton et al., 2001). In addition, ketamine produced depression of the thalamocortical portion of the brain and increases the activity of the limbic system which causes analgesia and sleep although the eyes often remain open with a slow nystagmic gaze along with preservation of the corneal and light reflexes (Boothe, 2005; Anonymous, 2009; Ozkan et al., 2010). In the case of these sheep, the anesthetic state was maintained around 60 min, followed by rapid recovery which coincides with the reported effects for ketamine xylazine mixture (Caracuel et al., 1992).

Conclusion

The sheep is a suitable experimental model for demonstrating the action of drugs that produce sedation and anesthesia as part of teaching practices in Veterinary Pharmacology and Veterinary Surgery. The effects by the action of xylazine, ketamine and atropine can be produced in about 60 min, which is the average duration of laboratory practices in Veterinary Pharmacology and other specialties. Hence, this experience can be transferred to other Ethiopian universities that do not have laboratory animal facilities.

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