Bangladesh Veterinary Journal (2021) 55(1-4): 10-18
pISSN 0378-8113 •eISSN 2708-6054
https://doi.org/10.32856/BVJ-55-2021.02

Research Article

OPEN ACCESS

Clinico-hemato-biochemical evaluation of general anesthesia with combination of Xylazine-Ketamine and Ketamine alone in sheep (*Ovis aries*)

Md. Sabuj Rahman[1§], Mst. Antora Akter[1§], Moinul Hasan[1], Md. Enamul Haque[2], Enamul Haque[3], Md. Rafiqul Alam[1], and Md. Mahmudul Alam[1*]

[1]Department of Surgery and Obstetrics, Bangladesh Agricultural University, Mymensingh-2202, Bangladesh
[2]Department of Physiology, School of Medicine, Ajou University, Suwon, South Korea
[3]RMIT University of Melbourne, Australia

Abstract

This study was designed to evaluate the effects of Xylazine-Ketamine and Ketamine alone on clinical parameters (rectal temperature, heart rate, respiratory rate and SpO2), haematological parameters (TEC, TLC, Hb and PCV) and biochemical parameters (AST, ALT, BUN, TP and Creatinine) during general anesthesia in sheep. Six healthy sheep were used for this experiment and divided into two groups named, Group A (Xylazine-Ketamine) and Group B (Only Ketamine). All the parameters measured and recorded before anesthesia, at 5 min, 10 min, 15 min, 20 min, 25 min, 30 min, hour post-induction of anaesthesia and after 24 hours of recovery. Temperature decreased significantly ($P < 0.05$) from control value at 10 min post-induction in both group A and B. This decrement continued up to 25 min post-induction and then started to increase. Heart rate increased ($P < 0.05$) significantly from control value at 10 min post-induction in sheep of Group A. This increment continued up to 25 min post-induction and then started to decrease. But in Group B, after 10 min of induction, heart rate fluctuated remarkably. Respiratory rate was decreased after 5 min post-induction and it was in the same trend up to 25 min. We also found fluctuation on the respiratory rate in Group B. We observed a decreasing pattern on SpO2 in both groups. In haematological parameters, we found a significant decreasing trend in all parameters up to 25 min post-induction in both groups. We found non-significant decrement of ALT and AST up to 25 min post-induction in both groups. The BUN and TP value were significantly ($P < 0.05$) decreased from control value up to 25 min post-induction in Group A, but in Group B value changed with a fluctuated trend. We got an increment on creatinine value in both groups, but in the case of Group B, the increment was high. Results suggest that combination of Xylazine-Ketamine can be used for general anesthesia in sheep rather than Ketamine alone although there are some systemic effects on the body.

Keywords: Sheep, Anaesthesia, Xylazine, Ketamine

INTRODUCTION

Similar to simple stomach animals, general anaesthesia is required in compound stomach animals as well. Though most of the surgical correction in ruminants can be done under local anesthesia and proper restraining (Taylor, 1991). Combination of drugs is seen commonly during the general anesthesia, mainly in ketamine and xylazine with or without diazepam (Taylor, 1991). General anaesthesia in ruminants may involve complex-

*Corresponding author's E-mail address: mahmuddso2004@gmail.com
§ Contributed equally
Article history: Received: 04 January 2021; Accepted: 19 March 2021.

ities like regurgitation, bloat, respiratory complication, nerve paralysis etc. To minimize these unwanted and restricting effects, ketamine is administered in combination with drug groups such as alpha-2 agonists. It possesses anxiolytic, anticonvulsant, hypnotic, sedative, skeletal muscle relaxant, and amnestic properties. During general anesthesia, vital organs of the body may lead to an unstable condition (Hossen *et al.*, 2004a). Several studies on the effect of general anaesthesia with the different combination in horse and pet animals were performed (Hodgson and Dunlop, 1990; Hossen *et al.*, 2004b; Kamal *et al.*, 2019) very few researches were done on small ruminant, therefore, this study was aimed to evaluate the effect of general anesthesia with the combination of Xylazine-Ketamine and Ketamine alone on the clinical, hematological and serum biochemical parameters in adult nonpregnant indigenous ewes.

MATERIAL AND METHODS

Experimental location and period

The study was conducted at Veterinary Teaching Hospital (VTH) of Bangladesh Agricultural University (BAU) and Department of Surgery and Obstetrics, Faculty of Veterinary Science, BAU, during the period from July to November 2019.

Experimental animals

Six healthy ewes were used in this experiment having the weight ranged from 12 to 14 kg and aged between 1 to 1.5 years. The sheep were housed in a well-ventilated room with veterinary supervision and accessed to food and water ad libitum.

Experimental design

The experimental animals were divided into two groups: Group A: xylazine-ketamine, Group B: Only Ketamine (Table 1).The experimental animals were closely monitored from 24 hours prior to anaesthesia. Clinical and physical examinations were performed thoroughly. Heart rate, respiratory rate and rectal temperature were recorded to ascertain that they were not suffering from any infectious diseases or any other disorders. The animals to be anaesthetized in the next morning were isolated from others and were kept in starvation for overnight.

Anesthetic procedure

The animals were premedicated and then placed on the operation table on lateral recumbency. An assistant grasped the animal's limbs and head. Anesthetic agents were injected using 1 ml and 5 ml disposable plastic syringe intramuscularly. Induction was examined and confirmed by puncture of a needle. Then mouth was opened and tongue was pulled out with tongue forceps and was connected to patient monitoring machine (Oxysmart- M, Oxycon Co. Ltd, China).

Table 1: Experimental design of the study

Group	**Induction**	**Anaesthetic agents**
Group A	Atropine Sulphate (Atrovet®, Techno Drugs Limited, Bangladesh) @0.05 mg/kg BW	Xylazine hydrochloride (Xyla®, Interchemie, Holland) @1.1 mg/kg BW and ketamine hydrochloride (Ketalar®, Popular, Bangladesh) @22 mg/kg BW
Group B	Atropine Sulphate (Atrovet®, Techno Drugs Limited, Bangladesh) @0.05 mg/kg BW	Ketamine hydrochloride (Ketalar®, Popular, Bangladesh) @22 mg/kg BW
Note: Each anesthetic agent was given after 5 min of previous inducing or anesthetic agents.		

Clinical examinations

Immediately before anesthetic administration, temperature, heart rate and respiratory rate were recorded as preanesthetic control value and again same parameters were recorded at 5, 10, 15, 20, 25, 30 minutes and 1hour post-induction for all groups. The recording was continued after 24 hours of anesthesia and 24 hours after of recovery. Clinical parameters like pulse rate, body temperature and blood oxygen saturation rate (SpO2) was live monitored from patient monitoring machine. For SpO_2, Pulse Rate and temperature, two different sensors were attached with the tongue of the animal. Simultaneously rectal temperature and pulse were recorded with the help of thermometer and stethoscope respectively to avoid error in patient monitoring machine. Respiratory rate was measured by counting the chest movement/ excursion of thoraco-abdomen.

Hematobiochemical examinations

Before the collection of a blood sample, the area was painted with gauze soaked with povidone iodine. Five ml blood from the jugular vein was collected from each sheep; 3 ml was transferred in a vacutainer without anticoagulant, to be used for serum biochemical analysis and remaining 2ml of blood was transferred in a vacutainer containing EDTA to perform routine haematological tests: Hemoglobin concentration (Hb), Total leukocyte count (TLC), Packed cell volume (PCV), Total Erythrocyte count (TEC) using automated hematology analyzer named (Sysmex XS-2000i®, Japan).

For biochemical analysis, blood sample transferred into clot activator tube were allowed to stay in the tube rack at room temperature for 30 minutes. Then sample centrifuged at 3000 rpm for 15 minutes and serum was collected in an Eppendorf tube using micropipette. Biochemical test was performed to monitor Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Total Protein (TP), Serum creatinine, Blood Urea Nitrogen (BUN) by kinetic method using Biochemistry Analyzer (Microlab®, Germany).

Statistical analysis

Data were presented as mean (±SE). IBM SPSS software version 20 was used to perform repeated measures analysis of variance to compare data, where the changes observed in the test levels, significantly different from control values. Probability $P < 0.05$ were considered statistically significant, as the level of significance.

RESULTS

Influences of general anaesthesia on clinical parameters in sheep

Effects of anaesthetic combinations on rectal temperature, heart rate, respiration rate, SpO_2 in sheep before anaesthesia, after 5, 10, 15, 20, 25, 30 min, 1-hour post-induction and 24 hours after recovery are shown in Table 2.

In this study, we found a decrease in rectal temperature from pre-anesthetized control value throughout the experimental period in Group A. The decrement at 10 minutes after induction (101.93 ± 0.16) in Group A was statistically significant ($P < 0.05$) and the decrement continued up to 25 minutes. Then the values returned to their control level after 24 hours of recovery. In Group B, temperature significantly decreased initially and then increased 15 minutes post-induction. Changes were inconstant here.

In Group A, the heart rate increased from pre-anesthetized control value (80.33 ± 2.03) until recovery. The increment at 10 min after induction (85.33 ± 3.05) was statistically significant ($P < 0.05$). Then, it returned to near baseline at 1-hour postinduction and to its control value after 24 hours of recovery. But in Group B heart rate changed dramatically. The value decreased from pre-anesthetized control value of 83 ± 2.0 to 81.33 ± 3.05 (at 10 min) and at 15 min post-induction it increased to 85.67 ± 4.16, which was statistically significant ($P < 0.05$). Then the value changed randomly up to 25 min.

In Group A, the respiratory rate decreased from pre-anesthetized control value (30.67 ± 3.06) and the significant ($P < 0.05$) decrement was noticed at 5 min of post-induction (29.88 ± 3.79). The decrement continued up to 25 min after induction. The value reached near baseline after an hour post-induction and returned to its control value after 24 hours of recovery. In the case of Group B, the respiratory rate decreased initially and then started fluctuating.

In group A, the SpO_2 decreased from pre-anesthetized control value (96.67 ± 4.16) to 5 min post-induction (87.10 ± 7.0), which was statistically significant ($P < 0.05$). The decrement continued up to 25 min post-induction. Then the value increased and returned to its baseline after 24 hours of recovery. In the case of Group B, the SpO_2 value decreased from pre-anesthetized control value (97 ± 3.6). Similar results were obtained in Group B as group A except the woken-up time. The animal woke up at 30 min of post-induction and it returned to its control value after 24 hours of recovery in Group B.

Influences of general anaesthesia on hematological parameters in sheep

Effects of anaesthetic combinations on TEC, TLC, Hb and PCV in sheep are shown in Table 3. In this study, we found a decreasing trend in TEC from pre-anaesthetized control value throughout the experiment in both groups. In Group A, the TEC decreased from pre-anesthetized control value (10.44 ± 0.07 thousands/cumm) at 5 minutes post-induction (9.76 ± 0.11 thousands/cumm), which was statistically significant ($P < 0.05$). The decrement continued up to 30 min post-induction. Then the value increased and returned to its baseline after 24 hours of recovery. Similarly, in Group B the TEC decreased from pre-anaestetized con-

trol value (10.37 ± 0.11 thousands/cumm) at 5 minutes (9.8 ± 0.12 thousands/ cumm) and that was significant ($P < 0.05$) statistically. In this group, the animal woke up after 30 min of induction. Then the value increased and returned to its baseline after 24 hours of recovery. In terms of TLC, we found that TLC in both groups decreased from pre-anaesthetized control value throughout the experiment. The value finally returned to its baseline after 24 hours of recovery.

We found a decrease in haemoglobin from pre-anaesthetized control value throughout the experiment in both groups and at 5 min post-induction significant ($P < 0.05$) decrement was observed. The value was then increased. It reached near its baseline after 1 hour of induction and returned to its control value after 24 hours of recovery. In Group B, animal woke up at 30 min post-induction.

The PCV decreased from pre-anaesthetized control value throughout the experiment in both groups. In Group A, PCV decreased from pre-anaestetized control value ($36.2 \pm 0.09\%$) and at 5 minutes ($35.43 \pm 0.19\%$), which was statistically significant ($P < 0.05$). The decreasing trend continued up to 30 minutes of post-induction and then started to increase. In Group B, PCV decreased from pre-anaestetized control value ($36.28 \pm 0.29\%$) and at 5 minutes ($35.6 \pm 0.15\%$) was significant ($P < 0.05$). The animal woke up after 30 min post-induction and we could not be able to take data of 1-hour post-induction. The value was then increased and returned to its baseline after 24 hours of recovery in all groups.

Influences of General Anaesthesia on serum enzyme in sheep

Effects of anaesthetic combinations on ALT, AST, BUN, TP and Creatinine in sheep are shown in Table 4. ALT value was abated slowly from pre-anaesthetized control value in both groups. In Group A, the ALT value reduced from control value and the reduction trend continued up to 25 minutes post-induction and started increasing from 30 minutes. We did not find any significant changes here. In Group B, very much inconsistent and fluctuated changes in ALT was observed except 30 min post-induction due to animal woke up at this point. ALT value increased gradually and returned near control value after 24 hours of recovery in both groups.

On the other hand, AST value reduced from pre-anaesthetized control value in both groups. In Group A, after 5 min of induction, AST value reduced to 16.5 ± 0.12 from control value (16.67 ± 0.88). The reduction continued up to 30 minutes. The value returned to near base value at 1hour post-induction and after 24 hours of recovery, all the values were quite reasonable. In Group B, a similar pattern was observed and we were unable to record data at 30 min post-induction because the animal woke up at this point.

BUN value increased from pre-anaesthetized control value in both groups. In Group A, 5 minutes after induction BUN value dramatically increased to 53.6 ± 0.21 from control value (51 ± 1.53) and it was statistically significant ($P < 0.05$). The increment continued up to 25 minutes and started to decrease. After 1hour post-induction the value demoted to near normal level. In Group B, BUN value increased to 54.30 ± 0.26 from control value (50.33 ± 0.89) at 5 min post-induction significantly ($P < 0.05$). The increment continued up to 15 minutes. Then the BUN value fluctuated and at 30 min post-induction the animal woke up. The BUN value returned near to the control value after 24 hours of recovery in both groups.

TP value was abated gradually from pre-anaesthetized control value up to 10 minutes post-induction in both groups. In Group A, 5 min after induction TP value reduced significantly ($P < 0.05$) to 5.59 ± 0.17 from control value (6.73 ± 0.12). The reduction trend continued up to 10 min post-induction. The value then started elevating and the elevation continued until recovery. The TP value then increased gradually and returned near baseline after 24 hours of recovery in both groups.

Serum creatinine value increased from pre-anaesthetized control value in both groups. In Group A, 5 minutes after induction creatinine value dramatically increased to 1.28 ± 0.08 from control value (1.21 ± 0.09), which was significant ($P < 0.05$) statistically. The increment continued up to 30 minutes and started decreasing from 30 min post-induction. In Group B, we found high increase and fluctuation in creatinine value. Creatinine value decreased gradually and returned near baseline after 24 hours of recovery in both groups.

Comparison of different anesthetic regimens on the onset of induction and duration of anesthesia in sheep

The effect of different anaesthetic combination in sheep on the onset of induction and duration of anaesthesia is presented in Table 5. The mean value of the onset of induction period with Xylazine-Ketamine and Ketamine were 12.00 ± 0.03 min and 18.00 ± 0.07 min respectively. The longest induction period was found with Xylazine-Ketamine combination.

Table 2: Effects of anaesthetic combination on rectal temperature, heart rate, respiration rate and SpO_2 in ewes

Parameter	Group	Ctrl	5 min	10 min	15 min	20 min	25 min	30 min	1 hr.	24hrs. after recovery
Temperature	A	103.8 ± 0.2^{a}	103.3 ± 0.15^{a}	101.43 ± 0.16^{b}	101.8 ± 0.15^{b}	101.5 ± 0.17^{b}	100.23 ± 0.25^{b}	101.10 ± 1^{a}	102.43 ± 0.57^{b}	103.7 ± 0.1^{a}
(°C)	B	103.3 ± 0.15^{a}	102.7 ± 0.36^{a}	101.93 ± 0.32^{b}	101.7 ± 0.36^{b}	101.56 ± 0.5^{b}	100.43 ± 0.67^{b}	*	102.7 ± 0.67^{a}	103.25 ± 0.12^{a}
Heart rate	A	80.33 ± 2.03^{a}	80.51 ± 4.16^{a}	85.33 ± 3.05^{b}	86.0 ± 3.46^{b}	88.67 ± 4.16^{b}	89.67 ± 4.16^{b}	90.66 ± 4.16^{b}	87.9 ± 5.29^{a}	80.23 ± 4.16^{a}
(Bit/Min)	B	83 ± 2.0^{a}	82.95 ± 4.13^{a}	81.33 ± 3.0^{a}	85.67 ± 4.16^{b}	80.33 ± 5^{a}	71.33 ± 1.15^{a}	*	79.33 ± 5.29^{b}	82.90 ± 3.05^{a}
Respiratory rate	A	30.67 ± 3.06^{a}	29.10 ± 3.79^{b}	28.5 ± 2.0^{b}	25.0 ± 4.5^{b}	24.33 ± 2.51^{b}	24.0 ± 2^{b}	28.33 ± 1.15^{a}	29.67 ± 4.16^{a}	30.64 ± 3.16^{a}
(breath/min)	B	30.67 ± 2.08^{a}	28.5 ± 2.0^{b}	27.67 ± 1.53b	28.4 ± 3.46^{b}	29.67 ± 0.57^{b}	24.50 ± 2.0^{b}	*	29.67 ± 2.0^{a}	30.62 ± 2.23^{a}
SpO2 (/min)	A	96.67 ± 4.16^{a}	87.10 ± 1.0^{b}	75.33 ± 7.4^{b}	67.67 ± 4.93^{b}	67 ± 6.6^{b}	63.66 ± 7.0^{b}	89.67 ± 2.08^{a}	96.67 ± 4.1^{a}	96.61 ± 4.22^{a}
	B	97 ± 3.6^{a}	87 ± 6.0^{b}	77 ± 4.35^{b}	72 ± 2.65^{b}	66.33 ± 3.64^{b}	63.67 ± 4.72^{b}	*	69 ± 4.0^{a}	97.0 ± 3.1^{a}

Values with different superscript letters (a, b) in the same row differ significantly at 5% level of significance; ±: Standard Error; *: Animal woke up

Table 3: Effects of anaesthetic combination on TEC, TLC, Hb and PCV in sheep

Parameter	Group	Ctrl	5 min	10 min	15 min	20 min	25 min	30 min	1 hr.	24hrs. after recovery
TEC (Thousands/cumm)	A	10.44 ± 0.07^{a}	9.76 ± 0.11^{b}	9.32 ± 0.12^{b}	9.16 ± 0.06^{b}	8.85 ± 0.04^{b}	8.53 ± 0.06^{b}	8.38 ± 0.03^{b}	10.21 ± 0.01^{a}	10.41 ± 0.07^{a}
	B	10.37 ± 0.11^{a}	9.8 ± 0.12^{b}	9.36 ± 0.07^{b}	9.18 ± 0.03^{b}	8.47 ± 0.28^{b}	8.22 ± 0.35^{b}	*	10.11 ± 0.33^{a}	10.29 ± 0.11^{a}
TLC (Millions/cumm)	A	8.5 ± 0.07^{a}	8.2 ± 0.05^{b}	8.15 ± 0.04^{b}	7.78 ± 0.07^{b}	7.46 ± 0.05^{b}	7.3 ± 0.06^{b}	7.00 ± 0.06^{b}	8.38 ± 0.08^{a}	8.48 ± 0.05^{a}
	B	8.72 ± 0.09^{a}	8.33 ± 0.04^{b}	8.12 ± 0.06^{b}	7.72 ± 0.14^{b}	7.33 ± 0.09^{b}	7.08 ± 0.08^{b}	*	8.28 ± 0.08^{a}	8.70 ± 0.05^{a}
Hb (%)	A	9.73 ± 0.12^{a}	9.23 ± 0.09^{b}	8.84 ± 0.07^{b}	8.43 ± 0.03^{b}	8.27 ± 0.29^{b}	8.01 ± 0.06^{b}	7.79 ± 0.04^{b}	9.53 ± 0.08^{a}	9.70 ± 0.14^{a}
	B	9.47 ± 0.18^{a}	9.47 ± 0.09^{b}	9.13 ± 0.03^{b}	8.88 ± 0.05^{b}	8.53 ± 0.08^{b}	8.43 ± 0.06^{b}	*	9.34 ± 0.07^{a}	9.46 ± 0.16^{a}
PCV (%)	A	36.2 ± 0.09^{a}	35.43 ± 0.19^{b}	34.73 ± 0.09^{b}	33.9 ± 0.1^{b}	33.47 ± 0.18^{b}	32.83 ± 0.2^{b}	32.6 ± 0.25^{b}	35.97 ± 0.12^{a}	36.25 ± 0.09^{a}
	B	36.28 ± 0.29^{a}	35.6 ± 0.15^{b}	34.87 ± 0.12^{b}	33.97 ± 0.18^{b}	33.37 ± 0.133^{b}	32.9 ± 0.17^{b}	*	35.11 ± 0.23^{a}	36.24 ± 0.29^{a}

Values with different superscript letters (a, b) in the same row differ significantly at 5% level of significance; ±: Standard Error; *: Animal woke up

Table 4: Effects of anaesthetic combination on ALT, AST, BUN, TP and Creatinine in sheep

Parameter	Group	Ctrl	5 min	10 min	15 min	20 min	25 min	30 min	1 hr.	24hrs. after recovery
ALT (iu/L)	A	20.33 ± 0.69^{a}	19.8 ± 0.17^{a}	19.7 ± 0.1^{a}	19.4 ± 0.12^{a}	19.2 ± 0.07^{a}	19.00 ± 0.06^{a}	20.00 ± 0.44^{a}	20.15 ± 0.73^{a}	20.31 ± 0.69^{a}
	B	19.87 ± 0.38^{a}	19.73 ± 0.20^{a}	19.57 ± 0.20^{a}	19.22 ± 0.25^{a}	19.18 ± 0.09^{a}	19.00 ± 0.12^{a}	*	19.12 ± 0.33^{a}	19.84 ± 0.38^{a}
AST (iu/L)	A	16.67 ± 0.88^{a}	16.5 ± 0.12^{a}	16.43 ± 0.132^{a}	16.16 ± 0.03^{a}	15.86 ± 0.06^{a}	15.4 ± 0.04^{a}	15.13 ± 0.09^{a}	15.63 ± 0.71^{a}	16.64 ± 0.88^{a}
	B	17 ± 1.53^{a}	16.87 ± 0.49^{a}	16.65 ± 0.43^{a}	16.47 ± 0.20^{a}	16.39 ± 0.31^{a}	16.19 ± 0.10^{a}	*	16.33 ± 0.18^{a}	17.01 ± 1.53^{a}
BUN (mg/dl)	A	51 ± 1.53^{a}	53.6 ± 0.21^{b}	55.46 ± 0.28^{b}	57.27 ± 0.07^{b}	58.17 ± 0.92^{b}	60.20 ± 0.26^{b}	55.8 ± 0.23^{a}	49.9 ± 1.3^{a}	50.9 ± 1.53^{a}
	B	50.33 ± 0.89^{a}	54.30 ± 0.26^{b}	55.43 ± 0.15^{b}	51.73 ± 0.03^{b}	50.90 ± 0.35^{b}	46.33 ± 0.03^{b}	*	49.0 ± 0.7^{a}	50.28 ± 0.89^{a}
TP (mg/dl)	A	6.73 ± 0.12^{a}	5.59 ± 0.16^{b}	4.66 ± 0.17^{b}	5.05 ± 0.14^{a}	6.28 ± 0.89^{a}	6.23 ± 0.05^{a}	6.34 ± 0.16^{a}	6.68 ± 0.08^{a}	6.71 ± 0.12^{a}
	B	6.65 ± 0.05^{a}	5.13 ± 0.21^{b}	4.3 ± 0.06^{b}	5.13 ± 0.11^{a}	6.03 ± 0.15^{a}	6.11 ± 0.17^{a}	*	6.45 ± 0.13^{a}	6.64 ± 0.05^{a}
CREATININE (mg/dl)	A	1.21 ± 0.09^{a}	1.28 ± 0.08^{b}	1.35 ± 0.04^{b}	1.42 ± 0.04^{b}	1.5 ± 0.02^{b}	1.65 ± 0.02^{b}	1.7 ± 0.04^{b}	1.32 ± 0.17^{a}	1.21 ± 0.09^{a}
	B	1.26 ± 0.09^{a}	1.38 ± 0.07^{b}	1.43 ± 0.03^{b}	1.32 ± 0.02^{b}	$1.54 \pm .01^{b}$	2.00 ± 0.01^{b}	*	1.38 ± 0.05^{a}	1.22 ± 0.09^{a}

Values with different superscript letters (a, b) in the same row differ significantly at 5% level of significance; $\pm$: Standard Error; *: Animal woke up

Table 5: Induction and duration of anaesthetic combinations used in sheep (n=6)

Anaesthetic Combination agents	**Induction of Time (min)**	**Duration of anaesthesia (min)**
Group-A (Xylazine-Ketamine)	12.00 ± 0.03	61.33 ± 0.03
Group-B (Ketamine)	18.00 ± 0.07	23.67 ± 0.05

$\pm$: StandardError

DISCUSSION

Effects of anaesthesia on clinical parameters in sheep

In the study, the significant diminution in rectal temperature in group A was observed, 5 min after induction resembling the finding of Islam *et al.* (2010) who reported that there is a decrease in rectal temperature in sheep anaesthetized with ketamine. Conversely, Nuha (2004) reported a significant decline in rectal temperature starting from 20 minutes post-induction of anaesthesia until full recovery. These results agree with the finding of Hall and Clark (1991) who states that ketamine depresses the basal metabolism leading to lowering of body temperature. The significant increase in heart rate after induction in both groups approves well with the finding of Islam *et al.* (2010) using Xylazine-ketamine although Afshar *et al.* (2005) found a decrease in heart rate with ketamine. We observed the significant ($P < 0.05$) reduction in respiration rate in both Group A and Group B for up to 25 min. Respiratory effects of xylazine are usually clinically insignificant, but a combination with other drugs and at high doses can cause respiratory depression, with a decrease in tidal volume and respiratory rate (Lee *et al.*, 2010). Reduced respiration rate might be due to depression of respiratory centers either by xylazine alone or by both xylazine-ketamine. We also observed the significant fall of SpO_2 after induction in Group A. Similar findings were also reported by Dubois *et al.* (2004) and Nusory (2011). A decline in SpO_2 has also been documented during the continuous infusion of ketamine in dogs (Sankar *et al.*, 2011). The initial decrease in SpO_2 could be due to depression caused by the anesthetic on the ventilatory function of the lungs (Kamal *et al.*, 2019).

Effects of anaesthesia on hematological parameters in sheep

Total Erythrocyte Count (TEC) showed a significant diminution in all groups. The value after one hour of induction reaches near the baseline and after 24 hours of recovery. The decline in TEC might be due to dilatation of spleen, resulting in splenic sequestration of erythrocytes under the influence of different anaesthetics. These findings are in agreement with the observations recorded after ketamine administration in dogs (Kamal *et al.*, 2019). Ismail et al. (2010) reported that there is a slight decrease in RBC with xylazine-ketamine anaesthesia in sheep.

The TLC lessened significantly in both Group A and Group B. Significant changes were observed up to 30 min post-induction. This finding correlates well with anaesthesia using xylazine-ketamine in deer (Ashraf *et al.*, 2019). White blood cell values showed no significant difference compared to baseline values (Peighambarzadeh *et al.*, 2014). These findings agree with the observations recorded by Ramaswamy *et al.* (1991) after ketamine administration in sheep. The low in TLC value during ketamine anaesthesia might be due to the segregation of blood cells in the spleen and lungs during anaesthesia (Steffy *et al.*, 1976). We found significant changes of haemoglobin (Hb) in both groups but a mild decrease in Hb (g/dl) after 5 min post-induction of anaesthesia. The findings well correspond with some previous studies in dogs (Munif *et al.*, 2020). The decrease in the Hb might have resulted from splenic pooling of blood, which occurs with most of the anaesthetics (Peighambarzadeh *et al.*, 2014).

A significant ($P < 0.05$) reduction in PCV% was found after 5 to 30 min post-induction in Group A. In both groups, a mild increase in PCV after 30 min of induction was observed. This finding correlates with Ismail, (2010) who found a significant escalation in PCV at 5, 10-, 15-, 20-, and 25-min post-induction in sheep and goats with xylazine-ketamine anaesthesia. Udegbunam and Udegbunam (2014) have reported that PCV in all groups diminished significantly ($P < 0.05$) at 5 min post induction and then increased at 30 min and 1 hour. In contrast, Peighambarzadeh *et al.* (2014) have reported that ketamine-xylazine combination produces a significant decrease in PCV values from 5 to 25 min compared with the baseline value.

Effects of anaesthesia on biochemical parameters in sheep

In our study, we observed a reduction in ALT value from its pre-anaesthetized control value in all groups. Khurana *et al.* (2014) have also observed a decline in ALT values within clinically normal range during Xylazine-Ketamine and only ketamine anaesthesia. The decrease in ALT activity in our study might be due to less alteration in cell membrane permeability in response to hemodynamic changes by the anesthetic agents.

The AST activity also reduced in both groups. Khurana *et al.* (2014) have also observed a diminution in AST values within the clinically normal range during xylazine-ketamine and alone ketamine anaesthesia. Better blood supply to the liver due to ketamine administration might have caused a decline in AST level (Khurana *et al.*, 2014).

This study showed both increased and decreased value of BUN from pre-anaesthetized control value in all groups. The increment in serum BUN levels has been reported after ketamine and xylazine administration in rabbit (Guzel *et al.*, 2006). Ketamine might reduce renal cortical blood flow by constricting the blood.

In all groups, we found significant changes but a mild decrease of TP from 5 min post-induction to 10 min post-induction. TP value started to rise after 15 min post-induction. Better blood supply to the liver due to ketamine administration might have caused a reduction in TP (Khurana *et al.*, 2014). The finding is in contrast with the finding of Pawde *et al.* (2000) who performed Xylazine-ketamine anesthesia in sheep. The escalation in TP activities might be due to the suppression of liver function during ketamine anesthesia (Basha and Ranganath, 2012).

In the present study, creatinine value amplified from pre-anaesthetized control value in both groups. Similar findings were also reported by Kamal *et al.* (2019) after Xylazine-ketamine anaesthesia in dogs. Ketamine could reduce renal cortical blood flow by constricting the blood vessels during continuous administration of ketamine in goats, and hence, reduces glomerular filtration rate and increases creatinine levels (Sankar *et al.*, 2011).

Effect on anaesthetic agents at the state of anaesthesia in sheep

The longest duration of anaesthesia was found in this study during xylazine-ketamine combination. Nuha (2004) also observed a significantly elongated duration of anesthesia induced with xylazine-ketamine than that obtained when using diazepam-ketamine. The induction of anaesthesia with xylazine-ketamine and diazepam-ketamine combinations resulted in a longer duration of recovery time compared with only ketamine (Nuha, 2004). This extended time might be due to the presence of an additive effect in the combination as suggested by Hossen *et al.* (2004b).

CONCLUSION

Based on the findings of this study, it can be concluded that Xylazine-Ketamine and alone Ketamine anesthetic combination exerts some effects on respiratory as well as on other vital organs. The findings from this study suggest Xylazine-Ketamine combinations can be used for general anaesthesia in sheep rather than Ketamine alone.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

References

Afshar FS, Baniadam A, Marashipour SP, 2005. Effect of xylazine ketamine on arterial blood pressure, arterial blood pH, blood gas, rectal temperature, heart and respiratory rates in goats. *Bulletin of the Veterinary Institute in Pulawy* 49: 481–484.

Ashraf MB, Akter MA, Saha M, Mishra P, Hoda N, Alam MM, 2019. Clinicopathological Evaluation on Capture Myopathy Due to Chemical Immobilization in Spotted Deer. *Turkish Journal of Veterinary Research* 3(2): 73–79.

Basha KMA, Ranganath L, 2012. Clinicophysiological and biochemical effects of isoflurane and sevoflurane anaesthesia in dogs. *Indian Journal of Veterinary Surgery* 33(2): 87–89.

Dubois WR, Prado TM, Ko JC, Mandsager KE, Morgan GL, 2004. A comparison of two i.m doses of xylazine-ketamine combination and tolazoline reversal in llamas. *Veterinary Anaesthesia and Analgesia* 31(2): 90–6.

Guzel O, Incl G, Cirakli ZT, Eraslan E, Aktas M, 2006. . *Medycyna Weterynaryjna* 62(12): 1383.

Hall LW, Clark KW, 1991. Veterinary Anaesthesia. Baillire Tindall Philadelphia, USA.

Hodgson DS, Dunlop CI, 1990. General anesthesia for horses with specific problems. *Veterinary Clinics of North America: Equine Practice* 6(3): 625–650.

Hossen MJ, Alam MM, Hashim MA, Juyena NS, 2004a. Certain haemato-biochemical values in anesthetized dogs. *Bangladesh Veterinary Journal* 38(3-4): 97–104.

Hossen MJ, Juyena NS, Hashim MA, Alam MM, Awal MA, 2004b. Evaluation of certain anaesthetic drugs in Dogs. *Bangladesh Veterinary Journal* 38(3-4): 87–9.

Hutch RC, 1976. Diazepam as premedication to Thiopentone anaesthesia horses. *Journal of the American Veterinary Medical Association* 150: 27.

Islam MM, Alam MR, Hashim MA, Runa RA, 2010. Effects of anaesthetics with or without premedication in sheep. *Bangladesh Veterinary Journal* 44(1-4): 43–52.

Kamal MM, Mishra P, Akter MA, Hasan M, Hashim MA, Alam MM, 2019. Effects of two anesthetic combinations (xylazine-ketamine and xylazine-propofol) on clinical and hematobiochemical profile in dogs. *Bangladesh Veterinary Journal* 53(1-4): 10–20.

Khurana A, Kumar A, Sharma SK, Kumar A, 2014. Electrocardiographic and hemato-biochemical effects of two balanced anesthetic protocols in dogs. *Veterinary World* 7(10): 835–841.

Lee JY, Jee HC, Jeong SM, Kim MC, Park CS, 2010. Comparison of anaesthetic and cardiorespiratory effects of xylazine or medetomidine in combination with tiletamine/ zolazepam in pigs. *Veterinary Record* 167(7): 245–249.

Munif MR, Alam MM, Alam MR, 2020. Pulse oximetry and clinical changes during electrosurgery in dogs anaesthetized with xylazine-thiopentone and xylazine-ketamine combinations. *Research in Agriculture, Livestock and Fisheries* 7(1): 97–105.

Nuha MO, 2004. Evaluation of selected anaesthetic protocols for total intravenous anaesthesia in goat kids undergoing laparotomy. Master's thesis, Faculty of Veterinary Medicine, U of K.

Nusory D, 2011. Propofol and ketamine as a general anaesthetic in dog. MV Sc. Ph.D. thesis, Assam Agricultural University, Gtizvaliati-22.

Pawde AM, Kinjavdekar P, Aithal HP, Pratap K, Bisht GS, 2000. Detomidinediazepam-ketamine anaesthesia in buffalo (*Bubalus bubalis*) calves. *Journal of Veterinary Medical Science* 47(3): 175–179.

Peighambarzadeh SZ, Tavana M, Peighambarzadeh SF, 2014. Effects of the ketamine/xylazine cocktail anaesthesia on haematological parameters in Lori-Bakhtiari sheep. *WALIA journal* 30(1): 9–11.

Ramaswamy V, Balasubramaniam NN, Gopal MS, Archibald D, 1991. Part II-Studies on the efficacy of ketamine HCl as general anaesthetic in combination with xylazine, diazepam and promazine in canines. *Indian Veterinary Journal* 68: 548–551.

Sankar P, Jastin WB, Rao GD, Prathaban S, Suresh KR, Leela, 2011. Cardiopulmonary and haematobiochemical alterations during ketamine or propofol anaesthesia in acepromazine-xylazine premedicated horses. *Indian Journal of Veterinary Surgery* 32(1): 23–26.

Steffy EP, Gillespie JR, Berry JD, Eger EI, Schalm OW, 1976. Effects of halothane and halothane-nitrous oxide on hematocrit and plasma protein concentration in dog and monkey. *American Journal of Veterinary Research* 37(8): 959–962.

Taylor PM, 1991. Anesthesia in sheep and goats. *Indian Veterinary Journal* 45: 145–177.

Udegbunam RI, Udegbunam SO, 2014. Anaesthetic potency and physiological effects of refrigerated solution of thiopentone sodium in rabbits. *Journal of Veterinary Sciences* 12(2): 14–18.