

## **Clinical and haematological changes upon administration of Xylazine-Ketamine and Xylazine-Thiopentone anaesthetic combinations in ewes**

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### **Abstract**

The study was done to evaluate the effect of Xylazine-Ketamine and Xylazine-Thiopentone combinations for general anaesthesia in sheep. Six healthy sheep were divided into two groups: Group XK (n = 3), anaesthetized with Xylazine-Ketamine and Group XT (n = 3), anaesthetized with xylazine-thiopentone. Anaesthesia was induced using 1.1 mg/kg xylazine with 10 mg/kg ketamine or 20 mg/kg thiopentone as a single intravenous injection. Induction, duration and recovery from anaesthesia were monitored. Respiratory rate, heart rate and rectal temperature were recorded 15 min before and 5 min after induction, and 15 and 30 min and 24 hours after recovery. Packed Cell Volume (PCV) (%), Haemoglobin (Hb) (g/dL), Total Leucocyte Count (TLC) (millions per cubic millimetre) and Total Erythrocyte Count (TEC; Thousands per cubic millimetre) were measured before anaesthesia, one hour after induction and 24 hours after recovery. Heart rate increased significantly in both XT and XK groups and returned to control value 24 hours after recovery. Respiration rate decreased at 15 min after induction, then highly increased at 30 min and then returned to control value 24 hours after recovery in XK group. Rectal temperature decreased significantly in both groups. Hb, TLC, and TEC decreased, but PCV increased significantly in both groups. The mean time of induction of anaesthesia was less in XT group ( $0.2 \pm 0.0$  min) than in group XK ( $2.7 \pm 0.1$  min). The duration of anaesthesia and its recovery was less in Group XK than in Group XT. A combination of Xylazine-Ketamine and Xylazine-Thiopentone can be used to induce short term anaesthesia in sheep with negligible effects on clinical and haematological parameters. (*Bangl. vet.* 2017. Vol. 34, No. 1, 9 – 19)

### **Introduction**

General anaesthesia is used for certain surgical intervention in sheep. Various sedatives, tranquillizing agents, pain killers and muscle relaxants are also used while animals undergo surgery. These anaesthetics help in overcoming resistance of the animals during examination, maintaining depth of anaesthesia, and increasing safety. For these purposes, the commonest drugs used are ketamine, diazepam, xylazine and atropine sulphate (Mahmud *et al.*, 2014).

In Bangladesh, injectable anaesthesia is performed in most surgical cases. Several drugs are used singly or in combination with other drugs to achieve balanced

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anaesthesia. These include barbiturates (thiopentone, methohexital), benzodiazepines (midazolam, diazepam), opioids (morphine, fentanyl, alfentanil, remifentanil), propofol, ketamine and miscellaneous drugs (droperidol, etomidate, xylazine; Hall & Clark, 2001; Yamashita *et al.*, 2007).

Intravenous anaesthetic agents are used in the absence of facilities for inhalational anaesthesia in veterinary practice in Bangladesh (Islam *et al.*, 2010).

Thiopentone and ketamine are popular. In this study, the effects of Xylazine-Ketamine and Xylazine-Thiopentone combination on clinical and haematological parameters were observed in sheep. The effects of anaesthetic combinations were studied pre-surgical, during surgery and post-surgical up to recovery of the animals from anaesthesia.

## Materials and Methods

### *Experimental animals*

Six apparently healthy ewes of 2 - 3 years old weighing 8 - 12 Kg were housed in a well-ventilated, concrete floor and tin-roofed shed, with access to food and water *ad libitum*.

Animals were maintained under uniform conditions of feeding and management under a veterinarian's supervision. Ewes were dewormed with anthelmintics (A-Mactin plus® Acme Pharmaceuticals, Bangladesh, Ltd) and vaccinated against PPR (PPR vaccine® LRI, Bangladesh) and FMD (Rakhsha, Indian Immunology Ltd). The sheep were fed roadside grass from 9 am to 5 pm and supplemented with 300 gms of concentrate once daily. The concentrate was a mixture of crushed maize (25%), wheat bran (50%), soybean meal (20%), fish meal (1%), Di-calcium phosphate (DCP) (1.5%), vitamins-mineral premix (0.5%) and iodized salt (3%).

### *Experimental design*

The experimental animals were randomly divided into 2 groups: XK (Xylazine-Ketamine) and XT (Xylazine-Thiopentone).

#### **Group-XK**

Xylazine hydrochloride (Ilium Xylazill-100®, Troy Laboratories Limited, India) was injected intramuscularly @ 1.1 mg/kg body weight and ketamine hydrochloride (G-Ketamine®, Gonoshasthaya Pharmaceuticals Ltd, Bangladesh) was @ 10 mg/kg intramuscularly 5 minutes after xylazine administration.

#### **Group-XT**

Freshly prepared thiopentone sodium (Thioton® 500, Tecno Drugs Ltd, Bangladesh) @ 20 mg/kg body weight, was given slowly intravenously 5 minutes after xylazine hydrochloride injection @ 1.1 mg/kg body weight.

### ***Preparation of the experimental animals***

The experimental animals were closely monitored from 24 hour prior to anaesthesia. Heart rate, respiratory rate and rectal temperature were recorded. The animals to be anaesthetized in the next morning were isolated from others and starved overnight. Before anaesthesia blood was collected by jugular venipuncture after cleaning with 10% Povidone Iodine (Povisep<sup>®</sup>, Jayson Pharmaceuticals, Bangladesh).

### ***Anaesthesia***

The sheep were restrained with the help of an assistant, and xylazine hydrochloride (1.1 mg/kg) was administered intramuscularly with 1 mL disposable syringe. After five minutes, ketamine hydrochloride (G-Ketamine<sup>®</sup>, Gonoshasthaya Pharmaceuticals Ltd, Bangladesh) (10 mg/kg), or thiopentone sodium (Thioton<sup>®</sup> 500, Tecno Drugs Ltd, Bangladesh) (20 mg/kg) were administered slowly through the jugular vein.

### ***Monitoring of clinical parameters***

#### ***Respiratory rate***

Respiratory rate was recorded by monitoring flank. Respiratory rate was recorded 15 mins before anaesthesia, 5, 15, 30 min after induction of anaesthesia, after recovery and 24 hours after recovery.

#### ***Heart rate***

Heart rate was recorded using stethoscope over the left side of the chest for one minute. Heart rate was recorded 15 mins before anaesthesia, 5, 15, 30 min after induction of anaesthesia, after recovery and 24 hours after recovery.

#### ***Rectal temperature***

The bulb of the clinical thermometer was inserted into the rectum at least 4 cm from the anus in contact with the rectal mucosa for 2 minutes. The temperature was recorded in Fahrenheit (°F) 15 mins before anaesthesia, 5, 15, 30 min after induction of anaesthesia, after recovery and 24 hours after recovery.

#### ***Haematological parameters***

Blood samples were collected before premedication and 60 minute and 24 hrs after induction of anaesthesia. Venous blood (4 mL) was collected by jugular venipuncture in vials containing Lithium Heparin and the following estimations were made within half an hour of blood collection.

- i. Packed cell volume (%);
- ii. Haemoglobin (gm/dL);
- iii. Total leucocyte count (millions per cubic millimetre);
- iv. Total erythrocyte count (Thousands per cubic millimetre).

***Monitoring of anaesthesia******Induction and duration of anaesthesia***

The period from time of injection to the onset of recumbency was recorded as the period of induction. The period from induction to a stage when reflexes reappeared was considered as the period of anaesthesia.

***Recovery from anaesthesia***

The recovery period was considered as the interval between reappearance of consciousness and the ewe standing.

***Statistical analysis***

Student's paired "t" test for correlated data was used to determine whether the changes observed in the clinical parameters significantly differ from control values. Results were assessed by the Least Significant Difference (LSD) test in "MSTAT" computer program.

**Results and Discussion*****Effects of anaesthetic combinations on clinical parameters in sheep******Heart rate***

Heart rate significantly increased after induction of anaesthesia in both groups (Table 1). This finding agrees with the findings of Islam *et al.* (2010). He reported a significant increase in heart rate with thiopentone and an increase with Xylazine-Ketamine combination. Amarpal *et al.* (2002) reported increased heart rate with thiopentone and depression of the cardiac portion of the vagal centre and/or arterial pressure receptor reflexes by thiopentone that might be responsible for this finding (Sogawa *et al.*, 2012). This result is in contrast to Ruffolo *et al.* (1993). They reported a significant decrease in heart rate after administration of xylazine. Afshar *et al.* (2005) found that heart rate decreased at 15 to 60 min. Lumb and Jones (1996) observed decreased heart rate with thiopentone sodium.

Table 1: Effects of anaesthetic combinations on heart rate in sheep (n = 6)

Anaesthetic agents	Heart rate					
	15 min before induction	5 min after induction	15 min after induction	30 min after induction	After recovery	24 hour after recovery
XT (n = 3)	80 ± 4	102.7 ± 6.1**	93.3 ± 1.2**	92.7 ± 3.1*	92 ± 5.4*	69.3 ± 2.3*
XK (n = 3)	90 ± 4	91.3 ± 2.3	80.7 ± 5.0	104 ± 6**	76.7 ± 3.1*	70 ± 2**

± = Standard error; \* = Significant at 5% level of probability; \*\* = Significant at 1% level of probability; XT = Xylazine-Thiopentone; XK = Xylazine-Ketamine

### Respiratory rate

More respiratory depression was observed in Xylazine-Thiopentone combination (Table 2). A significant decrease in respiratory rate was observed up to 30 minutes. Islam *et al.* (2010) found decrease in respiratory rate with thiopentone in sheep. Rana (2013) reported decreased respiratory rate in swine in both Xylazine-Thiopentone and Xylazine-Ketamine combination. Lumb and Jones (1996) and Thurmon and Smith (2007) reported that xylazine causes a dose-dependent depression of the respiratory centre causing a reduction of rate and tidal volume in swine. Murrell (2007) and Lee *et al.* (2010) reported that respiratory effects of xylazine are usually clinically insignificant, but in combination with other drugs can cause respiratory depression, with a decrease in tidal volume and respiratory rate. Ketamine is a potent respiratory depressant (Schifilliti, 2010). Decreased respiration rate might be due to depression of respiratory centres by xylazine alone or Xylazine-Ketamine. Moreover, thiopentone decreased respiration rate as a result of depression of CNS and reduction of the sensitivity of the respiratory centre to carbon dioxide (Hall *et al.*, 2001). However, non-significant increase in respiratory rate was observed following administration of Ketamine-Xylazine in goats by Kumar (1996). On the other hand, Afshar *et al.* (2005) found no changes in respiratory rate in sheep. The findings of this study correspond with those findings up to 30 min but after 30 min the respiratory rate increased significantly in XK group. This increasing rate in XK group in the present study was probably caused by surgical stress, as the animal was in major surgery.

Table 2: Effects of anaesthetic combinations on respiratory rate in sheep (n = 6)

Anaesthetic agents	Respiratory rate					
	15 min before induction	5 min after induction	15 min after induction	30 min after induction	After recovery	24 hour after recovery
XT (n = 3)	29.3 ± 4.2	26 ± 2	26 ± 3.8	28.7 ± 4.1	32.7 ± 7.6*	25.3 ± 2.3
XK (n = 3)	26.7 ± 3.1	23.3 ± 4.2	27.3 ± 4.2	83.3 ± 6.1**	37.3 ± 6.1*	25.3 ± 3.1

± = Standard deviation; \* = Significant at 5% level of probability; \*\* = Significant at 1% level of probability; XT = Xylazine-Thiopentone sodium; XK = Xylazine-Ketamine

### Rectal temperature

Significant decrease in rectal temperature was observed at 5 minute after induction with Xylazine-Ketamine and temperature gradually returned to its control value 24 hour after recovery (Table 3). In Xylazine-Thiopentone temperature increased in 5 min and gradually returned to its normal value 24 hour after recovery. This finding agree with Kumar and Sharma (1986), who reported that although rectal temperature increased significantly immediately after induction with thiopentone sodium, there was no significant effect of thiopentone sodium on rectal temperature in buffaloes. Thiopentone-Xylazine resulted in non-significant decrease in rectal temperature. Islam *et al.* (2010) found a decrease in rectal temperature in sheep after both

thiopentone and ketamine. These results suggest that thiopentone depresses metabolism leading to lowering of body temperature (Hall and Clarke, 1991).

Table 3: Effects of anaesthetic combinations on rectal temperature (°F) in sheep (n = 6)

Anaesthetic agents	Rectal temperature					
	15 min before induction	5 min after induction	15 min after induction	30 min after induction	After recovery	24 hour after recovery
XT (n = 3)	102 ± 0.2	102.3 ± 0.5	102.1 ± 0.1	101.6 ± 0.4	99.4 ± 1.2*	101.8 ± 0.2
XK (n = 3)	102.3 ± 0.8	102.2 ± 0.7*	102 ± 0.7	100.7 ± 1.3*	98.3 ± 0.8**	101.8 ± 0.2*

± = Standard deviation; \* = Significant at 5% level of probability; \*\* = Significant at 1% level of probability; XT = Xylazine-Thiopentone sodium; XK = Xylazine-Ketamine

### *Effects of anaesthetic combinations on haematological parameters in sheep*

#### *Haemoglobin*

In both groups (Xylazine-Ketamine and Xylazine-Thiopentone) there were no significance changes in haemoglobin, but mild decrease 1 hour after induction of anaesthesia (Table 4). After 24 hour from recovery, haemoglobin level increased in both groups. These findings agree with the observations recorded after ketamine administration in dogs by Bisen *et al.* (1994). Ismail *et al.* (2010) found that there are no significant changes in haemoglobin in sheep after Xylazine-Ketamine anaesthesia. Kilic (2008) found a decrease in haemoglobin after anaesthesia with ketamine. The ketamine and xylazine combination produced a decrease in haemoglobin (Peighambarzadeh *et al.*, 2014). Polycarp and Sunni (2015) reported a decrease in haemoglobin in rabbit after thiopentone anaesthesia. Radi *et al.* (2012) reported an increase in haemoglobin after thiopentone anaesthesia.

Table 4: Effects of anaesthetic combinations on Haemoglobin (g/dl) in sheep (n = 6)

Anaesthetic agents	Before anaesthesia	1 hour after induction	24 hours after induction
XT (n = 3)	6.67 ± 0.4	6.1 ± 0.4	7.3 ± 0.5
XK (n = 3)	7.73 ± 0.6	7.06 ± 0.4	7.2 ± 0.9

± = Standard deviation; \* = Significant at 5% level of probability; \*\* = Significant at 1% level of probability; XT = Xylazine-Thiopentone; XK = Xylazine-Ketamine

#### *Total Leukocyte count*

There were no significant changes of TLC before anaesthesia, 1 hour after induction or 24 hours after recovery in either group (Table 5). After anaesthesia with Xylazine-Ketamine WBC values showed no significant difference compared with baseline values (Peighambarzadeh, 2014). Ismail *et al.* (2010) reported a slight increase in white blood cell with Xylazine-Ketamine anaesthesia in sheep. Radi *et al.* (2012) reported no significant change of WBC after thiopentone anaesthesia. White blood cell count

(WBC) was significantly decreased in sheep anaesthetized with thiopentone (Edjtehadi, 1978). Polycarp and Sanni (2015) reported a decrease in WBC in rabbit after thiopentone anaesthesia. A lowering in TLC during ketamine anaesthesia might be due to segregation of blood cells in spleen and lungs during anaesthesia (Steffy *et al.*, 1976). These finding agree with the observations by Bisen *et al.* (1994) after ketamine administration in dogs.

Table 5: Effects of anaesthetic combinations on TLC (Millions per cubic millimeter) in sheep (n = 6)

Anaesthetic agents	Before anaesthesia	1 hour after of induction	24 hours after recovery
XT (n = 3)	8.1 ± 0.3	8.1 ± 0.1	8.04 ± 0.4
XK (n = 3)	7.8 ± 0.5	7.8 ± 0.2	7.6 ± 0.4

± = Standard Deviation; \* = Significant at 5% level of probability; \*\* = Significant at 1% level of probability; XT = Xylazine-Thiopentone; XK = Xylazine-Ketamine

#### **Total erythrocyte count**

Total Erythrocyte Count (TEC) decreased in both groups (Table 6). After 24 hour from recovery TEC increased in XT group but decreased in XK group.

The transient changes in TEC might be attributed to stress of anaesthesia (Jain, 1986). The decline in TEC might also be due to dilatation of spleen, resulting in splenic sequestration of erythrocytes (Hausner *et al.*, 1936). Weil and Chissy (1968) stated that the fall in circulating erythrocytes could be due to haemodilution produced by an alteration in the pre/post capillary resistance.

These finding are in agreement with the observations recorded after ketamine administration in dogs by Bisen *et al.* (1994). After anaesthesia with Xylazine-Ketamine, RBC values showed no significant difference compared with baseline values (Peighambarzadeh, 2014). Kilic (2008) found decreased RBC level in calves after ketamine anaesthesia. Ismail *et al.* (2010) reported a slight decrease in Red Blood Cell with Xylazine-Ketamine anaesthesia in sheep. Polycarp and Sanni (2015) reported a decrease in RBC in rabbit after thiopentone anaesthesia.

Table 6: Effects of anaesthetic combinations on TEC (Thousands per cubic millimetre) in sheep (n = 6)

Anaesthetic agents	Before anaesthesia	1 hour after induction	24 hours after induction
XT (n = 3)	8.0 ± 0.2	7.75 ± 0.0	8.1 ± 0.3*
XK (n = 3)	8.54 ± 0.4	8.1 ± 0.3	7.9 ± 0.3

± = Standard Deviation; \* = Significant at 5% level of probability; \*\* = Significant at 1% level of probability; XT = Xylazine-Thiopentone; XK = Xylazine-Ketamine

***Packed cell volume***

In group XT there was a significant increase in PCV% 1 hour after induction, and 24 hour after recovery from anaesthesia ( $P < 0.05$ ) (Table 7). In XK group PCV% increased slightly 1 hour after induction and 24 hour after recovery from anaesthesia. This finding corresponds well with Ismail *et al.* (2010) who found significantly increased PCV at 2 and 24 h after recovery in sheep and goats with Xylazine-Ketamine anaesthesia. Udegbunam and Udegbunam (2014) reported that PCV in all groups decreased significantly ( $P < 0.05$ ) by 10 min after induction, while PCV increased at 30 and 60 min. Polycarp and Sanni (2015) reported a decreased PCV in rabbit after thiopentone anaesthesia. Radi *et al.* (2012) reported no significant change in PCV after thiopentone anaesthesia. This finding contrasts with the report that Ketamine-Xylazine combination produced a significant decrease in PCV values from 30 minutes ( $23.4 \pm 1.0\%$ ) to 90 minutes ( $24.0 \pm 1.6\%$ ) compared with baseline value ( $29.63 \pm 1.47\%$ ) (Peighambarzadeh *et al.*, 2014). PCV and haemoglobin (Hb) were significantly decreased after thiopentone (Edjtehadi, 1978). Pooling of the circulating blood cells in the spleen or other reservoirs secondary to decreased sympathetic activity might be the reason for decrease in PCV as reported by Soliman *et al.* (1965) after administration of tranquillizers in dog. The decrease in PCV during anaesthesia might also be due to shifting of fluid from extra-vascular to intra-vascular compartment in order to maintain normal cardiac output (Wagner *et al.*, 1991).

Table 7: Effects of various anaesthetic combinations on PCV (%) during the course of anaesthesia (n = 6)

Anaesthetic agents	Before anaesthesia	1 hour after induction	24 hours after induction
XT (n = 3)	$31.3 \pm 2.5$	$34 \pm 1.7^*$	$34.7 \pm 2.4^*$
XK (n = 3)	$29.7 \pm 1.2$	$30 \pm 1.7$	$31.7 \pm 2.3^*$

$\pm$  = Standard Deviation; \* = Significant at 5% level of probability; \*\* = Significant at 1% level of probability; XT = Xylazine-Thiopentone; XK = Xylazine-Ketamine

***Effect of anaesthetic agents on the state of anaesthesia******Induction of anaesthesia***

The mean induction period with Xylazine-Thiopentone and Xylazine-Ketamine were  $0.2 \pm 0.0$  and  $2.7 \pm 0.1$  minutes. Thiopentone-Xylazine resulted in longer anaesthesia than when using Ketamine-Xylazine (Nuha, 2004). These results are in agreement with the findings of Kumar *et al.* (1983) and Kumar and Sharma (1986) who studied the effect of premedication with xylazine on thiopentone sodium anaesthesia in buffaloes.

***Duration and recovery period of anaesthesia***

The mean duration of anaesthesia was longer with Xylazine-Thiopentone ( $57.3 \pm 2.1$ ) than with Xylazine-Ketamine ( $30.3 \pm 1.2$ ). The mean recovery period of anaesthesia



was longer with Xylazine-Thiopentone ( $92.3 \pm 8.5$ ) than with Xylazine-Ketamine ( $57.7 \pm 1.5$ ) combination. Xylazine-Thiopentone resulted in a longer recovery time compared with Xylazine-Ketamine (Nuha, 2004). This longer time may be due to the presence of an additive effect in the combination (Hutch, 1976).

## Conclusions

The combination of Xylazine-Ketamine and Xylazine-Thiopentone can be used to induce short-term anaesthesia in sheep with minimum effects on clinical and haematological parameters.

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