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Clinico-physiological and haemato-biochemical evaluation of midazolam-ketofol anaesthesia in atropinized goats

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Abstract
The study was conducted on six healthy non-descript goats of either sex weighing between 20-25 kg by administrating atropine sulphate (0.04 mg/kg I/M) followed by midazolam (0.4 mg/kg I/M) and 15 min. later followed by induction of anaesthesia with ketofol (5mg/kg I/V). Sedation with drooping of head after midazolam administration within 8.20±0.58 min. After ketofol administration went into lateral recumbency and onset of anaesthesia was 0.62±0.14 min. Corneal, palpebral and anal pinch reflexes were abolished completely. Complete relaxation of all muscles of jaw, tail, anus, prepuce, neck and limb was observed but for short duration. There was complete analgesia and moderated salivation after ketofol anaesthesia. The average duration of anaesthesia was 33.71±1.08 min. after which sign of recovery such as raising of head, tail flicking appeared and complete recovery took 62.14±1.53 min. after ketofol anaesthesia. There was no significant variations in rectal temperature whereas a significant (P<0.01) increase in heart rate was observed up to 30 min. There was significant (P<0.01) decrease in respiration rate up to 20 min. Non-significant decrease in Hb, PCV and TLC was observed. No significant changes in haemato-biochemical parameters except serum glucose level which increased significantly (P<0.01) after ketofol anaesthesia upto 60 min. All the parameters were within normal physiological range. Therefore, it can be concluded that midazolam-ketofol combination may be safely used as general anaesthesia in atropinized goats for short duration.

Keywords: Anaesthesia, atropine sulphate, clinco-physiological, goat, haemato-biochemical, ketofol, midazolam

Introduction
Goat has particular importance in livestock due to its unique qualities such as high fertility, short kidding interval and good quality mutton, milk and hair. In addition, these species provide manure to enrich the soil**.** Many diseases are encountered requiring surgical procedures in goats which can be performed under regional/ local anesthesia after proper sedation. General anaesthesia with rapid, smooth induction and lesser recumbency time are desirable in goats due to complications like salivation, regurgitation, tympany and cardiopulmonary depression. But unfortunately no single anaesthetic has been found so far without depressing the vital function. Therefore, to get most desired effects of anaesthesia a combination of two or more drugs is used called as balanced anaesthesia which produce adequate level of sedation, analgesia, muscle relaxation, wide margin of safety and limit the cardiopulmonary depression.

Atropine sulphate is obtained from *Atropa belladonna* and is used preanaesthetic to prevent salivary, bronchial, tracheal and gastric secretions and also inhibit the bradycardiac effects of vagal stimulation. Midazolam exert its effects by occupying the benzodiazepine receptor and facilitating the inhibitory action of $GABA_A$ on postsynaptic transmission (Stegmann, 1998) [29]. It induces anticonvulsant, anxiolytic, sedative or hypnotic, amnesic and centrally mediated muscle relaxant effects (Posner *et al*., 2009) [20]. It is water soluble benzodiazepine that is considered to be fast acting with a short elimination half-life (Dzikiti *et al*., 2009) [7]. Midazolam is 4 times more potent in comparison to diazepam but is not used as widely as diazepam in veterinary. Midazolam has minimal effect on cardiopulmonary system in pigs (Smith *et al.*, 1991) [25], dogs (Butola and Singh, 2007) [3], calves (Kilic, 2008) [13] and buffalo calves (Kumar *et al*., 2014a) [15].

Use of midazolam for sedation in goats (Stegmann and Bester, 2001; Dzikiti *et al*. 2009) [30, 7] or in combination for general anaesthesia are limited.

Ketamine is a dissociative anaesthetic and has been used in veterinary anaesthesia for decades. It produces profound analgesia characterized by catatonic and amnesia with or without actual loss of consciousness (Hall *et al*., 2001) [10]. Ketamine is rarely used alone because of its association with poor muscle relaxation, tachycardia and catalepsy or muscle rigidity and it is therefore commonly used in combination with propofol, benzodiazepines and alpha2 agonist to minimize the untoward effects (Saikia *et al*., 2016) [23].

Propofol (2,6-di-isopropylphenol) is a non-opioid, non-barbiturate intravenous sedative hypnotic agent which has rapid smooth induction followed by a short period of unconsciousness and is one of the induction agents commonly used in goats (Dzikiti *et al*., 2009) [7]. Propofol is rapidly redistributed from the brain to other tissue and is also efficiently eliminated from plasma by hydroxylation, which explains its short action and the rapid recovery (Saikia *et al*., 2016) [23]. Propofol has only minimal analgesic property; this explains the need for concurrent administration of analgesic when propofol is used during painful procedures.

Intravenous anaesthetic agent used for induction and maintenance of anaesthesia in animals include propofol and ketamine (Lin *et al*., 1997) [17]. The combination of ketamine and propofol in predetermined ratio produces a mixture called as ketofol. Ketamine and propofol are two completely different sedative which mitigate each other's deficits due to their opposing physiological effects (Green *et al*., 2011) [8]. Propofol in ketofol provides rapid and smooth induction, maintenance of anaesthesia and recovery from anaesthesia and analgesic effects from ketamine (Wamaitha *et al*., 2019) [36]. Clinical reports on use of ketofol suggested some advantages such as limited incidence of propofol induced respiratory depression and decreased cardio-respiratory side effects over using ketamine or propofol alone (Shinde *et al*., 2018) [24]. The clinical efficacy of ketofol has been widely studied and demonstrated in dogs but there is paucity of literature available on the combination of above anaesthetic drugs in goats. Therefore, the purpose of this study is to evaluate the clinico-physiological and haemato-biochemical effects of midazolam-ketofol anaesthesia in atropinized goats.

Materials and Methods

This study was conducted on six healthy non-descript goats of either sex weighing between 20-25 kg. All the goats were fasted for food and water for 12-18 hr before start of experiment. Goats were premedicated with atropine sulphate (0.04 mg/kg I/M) and midazolam (0.4 mg/kg I/M) and then 10 min. later followed by induction of anaesthesia with ketofol (5mg/kg I/V). The ketofol mixture was prepared in the ratio of 5:1 with the five part of propofol (10mg/ml conc.) and one part ketamine (50mg/ml conc.) mixed in one syringe. The following clinic-physiological parameters were studied are onset of sedation / anaesthesia, spontaneous activity, lowering of head, salivation, onset of sternal or lateral recumbency and duration of anaesthesia. Depth of anaesthesia was judged by monitoring the loss of swallowing reflex, corneal, conjunctival, palpebral reflexes, relaxation of anal sphincter anal pinch, pedal reflexes and extent of muscle relaxation. Recovery from anaesthesia was monitored raising of head, trying to stand with ataxia and complete recovery i.e. standing without ataxia. Physiological parameters like heart rate, respiratory rate and rectal temperature were measured before and 10 minutes after premedication and then 10, 20, 30, 60, 90, 120 and 180 minutes after induction of ketofol anaesthesia. Three ml of blood sample were collected from jugular vein prior to administration of the premedication (atropine sulphate and midazolam) and then 30, 60, 120 minutes and 6hr after administration of ketofol. Immediately after collection, the blood samples were transferred in a sterile test tube containing Ethylene Diamine Tetra acetic acid (EDTA) as anticoagulant for estimation of haemoglobin (Hb), packed cell volume (PCV), total leucocyte count (TLC) and differential leucocyte count (DLC). For biochemical parameters, 5 ml venous blood was collected without anticoagulant in sterilized dry test tube and allowed to clot at room temperature. After 2 hr serum was separated and following parameters were estimated viz., serum glucose (mg/dl), serum urea nitrogen (mg/dl), creatinine (mg/dl) aspartate aminotransferase (AST) (U/L) and alanine aminotransferase (ALT) (U/L) at 0 min., and 30, 60, 120 minutes and 6 hrs after induction of ketofol anaesthesia. One way analysis of variance (ANOVA) was used to compare the means at different intervals with base values. All the data were expressed as mean±Standard Error which was analyzed as per the standard procedure outlined by Snedecor and Cochran (1994).

Results and Discussion

Clinical Parameters

The effects of midazolam-ketofol anaesthesia on clinical parameters in atropinized goats could be described as goats showed sedation with drooping of head and neck after midazolam administration within 8.20±0.58 min. All the animals remained conscious and able to stand when disturbed. Mild salivation was observed and midazalom failed to induce lateral or sternal recumbency during this period. A similar finding has been reported by Stegmanna (1998) [29] in goats after intravenous administration of midazolam. Midazolam's sedative effects are due to its agonist actions at gamma aminobutyric acid (GABA) receptors (Cao *et al.* 2002) [4]. Following sedation with midazolam, ketofol was administrated and all the animals went into lateral recumbency and consciousness also lost with onset of anaesthesia was 0.62±0.14 min. Eye remained partially closed throughout ketofol anaesthesia. Absence of corneal and palpebral reflexes was observed at 3 min. post midazolam-ketofol anaesthesia which was an indication of sufficient CNS depression in goats. The anal pinch reflex was abolished completely. There was complete relaxation of all muscles of jaw, tail, anus, prepuce, neck and limb but for short duration. The relaxation of muscle is due to inhibition of internuncial neurons at spinal level by midazolam (Hall *et al*., 2001) [10]. Laryngeal and pharyngeal reflexes were also depressed. Regurgitation nor bloat was not observed in any of the animal. The results of the present are in agreement with Abu-Ahmed (2013) [1] in goats and Kumar *et al.* (2014 a) [15] in buffalo calves after midazolam-ketamine anaesthesia. There was complete analgesia at fetlock, base of tail, abdomen, rib, peritoneum and base of horn. This might be due to ketamine which have potent analgesic property than propofol and midazolam. Kohrs and Durieux (1998) [14] reported that analgesia was produced by antagonistic effects of ketamine on N-methyl-D-aspartate receptors. There was moderated salivation and urination in all the goats after ketofol anaesthesia. Salivation recorded during present study might be due to deceased swallowing reflex. Sahay and Dass (2005) [22] also reported mild salivation after propofol-ketamine

administration in atropinized goats. Urination is a means of elimination of drugs by the kidney and it is a response of healthy kidney to eliminate these drugs from the body. The average duration of anaesthesia was 33.71±1.08 min after which sign of recovery such as raising of head, tail flicking appeared. In the present study, short duration of anaesthesia might be due to shorter half life of midazolam (Vree *et al*., 1981) [35]. Ketamine exerts its action on M-methyl-D-asparted (NMDA) receptor whereas propofol inhibits NMDA receptors by modulating channel gating and metabolic clearance of propofol from the body is at faster rate (Duke, 1995) [6]. All the animals returned to sternal recumbency at 46.85±1.50 min., the animals tried to stand with ataxia at 58.30±2.50 min. and complete recovery took 62.14±1.53 min. after ketofol anaesthesia. Goats started nibbling of grass immediately after recovery might be due to rapid and smooth recovery without struggling. Sahay and Dass (2005) [22] reported complete recovery in 39±1.74 min after propofol-ketamine administration in atropinized goats and Kilic (2008) [13] concluded that the combination of detomidine, midazolam, and ketamine resulted in anaesthesia lasting about 45 min in calves. Similarly, Maravi *et al*. (2018) [18] also reported duration of anaesthesia of 16.31±1.29 min. sternal recumbency at 20.00± 2.20 min and complete recovery at 27.33±2.04 min. in goats after propofol anaesthesia. Wamaitha *et al*. (2019) [36] observed that dogs anaesthesized with acepromazine-ketofol anaesthesia took 37.2 ±18.7 min. to stand. The findings of the present study are concurred with observations reported by Kumar *et al*. (2014 a) [15] in buffalo calves and Rina *et al*. (2018) [21] in yak after midazolam-ketamine anaesthesia. Kumar *et al*. (2014 b) [16], Shinde *et al*. (2018) [24] and Thejasree *et al*. (2018) [33] concluded that ketofol was an excellent induction agent and recovery from anaesthesia was rapid and without struggling in dogs.

Physiological Parameters:

The effects of midazolam-ketofol anaesthesia on physiological parameters in atropinized goats at various time intervals are shown in Table 1. There were non-significant variations in rectal temperature during the study period. Decrease in rectal temperature was recorded up to 30 mins following ketofol anaesthesia and the values returned towards the base values by 180 mins. The findings of the present study are concurred with observations reported by Abu-Ahmed (2013) [1] in Baladi goats, Kumar *et al*. (2014 a) [15] in buffalo calves and Rina *et al*. (2018) [21] in yak after midazolam-ketamine anaesthesia. Maravi *et al*. (2018) [18] observed a marginal decrease in rectal rectal temperature after propofol anaesthesia in goats. Contrarty to present study, Kilic (2008) [13] reported a significant (P<0.05) decrease in body temperature from 38.5±0.3ºC to 37.9±0.4 ºC during detomidine-midazolam-ketamine anaesthesia in calves. The results of present study are in agreement with Shinde *et al*. (2018) [24] and Thejasree *et al*. (2018) [33] who reported decrease in rectal temperature after ketofol anaesthesia in dogs.

A significant (P<0.05) increase in heart rate was observed after midazolam administration in goats which might be due to premedication with atropine sulphate. A similar finding has been reported by Stegmanna (1998) [29] in goats after intravenous administration of midazolam. However, decrease in heart rate after intravenous administration of midazolam has been reported by Smith *et al*. (1991) [25] in pigs, Jangra *et al*. (2008) [12] in goats and Kumar *et al*. (2014 a) [15] in buffalo calves. Following ketofol administration, heart rate significantly (P<0.01) increased from 81.85±2.40 to 92.42±2.54 beats/min. upto 30 min. post-anaesthesia and gradually return to near normalcy by 180 mins. The increase in the heart rate after ketofol administration may be due to cardiac stimulatory effects of ketamine. This increase rate could be due to increased sympathetic activation associated with loss of consciousness or compensatoy response to decreased arterial blood pressure caused by arterial vasodilation (Muir and Gadawski, 1998) [19]. Similar findings to present study have been observed by Kumar *et al*. (2014 b) [16], Shinde *et al*. (2018) [24] and Thejasree *et al*. (2018) [33] in dogs following ketofol anaesthesia. However, in the contrary, Bayan and Konwar (2014) [2] noticed no significant change in heart rate with ketofol anaesthesia in dogs.

The respiration rate significantly (P<0.05) decreased at 10 min. after midazolam administration in goats as midazolam causes respiratory depression (Greene, 2002) [9]. A similar finding has been reported by Smith *et al*. (1991) [25] in pigs after intravenous administration of midazolam. However, in the contrary, Stegmann (1998) [29] reported increase in respiration rate after intravenous administration of midazolam in goats. After ketofol administration, respiration rate significantly (P<0.01) decreased from 20.42±1.81 to 17.51±1.65 breaths/min. upto 20 min. post-anaesthesia and gradually return to near base value. Decreased respiration rate following ketofol anaesthesis might be due to respiratory depressant effect of ketamine (Haskins *et al*., 1985) [11] or propofol (Cullen and Reynoldson, 1997). Propofol caused decrease in respiratory rate by depression of central inspiratory drive and the ventilatory response to arterial CO_2 tension. Similar findings to present study are in agreement Thejasree *et al*. (2018) [33] in dogs following ketofol anaesthesia. Whereas, Sahay and Dass (2005) [22] observed non-significant alternations in rectal temperature, heart and respiratory rate following propofol-ketamine anaesthesia in atropinized goats. Propofol combined with ketamine (ketofol) results in higher pulse rate and mean arterial pressure with lower respiration rate (Taboada and Leece 2014) [32].

Haemato-biochemical Parameters

The effects of midazolam-ketofol anaesthesia on haemato-biochemical parameters in atropinized goats at various time intervals are shown in Table 2. In the present study, there was no significant changes in haemato-biochemical parameters except serum glucose level which increased significantly (P<0.01) after ketofol anaesthesia upto 60 min. A non significant decrease in haemoglobin, PCV and TLC were noted at 60 min following midazolam-ketofol anaesthesia. However, the values returned to near normalcy in 6 hrs and was within normal physiological range. The reason for decrease in Hb, and PCV might be due to pooling of blood in the spleen or other reservoirs secondary to decreased sympathetic activity. During anaesthesia, decrease in haemoglobin and PCV can also be attributed to shifting of fluid from extravascular compartment to intravascular compartment in order to maintain normal cardiac output in animals (Umar and Wakil, 2013) [34]. The decrease in TLC during ketamine anaesthesia may be due to increase in plasma volume during anaesthesia on account of vasodilatation resulting in vascular pooling (Steffy *et al*., 1976) [28]. Neutrophils count showed a non-significant increase whereas lymphocyte count also showed non-significant upto 60 min after ketofol anaesthesia respectively. The rise in neutrophils count and decrease in lymphocyte count might be due to adrenocortical stimulation and subsequent effect of

gluocoticoids on circulating neutrophils and lymphocytes (Soliman *et al.*, 1965) [27]. There was a non significant increase in monocyte and eosinophil count after ketofol anaesthesia upto 60 min. and returned to normalcy by 6 hr. Similarly, findings have been reported by Maravi *et al.* (2018) [18] following propofol administration in atropinized goats. Decrease in haemoglobin and PCV values during midazolam-ketamine anaesthesia was reported by Kilic (2008) [13] in calves, Abu- Ahmed (2013) [1] in Baladi goats and Kumar *et al.* (2014 a) [15] in buffalo calves.

There was non-significant variation in all biochemical parameters during midazolam-ketofol anaesthesia except serum glucose level which highly significant ($P<0.01$) increased (from 66.82 ±2.80 to 80.54±4.04 mg/dl) up to 60 min. which after decreased and returned to normalcy by 6 hrs of the observation period. But the increase was within normal physiological range. This increase might be due to release of catecholamine in stressful condition during anaesthesia, resulting in glycogenolysis or due to decreased glucose utilization, impaired insulin activity or increased adrenocortical hormone. During the period of anaesthesia, there was a decrease in basal metabolic rate with negligible muscular activity leading to decreased utilization of glucose. Similar finding have been documented by Maravi *et al.* (2018) [18] following propofol administration in atropinized goats. However, Rina *et al.* (2018) [21] reported non-significant increase in serum glucose level in yak after administration of midazolam-ketamine. A non-significant increase was observed in serum urea nitrogen, serum creatinine, AST and ALT upto 60 min after midazolam-ketofol anaesthesia which then decreased and returned to base value by 6 hrs. Anaesthetics may indirectly alter the renal function via change in cardiovascular and neuroendocrine activity (Stephen, 1996), but this did not happen in the present study as suggested by non significant transient increase in the level of creatinine which may be attributed due to the temporary inhibitory effect of drugs on the renal blood flow and consequent decrease in glomerular filtration rate which in turn might also have caused a rise in serum creatinine values. Similar observations were recorded by Kilic (2008) [13] in calves and Rina *et al.* (2018) [21] in yak after administration of midazolam-ketamine. Kumar *et al.* (2014 a) [15] also observed non-significant increase in AST activity after administration of midazolam- ketamine in buffalo caves. It corroborates with findings of Shinde *et al.* (2018) [24] and Thejasree *et al.* (2018) [33] following ketofol anaesthesia in dogs. All the haemato-biochemical changes induced by these combinations were compensated within 6 hrs and appeared within normal physiological range. Ketamine and propofol both possess advantages and disadvantages; therefore to reduce their undesirable effects, an attempt to combine them. Ketofol helps to mask the side effects of individual drugs which provide analgesia and adequate anaesthesia with good muscle relaxation. Therefore, it is concluded that midazolam-ketofol anaesthesia in goats provides adequate anaesthesia with smooth induction and rapid recovery without any deleterious effects on vital organs. Hence, ketofol can be safely used as general anaesthesia in goats for short duration.

Table 1: Effects of midazolam-ketofol anaesthesia on physiological parameters in atropinized goats at various time intervals (Mean±S.E.)

Parameters	Period of observation (min)								
	0	10 min after premedication	10 min after G.A.	20	30	60	90	120	180
Rectal Temperature (°F)	103.01 ±0.18	102.94 ±0.19	102.78 ±0.21	102.72 ±0.21	102.58 ±0.19	102.61 ±0.17	102.67 ±0.17	102.72 ±0.19	102.90 ±0.20
Heart Rate (Beats/ Minute)	71.85 ±2.37	81.85* ±2.40	85.57** ±2.26	90.85** ±2.69	91.42** ±2.54	80.28* ±2.34	76.71 ±3.61	76.20 ±2.11	74.51 ±2.32
Respiration Rate (breaths/ minute)	24.14 ±2.05	20.42* ±1.81	18.42** ±2.81	17.50** ±1.65	18.71** ±2.50	21.57* ±2.78	23.28 ±2.64	26.14 ±2.82	26.38 ±2.35

* $P<0.05$ = Significant at 5% level when compared to base value
** $P<0.01$ = Significant at 1% level when compared to base value

Table 2: Effects of midazolam-ketofol anaesthesia on haemato-biochemical parameters in atropinized goats at various time intervals (Mean±S.E.)

Parameters	0 min.	30 min.	60 min.	120 min.	6 hr
Haemoglobin (gm %)	8.11±0.22	7.38±0.32	7.51±0.32	7.88±0.30	8.20±0.30
Packed Cell Volume (%)	22.81±1.13	19.50±0.42	21.04±0.17	22.50±0.66	22.88±0.85
Total Leucocytes Count (x 10^3cumm^{-1})	32.74±0.60	32.05±0.60	31.87±0.88	31.98±0.95	32.85±1.03
Neutrophils (%)	34.42±1.17	36.14±1.20	37.28±2.10	37.62±2.21	35.57±1.99
Lymphocyte (%)	60.71±1.44	58.28±1.26	56.42±2.17	57.14±1.35	59.42±1.28
Eosinophil (%)	1.82±0.20	2.00±0.21	2.54±0.21	2.30±0.37	1.96±0.28
Monocyte (%)	3.14±0.67	3.57±0.42	3.04±0.73	2.92±0.48	3.10±0.45
Serum Glucose (mg/dl)	66.82±3.80	77.08±3.47**	80.54±4.04**	72.70±4.96*	68.38±3.99
Serum Urea Nitrogen (mg/dl)	18.11±1.01	20.91±1.81	22.91±2.63	19.27±1.43	18.32±1.13
Creatinine (mg/dl)	0.91±0.11	1.10±0.10	1.28±0.07	1.12±0.08	0.95±0.08
AST (U/L)	78.36±4.77	80.78±4.07	84.47±5.90	82.76±4.15	79.88±3.74
ALT(U/L)	20.20±1.17	22.75±1.45	24.04±2.34	23.92±2.75	21.54±1.32

* $P<0.05$ = Significant at 5% level when compared to base value
** $P<0.01$ = Significant at 1% level when compared to base value

References

1. Abu-Ahmed H. Sedative and haemato-biochemical effects of midazolam and midazolam ketamine combination in Baladi goats. Global Veterinaria, 2013; 10(6):742-747
2. Bayan H, Konwar B. Clinical evaluation of ketamine-propofol anaesthesia in dog. Indian J Field Veterinarian, 2014; 10(2):41-42
3. Butola V, Singh B. Midazolam as tranquilizer in dogs. Indian Vet. J. 2007; 84:1141-1145

4. Cao JL, Ding HL, Zhang LC, Duan SM, Zeng YM. Pretreatment with midazolam suppresses morphine withdrawal response in mice and rats. Acta Pharmacologica Sinica. 2002; 23:685-690.
5. Cullen LK, Reynoldson JK. Effects of tiletamine/zolazepam premedication on propofol anaesthesia in dogs. Veterinary Record. 1997; 140:363-366
6. Duke T. A new intravenous anaesthetic agent propofol. Canadian Veterinary Journal. 1995; 36:181-182
7. Dzikiti TB, Stegmann GF, Hellebrekers LJ, Auer REJ, Dzikiti LN. Sedative and cardiopulmonary effects of acepromazine, midazolam, acepromazine-butorphanol and midazolam-butorphanol on propofol anaesthesia in goats. J S Afr Vet Assoc. 2009; 80(1):10-16.
8. Green SM, Andolfatto G, Krauss B. Ketofol for procedural sedation? Pro and con. Ann. Emergency Med. 2011; 57:444-448.
9. Greene SA. Veterinary anaesthesia and pain management secrets. Hanley and belfus. Philadelphia, 2002.
10. Hall LW, Clarke KW, Trim CM. Principle of sedation, analgesia and premedication. In: Veterinary Anaesthesia 10th eds. W. B. Saunders, London, 2001.
11. Haskins SC, Farver TB, Patz JD. Ketamine in dogs. Am. J Vet. Res. 1985; 46(9):1855-1860
12. Jangra SK, Chawla SK, Peshin PK, Tayal R, Singh J, Behl SM. Cardiopulmonary effects of midazolam in goats. Indian J Vet. Surg. 2008; 29:2024
13. Kilic N. Cardiopulmonary, biochemical and haematological changes after detomidine-midazolam-ketamine anaesthesia in calves. Bull Vet Inst Pulawy. 2008; 52:453-456.
14. Kohrs R, Durieux ME. Ketamine: Teaching an old drug new trick. Anesth. Analg. 1998; 87:1186.
15. Kumar A, Kumar A, Singh S, Chaudhary RN. Evaluation of midazolam-ketamine as an anaesthetic combination in buffalo calves. Haryana Vet. 2014a; 53(2):117-120.
16. Kumar A, Kumar A, Tyagi PS, Sharma KS, Sharma R. Ketofol as a general anaesthetic agent in diazepam or midazolam premedicated and halothane anaesthetized dogs. Indian J Vet. Surg. 2014b; 35(1):31-34.
17. Lin HC, Purohit RC, Powe TA. Anaesthesia in sheep with propofol or with xylazine-ketamine followed by halothane. Veterinary Surgery. 1997; 26:247-252
18. Maravi MS, Dewangan, Rukmani, Tiwari SK. Effects of propofol on clinico-physiological and haemato-biochemical profiles in atriopinized goats. Indian J Small Rumin. 2018; 24(1):187-190
19. Muir WW, Gadawski JE. Respiratory depression and apnoea induced by propofol in dogs. Am J Vet. Res., 1998; 59(2):157-161
20. Posner LP, Burns P. Sedative Agents: Tranquilizers, Alpha-2 Agonists, and Related Agents, in Veterinary Pharmacology and Therapeutics, Riviere JE, Papich MG. Editors. Wiley. 2009, 337-380.
21. Rina T, Bayan H, Hanah SS, Bam J, Borah B. Statistical evaluation of acepromazine and midazolam as preanaesthetics to ketamine in yak. Intern. J. Appl. Res. Vet. Med., 2018; 16(2):131-139
22. Sahay S, Dass LL. Evaluation of propofol alone and with ketamine for anaesthesia in atropinized goats. Indian J Vet Surg. 2005; 26(2):96-98
23. Saikia B, Sarma KK, Kalita D, Sarmah BK, Phukan A, Goswami S. Propofol, ketamine and ketofol as total intravenous anaesthesia in dogs. Sch. J Agri. Vet. Sci., 2016; 3(2):100-102
24. Shinde PR, Chepte Thorate, Raulkar MG, Ali RV, Fani SS, Anam FA *et al*. Clinical efficacy of ketofol and propofol in dog. Int. J Sc. Env. Tech., 2018; 7(6):1949-1953
25. Smith AC, Zellner JL, Spinale FG, Swindle MM. Sedative and cardiovascular effects of midazolam in swine. Lab. Anim. Sci. 1991; 41:157-161.
26. Snedecore GW, Cochram WG. Statistical methods. 6th edition, Oxford and IBH, New Delhi: 1994, 258-296.
27. Soliman MK, Amrousi SE, Khamis MY. The influence of tranquilizers and barbiturates anaesthesia on the blood picture and electrolytes of dogs. Vet. Rec. 1965; 77:1256.
28. Steffy EP, Gillespie JR, Berry JD, Eger EI, Schalm OW. Effects of halothane and halothane- nitrous oxide on haematocrit and plasma protein concentration in dog and monkey. Am. J Vet. Res. 1976; 37:959-962.
29. Stegmann GF. Observations on the use of midazolam for sedation and induction of anaesthesia with midazolam in combinations with ketamine in the goat. J.S. Afr. Vet. Ass. 1998; 69(3):89-92.
30. Stegmann GF, Bester L. Sedative-hypnotic effects of midazolam in goats after intravenous and intramuscular administration. Vet Anaesth Analg., 2001; 28:49-55.
31. Stephen AG. Anaesthetic effects on renal function insufficiency. Lumb and Jones, Veterinary Anaesthesia. 3rd edn. 1996, 786.
32. Taboada MF, Leece E. Comparison of propofol with ketofol, a propofol-ketamine admixture, for induction of anaesthesia in healthy dogs. Vet. Anaesth. Analg. 2014; 41(6):575-582.
33. Thejasree P, Veena P, Dhanalakshmi N, Veerbrahmaiah K. Evaluation of propofol and ketofol anaesthesia following atropine, diazepam and fentanyl premedication in dogs. Int. J Curr. Microbiol. App. Sci. 2018; 7(11):3130-31370.
34. Umar MA, Wakil Y. Effects of the combination of ketamine and medetomidine anaesthesia on haematological parameters in Sahel goats. Sokoto Journal of Veterinary Sciences. 2013; 11(1):66-69.
35. Vree TB, Baars AM, Booji LH. Simultaneous determination and pharmacokinetics of midazolam and its hydroxymetabolites in plasma and urine of man and dogs by means of high performance liquid chromatography. Arneimittelforschung, 1981; 31:2215-2219.
36. Wamaitha MN, Mogoa EM, Mande JD. Evaluation of anaesthesia produced by kefofol in acepromazine or medetomidine sedated dogs. J Adv. Vet. Anim. Res., 2019; 6(2):215-221.