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Haemato-biochemical evaluation of midazolam propofol induction combination isoflurane anaesthesia in cattle

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Abstract
Six animals were administered Midazolam (3mg/kg) intravenously, 10 minutes later Propofol was given @3mg/kg body weight intravenously for induction of anaesthesia followed by immediate intubation; maintenance of anaesthesia was done under isoflurane. Anaesthetic combinations were compared by haematological and biochemical observations.
Haematological observations in the present study revealed that haemoglobin, packed cell volume and total erythrocyte count decreased significantly at maximum depth of anaesthesia in all the animals. Neutrophilia with relative lymphocytopenia were recorded during anaesthesia suggesting, certain amount of anaesthetic stress was produced by these combinations. In all the animals most of the biochemical parameters showed the changes, which were within the normal range, suggesting that the anaesthetic combinations used in the present study do not produce adverse effect on these parameters.

Keywords: midazolam, propofol, isoflurane, cattle

1. Introduction
Cattle being docile animals allow many of the surgical and diagnostic procedures to be performed under physical restraint in conjunction with local or regional anaesthesia blockade with or without sedation. However, the resulting conditions are sub-optimal for a number of situations for complex and prolonged surgical procedures and the use of anaesthesia is desired (Adetunji *et al*., 1984) [1].
\General anaesthesia may be preferred over local analgesia for many surgical interventions, as it provides complete unconsciousness, better insensitivity to pain, good muscle relaxation, and freedom from reflex responses and loss of motor ability (Thurmon *et al*., 1996) [2].
Intravenous anaesthesia involves the delivery of a bolus dose or a fast loading infusion to achieve an adequate blood concentration of the drug. In veterinary practice, intravenous anaesthetic drugs are commonly used for induction of anaesthesia inorder to facilitate endotracheal intubation, oxygen administration and artificial ventilation. Maintenance of anaesthesia can be obtained by infusion of intermittent boluses (IBI) or by continuous rate infusion (CRI), which causes a cumulative effect and prolonged recovery (Malik, 2014) [3]. Hence, inhalant anaesthetic agents, which provide predictable and rapid adjustment of anaesthetic depth and help to minimize the patient morbidity and mortality, form the foundation for maintenance of general anaesthesia (Mckenzi, 2008) [4]. Anatomical considerations in cattle carry the risk of complications like tympany, regurgitation and aspiration pneumonia, which could be minimized by fasting the animal before anesthesia. Heavy body weight in adult cattle carries greater risk of developing myopathies and neuropathies following prolonged recumbency so; good positioning and protective padding must be ensured.
Currently ketamine is used as induction agent in cattle, along with several pre- anesthetic agents, xylazine (Arai *et al*., 2006) [1], diazepam (Riazuddin *et al*., 2004a) [7], acepromazine (Kumar *et al*., 2012) [5] and guaifenesin (Riazuddin *et al*., 2004b) [6] under isoflurane anesthesia.

2. Materials and Method
2.1. Source of Animals
The study was conducted in 06 clinical cases presented to VCC, Veterinary College, Bidar,

with various surgical conditions to evaluate haemato-biochemical observations for midazolam-propofol induction combinations under isoflurane anaesthesia in cattle.

2.2 Grouping of animals and anaesthetic protocol
In all the animals, midazolam was administered at the dose rate of 0.4 mg per kg body weight intravenously, five minutes later the animals were restrained in lateral recumbency and anaesthesia was induced by administering propofol intravenously, at the dose rate of 3mg/kg body weight, followed by immediate intubation, the animals were maintained on 5 per cent to 1 per cent of isoflurane.

2.3 Haematological evaluation
The heamatological observations *viz*, Heamoglobin, Packed cell volume, TEC, TLC and DLC was estimated before administration of any drug, immediately after induction (0 min) and then at 30 min, 60 min and24 hr. After induction of anesthesia.

2.4 Biochemical evaluation
The biochemical observations *viz*, alanine transaminase, aspertate transaminase, creatinine and serum urea nitrogen was estimated before administration of any drug, immediately after induction (0 min) and then at 30 min, 60 min and 24 hr. after induction of anesthesia.

3. Results
Haematological observations
The haemoglobin (Mean ±SE) in all the animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes, 60 minutes and 24hrs after induction were; 10.15±0.75, 10.48±0.62, 09.35±0.86, 09.23±0.90 and 09.20±0.62 respectively (table no1). The comparison between the groups at different intervals revealed that there was no statistically significant (P>0.05) difference in the haemoglobin.

Packed cell volume (%)
The packed cell volume (Mean ±SE) in all the animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes, 60 minutes and 24hrs after induction were; 35.48±2.83, 33.15±2.93, 30.40±2.96, 28.40±3.40 and 30.20±2.17 (table no1) respectively.

Total erythrocyte count (x106 /µl)
The total erythrocyte count (Mean ±SE) in all the animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes, 60 minutes and 24hrs after induction were; 7.62±0.53, 7.26±0.54, 6.79±0.52, 6.49±0.56 and 7.11±0.40 (table no.1) respectively.

Total leucocyte count (x103 /µl)
The total leucocyte count (Mean±SE) in all the animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes, 60 minutes and 24hrs after induction were; 11.72±1.49, 09.63±0.94, 08.20±0.57, 08.77±0.56 and 10.12±0.84 (table no1) respectively

Neutrophils (%)
The total neutrophils (Mean ±SE) in all the animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes, 60 minutes and 24hrs after induction were; 32.40±1.33, 34.10±1.47, 41.30±1.37, 32.43±1.47 and 40.10±2.12 (table no2) respectively.

Lymphocytes (%)
The lymphocytes (Mean ±SE) in all the animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes, 60 minutes and 24hrs after induction were; 61.80±1.54, 59.43±1.76, 50.10±2.28, 47.23±1.83 and 53.27±2.14 (table no2) respectively.

Biochemical observations
Alanine transaminase (IU/L)
The alanine transaminase (Mean ±SE) in all the animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes, 60 minutes and 24hrs after induction were; 24.50±2.71, 23.67±1.45, 23.67±2.19, 26.17±2.68 and 27.83±3.74 (table no3) respectively.

Aspartate transaminase (IU/L)
The Aspartate transaminase (Mean ±SE) in all the animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes, 60 minutes and 24hrs after induction were; 69.00±11.60, 73.83±10.11, 74.17±11.06, 91.00±11.97 and 94.20±14.98 (table no3) respectively.

Creatinine (mg/dl)
The Creatinine (mg/dl) (Mean ±SE) in all the animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes, 60 minutes and 24hrs after induction were; 1.73±0.16, 1.74±10.16, 1.89±0.14, 1.81±0.7 and 1.82±0.25 (table no3) respectively.

Serum Urea Nitrogen (mg/dl)
Serum Urea Nitrogen (mg/dl) (Mean ±SE) in all the animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes, 60 minutes and 24hrs after induction were; 27.63±3.64, 27.27±4.15, 27.95±3.74, 31.15±4.47 and 26.60±2.26 (table no3) respectively.

4. Discussion
Haematological observations
Haemoglobin decreased significantly from 60 minutes to 24hrs after induction, and there was gradual increase in the post-anesthetic period, however, it remained come to physiological limits after 24hrs hours after anesthesia.
Packed cell volume, total erythrocyte count, total leucocyte count significant decreased from 30 minutes to 60 minutes and after 24 hrs its come to normal physiological limits of post induction. The decrease in haemoglobin during sedation may be caused by the shifting of fluid from the extravascular compartment to the intravascular compartment in order to maintain normal cardiac output (Wagner *et al*., 1991) [8]. The decreased haemoglobin has been reported after administration of dexmedetomidine in dogs (Gupta, 2010) [9] and sheep (Monsang, 2011) [10]. De Moor and Desmet (1979) [11] reported a decrease in haemoglobin after giving xylazine in cattle. Decrease in total erythrocyte count is due to stress response towards anaesthetic drugs. Amreshkumar *et al*. (1979) [12] stated that these changes could be due to result of animal response to stress caused by anaesthetic drugs. A significant increase in neutrophils with a subsequent significant decrease in lymphocytes was observed under ketamine-isoflurane anaesthesia in all the animals. These changes were nearer to normal levels and were probably related to response of animal to anaesthesia and surgery.

Peshin *et al*. (1980) [13] reported a decrease in lymphocytes with subsequent increase in neutrophils in dogs administered with xylazine.

Biochemical observations

Alanine transaminase and aspertate transaminase fluctuated within normal limits in all animals. Alanine transaminase and aspertate transaminase increased significantly at 24 hours after induction and they remained significantly higher even 48 hours after anesthesia in all the animals similar findings has been reported by Nuh (2008) [14] after detomidine-midazolam-ketamine anesthesia in calves, however, they reported that the values returned to the pre-anesthetic level by 24 hours after anesthesia. Abu-Ahmed (2013) [15] observed no significant change in the alanine transaminase and aspertate transaminase during midazolam ketamine anesthesia in goats. All the general anesthetics lower the circulation to liver (Malik and Singh, 2007) [16] and the changes in alanine transaminase and aspertate transaminase during present study might be due to this fact.

Creatinine values remained within normal limits and no significant change in the values were observed throughout anesthesia in all animals. Similar findings were recorded after midazolam-ketamine anesthesia in goats (Abu-Ahmed, 2013) [17] and isoflurane anesthesia in sheep (Hikasa *et al*, 2000) [18].

A significant increase in the serum urea nitrogen was observed in all the animals. Increased hepatic urea production from amino acid degradation might account for the observed increase in serum urea nitrogen. Increase in serum urea nitrogen was reported after detomidine-midazolam-ketamine anesthesia in calves (Nuh, 2008) [19], however Abu-Ahmed (2013) [20] observed no significant change in the serum urea nitrogen during midazolam-ketamine anesthesia in goats.

5. Conclusion

In conclusion Haematological and biochemical observations revealed that haemoglobin, packed cell volume and total erythrocyte count decreased significantly at maximum depth of anesthesia in all the animals followed by all the biochemical parameters are within limits, the above said combination for surgery in cattle may be good for general anaesthesia.

Table 1: Mean ±SE values of Haematological parameters at different intervals in all the animals

S. No	Parameters	Time	Midazolam+ propofol+ isoflurane Anaesthetic combinations
1	Haemoglobin (g/dl)	Before	10.15±0.75
		0 Min	10.48±0.62
		30 Min	09.35±0.86*
		60 Min	09.23±0.90*
		24 Hr	09.20±0.62**
2	Packed Cell Volume (%)	Before	35.48±2.83
		0 Min	33.15±2.93
		30 Min	30.40±2.96*
		60 Min	28.40±3.25**
		24 Hr	30.42±2.17*
3	Total Erythrocyte Count ($x10^6$ /µl)	Before	7.62±0.53
		0 Min	7.26±0.54
		30 Min	6.79±0.52**
		60 Min	6.49±0.56**
		24 Hr	7.11±0.40*
4	Total Leucocyte Count ($x10^3$ /µl)	Before	11.72±1.49
		0 Min	09.63±0.94
		30 Min	08.20±0.57* [b]
		60 Min	08.77±0.56*
		24 Hr	10.12±0.84

*Means bearing superscript*differ significantly at $P<0.05$ from interval 'before' within the group

Means bearing superscriptdiffer significantly at $P<0.01$ from interval 'before' within the group a, b means bearing superscript a, b differ significantly at $P<0.05$ level between groups at corresponding intervals

Table 2: Mean ±SE of Differential leucocyte count (%) at different intervals in all the animals

S. No	Parameters	Time	Midazolam+ propofol+ isoflurane Anaesthetic combinations
1	Neutrophils (%)	Before	32.40±1.33
		0 Min	34.10±1.47
		30 Min	41.30±1.37**
		60 Min	42.43±1.47***
		24 Hr	40.10±2.12***
		48 Hr	32.33±2.13
2	Lymphocytes (%)	Before	61.83±1.54
		0 Min	59.43±1.76*
		30 Min	50.10±2.28***
		60 Min	47.23±1.83***
		24 Hr	53.27±2.14***
		48 Hr	61.00±2.19

*Means bearing superscript*differ significantly at $P\leq0.05$ from interval 'before' within the group

Means bearing superscriptdiffer significantly at $P\leq0.01$ from interval 'before' within the group

Means bearing superscriptdiffer significantly at $P\leq0.001$ from interval 'before' within the group

a, b means bearing superscript a, b differ significantly at $P\leq0.05$ level between groups at corresponding intervals

Table 3: Mean ±SE values of biochemical parameters at different intervals in all the animals

S. No	Parameters	Time	Group-II
1	Alanine Transaminase (IU/L)	Before	24.50±2.71
		0 Min	23.67±1.45
		30 Min	23.67±2.19
		60 Min	26.17±2.68
		24 Hr	27.83±3.74 [b]
2	Aspartate Transaminase (IU/L)	Before	69.00±11.60 [b]
		0 Min	73.83±10.11
		30 Min	74.17±11.06
		60 Min	91.00±11.97
		24 Hr	94.20±14.98*
3	Creatinine (mg/dl)	Before	1.73±0.16
		0 Min	1.74 ±0.16
		30 Min	1.89±0.14
		60 Min	1.81±0.07
		24 Hr	1.82±0.25
4	Serum Urea Nitrogen (mg/dl)	Before	27.63±3.64 [b]
		0 Min	27.27±4.15 [b]
		30 Min	27.95±3.74 [b]
		60 Min	31.15±4.47 [b]
		24 Hr	26.60±2.26

*Means bearing superscript*differ significantly at $P \leq 0.05$ from interval 'before' within the group

Means bearing superscriptdiffer significantly at $P \leq 0.01$ from interval 'before' within the group a, b means bearing superscript a, b differ significantly at $P \leq 0.05$ level between groups at corresponding

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