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Heamato-biochemical evaluation of midazolam-propofol and xylazine-propofol induction combinations for isoflurane anaesthesia in cattle

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Abstract
Twelve animals were randomly divided in to two groups *viz*., Group-I and Group-II consisting of six animals in each group. Group –I animals received Xylazine (0.08mg/kg) intravenously, 10 minutes later Propofol was given @3mg/kg body weight intravenously for induction of anaesthesia. In Group-II animals' Medazolam (3mg/kg) was administered intravenously, 10minutes later Propofol was given @3mg/kg body weight intravenously for induction of anaesthesia followed by immediate intubation, maintenance of anaesthesia was done under isoflurane in both the groups. Anaesthetic combinations were compared by haematological and biochemical observations.

Haematological observations in the present study revealed that haemoglobin, The haemoglobin (Mean ±SE) in Group-I animals; (10.58±0.63, 10.65±0.55, 09.65±0.45 and 08.90±0.50 respectively) and in Group-II animals (11.25±0.75, 10.78±0.62, 09.65±0.86 and 09.13±0.90 respectively).packed cell volume and total erythrocyte count decreased significantly at maximum depth of anaesthesia in both the groups. Neutrophilia (Mean ±SE values of neutrophils are 32.17±2.04, 34.50±2.06, 42.67±2.35 and 45.67±2.50) with relative lymphocytopenia (Mean ±SE 63.33±2.15, 61.50±2.09, 52.33±2.83 and 49.50±2.72) were recorded in both groups during anaesthesia suggesting, certain amount of anaesthetic stress was produced by these combinations. In both groups 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, xylazine, isoflurane, cattle

1. Introduction

General anaesthesia in cattle involves complexities like regurgitation, bloat, respiratory complication, nerve paralysis etc., which are not often encountered in small animals however, carefully selected and properly managed general anaesthetic technique provide optimal conditions for surgery (Arai *et al*., 2006) [1].

Cattle and buffaloes usually accept physical restraint well and that to in conjuction with local or regional anaesthesia is often sufficient for completion of many surgical procedures. However, many times in non-co-operative animals and in diagnostic and surgical procedure that are more complex like, diaphragmatic hernia, traumatic pericarditis and orthopedic surgeries where technical and anatomical aspects of the surgical procedures warrant absolute control of movement during surgery (Kumar *et al*., 2013) [2]. General anaesthesia is required in cattle and buffaloes for complex surgical or diagnostic procedures. Inhalation anaesthesia requires specific equipment and may only be possible in the hospital environment. It is rarely feasible for use in the field.

In recent years, intravenous anaesthetics with rapid onset, redistribution and clearance have become available, which creates the possibility of maintaining anaesthesia even in large ruminants using these intravenous agents (Malik *et al*., 2012) [3]. Moreover, the use of intravenous anaesthetic agents for induction and maintenance of anaesthesia may facilitate endotracheal intubation, oxygen administration or artificial ventilation if it is required.

Various sedatives and tranquilizing agents are used as pain killers and/or muscle relaxants while animals undergo minor or major surgeries. These drugs are needed in veterinary practice and are indispensable as they help in overcoming resistance of the animals during examination, maintaining depth of anesthesia, reducing the amount of anesthetic agents and increasing margins of safety (Mahmud *et al*., 2014) [4]. Midazolam, water soluble benzodiazepine having sedative, hypnotic, anticonvalsant and muscle relaxant properties. It has been shown to have

both analgesic and muscle relaxant effect (Ritcher, 1981) [5] with minimum adverse effects on cardiovascular system (Jones *et al*., 1979) [6]. Propofol is one of the intravenous anaesthetics with rapid induction, distribution, metabolism and elimination that makes it a good choice for induction and maintenance of anaesthesia by repeated bolus infusion or continuous intravenous infusion. Little work has been done on propofol usage in large ruminants.

Currently ketamine is used as induction agent in cattle, along with several pre-anaesthetic agents, xylazine (Arai *et al*., 2006)[7] diazepam (Riazuddin *et al*., 2004a) [8] acepromazine (Kumar *et al*., 2012) [9] and guaifenesin (Riazuddin *et al*., 2004 *b*) [10] under isoflurane anaesthesia. However, there is paucity of reports or studies on propofol anaesthesia in cattle in India. Therefore the present clinical study was to compare heamato-biocheemical evaluation of midazolam-propofol and xylazine-propofol induction combinations for isoflurane anaesthesia incattle.

2. Materials and Method

2.1 *Source* of animals

The study was conducted in 12 clinical cases presented to VCC, veterinary college, Bidar, with various surgical conditions to evaluate heamato-biochemical observations for midazolam-propofol and xylazine-propofol induction combinations under isoflurane anaesthesia in cattle.

2.2 Grouping of animals and anaesthetic protocol

Twelve clinical cases were randomly divided in two groups *viz*., group-I and group-II with six animals in each group. The animals in Group-I received xylazine at the dose rate of 0.08mg/kg body weight intravenously, after tenminutes of xylazine administration, the animals were restrained in lateral recumbency and anaesthesia was induced by administering propofol, at the dose rate of 3mg/kg body weight intravenously, followed by immediate intubation, the animals were maintained on 5 per cent to 1 per cent of isoflurane. In the animals of Group-II, 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. Heamatological 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, 24 hr and 48 hr after induction of ane sthesia.

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, 24 hr and 48 hr after induction of anesthesia.

3. Results

Haematological observations

Haemoglobin (g/dl)

The haemoglobin (Mean ±SE) in Group-I animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes and 60 minutes after induction were; 10.58±0.63, 10.65±0.55, 09.65±0.45 and 08.90±0.50 respectively. The Mean ±SE values 24 hour and 48 hour post anesthesia were; 09.83±0.67 and 09.88±0.70 respectively in Group-I animals. The haemoglobin (Mean ±SE) in Group-II animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes and 60 minutes after induction were; 11.25±0.75, 10.78±0.62, 09.65±0.86 and 09.13±0.90 respectively. The Mean ±SE values 24 hour and 48 hour post anaesthesia were; 09.70±0.62 and 09.98±0.62 respectively in Group-II animals.

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 Group-I animals before anesthesia, immediately after induction (0 minute) and then at 30 minutes and 60 minutes after induction were; 33.77±2.13, 34.33±2.10, 30.33±1.70 and 28.90±1.71 respectively. The Mean ±SE values 24 hour and 48 hour of post anesthesia were; 31.83±2.42 and 31.65±2.59 respectively in Group-I animals. The packed cell volume (Mean ±SE) in Group-II animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes and 60 minutes after induction were; 36.68±2.83, 34.05±2.93, 31.80±2.96 and 29.50±3.25 respectively. The Mean ±SE values 24 hour and 48 hour post anesthesia were; 31.52±2.17 and 31.05±2.76 respectively in Group-II animals. The comparison within the group at different intervals revealed that the packed cell volume decreased significantly (P≤0.05) between 30 minutes and 60 minutes post induction when compared to pre-anesthetic level in Group-I animals.

Total Erythrocyte Count (x10^6 /µl)

The total erythrocyte count (Mean ±SE) in Group-I animals before anesthesia, immediately after induction (0 minute) and then at 30 minutes and 60 minutes after induction were; 6.87±0.44, 6.87±0.43, 6.37±0.34 and 5.92±0.35 respectively. The Mean ±SE values 24 hour and 48 hour post anesthesia were; 6.51±0.51and 6.46±0.54 respectively in Group-I animals. The total erythrocyte count (Mean ±SE) in Group-II animals before anesthesia, immediately after induction (0 minute) and then at 30 minutes and 60 minutes after induction were; 6.82±0.53, 6.36±0.54, 5.99±0.52 and 5.59±0.56 respectively. The Mean ±SE values 24 hour and 48 hour post anesthesia were; 6.01±0.40 and 6.16±0.43 respectively in Group-II animals.

The comparison within the group at different intervals revealed that the total erythrocyte count decreased significantly (P≤0.01) between 30 minutes and 60 minutes post induction when compared to pre-anesthetic level in both the groups.

Total Leucocyte Count (x10^3 /µl)

The TLC (Mean ±SE) in Group-I animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes and 60 minutes after induction were; 13.55±2.46, 14.15±2.51, 11.80±1.87 and 11.35±2.70 respectively. The Mean ±SE values 24 hour and 48 hour post anesthesia were; 15.92±2.12 and 15.48±2.08 respectively in Group-I animals. The total leucocyte count (Mean ±SE) in Group-II animals before anesthesia, immediately after induction (0 minute) and then at 30 minutes and 60 minutes after induction were;

10.82±1.49, 08.93±0.94, 07.60±0.57 and 06.97±0.56 respectively. The Mean ±SE values 24 hour and 48 hour post anesthesia were; 11.42±0.84 and 10.45±0.84 respectively in Group-II animals.

In the animals of Group-II the total leucocyte count decreased significantly ($P \leq 0.05$) between 30 minutes and 60 minutes post induction when compared to pre-anesthetic level, however, it again increased 24 hours of post anesthesia.

Neutrophils (%)

The neutrophil count (Mean ±SE) in Group-I animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes and 60 minutes after induction were; 32.17±2.04, 34.50±2.06, 42.67±2.35 and 45.67±2.50 respectively. The Mean ±SE values 24 hour and 48 hour post anesthesia were; 39.33±3.16 and 33.50±2.58 respectively in Group-I animals. The neutrophil count (Mean ±SE) in Group-II animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes and 60 minutes after induction were; 33.00±1.53, 35.00±1.67, 44.00±1.67 and 46.83±1.67 respectively. The Mean ±SE values 24 hour and 48 hour post anesthesia were; 41.00±2.02 and 33.33±2.23 respectively in Group-II animals.

The comparison within the group at different intervals revealed that the neutrophil count increased significantly between 30 minutes ($P \leq 0.01$) and 60 minutes ($P \leq 0.001$) post induction when compared to pre-anesthetic level in both the groups.

Lymphocytes (%)

The lymphocyte count (Mean ±SE) in Group-I animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes and 60 minutes after induction were; 63.33±2.15, 61.50±2.09, 52.33±2.83 and 49.50±2.72 respectively. The Mean ±SE values 24 hour and 48 hour post anesthesia were; 57.17±3.40 and 63.00±2.94 respectively in Group-I animals. The lymphocyte count (Mean ±SE) in Group-II animals before anesthesia, immediately after induction (0 minute), and then at 30 minutes and 60 minutes after induction were; 62.83±1.54, 60.83±1.76, 51.00±2.28 and 48.33±1.93 respectively. The Mean ±SE values 24 hour and 48 hour post anesthesia were; 55.17±2.04 and 63.00±2.29 respectively in Group-II animals.

The comparison within the group at different intervals revealed that the lymphocyte count decreased significantly between 30 minutes ($P \leq 0.05$) and 60 minutes ($P \leq 0.001$) post induction when compared to pre-anesthetic level in both the groups.

4. Discussion

Haematological observations

Haemoglobin decreased significantly 30 minutes after induction, and there was gradual increase in the post-anesthetic period, however, it remained significantly below even 48 hours after anesthesia.

Packed cell volume has no statistical significant difference between the groups and decreased significantly between 30 and 60 minutes post induction.

Total erythrocyte count decreased significantly between 30 minutes and 60 minutes post induction. It again increased 24 hours post anesthesia in group I animals, however, in group II animals remained significantly lower till 48 hrs post anaesthesia.

The decrease in the haemoglobin, packed cell volume and total erythrocyte count values is in agreement with earlier workers (Hikasa *et al*., 2000 [11]; Ajadi *et al*., 2008; [12] Nuh, 2008 and Abu-Ahmed, 2013) [13]. The decrease in the haematocrit values might be attributed to the combined effect of drugs on venous tone, pooling of blood in spleen, vasodilatation and subsequent haemodilution, as has been observed with midazolam-ketamine anesthesia in horses (Malik and Singh, 2007) [14].

Total leucocyte count decreased significantly between 30 and 60 minutes post induction when compared to pre-anaesthetic level, however it again increased 24 hours post anaesthesia in both groups. It was observed those 30 minutes of induction statistically significant between the groups. Fluctuated within normal limits in all animals. Decrease in the total leucocyte count was observed at maximum depth of anesthesia in both groups, and subsequently it increased to base value by 24 hours post-anesthesia. Similar findings have been reported after midazolam-ketamine anesthesia in horses (Malik and Singh, 2007) [15], in goat (Abu-Ahmed, 2013) [16] and in calves (Nuh, 2008), and after fentanyl-medetomidine-thiopentone-isoflurane anesthesia in buffaloes (Singh *et al*., 2013) [17]. In the present study inter-compartmental fluid shift or splenic pooling of cells might have caused decrease in total leucocyte count.

Neutrophilia with relative lymphocyteopenia were recorded in both groups during anesthesia and might have been the result of the stress caused by the pre-anesthetics and anesthetic drugs and subsequent stimulation of adrenal gland (Singh *et al*., 2013) [18]. Similar findings had been reported after medetomidine- butorphanol,-thiopental and halothane anesthesia (Malik *et al*., 2011) [18] and fentanyl-medetomidine-thiopentone-isoflurane anesthesia (Singh *et al*., 2013) [17] in buffaloes. In the present study neutrophils and lymphocytes returned to base values 48 hours after anesthesia. There was no statistical difference in eosinophil count was recorded in Group-I animals, increased significantly between 30 minute and 60 minute post induction in group II animals. However, it returned to base level at 24 hours post induction.

There was no statistically significant difference in the basophil and monocyte count count between and within the groups.

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 both group of animals, similar findings has been reported by Nuh (2008) 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) 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) [24] 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) and isoflurane anesthesia in sheep (Hikasa *et al*, 2000) [3]. However, increase in the creatinine values were reported after

acepromazine-ketamine and diazepam-ketamine anesthesia in goats (Akhare *et al.*, 2003), xylazine-butorphanol-midazolam-ketamine anesthesia in horses (Malik and Singh, 2007) and detomidine-midazolam-ketamine anesthesia in calves (Nuh, 2008).

A significant increase in the serum urea nitrogen was observed in both groups of animals. Increased hepatic urea production from amino acid degradation might account for the observed increase in serum urea nitrogen. However, it is unlikely that this could be caused by renal damage because all the creatinine values in the present study were within the normal physiological limits. Similar increase in serum urea nitrogen was reported after detomidine-midazolam-ketamine anesthesia in calves (Nuh, 2008), however Abu-Ahmed (2013) observed no significant change in the serum urea nitrogen during midazolam-ketamine anesthesia in goats.

In conclusion haematological observations revealed that haemoglobin, packed cell volume and total erythrocyte count decreased significantly at maximum depth of anesthesia in both the groups. Decrease in the total leukocyte count was observed at maximum depth of anesthesia in both groups. Neutrophilia with relative lymphocytopenia were recorded in both groups during anesthesia. No significant difference in the monocyte and basophil count was observed in both groups. In both groups 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. Xylazine-propofol combinations could be used in healthy surgical condition patients whereas, midazolam-propofol combinations could use in healthy and also in compromised surgical condition patient.

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