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Haemato-biochemical and blood gas changes in cattle under multimodal general anaesthesia using guaiphenesin-ketamine-isoflurane with butorphanol-xylazine-ketamine premedication

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Abstract

The study was carried out in six female cattle of different breeds, aged between six months to 10 years and weighing 100–480 kg, to assess haemato-biochemical and blood gas alterations during multimodal general anaesthesia. Pre-anaesthetic sedation was achieved with intramuscular injection of butorphanol, xylazine and ketamine at the dose rate of 0.01, 0.02 and 0.04 mg/kg body weight. Following sedation, all the animals were positioned in left lateral recumbency, and anaesthesia was induced with intravenous administration of double drip containing ketamine (1.0 mg/mL) and guaiphenesin (50 mg/mL) to effect. Intubated the trachea and anaesthesia was maintained using isoflurane in 100% oxygen. A significant leukopenia was observed after induction of anaesthesia. No significant changes were observed in total erythrocyte count, volume of packed red cells, platelet count, or haemoglobin concentration before and during maintenance of anaesthesia. A non-significant anaemia, lymphocytosisand neutropenia, along with mild fluctuations in aspartate aminotransferase and a significant reduction in alanine aminotransferase level wererecorded during maintenance of anaesthesia. Blood pH showed a significant reduction ($p<0.01$) after induction and during maintenance, whereas $PvCO_2$ ($p<0.01$), PvO_2 ($p<0.01$) and glucose values increased significantly post-induction and during maintenance of anaesthesia. Blood bicarbonate and base excess levels, however, remained unaltered throughout the procedure.

Keywords: *Multimodal general anaesthesia, cattle, blood gas, haemato-biochemical changes*

Anaesthetic management in cattle is inherently challenging due to species-specific anatomical and physiological features such as their large body mass, complex ruminant digestive system, and higher risk of regurgitation, tympany, hypoventilation, hypoxaemia and prolonged recovery (Abrahamsen, 2008; Lin and Walz, 2014). These factors make it essential to adopt balanced anaesthetic protocols that provide sufficient sedation, analgesia and muscle relaxation while

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minimising cardiopulmonary depression and metabolic disturbances.

Multimodal anaesthesia has gained increasing importance in bovine practice, as the combination of different agents reduced the dosage of each drug required, thereby improving the quality of anaesthesia and reducing adverse effects (Short, 1987; Hall et al., 2001). It disrupts more than one part of the pain pathway and reduces peripheral and central sensitisation and tachyphylaxis (Soumya et al., 2024). In cattle, guaiphenesin, ketamine and isoflurane represent a widely studied multimodal combination. Guaiphenesin acts as a centrally acting muscle relaxant with minimal impact on cardiopulmonary function, ketamine provides dissociative anaesthesia and analgesia, and isoflurane ensures rapid titration of anaesthetic depth and smooth recovery (Thurmon et al., 1986; Grandy et al., 1989).

Premedication further enhances anaesthetic safety and stability. The combination of butorphanol, xylazine and ketamine has been reported to provide synergistic sedation, analgesia and muscle relaxation in cattle, while also reducing the requirement for induction and maintenance agents (Pawde et al., 2000; Clarke et al., 2014). Butorphanol, a kappa-opioid agonist, provides visceral analgesia, xylazine, an α2-adrenergic agonist, induces sedation and muscle relaxation, and ketamine augments analgesia and improves induction quality. Subsequent induction using guaiphenesin–ketamine allows smooth intubation with adequate muscle relaxation and maintenance with isoflurane provides controllable depth of anaesthesia with faster recovery compared to injectable protocols alone (Lin and Walz, 2014).

Recent studies have emphasised the clinical efficacy and safety of such multimodal anaesthetic protocols in cattle. Saranya et al. (2021) reported that guaiphenesin–ketamine induction followed by isoflurane maintenance ensured stable anaesthesia with minimal haemodynamic alterations. Sindhu (2021) and Praveen et al. (2021) highlighted the advantages of incorporating opioid–α2 agonist combinations, such as butorphanol and xylazine, in improving sedation and analgesia. Jayakrishnan (2023) further demonstrated that monitoring haemato-biochemical and blood gas parameters during anaesthesia provided critical insights into oxygenation, ventilation, acid–base balance and metabolic homeostasis, thereby establishing the safety of multimodal protocols in bovine anaesthesia.

Given the clinical importance of maintaining haemodynamic and metabolic stability during anaesthesia, the present study was undertaken to evaluate haemato-biochemical and blood gas changes in cattle premedicated with butorphanol–xylazine–ketamine, induced with guaiphenesin–ketamine and maintained on isoflurane. The findings are expected to contribute to refining multimodal anaesthetic strategies for safe and effective use in cattle.

Materials and methods

Six crossbred female cattle, aged between six months and 10 years and weighing 100–480 kg, were presented for elective surgical interventions. The animals, designated as I to VI, underwent standard pre-anaesthetic preparation, which included withholding feed for 24 hours and water for 12 hours prior to surgery. The surgical procedures performed were horn amputation (animal I), umbilical herniorrhaphy (animals II, III and VI), excision of third eyelid dermoid (animal IV) and excision of interdigital fibroma (animal V).

A combination of butorphanol, xylazine and ketamine was administered intramuscularly as pre-anaesthetic medication at dose rates of 0.01, 0.02 and 0.04 mg/kg body weight, respectively. The onset of sedation was characterised by signs such as salivation, lacrimation, bellowing and attainment of recumbency.

Following the attainment of sedation, all the animals were positioned in left lateral recumbency, and anaesthetic induction was achieved by intravenous administration of double drip solution containing ketamine (1 mg/mL) and guaiphenesin (50 mg/mL) to effect. After induction, endotracheal intubation was performed using an appropriately sized cuffed endotracheal tube, which was connected to a large animal anaesthesia machine with a closed circuit. Anaesthesia was subsequently maintained with isoflurane (1–3%) delivered in 100% oxygen.

All the animals were monitored from premedication until recovery by recording physiological and anaesthetic parameters at five-minute intervals. Blood samples were collected prior to administration of pre-anaesthetics, after induction of anaesthesia and 15 minutes after commencement of isoflurane anaesthesia, and were analysed for haematological parameters, including total erythrocyte count (TEC), total leukocyte count (TLC), differential leukocyte count (DLC), haemoglobin concentration (Hb), platelet count (PLT), and volume of packed red cells (VPRC). Serum biochemical parameters such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were also evaluated. For blood gas analysis, venous blood samples were collected in heparinised vials and parameters assessed included blood pH, partial pressure of carbon dioxide (P_vCO_2), partial pressure of oxygen (P_vO_2), bicarbonate concentration (HCO_3^-), base excess and glucose using an automated blood gas analyser. Variations in haemato-biochemical and blood gas values during anaesthesia were subjected to statistical analysis.

Results and discussion

The mean total erythrocyte count (10^6/μL) was 5.51 ± 0.73 prior to pre-anaesthetic administration, 5.13

± 0.39 following induction of anaesthesia and 4.47 ± 0.35 at 15 minutes after commencement of isoflurane administration (Table 1), showing a non-significant reduction. This observation is consistent with earlier reports by Muchalambe et al. (2018), Praveen et al. (2021) and Jayakrishnan (2023) in cattle. The mean total leukocyte count (10^3/µL) decreased significantly from 11.98 ± 2.97 before anaesthesia to 10.07 ± 2.72 and 9.75 ± 1.84 after induction and 15 minutes after starting isoflurane respectively (Table 1). The reduction in leukocyte count could be associated with ketamine induced suppression of leukocyte proliferation, migration and activity, leading to a temporary reduction in total leukocyte count in the bloodstream, as suggested by Cullen (1996) and Sindhu (2021). But the recorded values were within normal physiological range.

Similarly, the mean haemoglobin concentration (g/dL) decreased from 6.57 ± 0.66 to 6.23 ± 0.39 and 5.38 ± 0.37, the mean platelet count (10^3/µL) from 363.50 ± 69.89 to 255.17 ± 27.86 and 283.17 ± 75.33, and the mean volume of packed red cells (%) from 22.83 ± 2.09 to 21.38 ± 0.93 and 18.83 ± 1.14 before pre-anaesthetic administration, after induction and 15 minutes after commencement of isoflurane (Table 1). These reductions were not statistically significant.

The reduction in volume of packed red cells has been documented following xylazine administration in calves by Picavet et al. (2004) and during isoflurane anaesthesia in cattle by Praveen et al. (2021) and Jayakrishnan (2023). Kilic (2008) and Muchalambe et al. (2018) attributed this reduction to fluid shifts from the extravascular to intravascular compartment as a compensatory mechanism to maintain cardiac output. Additionally, sequestration of blood cells in the spleen due to reduced sympathetic activity has been suggested as another cause for decrease in volume of packed red cells, erythrocyte count, leukocyte count, platelet count and haemoglobin concentration (Kilic, 2008). In the present study, however, total erythrocyte count, haemoglobin and VPRC values remained below the normal physiological range both before anaesthesia after induction of anaesthesia and 15 minutes after starting administration of isoflurane, which may be attributed to a history of haemoprotozoan infection in two of the cattle.

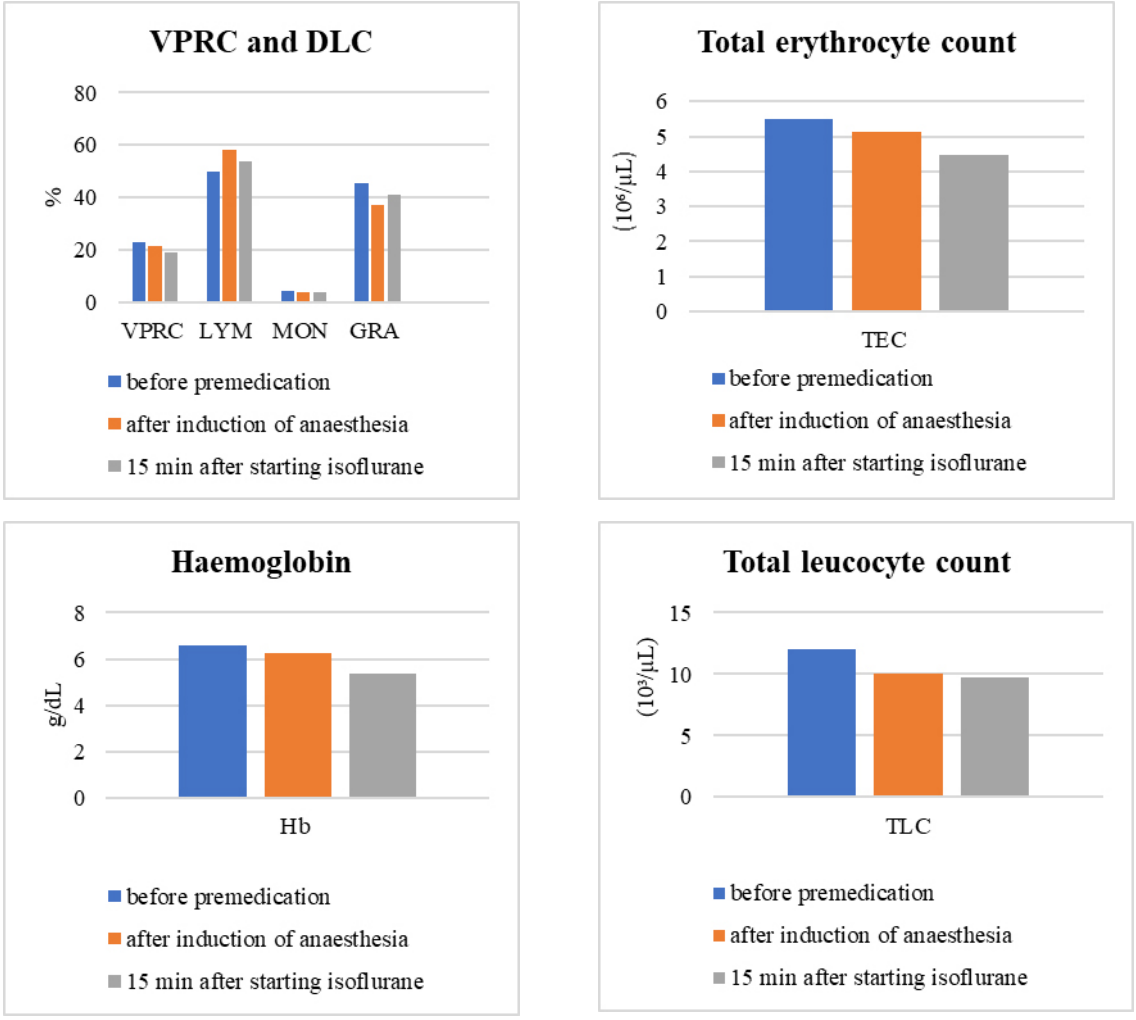

Fig. 1. Graph indicating changes in haematological parameters

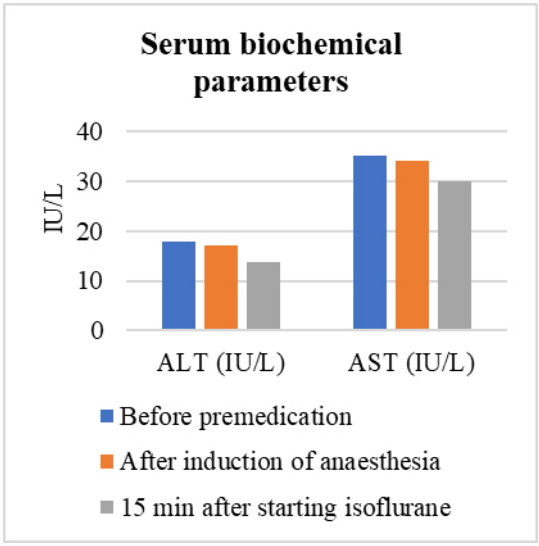

Fig. 2. Graph indicating changes in serum biochemical parameters

The mean lymphocyte count (%) was 49.87 ± 6.70 prior to pre-anaesthetic administration, 58.18 ± 3.29 after induction and 53.68 ± 3.76at 15 minutes after onset of isoflurane anaesthesia. The corresponding mean granulocyte counts (%) were 45.23 ± 7.42, 37.02 ± 3.80 and 40.78 ± 3.89, while the mean monocyte counts (%) were 4.10 ± 0.53, 3.85 ± 0.70 and 3.87 ± 0.51, respectively (Table 1). The observed lymphocytosis accompanied by granulocytopenia was non-significant and may be attributed to stress induced by the administration of pre-medicants and anaesthetic agents, leading to adrenal gland stimulation and release of corticosteroids and catecholamines from the adrenal glands. Catecholamines could cause lymphocyte demargination from the marginal pool of blood vessels into circulation, temporarily causing lymphocytosis (Singh et al., 2013).

Serum alanine aminotransferase (ALT) showed a significant decrease following anaesthesia. The mean ALT activity (IU/L) was 18.00 ± 2.82 before pre-anaesthetic administration, 17.00± 2.41after induction of anaesthesia and 13.83 ± 1.87at 15 minutes after starting isoflurane, while the corresponding AST values were 35.17 ± 5.38, 34.22 ± 5.03 and 30.00 ± 6.66, respectively (Table 1) which showed a non-significant reduction on anaesthesia. The reduction in ALT and AST could be due to decreased extra-hepatic release from muscle or other sources during deep sedation or immobilisation (Malik & Singh, 2007).

The mean blood pH values recorded were 7.47 ± 0.02, 7.41 ± 0.03 and 7.36 ± 0.03 prior to anaesthesia, post-induction and 15 minutes after initiation of isoflurane anaesthesia, respectively (Table 2). A significant ($p<0.01$) reduction in pH was observed following induction and during isoflurane maintenance, likely due to respiratory depression leading to respiratory acidosis (Benato et al., 2013). Similar findings of decreased arterial pH during anaesthesia have been reported in calves by Picavet et al. (2004) and Kilic (2008) under xylazine–guaiphenesin–ketamine and dexmedetomidine–midazolam–ketamine protocols, respectively and in buffaloes by Harmanjeet et al. (2013). In the present study, the baseline pH was slightly above the physiological range, while subsequent values remained within normal limits during anaesthesia.

The mean venous partial pressure of carbon dioxide ($PvCO_2$, mmHg) was 34.03 ± 1.77, 43.30 ± 1.89 and 47.10 ± 3.72 at baseline, after induction and 15 minutes following initiation of isoflurane anaesthesia, respectively (Table 2). A significant ($p<0.01$) elevation in $PvCO_2$ was recorded post-induction and during isoflurane maintenance compared to baseline values. Comparable increases in $PaCO_2$ have been described in sheep (Hikasa et al., 2000), buffaloes (Harmanjeet et al., 2013) and cattle (Praveen et al., 2021). The hypercapnia observed in the present study may be attributed to hypoventilation and the

Table 1. Haematological and serum biochemical parameters before and during multimodal anaesthesia in cattle (n=6)

Parameters	Before anaesthesia	After induction	15 min after starting isoflurane	F-value (p-value)
TLC (10^3/µL)	11.98^a ± 2.97	10.07^b ± 2.72	9.75^{ab} ± 1.84	8.571*(0.036)
TEC (10^6/µL)	5.51 ± 0.73	5.13 ± 0.39	4.47 ± 0.35	3.744 (0.121)
HGB (g/dL)	6.57 ± 0.66	6.23 ± 0.39	5.38 ± 0.37	4.181 (0.105)
VPRC (%)	22.83 ± 2.09	21.38 ± 0.93	18.83 ± 1.14	3.441 (0.135)
PLT (10^3/µL)	363.50 ± 69.89	255.17 ± 27.86	283.17 ± 75.33	3.071 (0.156)
LYM%	49.87 ± 6.70	58.18 ± 3.29	53.68 ± 3.76	1.855 (0.269)
MON%	4.10 ± 0.53	3.85 ± 0.70	3.87 ± 0.51	3.985 (0.112)
GRA%	45.23 ± 7.42	37.02 ± 3.80	40.78 ± 3.89	1.778 (0.280)
ALT (IU /L)	18.00^a ± 2.82	17.00^{ab} ± 2.41	13.83^b ± 1.87	3.379 (0.138)
AST (IU /L)	35.17 ± 5.38	34.22 ± 5.03	30.00 ± 6.66	1.482 (0.330)

Analysis done by repeated measures ANOVA followed by Least Significant Difference method using SPSS version 24.0

**Significant at 0.05 level (p<0.05); Means having different letter as superscript differ significantly within a row*

Table 2. Changes in blood gas parameters during different stages of multimodal anaesthesia in cattle (n=6).

Parameters	Before anaesthesia	after induction of anaesthesia	15 min after starting isoflurane	F-value (p-value)
pH	$7.47^{a} \pm 0.02$	$7.41^{b} \pm 0.03$	$7.36^{b} \pm 0.03$	18.462^{**} (0.010)
P_vCO_2(mmHg)	$34.03^{b} \pm 1.77$	$43.30^{a} \pm 1.89$	$47.10^{a} \pm 3.72$	35.794^{**} (0.003)
P_vO_2(mmHg)	$36.38^{b} \pm 1.77$	$48.57^{b} \pm 5.59$	$87.87^{a} \pm 5.50$	39.295^{**} (0.002)
HCO_3^-(mmol/L)	24.95 ± 0.47	27.85 ± 1.22	26.62 ± 2.08	3.216 (0.147)
BE(mmol/L)	1.35 ± 0.61	3.33 ± 1.69	1.12 ± 2.41	1.788 (0.279)
Glucose (mg/dL)	$98.50^{b} \pm 5.39$	$183.00^{a} \pm 14.85$	$171.67^{a} \pm 10.65$	38.887^{**} (0.002)

Analysis done by repeated measures ANOVA followed by Least Significant Difference method using SPSS version 24.0

*** Significant at 0.01 level (p<0.01); Means having different letter as superscript differ significantly within a row*

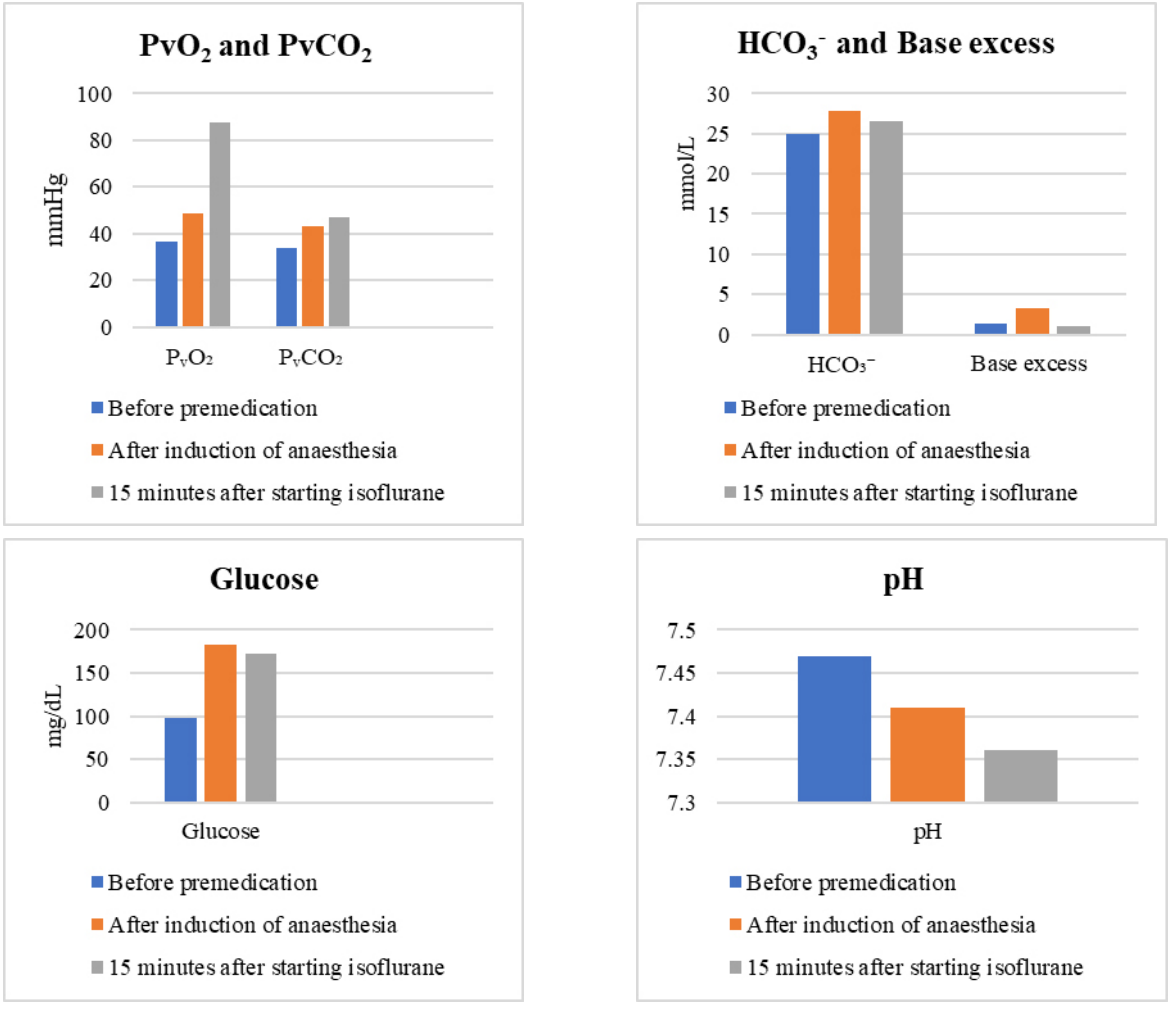

Fig. 3. Graph indicating changes in blood gas parameters

lateral recumbency of the animals during surgery (Benato et al., 2013).

The mean venous partial pressure of oxygen (PvO_2, mmHg) was 36.38 ± 4.27, 48.57 ± 5.59 and 87.87 ± 5.50 at the respective observation periods (Table 2). PvO_2 increased significantly during maintenance with isoflurane. The elevation observed 15 minutes after commencement of isoflurane anaesthesia might be explained by the high oxygen concentration delivered through fresh gas flow following intubation. These findings are consistent with those reported by Picavet et al. (2004).

The mean blood bicarbonate concentration (mmol/L) recorded was 24.95 ± 0.47, 27.85 ± 1.22 and 26.62 ± 2.08 at baseline, post-induction and 15 minutes after initiation of isoflurane anaesthesia (Table 2). Although a slight rise was observed at post-induction, the variations were not statistically significant. The increase in bicarbonate values during anaesthesia might represent a

compensatory response to counteract respiratory acidosis resulting from elevated $PvCO_2$ (Benato et al., 2013).

The mean blood base excess (mmol/L) was 1.35 ± 0.61, 3.33 ± 1.69 and 1.12 ± 2.41 at baseline, post-induction and 15 minutes after initiation of isoflurane anaesthesia, respectively. A non-significant increase in base excess was observed following induction of anaesthesia; however, the values remained within the normal physiological range. These findings are similar with those of Picavet et al. (2004) and Praveen et al. (2021) who reported a non-significant increase of base excess in calves. The elevated base excess values in the present study might be attributed to respiratory acidosis resulting from increased $PvCO_2$ during anaesthetic maintenance (Benato et al., 2013).

The mean blood glucose level rose from 98.50 ± 5.39 mg/dL before premedication to 183.00 ± 14.85 mg/dL after guaifenesin–ketamine induction and 171.67 ± 10.65 mg/dL during isoflurane maintenance, showing a significant but physiologically normal increase. This rise is likely due to ketamine-induced sympathoadrenal stimulation and isoflurane's suppression of insulin secretion and sensitivity, along with reduced muscular glucose use under anaesthesia (Tanaka et al., 2005; Hughes et al., 2012; Mostafa et al., 2022; Kitamura et al., 2023).

Conclusion

In the present investigation, the haematological, serum biochemical, and blood gas values remained within normal physiological limits, indicating that the anaesthetic protocol employed did not exert any detrimental effects on the body systems.

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Conflict of interest

The authors declare that they have no conflict of interest.

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