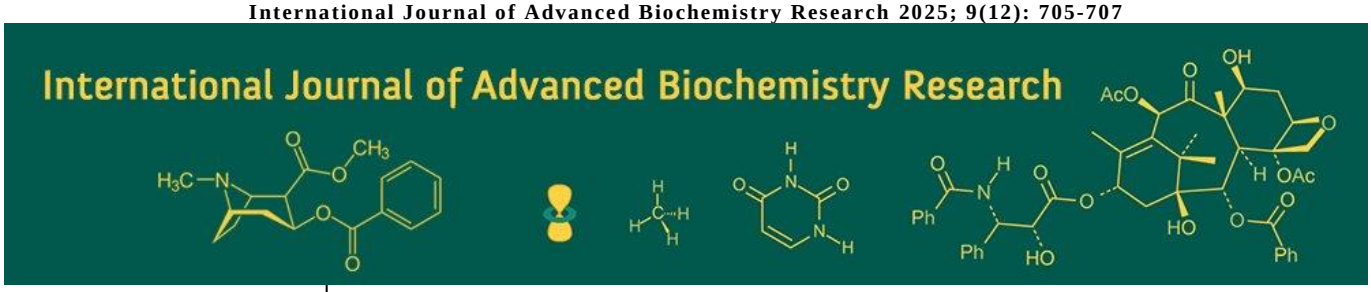

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Haematobiochemical alterations following multimodal anaesthesia using medetomidine-butorphanol-midazolam-ketamine and isoflurane with or without lignocaine continuous rate infusion in bovines

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Abstract
The present study was undertaken to evaluate the haemato-biochemical alterations associated with a multimodal anaesthetic protocol using medetomidine @ 5 µg/kg, butorphanol (0.05 mg/kg), midazolam (0.20 mg/kg), ketamine (4 mg/kg) and isoflurane for maintenance of anaesthesia, with or without lignocaine administered as a continuous rate infusion (50 µg/kg/min), in bovines undergoing various surgical procedures. Clinically healthy bovines were randomly allocated into two groups. Animals in Group I were maintained under isoflurane anaesthesia alone, whereas those in Group II received isoflurane in combination with lignocaine continuous rate infusion. Blood samples were collected at predefined intervals before induction of anaesthesia, during maintenance, and during recovery for assessment of haemato-biochemical parameters. Haematological evaluation included Hb concentration, PCV, total erythrocyte count, total leukocyte count and differential leukocyte count. Biochemical analysis comprised serum aspartate aminotransferase, blood urea nitrogen and serum creatinine. The study revealed a transient reduction in Hb concentration, PCV and total erythrocyte count during anaesthesia in both groups, while total leukocyte count and differential leukocyte counts remained within physiological limits. Mild, non-significant elevations in serum aspartate aminotransferase and blood urea nitrogen were observed during anaesthesia, with serum creatinine values remaining stable. All altered parameters returned towards baseline values during recovery. The inclusion of lignocaine continuous rate infusion did not produce any adverse haemato-biochemical effects.

Keywords: Bovine, multimodal anaesthesia, haemato-biochemical parameters, lignocaine infusion

Introduction
Haemato-biochemical parameters are widely used indicators to assess the systemic safety of anaesthetic protocols in large animals (Arnemo and Soli, 1993; Malik *et al.*, 2011) [1, 7]. General anaesthesia may influence these parameters due to haemodilution, splenic sequestration of erythrocytes, altered hepatic perfusion and stress-induced endocrine responses (Ranheim *et al.*, 1999; Rioja *et al.*, 2008) [8, 9]. Multimodal anaesthesia combines drugs with different mechanisms of action to achieve balanced anaesthesia while minimizing adverse effects (Wolfensberger and Larenza, 2007) [1]. Isoflurane is commonly used for maintenance of anaesthesia in bovines due to its rapid titratability and smooth recovery profile (Cantalapiedra *et al.*, 2000) [2]. Lignocaine administered as a continuous rate infusion has been reported to provide analgesic and anaesthetic-sparing effects without significant systemic disturbances (Vesal *et al.*, 2011) [11].

Materials and Methods
The 12 cases of bovines presented for elective and therapeutic surgical procedures were selected for the study. Animals were randomly divided into two groups. The two groups were premedicated with medetomidine and butorphanol followed by induction with midazolam and ketamine. Anaesthesia was maintained using isoflurane in oxygen. In Group II, lignocaine was administered intravenously as a continuous rate infusion during maintenance. Blood samples were collected before induction, 0th minute, 120th minute, 24 hours and 48

hours after surgery. Haematological parameters including haemoglobin concentration, packed cell volume, total erythrocyte count, total leukocyte count and differential leukocyte count were analysed. Biochemical parameters such as serum aspartate aminotransferase, blood urea nitrogen and serum creatinine were estimated using standard laboratory procedures.

Results

The haemato-biochemical parameters recorded at different time intervals are expressed as Mean±standard error.

In Group I, Hb concentration showed a significant reduction from the pre-induction value of 10.21±0.32 g/dL to 9.12±0.28 g/dL during the maintenance phase of anaesthesia, which subsequently increased to 9.96±0.30 g/dL during recovery. Similarly, in Group II, haemoglobin values significantly decreased from 10.34±0.29 g/dL before induction to 9.05±0.26 g/dL during anaesthesia and returned towards baseline (10.02±0.27 g/dL) during recovery (Table 1).

Packed cell volume exhibited a comparable trend in both groups. In Group I, packed cell volume significantly decreased from 31.42±0.88% to 28.36±0.75% during anaesthesia, whereas in Group II it declined from 32.10±0.81% to 28.14±0.72% during maintenance. Values in both groups showed recovery towards pre-induction levels during the recovery phase (Table 1).

Total erythrocyte count decreased marginally during anaesthesia in both groups, with Group I showing a reduction from 6.82±0.21 $\times10^6$/µL to 6.15±0.19 $\times10^6$/µL, and Group II from 6.94±0.23 $\times10^6$/µL to 6.10±0.18 $\times10^6$/µL. Total leukocyte count remained within physiological limits throughout the observation period, with no statistically significant differences between the two groups. Differential leukocyte count revealed a significant transient increase in neutrophil percentage during anaesthesia, accompanied by a corresponding significant decrease in lymphocyte percentage in both groups, which normalized during recovery (Table 1).

Biochemical parameters showed mild, non-significant alterations during anaesthesia (Table 2). Serum aspartate aminotransferase levels increased from 62.18±3.21 IU/L to 68.94±3.56 IU/L in Group I and from 61.44±3.08 IU/L to 69.22±3.47 IU/L in Group II during maintenance of anaesthesia. Blood urea nitrogen values showed a slight increase during anaesthesia in both groups (Group I: 21.34±1.12 mg/dL to 24.18±1.26 mg/dL; Group II: 20.98±1.08 mg/dL to 24.62±1.31 mg/dL). Serum creatinine values remained stable throughout the study period in both groups. All biochemical parameters returned towards baseline values during recovery.

Table 1: Mean ± SE of Hematological parameters at different intervals in bovines of Group I and Group II

Parameter	Group	Before induction	0th minute	120th minute	24 hours	48 hours
Hb (g/dL)	I	8.08±0.18	7.98±0.18	7.25±0.15*	7.53±0.15*	7.52±0.18*
	II	8.13±0.19	8.12±0.14	7.22±0.14*	7.50±0.18*	7.40±0.17*
PCV (%)	I	29.87±0.68	29.03±0.75	26.75±0.66**	28.20±0.73	29.35±0.62
	II	31.20±0.60	30.27±0.43	28.80±0.86	28.77±0.49**	28.77±0.36**
TEC (x10^6/µL)	I	6.17±0.22	6.17±0.30	6.01±0.30	5.85±0.29	5.36±0.26
	II	6.47±0.15	6.27±0.13	5.98±0.13	5.77±0.27	5.77±0.26
TLC (x10^3/µL)	I	7.25±0.31	7.21±0.29	7.72±0.27	8.12±0.27	8.02±0.33
	II	7.37±0.27	7.35±0.27	7.65±0.28	7.92±0.26	7.64±0.30
Neutrophils (%)	I	32.12±0.80	31.32±0.81	32.07±0.89	31.82±1.15	33.66±1.21
	II	31.65±0.69	33.47±0.66	33.37±0.68	34.02±0.45*	35.07±0.78**
Lymphocytes (%)	I	59.56±0.93	57.52±1.01	55.32±0.92**	55.03±1.25**	54.52±1.15**
	II	58.18±0.97	54.85±0.95	53.49±0.58**	52.15±0.65**	52.93±0.79**
Monocytes (%)	I	1.55±0.43	1.79±0.30	1.61±0.12	1.93±0.10	1.47±0.19
	II	1.78±0.30	2.75±0.47	2.17±0.17	1.50±0.15	1.46±0.07
Eosinophils (%)	I	6.09±0.48	5.75±0.24	5.64±0.37	5.18±0.33	5.81±0.29
	II	6.39±0.42	6.67±0.40	6.45±0.25	6.16±0.30	5.84±0.38

Means bearing superscript ** differ significantly ($p\leq0.01$) from interval before sedation within the group
Means bearing superscript * differ significantly ($p\leq0.05$) from interval before sedation within the group

Table 2: Mean ± SE of Biochemical parameters at different intervals in bovines of Group I and Group II

Parameter	Group	Before induction	0th minute	120th minute	24th hour	48th hour
Aspartate aminotransferase (IU/L)	I	74.00±3.13	72.67±3.46	75.00±3.95	74.40±3.21	76.47±3.29
	II	70.70±1.87	69.98±2.33	71.02±2.39	71.75±2.14	72.53±1.92
Blood Urea Nitrogen (mg/dL)	I	18.93±0.70	18.97±0.56	19.74±0.69	20.04±0.90	19.65±0.82
	II	19.00±0.96	18.37±0.55	19.50±0.59	18.83±0.41	19.92±0.48
Serum Creatinine (mg/dL)	I	0.94±0.03	0.94±0.03	0.98±0.03	0.97±0.03	0.99±0.04
	II	0.96±0.05	0.88±0.03	1.01±0.03	1.03±0.05	1.00±0.04

Discussion

The transient reduction in Hb concentration, PCV and total erythrocyte count observed during anaesthesia may be attributed to haemodilution and splenic sequestration of erythrocytes induced by alpha-2 agonists (Ranheim *et al.*, 1999; Grimsrud *et al.*, 2012) [8, 3]. Stability of total leukocyte count indicates minimal immunological impact of the anaesthetic protocol. Temporary neutrophilia and lymphopenia observed during anaesthesia are consistent with stress-mediated corticosteroid release (Venkatgiri *et al.*, 2017) [10]. Mild elevations in serum aspartate aminotransferase and blood urea nitrogen may reflect transient alterations in hepatic and renal perfusion during anaesthesia (Kilic, 2008; Kawhale *et al.*, 2020) [6, 5]. The absence of significant changes in serum creatinine confirms preservation of renal function. Lignocaine continuous rate

infusion did not adversely affect haematobiochemical parameters, corroborating earlier findings (Vesal *et al.*, 2011; Jayakrishnan *et al.*, 2023) [11, 4].

Conclusion

The multimodal anaesthetic protocol using medetomidine, butorphanol, midazolam, ketamine and isoflurane, with or without lignocaine continuous rate infusion, caused only mild and transient haematological and biochemical changes in bovines. All alterations remained within physiological limits, indicating that the protocol is safe for clinical use.

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