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RESEARCH ARTICLE

Effects of Anesthesia Protocols for Umbilical Hernia Surgery on Blood Gas Parameters in Calves

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ABSTRACT

This study aimed to evaluate the physiological effects of different preanesthetic sedative and lidocaine combinations in neonatal calves undergoing umbilical herniorrhaphy based on blood gas analyses. Twenty-five clinically healthy calves (42.3±15.8 days old; 79.6±7.2 kg) diagnosed with umbilical hernia were divided into five groups. Preanaesthetic drugs were administered intravenously, and local infiltration anesthesia was performed with lidocaine (4 mg/kg) in all calves. Based on the sedative–lidocaine combinations, the treatment groups were defined as follows: xylazine–lidocaine (XL), dexmedetomidine–lidocaine (DL), medetomidine–lidocaine (MeL), midazolam–lidocaine (MiL), and butorphanol–lidocaine (BL). Venous blood samples were collected from each calf before anesthesia and at 5, 15, 30, and 60 min after induction. The following parameters were analyzed: pH, pCO_2, pO_2, HCO_3^-, Base Excess, sO_2, Hb, Hct, Na^+, K^+, Cl^-, Ca^{2+}, glucose, lactate, and creatinine levels. Although no significant differences were observed between the groups for most parameters, time-dependent changes within the groups were notable. In the DL group, marked acidosis and hypoxemia were detected at the 5th min ($p<0.05$), whereas in the BL group, potassium and lactate levels increased significantly ($p<0.05$). The MeL group exhibited significant hyperglycemia ($p=0.004$), whereas the MiL group demonstrated the most stable values in terms of oxygenation and acid–base balance. In conclusion, the MiL combination is the most stable and safe anesthesia protocol in terms of hemodynamic and metabolic parameters during umbilical herniorrhaphy in neonatal calves. Furthermore, the interpretation of blood gas dynamics was strengthened by concurrent cardiopulmonary monitoring, which confirmed that the most pronounced metabolic disturbances in the DL and BL groups coincided with marked hypoxemia and respiratory instability. These findings provide important clinical insights into safe anesthetic management under field conditions.

Keywords: Calves, Local Anesthesia, Preanesthetic, Umbilical Hernia, Venous Blood Gases

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Buzağılarda Göbek Fıtığı Cerrahisine Yönelik Anestezi Protokollerinin Kan Gazı Parametrelerine Etkisi

ÖZ

Bu çalışma, göbek fıtığı ameliyatı geçiren neonatal buzağılarda farklı preanestezik sedatif ve lidokain kombinasyonlarının fizyolojik etkilerini, kan gazı analizlerine dayanarak değerlendirmeyi amaçlamıştır. Göbek fıtığı tanısı konulan klinik olarak sağlıklı yirmi beş buzağı (42,3±15,8 günlük; 79,6±7,2 kg) beş gruba ayrıldı. Preanestezik ilaçlar intravenöz olarak uygulanmış ve tüm buzağılara lidokain (4 mg/kg) ile lokal infiltrasyon anestezisi yapıldı. Sedatif–lidokain kombinasyonlarına göre tedavi grupları şu şekilde tanımlandı: ksilazin–lidokain (XL), deksmedetomidin–lidokain (DL), medetomidin–lidokain (MeL), midazolam–lidokain (MiL) ve butorfanol–lidokain (BL). Her buzağıdan anestezi öncesi ve indüksiyondan 5., 15., 30. ve 60. dakikalarda venöz kan örnekleri alındı. Şu parametreler analiz edildi: pH, pCO_2, pO_2, HCO_3^-, Baz fazlalığı, sO_2, Hb, Hct, Na^+, K^+, Cl^-, Ca^{2+}, glukoz, laktat ve kreatinin düzeyleri. Çoğu parametre açısından gruplar arasında anlamlı bir fark gözlenmemekle birlikte, gruplar içinde zamana bağlı değişiklikler belirgindi. Deksmedetomidin–lidokain grubunda 5. dakikada belirgin asidoz ve hipoksemi ($p<0,05$) tespit edilirken, BL grubunda potasyum ve laktat düzeyleri anlamlı derecede arttı ($p<0,05$). MeL grubu, belirgin hiperglisemi ($p=0,004$) gösterirken, MiL grubu oksijenasyon ve asit-baz dengesi açısından en stabil değerleri sergiledi. Sonuç olarak, MiL kombinasyonu, neonatal buzağılarda göbek fıtığı onarımı sırasında hemodinamik ve metabolik parametreler bakımından en stabil ve güvenli anestezi protokolüdür. Ayrıca, kan gazı değişimlerinin yorumlanması kardiyopulmoner parametrelerle desteklenmiş ve özellikle DL ile BL gruplarında saptanan metabolik bozulmaların belirgin hipoksemi ve solunumsal instabilite ile eş zamanlı ortaya çıktığı doğrulanmıştır. Bu bulgular, saha koşullarında güvenli anestezi yönetimi için önemli klinik bilgiler sunmaktadır.

Anahtar Kelimeler: Buzağılar, Lokal Anestezi, Preanestezik, Umbilikal Herni, Venöz Kan Gazları

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INTRODUCTION

Umbilical hernia is a congenital or early postnatal surgical pathology that is commonly encountered in neonatal calves. Umbilical infections have been reported to play an essential role in cases that develop within the first two months, with an incidence rate of up to 21% in male calves (Salim et al. 2015). Although clinical diagnosis can easily be performed through physical examination, treatment is typically performed surgically via umbilical herniorrhaphy. However, the anesthesia protocol chosen during the operation has direct physiological effects on various systems, particularly on respiratory and circulatory functions (Adcock & Tucker 2018; Nikolayenkova-Topie et al. 2020).

Although inhalation anesthesia is efficient in ruminants, its practical use is limited owing to its cost, equipment requirements, and field conditions (Kim et al. 2021). Agents such as ketamine and thiopental administered via injection are also limited in their use owing to the risk of gastrointestinal and respiratory complications (Nikolayenkova-Topie et al. 2020). Hence, the combination of preanesthetic sedatives and local anesthetics stands out in terms of both physiological stability and ease of application (Cuypers et al. 2024).

Although various physiological effects of sedative agents, such as xylazine, medetomidine, dexmedetomidine, midazolam, and butorphanol, have been identified in ruminants, data on the systemic changes they cause during umbilical herniorrhaphy in calves are insufficient (Greene 2003; Vigneshwaran et al. 2020). Lidocaine is widely used for infiltrative local anesthesia; however, the physiological effects of combination protocols remain limited (Adcock and Tucker 2018).

Therefore, it was hypothesized that each sedative–lidocaine protocol would produce distinct alterations in acid–base status, oxygenation, and metabolic balance, and that the protocol offering the greatest stability supported by both blood gas and cardiopulmonary indicators would be identified as the most physiologically appropriate option for neonatal calves.

MATERIALS and METHODS

The study protocol was approved by the Local Ethics Committee on Animal Experiments, Harran University (session and permit number: 2025/008/07).

Study Groups

This study was conducted on a total of 25 clinically healthy calves aged 0–3 months who were diagnosed with umbilical hernia via physical examination and brought to the Animal Hospital of Harran University Faculty of Veterinary Medicine for clinical evaluation and surgical intervention. The calves were randomly assigned to five equal groups (n = 5) with a balanced sex distribution. Sample size calculation was performed using G*Power 3.1 software (Faul et al., 2007). The analysis was based on a repeated-measures ANOVA model with five independent groups and five time points. An effect size of f = 0.40 (large effect) was chosen because previous studies evaluating cardiopulmonary and blood gas responses to sedative and anesthetic protocols in calves and small ruminants (Blaze et al., 1988; Lin et al., 1989; Kılıç et al., 2015) have demonstrated moderate-to-large physiological changes, particularly in pH, pCO_2, and oxygenation variables. These studies indicate that anesthetic-related respiratory and metabolic effects typically fall within a large effect size range; therefore, f = 0.40 was considered a biologically and clinically justified expectation for differences among treatment groups. Using $\alpha = 0.05$ and statistical power $(1–\beta) = 0.80$, the minimum required sample size was calculated as n = 5 animals per group, yielding a total sample size of 25 calves. The working hypothesis of the study was that different sedative–lidocaine combinations would induce variable effects on blood gas parameters, and that one of these protocols would provide a more stable physiological profile than the others. Although body temperature, heart rate, respiratory rate, and oxygenation status were monitored throughout the procedure to ensure animal safety and physiological stability, the primary focus of this study was the assessment of blood gas parameters; therefore, these variables were not included in the final analysis. Each group received a different preanesthetic sedative agent administered intravenously (IV) via the jugular vein. Lidocaine (Vilcain 2%, Vilsan İlaç Sanayi ve Tic. A. Ş., Ankara, Turkey) was administered subcutaneously at a dose of 4 mg/kg using the standard infiltrative technique in all individuals. The experimental groups were formed as follows: Group 1 (XL): Xylazine (Alfazyne 2%® injection, Alfasan International B.V., Netherlands) (0.05–0.1 mg/kg, IV) + Lidocaine; Group 2 (DL): Dexmedetomidine (Hipnodex® fliptop vials, Haver Farma, Istanbul, Turkey) (0.001 mg/kg, IV) + Lidocaine; Group 3 (MeL): Medetomidine (Domitor, Orion; Turku, Finland) (0.02 mg/kg, IV) + Lidocaine; Group 4 (MiL): Midazolam (Zolamid®, Vem İlaç, Ankara, Turkey) (0.1 mg/kg, IV) + Lidocaine; Group 5 (BL): Butorphanol (Butomidor®, Richterpharma AG, Wels, Austria) (0.01–0.02 mg/kg, IV) + Lidocaine (Condino et al. 2010; Abou-Ghanema et al. 2014; Samimi et al. 2019; Vingneshwaran et al. 2020; Maidanskaia et al. 2023).

Cardiopulmonary Monitoring

Pulse, respiratory rate (RR), mean arterial pressure (MAP), peripheral oxygen saturation (SpO_2), and end-tidal carbon dioxide ($EtCO_2$) were continuously monitored in all calves from the onset of sedation. Measurements were recorded at 0, 5, 15, 30, and 60

minutes using a Mindray® uMEC12Vet multiparameter monitor.

Blood Sampling and Blood Gas Analysis

Venous blood samples (4–5 mL) were collected from the jugular vein of each calf using heparinized syringes at five time points: before anesthetic administration (0 min) and at 5, 15, 30, and 60 min after administration. The samples were analyzed using a portable blood gas analyzer (Epoc ® Blood Analysis System; Siemens Healthineers, Germany) within a maximum of 5 min. The physiological parameters evaluated in this study included acid–base balance (pH, pCO_2, HCO_3^-, base excess [BE]), gas exchange (pO_2, oxygen saturation [sO_2]), hematocrit and hemoglobin levels (Hct, Hb), electrolyte concentrations (sodium [Na^+], potassium [K^+], chloride [Cl^-], ionized calcium [Ca^{2+}]), as well as metabolic indicators such as glucose, lactate, and creatinine concentrations. The findings were compared with reference ranges reported in the literature for healthy calves (Gülersoy et al. 2023; Tokimitsu et al. 2024).

Surgical Procedure

All umbilical herniorrhaphy operations were performed under aseptic conditions by the same surgical team in compliance with standard procedures. Following surgical intervention, a combination of penicillin and streptomycin (Vetimisin®, VETAŞ, Turkey) was administered to all calves for seven days to minimize the risk of postoperative infection. For postoperative analgesia, meloxicam (Melox® Ampoule, Nobel İlaç San. ve Tic. A. Ş., Turkey) was administered subcutaneously once daily for 3 days. All procedures were completed uneventfully, and no major postoperative complications were observed.

Statistical Analysis

Statistical analysis was conducted using IBM SPSS Statistics for Windows, Version 22.1 (IBM Corp., Armonk, NY, USA). The normality of the data distribution was assessed using the Kolmogorov-Smirnov test. Parametric data that met the normality assumption were defined as means ± standard deviation (SD). One-way ANOVA (ANOVA) was used to analyze time-dependent changes within groups, and two-way ANOVA (two-way Repeated Measures ANOVA) was used to evaluate group and time interactions. Differences between groups were analyzed using one-way ANOVA, and Tukey's post hoc test was applied in cases with significant results. For non-parametric data, the Kruskal-Wallis and Mann-Whitney U tests were used for pairwise comparisons. In all tests, a p-value of <0.05 was considered statistically significant.

RESULTS

A total of 25 calves (13 male, 12 female) with a mean age of 42.3±15.8 days and a mean body weight of 79.6±7.2 kg were included in the study. The parameters evaluated were pH, pCO_2, HCO_3^-, BE, pO_2, sO_2, Hct, Hb, Na^+, K^+, Cl^-, Ca^{2+}, as well as the metabolic indicators glucose, lactate, and creatinine (Tables 1-6). The findings were statistically evaluated both within groups (Repeated Measures ANOVA) and between groups (Two-Way ANOVA, post-hoc Tukey test).

Cardiopulmonary Findings

Time-dependent alterations in cardiopulmonary parameters were observed across sedative–lidocaine protocols ($p=0.02$). Median cardiopulmonary values demonstrated protocol dependent temporal fluctuations across the study period. In the BL group, pulse rate showed a pronounced elevation, rising from a baseline median of 119 beats/min to 182 beats/min at 5 min, 176 beats/min at 15 min, 170 beats/min at 30 min, and reaching the highest median value of 200 beats/min at 60 min, representing a significantly sustained tachycardic pattern compared with all other groups ($p < 0.001$). In contrast, the DL group displayed a transient early increase in pulse rate (125 → 147 beats/min at 5 min, $p = 0.014$), whereas the XL, MeL, and MiL groups exhibited comparatively stable pulse medians without significant time-related alterations ($p>0.05$). Median MAP values also varied among protocols. The DL group showed a marked transient decline at 15 minutes (98 → 76 mmHg, $p = 0.009$), while MeL demonstrated an early increase (122 → 128 mmHg at 5 min) followed by stabilization. MAP fluctuations in XL, MiL, and BL remained within physiologic limits and did not reach statistical significance. Respiratory rate medians exhibited clear protocol-specific changes. In the DL group, RR decreased from 35 breaths/min at baseline to 28 breaths/min at 5 min ($p = 0.026$), indicating early respiratory depression. Conversely, the BL group showed a significant RR elevation at 15 minutes (30 → 37 breaths/min, $p = 0.018$). The XL group demonstrated a significant decline at 15 minutes (34 → 19 breaths/min, $p = 0.042$), whereas MeL and MiL displayed relatively stable respiratory patterns. Oxygenation parameters revealed that MeL experienced the earliest and most pronounced desaturation, with SpO_2 medians dropping from 93% at baseline to 71% at 5 minutes ($p = 0.012$). The BL group, despite a higher initial median SpO_2 (99%), showed a progressive decline culminating in a significant reduction at 60 minutes (82%, $p = 0.028$). In contrast, MiL and XL maintained more stable oxygen saturation throughout. $EtCO_2$ medians fluctuated within physiological ranges in all groups,

without significant temporal changes ($p > 0.05$): XL (33–39%), MeL (32–41%), DL (31–46%), MiL (35–42%), and BL (28–41%). The maintenance of $EtCO_2$ within normal limits suggests that the mild pCO_2 variations identified in blood gas analysis were not primarily ventilation-driven but more likely influenced by drug-specific metabolic and cardiovascular effects. (Figure 1a-e).

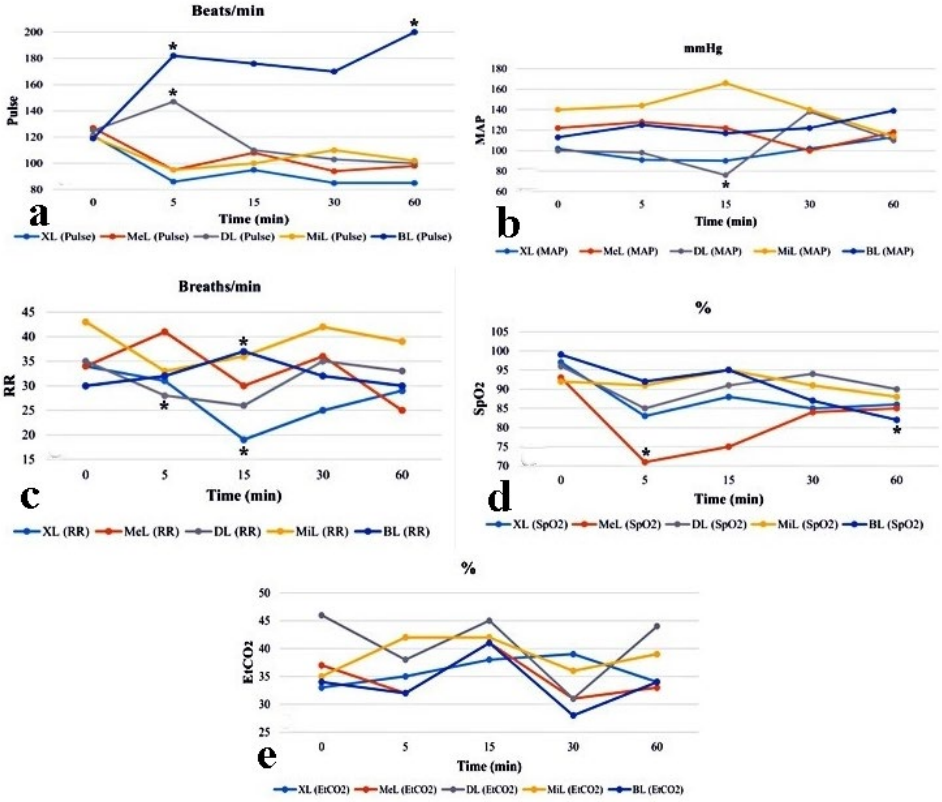

Figure 1: Cardiopulmonary parameter changes following different sedative–lidocaine protocols in neonatal calves. Line graphs illustrate time-dependent alterations in (a) Pulse, (b) mean arterial pressure (MAP), (c) respiratory rate (RR), (d) peripheral oxygen saturation (SpO_2) and (e) end-tidal carbon dioxide (EtCO2) measured at 0, 5, 15, 30, and 60 minutes after administration of the sedative–lidocaine protocols. The treatment groups were: XL (xylazine–lidocaine), MeL (medetomidine–lidocaine), DL (dexmedetomidine–lidocaine), MiL (midazolam–lidocaine), and BL (butorphanol–lidocaine). Values represent mean measurements at each time point. Asterisks (★) in the main text indicate statistically significant changes ($p < 0.05$) within groups.

Table 1: Mean (± SD) values of venous blood gas parameters measured at different time points in the group receiving xylazine and lidocaine (XL) combination.

XL					
Parameter	**0 min**	**5 min**	**15 min**	**30 min**	**60 min**
pH	7.40±0.05	7.36±0.01	7.33±0.012	7.32±0.012	7.36±0.04
pCO_2 (mmHg)	44±5	50.1±5.05	55.4±4.02	53.9±3.9	49±5
HCO_3^- (mmol/L)	24±3	29±1.1	29.6±1.4	25.3±0.3	25±3
BE (mmol/L)	0±4	3.7±2.8	3.7±2.6	-1.3±1.2	0±3
pO_2 (mmHg)	65±10	37.3±2.24	35.2±2.10	49.2±2.6	60±8
sO_2 (%)	75±5	23±3.11	17±3.41	47.7±3.5	73±4
Hct (%)	32±4	21±2.78*	24±2.15	21±2.62	31±3
Hb (g/dL)	11±1.5	7±0.52*	8.2±0.44	7±0.98	10.8±1.2
Na^+ (mmol/L)	138±3	135±0.48	136±0.77	133±0.8	137±3
K^+ (mmol/L)	4.5±0.5	4±0.55	4.1±0.80	4.1±0.61	4.6±0.4
Cl^- (mmol/L)	100±3	100±0.66	98±0.77	98±0.8	100±3
Ca^{2+} (mmol/L)	1.2±0.1	1.22±0.1	1.2±0.2	1.27±0.1	1.14±0.1
Glucose (mg/dL)	95±15	66±6.50	78±2.80	171±6.8	88±10
Lactate (mmol/L)	1.2±0.5	0.59±0.30	0.98±0.22	1.3±0.99	1.8±0.4
Creatinine (mg/dL)	1.0±0.2	1.30±0.11	1.37±0.19	1.01±0.44	1.1±0.2

Note: pH: hydrogen; pCO_2: partial pressure of carbon dioxide; HCO: bicarbonate; BE: base excess; pO_2: partial pressure of oxygen; sO_2: oxygen saturation; Hct: hematocrit; Hb: hemoglobin; Na^+: sodium; K^+: potassium; Cl^-: chloride; Ca^{2+}: ionized calcium; Glucose: blood sugar; Lactate: lactic acid; Creatinine: product of muscle metabolism. Asterisk (*) indicates a statistically significant difference ($P < 0.05$

Table 2: Mean (± SD) values of venous blood gas parameters measured at different time points for the group administered with the dexmedetomidine and lidocaine combination (DL).

DL					
Parameter	**0 min**	**5 min**	**15 min**	**30 min**	**60 min**
pH	7.41±0.03	7.24±0.05*	7.30±0.04	7.26±0.1	7.34±0.05
pCO_2 (mmHg)	42±4	55.2±3.1	55.92±1.75	47.82±0.71	52±6*
HCO_3^- (mmol/L)	23±2.5	27.58±2.36	26.92±1.48	22.12±4.77	26±2
BE (mmol/L)	1±2	1.46±3.07	0.48±2.08	--5.5±2.4	-1±3
pO_2 (mmHg)	70±6	25.4±5.9*	24.86±8.16	30.22±6.19	62±7
sO_2 (%)	76±4	48.4±7.1*	48.40±7.18	48.40±7.12	75±3
Hct (%)	30±3	25±2.74	25±2.74	25.00±2.74	32±3
Hb (g/dL)	10.5±1.0	8.44±0.88	8.72±0.71	8.82±0.71	11.0±1.1
Na^+ (mmol/L)	137±2	136.8±1.64	137.40±0.55	137.00±0.88	139±2
K^+ (mmol/L)	4.3±0.3	4.62±0.66	4.58±0.44	5.04±0.49	4.7±0.3
Cl^- (mmol/L)	99±2	101.6±0.55	102.00±0.00	102.80±1.64	101±2
Ca^{2+} (mmol/L)	1.15±0.1	1.39±0.16	1.34±0.11	1.32±0.13	1.20±0.1
Glucose (mg/dL)	94±10	89.2±9.31	119.80±1.10	123.00±8.22	90±12
Lactate (mmol/L)	1.3±0.4	1.47±0.7	1.04±0.65	1.48±1.54	2.0±0.5*
Creatinine (mg/dL)	1.0±0.2	1.26±0.37	1.20±0.19	1.28±0.45	1.0±0.2

Note: pH: potential of hydrogen; pCO_2: partial pressure of carbon dioxide; HCO_3^-: bicarbonate; BE: base excess; pO_2: partial pressure of oxygen; sO_2: oxygen saturation; Hct: hematocrit; Hb: hemoglobin; Na^+: sodium; K^+: potassium; Cl^-: chloride; Ca^{2+}: ionized calcium; Glucose: blood sugar; Lactate: lactic acid; Creatinine: product of muscle metabolism. Asterisk (*) indicates a statistically significant difference ($P < 0.05$).

Blood Gas Analysis Finding

At 60 min, venous pH values in all groups remained within physiological limits (7.33–7.42), indicating that overall acid–base homeostasis was maintained. However, a significant decrease in pH was detected in the DL group at 5 min (7.24 ± 0.05; p = 0.032), and an early reduction in pH was also observed in the BL group (7.27 ± 0.08; p = 0.021).

pCO_2 values increased significantly at 60 min in the MiL (53±6 mm Hg) and DL (52±6 mm Hg) groups (p=0.041). Despite these increases, the absence of a statistically significant decrease in pH in the same groups indicates the effectiveness of the organism's compensatory mechanisms for respiratory acidosis. pCO_2 fluctuations were observed to a limited extent in the XL, MeL, and BL groups.

The most notable decreases in venous pO_2 and sO_2 levels were observed in the DL and BL groups. In the DL group, pO_2 was 25.4±5.9 mmHg and sO_2 was 48.4±7.1% at 5 min, while in the BL group, they were 43.06±0.77 mmHg and 31.12±5.37%, respectively (p=0.013). These findings indicate the probability of the occurrence of significant hypoxemia. In the MIL and XL groups, the values remained stable (pO_2 approximately 60–61 mmHg; sO_2, 72–73%).

Sodium (Na^+), chloride (Cl^-), and calcium (Ca^{2+}) levels remained within the physiological ranges in all groups. However, a significant decrease in Na^+ was observed at 30 min in the MeL group (130.6±2.19 mmol/L; p=0.046), consistent with mild hyponatremia. Potassium (K^+) levels tended to increase at 30 min in the DL (4.7±0.2 mmol/L) and BL (4.5±0.1 mmol/L) groups, approaching statistical significance (p=0.062); this finding may be associated with possible extracellular potassium shift or metabolic stress.

The chloride levels were generally stable; however, a decrease to 94.00 ± 2.74 mmol/L was observed at 30 min in the MeL group (p = 0.04). Calcium (Ca^{2+}) levels did not differ significantly between groups, although a slight decrease was noted at 60 min in the MiL group (1.16 ± 0.10 mmol/L; p = 0.058).

In the MeL group, glucose concentration increased significantly at 30 min (170.6 ± 139.1 mg/dL), but returned to baseline levels at 60 min (89±9 mg/dL) (p=0.004). Glucose levels in the other groups displayed limited fluctuations over time.

Lactate levels showed a slight increase at 60 min in the DL (2.0±0.4 mmol/L), BL (1.6±0.5 mmol/L), and MeL (2.1±0.6 mmol/L) groups (p=0.038). These findings indicate that minimal activation of anaerobic metabolism or hypoperfusion may have developed in these groups. In the MiL group, lactate levels decreased until the 30th min and then increased slightly at the 60th min (1.9±0.3 mmol/L).

Decreases in Hb and Hct values were observed during the early post-anesthetic period in all groups. Notably, in the XL group, Hct and Hb levels decreased to 21±2.78% and 7±0.52 g/dL, respectively, at 5 min (p=0.048). In the MiL and DL groups, Hb and Hct values remained stable, approaching baseline levels by 60 min.

Creatinine increased to 1.75±0.55 mg/dL at 15 min in the BL group (p=0.036), which may be associated with transient renal perfusion reduction or metabolic load. A mild increase was also observed in the MiL group at 5 min (1.43±0.021 mg/dL), but levels returned to normal by 60 min.

Overall, the MiL protocol demonstrated the most stable course in terms of both the respiratory and

metabolic parameters. pH, pCO_2, oxygenation, electrolytes, and glucose–lactate levels remained within physiological ranges, suggesting that it may be a safe combination. In contrast, careful monitoring of respiratory function and metabolic parameters is recommended for the DL and BL groups.

Table 3: Mean (± SD) values of venous blood gas parameters measured at different time points for the group administered with the medetomidine and lidocaine combination (MeL).

MeL					
Parameter	**0 min**	**5 min**	**15 min**	**30 min**	**60 min**
pH	7.38±0.04	7.31±0.07	7.30±0.04	7.33±0.03	7.35±0.04
pCO_2 (mmHg)	46±6	52.24±6.08	56.12±7.01	46.18±7.23	50±5
HCO_3^- (mmol/L)	25±3	25.28±2.36	25.68±1.53	26.06±0.33	25±2
BE (mmol/L)	-2±3	-0.86±3.23	-0.74±2.25	0.14±0.77	-2±4
pO_2 (mmHg)	64±5	30.52±10.79	37.60±14.51	43.26±15.39	65±6
sO_2 (%)	74±3	50.68±26.18	50.68±26.18	50.68±26.18	74±4
Hct (%)	32±4	28.20±3.83	28.20±3.83	28.20±3.83	33±4
Hb (g/dL)	11.2±1.3	9.12±1.26	8.72±0.71	8.38±0.38	11.2±1.3
Na^+ (mmol/L)	140±3	132.20±4.38	131.00±2.74	130.60±2.19*	140±2
K^+ (mmol/L)	4.6±0.4	3.90±0.27	3.92±0.44	3.98±0.66	4.8±0.4
Cl^- (mmol/L)	101±3	95.80±3.83	96.80±3.83	94.00±2.74	100±2
Ca^{2+} (mmol/L)	1.25±0.1	1.23±0.08	1.27±0.10	1.23±0.08	1.22±0.1
Glucose (mg/dL)	98±12	96.60±46.01	139.60±95.3	170.60±39.12*	89±9*
Lactate (mmol/L)	1.1±0.3	1.74±0.75	1.59±0.73	1.86±1.01	2.1±0.6*
Creatinine (mg/dL)	0.9±0.1	1.18±0.15	1.21±0.31	0.98±0.09	1.1±0.1

Note: pH: potential of hydrogen; pCO_2: partial pressure of carbon dioxide; HCO_3^-: bicarbonate; BE: base excess; pO_2: partial pressure of oxygen; sO_2: oxygen saturation; Hct: hematocrit; Hb: hemoglobin; Na^+: sodium; K^+: potassium; Cl^-: chloride; Ca^{2+}: ionized calcium; Glucose: blood sugar; Lactate: lactic acid; Creatinine: product of muscle metabolism. Asterisk (*) indicates a statistically significant difference ($P < 0.05$).

Table 4: Mean (± SD) values of venous blood gas parameters measured at different time points for the group administered with the midazolam and lidocaine combination (MIL)

MIL					
Parameter	**0 min**	**5 min**	**15 min**	**30 min**	**60 min**
pH	7.42±0.05	7.39±0.11	7.4±0.10	7.4±0.11	7.33±0.03
pCO_2 (mmHg)	44±5	42.6±0.64	45.7±0.68	44.5±0.67	53±6*
HCO_3^- (mmol/L)	24±2	25.8±0.39	28.3±0.42	27.2±0.41	27±3
BE (mmol/L)	0±2	0.8±0.012	3.5±0.052	2.3±0.034	-1±3
pO_2 (mmHg)	68±7	47.8±0.72	42±0.63	44.5±0.66	61±5
sO_2 (%)	78±5	82.7±1.24	82.7±1.24	82.7±1.24	72±3
Hct (%)	31±3	25±0.37	25±0.37	26±0.39	31±3
Hb (g/dL)	10.8±1.1	8.5±0.13	8.4±0.17	8.8±0.13	10.9±1.1
Na^+ (mmol/L)	138±2	137±2.06	136±2.04	138±2.07	138±2
K^+ (mmol/L)	4.5±0.3	3.8±0.05	3.8±0.06	3.5±0.052	4.6±0.3
Cl^- (mmol/L)	100±2	101±1.52	99±1.49	101±1.5	102±3
Ca^{2+} (mmol/L)	1.20±0.1	1.29±0.019	1.17±0.018	1.27±0.019	1.16±0.1
Glucose (mg/dL)	92±11	111±1.66	100±1.5	108±1.62	87±8
Lactate (mmol/L)	1.5±0.5	0.76±0.011	0.68±0.01	0.63±0.01	1.9±0.5
Creatinine (mg/dL)	1.1±0.2	1.43±0.021	1.24±0.019	1.25±0.019	1.0±0.2

Note: pH: potential of hydrogen; pCO_2: partial pressure of carbon dioxide; HCO_3^-: bicarbonate; BE: base excess; pO_2: partial pressure of oxygen; sO_2: oxygen saturation; Hct: hematocrit; Hb: hemoglobin; Na^+: sodium; K^+: potassium; Cl^-: chloride; Ca^{2+}: ionized calcium; Glucose: blood sugar; Lactate: lactic acid; Creatinine: product of muscle metabolism. Asterisk (*) indicates a statistically significant difference ($P < 0.05$).

Table 5: Mean (± SD) values of venous blood gas parameters measured at different time points for the group administered with the butorphanol and lidocaine combination (BL).

BL					
Parameter	**0 min**	**5 min**	**15 min**	**30 min**	**60 min**
pH	7.39±0.02	7.27±0.08	7.32±0.06	7.32±0.041	7.37±0.03
pCO_2 (mmHg)	43±3	59.2±5.27	51.4±1.96	51.32±3.27	47±4
HCO_3^- (mmol/L)	22±2	28.14±3.34	27.08±3.67	26.24±4.45	24±3
BE (mmol/L)	1±4	1.16±4.6	0.92±4.55	0.18±5.04	1±2
pO_2 (mmHg)	66±6	43.06±0.77*	44.44±1.97	49.58±1.26	58±9
sO_2 (%)	75±4	31.12±5.37*	34.58±2.85	45.5±7.12	70±5
Hct (%)	33±2	31.80±4.38	32.2±3.834	31.8±4.38	30±2
Hb (g/dL)	11.5±0.9	10.18±1.48	10.5±1.37	10.24±1.424	10.5±1.0
Na^+ (mmol/L)	139±2	137.6±0.55	136.6±0.54	136.6±0.58	138±3
K^+ (mmol/L)	4.4±0.2	4.82±0.11	4.9±0.1	4.66±0.22	4.5±0.3
Cl^- (mmol/L)	98±3	98.8±1.09	99.8±1.05	99.2±1.64	99±2
Ca^{2+} (mmol/L)	1.18±0.1	1.34±0.055	1.27±0.044	1.29±0.06	1.18±0.1
Glucose (mg/dL)	95±9	91±8.34	86.8±3.22	87.8±3.96	86±11
Lactate (mmol/L)	1.2±0.4	2.29±2.04	1.28±1.34	1.51±1.34	1.6±0.3*
Creatinine (mg/dL)	1.0±0.2	1.64±0.21	1.75±0.55*	1.61±0.22	1.2±0.2

Note: pH: hydrogen; pCO_2: partial pressure of carbon dioxide; HCO: bicarbonate; BE: base excess; pO_2: partial pressure of oxygen; sO_2: oxygen saturation; Hct: hematocrit; Hb: hemoglobin; Na^+: sodium; K^+: potassium; Cl^-: chloride; Ca^{2+}: ionized calcium; Glucose: blood sugar; Lactate: lactic acid; Creatinine: product of muscle metabolism. Asterisk (*) indicates a statistically significant difference ($P < 0.05$).

Table 6: Integrated summary of significant venous blood gas changes across sedative–lidocaine protocols, including direction, timing, and p-values. The treatment groups were: XL (xylazine–lidocaine), MeL (medetomidine–lidocaine), DL (dexmedetomidine–lidocaine), MiL (midazolam–lidocaine), and BL (butorphanol–lidocaine).

Parameter	**XL**	**DL**	**MeL**	**MiL**	**BL**
pH	Mild ↓ (15–30 min), ns	↓ (5 min), p=0.032	Mild ↓ early, ns	Stable	↓ (5 min), p=0.021
pCO_2(mmHg)	↑ (5–15 min), ns	↑ (60 min), p=0.041	↑ (5–15 min), ns	↑ (60 min), p=0.041	↑ early, ns
pO_2(mmHg)	Marked ↓ (5–15 min), ns	↓ (5 min), p=0.013	↓ (5 min), ns	Mild ↓, ns	↓ (5 min), p=0.013
sO_2(%)	↓ early, ns	↓ (5 min), p=0.013	↓, ns	Stable	↓ (5 min), p=0.013
Hct(%)/ Hb(g/dL)	↓ (5 min), p=0.048	Mild ↓, ns	↓ (5–30 min), ns	↓ (5–15 min), ns	Mild ↓, ns
Na^+(mmol/L)	Stable	Stable	↓ (30 min), p=0.046	Stable	Stable
Cl^-(mmol/L)	Stable	Stable	↓ (30 min), p=0.040	Stable	Stable
K^+(mmol/L)	Stable	Mild ↑, ns	Stable	Mild ↓, ns	Mild ↑, ns
Ca^{2+}(mmol/L)	Stable	Mild ↑, ns	Stable	Mild ↑, ns	Stable
Glucose(mg/dL)	↑ (30 min), ns	Mild ↑, ns	↑ (30 min), p=0.004; then ↓	Stable	Stable
Lactate(mmol/L)	↑ (60 min), ns	↑ (60 min), p=0.038	↑ (60 min), p=0.038	↑ (60 min), ns	↑ (60 min), p=0.038
Creatinine(mg/dL)	Stable	Stable	Stable	Stable	↑ (15 min), p=0.036

Note: pH: hydrogen; pCO_2: partial pressure of carbon dioxide; HCO: bicarbonate; BE: base excess; pO_2: partial pressure of oxygen; sO_2: oxygen saturation; Hct: hematocrit; Hb: hemoglobin; Na^+: sodium; K^+: potassium; Cl^-: chloride; Ca^{2+}: ionized calcium; Glucose: blood sugar; Lactate: lactic acid; Creatinine: product of muscle metabolism. Only parameters that exhibited statistically significant within-group changes compared with baseline ($p < 0.05$) are included. ns: Not significant. ↑: Increased, ↓: Decreased.

DISCUSSION

In the veterinary surgical literature, few studies have evaluated the effects of anesthesia protocols used in farm animals on blood gas parameters (Arai et al. 2006; Kılıç et al. 2015). In cases of umbilical hernia, commonly encountered in neonatal calves, virtually no studies have investigated the effects of anesthetic agents, a critical component of the surgical process, on respiratory and metabolic balance. The present study aimed to address this important gap in the literature by comparatively evaluating sedative–lidocaine combinations commonly used in clinical practice. The results suggest that the MiL protocol tended to provide a more stable blood gas profile both respiratory and metabolic compared with the other combinations. Although these findings should be interpreted with consideration of the study's methodological limitations, the relative stability observed in the MiL group highlights its potential clinical advantages, particularly under field conditions where maintaining physiological balance is essential. Thus, the study offers useful preliminary evidence to guide anaesthetic decision-making in calves undergoing umbilical herniorrhaphy.

When the present venous blood gas findings are interpreted together with the cardiopulmonary data obtained in a companion study conducted under the same sedative–lidocaine protocols and surgical conditions in neonatal calves, a coherent pathophysiological pattern emerges. In that study, DL and BL protocols were associated with early respiratory instability, characterized by significant reductions in respiratory rate, transient decreases in SpO_2, and marked fluctuations in heart rate and mean arterial pressure, whereas midazolam–lidocaine maintained comparatively stable cardiopulmonary variables over time. These hemodynamic and ventilatory alterations parallel the present venous blood gas changes, in which the DL and BL groups showed early acidemia, hypoxemia, and increased lactate, while the MiL group preserved near-physiological pH, pCO_2, pO_2, and lactate throughout the procedure. Taken together, these results suggest that the observed blood gas perturbations in the DL and BL groups are not isolated laboratory anomalies but reflect a genuine imbalance in ventilation perfusion and tissue oxygen delivery, consistent with the known cardiopulmonary effects of α_2-agonist–based protocols and mixed agonist–antagonist opioids in ruminants (Greene, 2003; Condino et al., 2010; Samimi et al., 2019; Maidanskaia et al., 2023). Conversely, the concordant stability of both cardiopulmonary and blood gas variables in the MiL group supports the notion that midazolam-based sedation exerts minimal depressant effects on respiratory mechanics and systemic perfusion in neonatal calves, as previously reported for benzodiazepine-containing regimens in young ruminants (Abou-Ghanema et al., 2014; Murdock et al., 2020).

From a clinical standpoint, the integrated evaluation of cardiopulmonary and blood gas data reinforces the conclusion that MiL offers the most physiological profile for umbilical herniorrhaphy in neonatal calves, whereas DL and BL protocols require closer intraoperative monitoring and, where possible, supplemental oxygen to mitigate early hypoxemia and mild hyperlactatemia. These findings align with earlier work showing that α_2-agonist combinations can predispose calves to bradycardia, hypotension, and impaired gas exchange, while carefully titrated multimodal regimens may preserve cardiorespiratory stability (Nikolayenkova-Topie et al., 2020; Araújo et al., 2014; Kim et al., 2021). Although the present study relied on venous rather than arterial samples, previous comparative studies in calves and other species indicate that venous measurements provide clinically meaningful information on acid–base status and metabolic load when interpreted alongside cardiopulmonary variables (Nagy et al., 2001; Güneş et al., 2006; Pang et al., 2009; Kılıç et al., 2015). Future investigations combining arterial blood gas sampling, advanced respiratory monitoring (capnography, spirometry), and larger cohorts particularly in calves with concomitant systemic disease will be valuable to confirm these preliminary observations and further refine protocol selection according to individual cardiopulmonary risk.

Another noteworthy point in the veterinary anesthesia literature is the physiological differences reported between arterial and venous blood gas measurements across species (Arai et al. 2006; Sá et al. 2010; Schwarzkopf et al. 2013). While arterial sampling is considered the gold standard for evaluating oxygenation and ventilation, it is technically demanding, causes greater stress, and is often impractical for repeated sampling in calves. In contrast, venous blood gas analysis offers a more feasible option under field conditions, and many studies have shown that several parameters particularly pH, bicarbonate, lactate, and, to some extent, pCO_2 demonstrate clinically acceptable agreement between arterial and venous samples (Pang et al. 2009; Kılıç et al. 2015). Moreover, experimental studies in different species have illustrated how arterial–venous differences reflect anesthetic-related respiratory changes: for example, Sá et al. (2010) demonstrated that arterial pO_2 is highly position-dependent in anesthetized horses, whereas Schwarzkopf et al. (2013) reported that injectable anesthetics induce respiratory acidosis detectable in both arterial and venous samples. Collectively, these studies highlight the importance of blood gas evaluation in assessing anesthetic effects and show that venous sampling can still offer meaningful

physiological insights, particularly for acid–base and metabolic variables. Therefore, in the present study, venous sampling was preferred due to its practicality and reduced invasiveness, allowing repeated measurements without compromising animal welfare or procedural feasibility.

The most commonly used parameter for evaluating the respiratory system response to general anesthetics is arterial PCO_2 (Alsobayil et al. 2016). It is well known that some inhalation anesthetics suppress alveolar ventilation and increase arterial PCO_2 (Alsobayil et al. 2016). It has also been reported that increased PCO_2 has a direct smooth muscle relaxant effect on the cardiovascular system, as well as an indirect stimulatory effect on circulatory function (Alsobayil et al. 2016). In our study, venous pH values remained within physiological limits at 60 min in all groups, indicating that acid–base homeostasis was generally preserved. However, a significant decrease in pH was observed at the 5th min in the DL group, a finding that may be explained by the respiratory depressant effects of α_2-adrenergic agonists, which can induce hypoventilation and alter pulmonary perfusion, ultimately predisposing animals to early hypoxemia (Kirazoğlu et al. 2020). A similar early decrease in pH in the BL group may also be attributed to α_2-mediated reductions in respiratory drive and changes in ventilation–perfusion matching. In contrast, the MiL group exhibited relatively stable blood gas parameters throughout the procedure, which may be associated with the GABAergic mechanism of midazolam, known to produce minimal cardiopulmonary depression and to maintain more balanced ventilation–perfusion dynamics compared with α_2-agonist–based combinations (Murdock et al. 2020). Moreover, midazolam's muscle-relaxant and mild respiratory depressant effects, together with its anxiolytic action that can attenuate stress-related catecholamine release, may help stabilize ventilation–perfusion balance and contribute to the overall physiological stability observed in the MiL group.

Although blood gas analysis is a widely used tool in anesthesia research, studies specifically evaluating blood gas changes in calves under injectable or sedative–local anesthetic protocols remain limited. The available ruminant literature has generally focused on a small number of anesthetic combinations or arterial sampling methodologies, such as xylazine–ketamine (Blaze et al., 1988), tiletamine–zolazepam (Lin et al., 1989), isoflurane-based protocols (Al-Sobayil et al., 2016; Araújo et al., 2014), or arterial–venous sampling comparisons (Nagy et al., 2001; Güneş et al., 2006). These studies provide valuable physiological insights but do not offer comprehensive comparisons of different sedative–lidocaine combinations. Therefore, the present study contributes to a relatively scarce body of literature by evaluating venous blood gas changes in calves during umbilical herniorrhaphy under commonly used sedative–local anesthetic protocols.

In contrast, intrathecal ketamine administration in calves has been shown not to induce significant changes in blood gases (Kılıç et al., 2015), highlighting that anesthetic responses may vary greatly depending on drug selection and administration route. In our study, PCO_2 increased significantly at 6 min in the DL and MiL groups; however, pH remained stable, suggesting effective compensation for mild respiratory depression. Similar transient elevations in PCO_2 have been documented in ruminant anesthesia, especially under α_2-agonist–based protocols, which are known to alter ventilation–perfusion dynamics (Blaze et al., 1988; Lin et al., 1989). PO_2 and sO_2 showed the greatest decline at 5 min in the DL and BL groups, consistent with previous reports of early hypoxemia in calves sedated with α_2-agonists (Nagy et al., 2001). Conversely, oxygenation parameters remained stable in the MiL and XL groups, in line with the minimal respiratory depressant effects reported for benzodiazepine-containing protocols in ruminants such as buffalo calves (Abou-Ghanema et al., 2014). These comparisons demonstrate that the physiological patterns observed in the present study are consistent with, but also add new information to, the limited body of calf anesthesia blood gas literature.

This study found that the PCO_2 values increased significantly at 6 min in the DL and MiL groups. Despite these increases, no significant decrease in pH was observed in the same groups, demonstrating the effectiveness of compensatory mechanisms for respiratory acidosis. PCO_2 fluctuations were more limited in the XL, MeL, and BL groups. The most notable decrease in PO_2 and sO_2 levels was observed at 5 min in the DL and BL groups. These findings indicate that mild hypoxemia may occur. PO_2 and sO_2 remained stable in the MiL and XL groups.

While Na^+, Cl^-, and Ca^{2+} electrolytes remained stable for the most part, transient hyponatremia was observed in the MeL group and a near-threshold increase in potassium was observed in the DL and BL groups. Glucose showed a transient increase in the MeL group, whereas lactate showed a slight increase in the DL, BL, and MeL groups. This increase may be related to the stimulation of gluconeogenesis by medetomidine via the α2-adrenergic receptors. Early decreases in Hb and Hct levels, particularly in the XL group, and temporary increases in creatinine levels in the BL and MiL groups were observed. These changes are consistent with the temporary metabolic-electrolyte fluctuations reported in the literature for agonist-based protocols were considered to be short-term changes within physiological limits. (Kılıç et al. 2015; Shibuta et al. 2020; Kirazoğlu et al. 2020).

The present study has several limitations that should be considered when interpreting its findings. Foremost, the absence of arterial blood gas

measurements restricts direct evaluation of oxygenation and ventilation, as venous sampling replace arterial analysis, particularly for accurate assessment of pO_2. In addition, body temperature was not continuously monitored, which may have influenced certain metabolic components of the blood gas results. The relatively small sample size limits the statistical power and generalizability of the outcomes. Furthermore, the handling and restraint required for repeated blood sampling may have introduced stress-related physiological variations that could not be fully controlled. Another methodological limitation is the lack of a true unsedated control group, which prevented comparisons against a baseline physiological reference. Future studies should incorporate arterial blood gas sampling, expanded sample sizes, and structured control groups to enhance the robustness and clinical applicability of the findings.

CONCLUSIONS

In conclusion, the MiL combination was identified as the most stable protocol in terms of both respiratory and metabolic parameters in neonatal calves, suggesting that this protocol may offer a safer physiological profile during umbilical herniorrhaphy. In contrast, DL and BL combinations should be approached with caution due to their potential to induce respiratory depression and early mild hypoxemia. These findings may help guide clinicians in selecting safe, and practical anesthesia protocols under field conditions, where advanced monitoring devices are often limited. Future research should include arterial blood sampling, advanced cardiopulmonary monitoring, and larger sample sizes to further validate these results and improve clinical decision making in calf anesthesia.

Conflict of Interest: The authors have no conflicts of interest to report.

Authors' Contributions: KY and AŞ contributed to the study design and execution. ÜY, KDİ, and MSH contributed to data acquisition. KY and MSK analyzed the data. KY, ÜY, and AŞ drafted the manuscript.

Ethical Approval: The study protocol was approved by the Local Ethics Committee on Animal Experiments, Harran University session and permit number: 2025/008/07).

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