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ORIGINAL ARTICLE

Effects of xylazine-ketamine anesthesia with atropine premedication on hematological parameters in puppies

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Abstract

Background: General anesthesia can alter hematological parameters, influencing clinical interpretation of laboratory results. Understanding these effects in pediatric animals is crucial for safe anesthetic management.

Methods: Nine clinically healthy local-breed puppies, approximately 4 weeks old, were administered atropine (0.05 mg/kg, IV), followed by xylazine (1 mg/kg, IV) and ketamine (10 mg/kg, IV). Blood samples were collected before anesthesia, during anesthesia, and after recovery. Hematological parameters (WBC, Lym%, Gran%, Mid%, RBC, HGB, HCT, MCV, MCH, MCHC, RDW, PLT, MPV, PDW, PCT, P-LCR, and P-LCC) were analyzed using a Dymind Automated Hematology Analyzer. Data were expressed as mean ± SD. Statistical analysis was performed using repeated measures ANOVA, with p-values < 0.05 considered statistically significant.

Results: Statistically significant decreases were observed in RBC ($p = 0.0037$), HGB ($p = 0.0109$), HCT ($p = 0.0063$), MCH ($p = 0.0251$), RDW-SD ($p = 0.0135$), and platelet count ($p = 0.0072$) during anesthesia, followed by partial recovery post-anesthesia. Other parameters, including WBC, lymphocyte percentage, granulocyte percentage, MCV, MCHC, MPV, and RDW-CV, showed no significant variation. The puppies showed induction average 1.49 minutes, duration average 34 minutes, and recovery 76.66 minutes with suitable depth and muscle relaxation.

Conclusion: Xylazine-ketamine anesthesia with atropine premedication induces transient but significant hematological alterations, mainly affecting red blood cell indices and platelet counts in puppies. These findings are important for interpreting hematological results during the perioperative period in pediatric canine patients. The given combination of anesthetics produces suitable anesthesia for major surgery.

Keywords: Hematological parameters, Anesthesia, Puppies, xylazine-ketamine.

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Introduction

Anesthesia is a reversible process used to safely and effectively restrain surgical patients, allowing surgical procedures to be performed with minimal pain and stress (William, 1996; Thurmon *et al*., 2007). It is an essential requirement in both animals and humans before surgery to ensure patient safety and optimal performance by the surgical team (Reddy *et al*., 1994).

Ketamine is a non-barbiturate anesthetic that induces a dissociative state in which the patient appears awake but does not perceive pain (Liu *et al*., 2016). However, ketamine increases muscle tone, resulting in muscle rigidity. Therefore, it is often used in combination with muscle relaxants such as alpha-2 adrenoceptor agonists (Welsh *et al*., 2003).

Xylazine is a non-opioid alpha-2 adrenoceptor agonist with sedative, muscle relaxant, and analgesic properties (Fereidoon *et al*., 2005). The combination of xylazine and ketamine provides smooth induction of anesthesia and safe recovery in veterinary practice (Durrani *et al*., 2003).

Atropine is a commonly used premedication that reduces muscle spasm, salivation, and gastrointestinal and respiratory secretions during anesthesia (Liga *et al*., 2011). It is also used to prevent bradycardia, a common side effect of alpha-2 agonists (Ko *et al*., 2001).

The combination of subcutaneous ketamine and intravenous xylazine has been reported to cause no significant changes in hematological parameters in dogs, except for a slight decrease in mean corpuscular hemoglobin concentration (MCHC) and eosinophil count (Babalola *et al*., 2021). Another study found that the combination of atropine, xylazine, and ketamine did not significantly alter blood parameters in dogs (Ayalew *et al*., 2016). Similarly, Gebremedhin (2018) reported that hematological values remained unchanged following xylazine-ketamine anesthesia in dogs.

However, hematological parameters can be altered by pharmacological agents, hormones, or splenic contraction (Hall *et al*., 2001). The effect of the drug on the developing physiology of puppies may vary from adult dogs and require in-depth evaluation (Kumar *et al*., 2014; Hellyer *et al*., 2012).

The combination of xylazine-ketamine anesthesia is frequently used for adult and young dogs, but there is limited research on hematological parameters in young dogs (Sarma *et al*., 2002; Kumar *et al*., 2014; Adetunji *et al*., 2002).

Therefore, this study was performed to investigate the effects of general anesthesia on hematological parameters in puppies.

Materials and methods

Experimental Animals: Nine (9) healthy local-breed puppies, approximately 4 weeks of age, were used in this study. The puppies were humanely captured from the streets within the university campus and housed individually in clean, well-ventilated cages under standard management conditions. All animals were vaccinated against rabies using **Rabisin®** (1 mL, subcutaneously; Boehringer Ingelheim, vial size: 10 mL) before the experimental procedures.

Anesthetics and premedicant used in the experiment: Atropine sulphate @ 0.05 mg/kg, IV (Tropin Vet ®- 10 ml vial, The ACME Laboratories Limited), Xylazine @ 1 mg/kg, IV (Xylazine Injection USP ®- 30 ml vial, Farmer's Pharma Private Limited) and Ketamine @ 10 mg/kg, IV (G- Ketamine ®- 10 ml vial, Gonoshasthaya Pharmaceuticals Ltd.).

Experimental procedure: The puppies were fasted for 3 hours without water and 6 hours without food. Then they were premedicated with atropine sulphate and anesthetized by a combination of xylazine and ketamine. Blood samples were collected (2 ml each) from the cephalic vein before anesthesia, during anesthesia (10 minutes after induction), and 30 minutes after recovery from anesthesia (each dog bled 3 times). The blood samples, immediately after collection, were kept in a K_2EDTA tube and mixed properly for hematological test.

Figure 1: Fasting

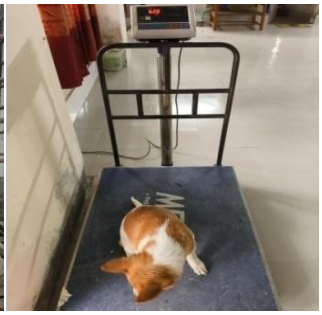

Figure 2: Weighing

Figure 3: Blood collection

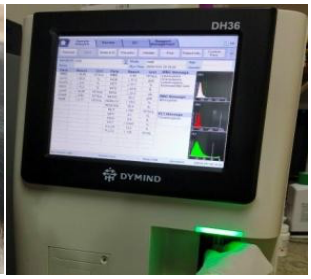

Figure 4: Blood testing

Hematological parameters: Dymind hematology analyzer (Model: DH36, Manufacturer: Dymind, Country: China) used to measure the following parameters: White Blood Cells (WBC), Lymphocyte% (Lym%), Granulocyte% (Gran%), Mid cell% (Mid%), Red Blood Cells (RBC), Hemoglobin (HGB), Hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Red Blood Cell Distribution Width (RDW), Platelet count (PLT), Mean Platelet Volume (MPV), Platelet Volume Distribution Width (PDW), Platelet Crit (PCT), Platelet-Large cell Ratio (P-LCR), Platelet- Large Cell Count (P-LCC).

Clinical parameters: Induction time of anesthesia after administration of anesthetic intravenously, depth of anesthesia, duration, and recovery time were recorded.

Statistical analysis: The obtained data were expressed as mean ± S.D. The data were analyzed using SPSS software, and a P value less than 0.05 was considered statistically significant.

Results

Table 1: Changes in the hematological parameters during anesthesia using atropine- xalazine- ketamine combination in puppies (n=9)

SL. No.	Parameters	Preanesthetic control values (Mean ± SEM)	Values during anesthesia (Mean ± SEM)	Values after recovery (Mean ± SEM)	p-Value
1	RBC (10^6/uL)	4.81±0.15	4.36±0.09	4.46±0.09	0.0037
2	WBC (10^3/uL)	16.69 ± 1.05	15.34 ± 0.74	15.37 ± 0.55	0.169
3	HGB (g/dL)	10.3±0.36	9.75±0.25	9.90±0.21	0.0109
4	Lymphocyte (%)	84.77 ± 1.43	93.82 ± 3.98	93.82 ± 3.98	0.895
5	Granulocyte (%)	4.63±0.67	7.28±1.41	4.53±0.62	0.166
6	HCT (%)	30.9±1.2	27.9±0.7	28.7±0.7	0.0063
7	MCV (fL)	63.2±0.6	63.9±0.4	62.8±0.5	0.1362
8	MCH (pg)	22.0±0.1	22.4±0.2	22.2±0.2	0.0251
9	MCHC (g/dL)	34.6±0.1	34.9±0.1	34.8±0.1	0.6545
10	RDW-CV (%)	17.0±0.6	16.4±0.4	16.7±0.5	0.1419
11	RDW-SD (fL)	37.1±0.7	35.6±0.7	35.7±0.6	0.0135
12	PLT (10^3/uL)	586.6±54.4	522.3±47.8	513.8±56.9	0.0072

13	MPV (fL)	8.5±0.1	8.4±0.1	8.3±0.1	0.4563
14	PDW (fL)	10.0±0.2	9.8±0.2	9.8±0.2	0.3689
15	PCT (%)	0.491±0.033	0.441±0.038	0.466±0.037	0.0429
16	P-LCR (%)	17.8±0.8	17.4±0.7	16.8±0.7	0.1620
17	P-LCC (10^9/L)	99.2±4.7	91.2±4.5	86.6±4.4	0.0025

Table 2: Induction of anesthesia, duration, and recovery period using atropine- xalazine-ketamine combination in puppies (n=9)

Parameters	**Minutes (Average)**
Induction	1.494
Duration	34
Recovery	76.667

Table 3: Depth of anesthesia during blood collection

Puppies	**Pedal Reflex**	**Corneal Reflex**	**Muscle relaxation**
1	---	+	+++
2	---	+	+++
3	---	+	+++
4	---	+	+++
5	---	+	+++
6	---	+	+++
7	---	+	+++
8	---	+	+++
9	---	+	+++

Note: --- (no pedal reflex), + (Sluggish), +++ (Marked relaxation)

Discussion

This study explored the consequences of general anesthesia on different hematological parameters in puppies, directing attention to values measured before anesthesia (pre-induction), during anesthesia (maintenance), and after recovery (post-anesthesia). The statistically significant alterations observed in several hematological parameters enhance the physiological impact of anesthesia, which has a significant message for veterinary clinical practice.

A marked decrease in red blood cell (RBC) count, hematocrit (HCT), and hemoglobin (Hb) concentration was noticed during anesthesia compared to control values. Such declines are due to splenic sequestration of RBC and hemodilution, which are common effects of ketamine and xylazine. Xylazine produces splenic contraction and relaxation, which causes temporary pooling of RBCs in the spleen, resulting in reduced Hb, RBCs, and HCT in blood circulation (Thurmon *et al*., 1996).

Ketamine intensifies the cardiovascular and sedative effects of xylazine (Thurmon *et al.,* 1996; Hellyer *et al.*, 2007), resulting reduction of peripheral vasodilation and sympathetic tone, which enhances splenic sequestration and fluid shift (Hall *et al.,* 2001).

Post-anesthesia, partial recovery of these indices suggests a reversible physiological response, though values remained lower than baseline in some cases. These findings align with the work of Stepien *et al.* (2009), who noted transient anemia in dogs after anesthetic exposure, particularly in younger or smaller animals due to immature regulatory mechanisms.

Total white blood cell (WBC) counts showed an increase during anesthesia but returned to baseline levels post-recovery. However, differential counts revealed statistically significant neutrophilia and lymphopenia during anesthesia. These changes are likely stress-related, mediated by endogenous corticosteroid release during anesthesia and surgical stimulation (Jones and Allison, 2007). Glucocorticoids induce mobilization of neutrophils and apoptosis or redistribution of lymphocytes, contributing to the leukocyte profile observed (Feldman *et al.,* 2006).

Post-anesthetic normalization of differential counts supports the transient nature of this stress leukogram, which has been widely reported in both canine and feline models undergoing surgical procedures (Day, 2002).

Platelet counts exhibited a significant decrease during anesthesia. Anesthetic-induced thrombocytopenia is uncommon but may result from hemodilution or altered platelet distribution (Thompson *et al.,* 2003). Platelet indices, such as mean platelet volume (MPV) and plateletcrit (PCT), also changed significantly, indicating a functional response to altered vascular tone or endothelial interaction during anesthesia.

Interestingly, platelet counts returned to near-baseline values after recovery, reinforcing the idea of reversible physiological redistribution rather than true consumption or destruction. Similar trends were reported by Bazzano *et al*. (2014), who studied platelet dynamics in dogs undergoing elective neutering.

Mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) increased slightly but significantly during anesthesia. These changes may be linked to osmotic shifts due to intravenous fluid administration or early erythrocyte swelling (Kramer *et al.,* 2002). Mean corpuscular hemoglobin concentration (MCHC), however, decreased during anesthesia, supporting the hypothesis of dilutional effects rather than intrinsic erythrocyte pathology.

The hematological alterations observed are consistent with the known pharmacodynamics of commonly used anesthetic agents. For example, propofol and isoflurane reduce systemic vascular resistance and affect sympathetic regulation, which can lead to sequestration and dilution effects (Steffey and Mama, 2007). These mechanisms are especially pronounced in puppies due to their immature hepatic and renal function, which limits their compensatory capacity (Olsson *et al.,* 2006).

Additionally, young animals have a more active bone marrow and higher baseline hematological turnover, making them more sensitive to transient disruptions (Cowell and Tyler, 2002).

Understanding these hematological responses is critical in pediatric veterinary anesthesia. Hemodilution or transient anemia may increase the risk of tissue hypoxia,

particularly in procedures involving blood loss or prolonged recovery. Similarly, stress leukograms may complicate the interpretation of concurrent infections or inflammatory conditions in puppies undergoing surgery. The findings suggest that clinicians should interpret hematological data with caution when collected perioperatively. Where possible, baseline hematological parameters should be obtained well before anesthesia, and post-anesthetic samples should be delayed until full recovery to avoid misleading conclusions.

The induction period of this study was 1.49 minutes (average) after combined administration of xylazine and ketamine intravenously, indicating a quick start of anesthesia. This finding is harmonious with the report of Aithal *et al*., 1996, and Thurmon *et al*., 1996, who documented 1 to 2-minute induction time in dogs and puppies using xylazine and ketamine intravenously. The observation for duration of anesthesia was 34 minutes (average), which aligns with the report of Thurmon *et al*., 1996, and Ramaswamy *et al*., 1995, who reported duration ranging from 30 to 45 minutes based on dose, age, and condition of physiology. Recovery period from anesthesia was found to be 76.667 minutes (average), which aligns with the standard recovery period of 60 to 90 minutes in puppies reported by Ramaswamy *et al*., 1995.

During blood collection in the deep anesthesia stage, puppies showed strong muscle relaxation, total loss of pedal reflex, and slight presence of corneal reflex. In small animals, loss of pedal reflex is a standard indicator of surgical anesthesia (Thurmon *et al*., 1996). The slight presence of corneal reflex is common and it does not indicate inadequate anesthesia (Hall *et al*., 2001). The strong muscle relaxation is due to the effect of xylazine. Ketamine produces anesthesia but tends to produce muscle tone (Greene, 1996). After combined use, xylazine mitigates the muscle rigidity tendency of ketamine, resulting in good relaxation of the muscle (Mama *et al*., 1993).

Those clinical parameters indicate that the xylazine-ketamine combination produces suitable anesthesia for surgery on a puppy for a reasonable period.

Conclusions

General anesthesia in puppies induces significant but largely reversible alterations in hematological parameters, particularly erythrocyte indices, platelet counts, and differential leukocyte count. These changes are likely driven by hemodynamic shifts, fluid therapy, and anesthetic-mediated physiological modulation. Awareness of these alterations is essential for accurate interpretation of perioperative laboratory results and for ensuring safe anesthetic management in pediatric veterinary patients.

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Conflict of interest

The author does not have any conflicts of interest.

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