IOSR Journal of Agriculture and Veterinary Science (IOSR-JAVS)
e-ISSN: 2319-2380, p-ISSN: 2319-2372. Volume 18, Issue 11 Ser. 1 (November. 2025), Pp 30-38
www.iosrjournals.org

Cardiovascular Effect of Tiletamine-Zolazepzm and Ketamine-Diazepam Combinations in Male Rabbits

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Abstract
The Present study was conducted at Nepal Polytechnic Institute, Bharatpur, Nepal. The objectives of this study were to evaluate the effect of Tiletamine-Zolazepam (TZ) combination at different dose rate and Ketamine-Diazepam (KD) combination in rabbits for their impact on physiological parameters and biochemical parameters, and tissue structure of the heart. The study was carried out in rabbits in which 12 apparently healthy male rabbits were allocated to four treatment groups A, B, C and D. Group A, B and C rabbits received Tiletamine-Zolazepam combination at the dose rate of 32, 7.5 and 3.5 mg/kg body weight respectively and group D rabbits received ketamine-diazepam at dose rate of 20 and 1 mg/kg body weight respectively. The blood was collected before and after 120 minutes after the induction of anesthesia. The physiological parameters like heart rate, respiratory and temperature were monitored for 120 minutes. The respiratory rate significantly decreased at 20,30 and 40 min ($p< 0.05$), duration of loss of with drawl reflex and recovery time was significantly greater for group A and temperature increased at 0 to 120 minutes in group A and B. But comparison to other doses, the very mild degenerative changes were seen at TZ-3.5mg/kg body weight. which resulted in less damage than other group doses. Also, it results to the shortest recovery interval time after anesthetic induction. As a result of our study, we suggest that TZ-3.5 mg/kg can be safely administered.
Keywords: *Analgesics, Cardiovascular effects, Heart rate, histopathology*

Date of Submission: 12-11-2025 Date of Acceptance: 23-11-2025

I. INTRODUCTION

Background

Anesthetics are drugs that induce loss of sensation and can significantly affect the cardiovascular, respiratory, and other body systems. Tranquilizers and injectable agents such as ketamine, Telazol®, propofol, and the tiletamine–zolazepam combination are commonly used, although their use in rabbits carries higher risk. Tiletamine is a non-narcotic dissociative anesthetic known for rapid induction and cataleptoid anesthesia when used at appropriate doses (Saha et al., 2007). Zolazepam, a benzodiazepine, enhances GABAA_AA receptor activity, providing sedation, muscle relaxation, and a wide safety margin in animals. Together00, tiletamine and zolazepam are widely used as general anesthetics in species such as dogs, rabbits, goats, and horses. Ketamine is another dissociative anesthetic that causes minimal cardiovascular and respiratory depression. Its associated muscle rigidity can be reduced with diazepam. Although ketamine's cardiovascular-stimulating effects make it useful in poor-risk patients, diazepam may cause species-specific variability and its solvent, propylene glycol, can lead to hypotension (Short, 1987).

Statement of Problem

Rabbits are the third most commonly anesthetized species but have a seven-fold higher risk of anesthetic-related death than dogs and cats (Brodbelt, 2009). Ketamine, a dissociative anesthetic, often causes cataleptic sleep, poor muscle relaxation, convulsions, and prolonged recovery. The combination of tiletamine and zolazepam (TZ) provides both anesthetic and sedative effects; however, tiletamine, like ketamine, has no specific antidote and does not induce muscle relaxation or suppress cranial and spinal reflexes (Topal et al., 2023). Diazepam (5–60 mg/kg) can produce unconsciousness and immobility but may cause polypnea, particularly when compared with xylazine–ketamine combinations (5–35 mg/kg). In rabbits, TZ at 20 mg/kg produces only superficial anesthesia and increases heart rate due to tiletamine's sympathetic stimulation and zolazepam's minimal cardiovascular effects. Reports comparing the anesthetic effects of TZ with ketamine–diazepam (KD) combinations in rabbits remain limited.

Rationale of Study

Tiletamine–zolazepam (TZ) has been shown to cause minimal changes in heart rate but can induce hypertension in rats due to its cardio-stimulatory effects (Wilson et al., 1993). Higher doses of TZ (32 mg/kg and

7.5 mg/kg) have also been linked to renal tubular necrosis and mild nephrosis in rabbits (Nephrotoxicity of Tiletamine…, 1992). However, no studies have compared the therapeutic effectiveness of TZ at different doses (32, 7.5, and 3 mg/kg BW) with single-dose ketamine–diazepam combinations, particularly regarding their anesthetic depth, hematological changes, and cardiac pathology. This study aims to fill that gap by evaluating and comparing the cardiovascular effects and overall safety profiles of these anesthetic regimens in rabbits.

II. METHODOLOGY

Ethical Statement

The study was started after the approval of the Nepal Veterinary Council (32/2080/81).

Animals

In this investigation, 12 apparently healthy male rabbits weighing 1-2 kg each underwent four different anesthetic protocols. The rabbits were single housed in cages for 7days for acclimatization before the experiments and were given locally available grass and water ad libitum. Before initiating the experiment, the animals were kept off fed for 6 hours and water was withheld for 2 hours.

Experimental design

The rabbits were randomly assigned into 4 groups A, B, C and D each group containing 3 rabbits. Tiletamine-Zolazepam (ZoletilTM 50 veterinary) was administered in group A, B, C at the dose rate of 32 mg/kg, 7.5 mg/kg and 3.5 mg/kg respectively. Group D received Ketamine (Kmine) and Diazepam (LoriR)@ 20 mg/kg and 1 mg/kg, respectively.

Drugs/Group	Group A	Group B	Group C	Group D
T-Z (1:1)	32 mg/Kg	7.5 mg/Kg	3.5mg/kg	-
K+D	-	-	-	20+1 mg/Kg

Anesthetization and monitoring period

On the day of the experiment, rabbits were weighed and transported from the housing room to the operating room using a pet carrier. Baseline heart rate, respiratory rate, and body temperature were recorded before anesthesia. The hair on the hind limb and ear was trimmed, and lignocaine gel was applied topically for local desensitization. Anesthesia was administered via the saphenous vein. Anesthetic depth was assessed by the absence of pedal withdrawal to toe pinch, loss of ear-pinch response, and loss of the righting reflex when placed in lateral recumbency. Heart rate, respiratory rate, and body temperature were monitored before induction and then at 10-minute intervals for 120 minutes after anesthetic administration. Heart rate was measured using a stethoscope placed on the lower left lateral thoracic wall, respiratory rate was visually observed, and body temperature was recorded using a digital rectal thermometer.

Histopathological Examination

Following the slaughter of the rabbit on the 8th day after anesthesia for histological analysis, kidney samples from all rabbits were collected and placed in buffered formalin. Hematoxylin and eosin-stained 4 µm slices were cut after standard tissue processing. Different areas of the kidney were investigated for signs of tubular degeneration and inflammatory cells, hemorrhages and proteineous materials.

Statistical analysis

Data for heart rate, respiratory rate, temperature, induction time and recovery times were analyzed using a one-way ANOVA and then Tukey's test for equal variance with repeated measures in each group to assess changes with time. Data for serum creatine and BUN were analyzed by using two-way ANOVA and then Tukey's HSD for post hoc test for equal variance with repeated measures in each group to asses change with time. For all statistical comparisons, differences were considered significant when p value was <0.05. The calculation was performed utilizing (Minitab 17). All values are presented as means ± Standard error mean (SE mean).

III. RESULTS

Table 1: Induction time, duration of loss of ear pinch reflex, duration of loss of pedal pinch reflex and recovery time in the Group A (32mg/kg), Group B (TZ-7.5 mg/kg), Group C (TZ-3.5),Group D (KD (20+1) mg/kg) groups ($\bar{x}$ ±SEM, n=3)

Note: a, b, c- means with different superscript letters differ significantly in the same row at p<0.05

The data regarding anesthesia induction are presented in Tab. 1. There was no significance difference between the groups regarding to the induction time (p> 0.05) (Tab. 1). The pedal withdrawal reflexes and ear pinch were lost in all groups. The duration of loss of ear pinch was longest in the Group A, followed by Group C and Group D and Group B (p>0.05). The duration of loss of pedal withdrawal reflexes was longest in the Group A (56.67±1.67), followed by Group B (29.67 ± 9.17) and then Group D (23.0±9.64) and Group C (19.67±2.91) (p<0.05). The recovery time was longest in the group A (252.7±20.4) followed by group B (136.0±15.6), group D (120.67±2.33) and group C (51.3±10.3) (p<0.001).

Criteria	Group A	Group B	Group C	Group D	p value
Onset time(Min)	0.2233±0.0410	0.1633±0.0491	0.1867 ± 0.0133	0.440±0.280	0.538
Duration of loss of ear pinch (Min)	46.0±23.1	13.67±6.84	19.00±3.06	14.00 ± 4.58	0.273
Duration of loss of pedal withdrawl reflex(Min)	56.67 ± 1.67	29.67 ± 9.17^{ab}	19.67 ± 2.91^{b}	23.0 ± 9.64 ^{b}	0.019
Recovery Time(Min)	252.7 ± 20.4^{a}	136.0 ± 15.6 ^{b}	51.3± 10.3^{b}	120.67 ± 2.33^{c}	0

Table 2: Heart rate at various times in the Group A (TZ-32mg/kg), Group B (TZ-7.5 mg/kg), Group C (TZ-3.5), and Group D (KD (20+1) mg/kg) groups ($\bar{x}$±SEM, n=3)

Time	Heart rate (beats per minute)				P value
	Group A	Group B	Groupo C	Group D	
Before	188±28	252±46.1	229.33±5.33	273.3±21.90	0.279
0	285±11.9	274±33.2	261.3±22.8	260.0±45.40	0.926
10	268±18.5	206±24.0	228.7±15.8	271.3±20.40	0.135
20	269±23.4	252.0±35.9	240.7±34.3	229.3±21.30	0.8
30	250.7±14.8	240.0±20.8	223.3±32.7	220.0±26.00	0.793
40	253.3±19.6	246.7±17.5	190.7±21.5	257.3±13.50	0.1
50	253.3±17.9	214.7±10.9	210.0±42.3	262.0±21.40	0.424
60	253.3±13.5	210.7±16.2	194.0±15.9	256.0±22.30	0.083
70	222.7±14.7	220.0±14.4	214±16.4	256.0±24.10	0.402
80	226.7±15.4	221.3±10.4	238.7±22.4	124.7±49.70	0.077
90	249.33±1.33	232±17.4	208.0±44.1	202.7±17.00	0.556
100	244.00±18.5	213.33±8.74	177.3±20.2	208.0±21.20	0.087
110	210±18.5	210.67±5.81	224.0±43.9	222.67±9.610	0.964
120	230.7±35.9	208.0±8.0	173.7±47.2	228.0±6.93	0.546

The data regarding heart rate is shown in Table 2. The mean heart rate (beats per minute) at the infusion time to the end of experimental time frame was found non-significance for all the anesthetic combinations. The mean heart rate gradually decreases for the 70th minute after the infusion for group A b.wt. from 285 beats/min to 222 beats/min and then increases to 249 beats/min on the 90th minute with fluctuate heart beats on the gradual reading on 10 minutes interval. For group B, the highest mean heart beat was recorded at the time of infusion (274 beats/min) and lowest at 120 minutes (208 beats/min) with gradual decreases in hear beat with the time intervals, but for group C, although the mean highest hear rate was recorded at the infusion time (261.3 beats/min) and lowest at 120 min (173.4 beats/min), the heart rate exhibited fluctuations, oscillating between high and low levels during each recording. For group D, heart rate was between 260 to 256 beats/min from infusion time until 70th minutes but sharply decreased to 124 beats/min on the 80th minutes though on the 90th minutes, heart rate again rises to 202.7 beats/min on 100th minute with gradual increase to 228 beats/min on 120th minute.

Table 3: Temperature at a various times in Group A TZ -32mg/kg bwt, Group B TZ 7.5mg/kgbwt ,Group C TZ 3.5 mg/kg bwt, Group D KD 20mg/kg+1mg/kg (means ±SEM,N=3)

Time	Temperature in degree Celsius				P value
	Group A	Group B	Group C	Group D	
Before	37.83±0.41^{a}	39.20±0.31^{a}	38.73±0.15^{a}	38.87±0.69 ^{a}	0.22
0	38.07±0.43^{a}	39.80±0.12^{a}	39.07±0.43^{a}	39.27±0.69 ^{a}	0.14
10	38.20±0.45^{b}	39.80±0.17^{a}	39.33±0.12 ^{ab}	39.67±0.45 ^{ab}	0.03

20	38.33±0.17[a]	39.53±0.52[a]	39.07±0.29 [a]	39.23±0.38 [a]	0.19
30	38.30±0.31[a]	39.53±0.50[a]	38.80±0.36 [a]	39.20±0.42 [a]	0.23
40	38.17±0.23[a]	39.10±0.31[a]	39.37±0.35 [a]	38.85±0.40 [a]	0.13
50	38.13±0.24[a]	39.60±0.31[a]	39.23±0.48 [a]	38.70±0.35 [a]	0.07
60	38.30±0.21[a]	39.47±0.54[a]	38.97±0.37 [a]	38.80±0.21 [a]	0.22
70	38.27±0.20[b]	39.83±0.29[a]	39±0.25 [ab]	38.60±0.50 [ab]	0.04
80	38.07±0.20[a]	39.43±0.17[a]	38.67±0.44 [a]	38.57±0.43 [a]	0.10
90	38.47±0.44[a]	39.63±0.27[a]	38.67±0.53 [a]	38.53±0.57 [a]	0.25
100	38.43±0.41[a]	39.47±0.32[a]	39±0.25 [a]	38.03±0.32 [a]	0.06
110	38.33±0.44[a]	39.57±0.38[a]	39.27±0.35 [a]	38.30±0.36 [a]	0.11
120	38.53±0.41[a]	39.47±0.35[a]	38.83±0.41 [a]	38.47±0.29 [a]	0.28

Compared to the preanesthetic values, the temperature increased at 0 to 120 minute in the group A and B. The temperature was increased at o to70,110,and 120 minutes (p>0.05),and decreased at 80 and 90 minutes in group C (p> 0.05).Temperature was increased at 0,10,20,30minutes and decreased at 40 to 120 minutes in group D .

Table 4: Respiratory rate at a various time in TZ 32mg/kg bwt,TZ 7.5mg/kgbwt, TZ 3.5mg/kg bwt and KD20mg/kg+1mg/kg (means ±SEM,N=3)

Time	**Respiratory rate(per minute)**				
	Group A	**Group B**	**Group C**	**Group D**	**p value**
Before	182.7±36.3	264±8.33	239±25.2	286.7±15.4	0.07
0	78.7±45.0	73.3±23.4	70.7±24.7	101.3±23.1	0.887
10	46.7±12.7[a]	88.0±14.0[a]	139.3±46.9[a]	106.0±20.2[a]	0.192
20	44.0±10.6[a]	178.7±14.0[a]	209.33±9.33[a]	148.0±10.6[b]	0.004
30	48.0±6.93 [a]	216.0±16 [a]	218.7±25.4 [a]	142.7±17.3 [b]	0.000
40	48.0±4.62	209.3±24.9	222.0±12.2[a]	138.7±27.1[b]	0.001
50	60.0±8.33[a]	208±10.6[a]	224.00±8[b]	148.0±13.9[c]	0
60	77.33±7.0[a]	197±10.1[a]	216±48.7[ab]	149.3±14.8[b]	0.023
70	93.3±30.8	217.3±19.2	174.7±40.7	116.0±6.11	0.046
80	101.3±33.4	210.7±40.4	188.0±51.0	161.3±26.0	0.297
90	133.3±33.4	226.7±32.0	228.0±37.2	140.0±14.0	0.098
100	138.7±46.7	221.3±19.6	233.3±27.6	146.7±27	0.144
110	134.0±50.7	229.33±9.33	248.0±6.11	128.0±30.2	0.043
120	120.0±48.5	102.7±0.603	101.77±0.26	102.0±1.27	0.024

Before anesthesia, there was no any significant differences between the groups. Yet, during specific time intervals (20,30,40 and 50min), Group A exhibited significantly reduced respiratory rates compared to the other groups At 120 min, respiratory rates in all groups became similar, with no significant differences observed.

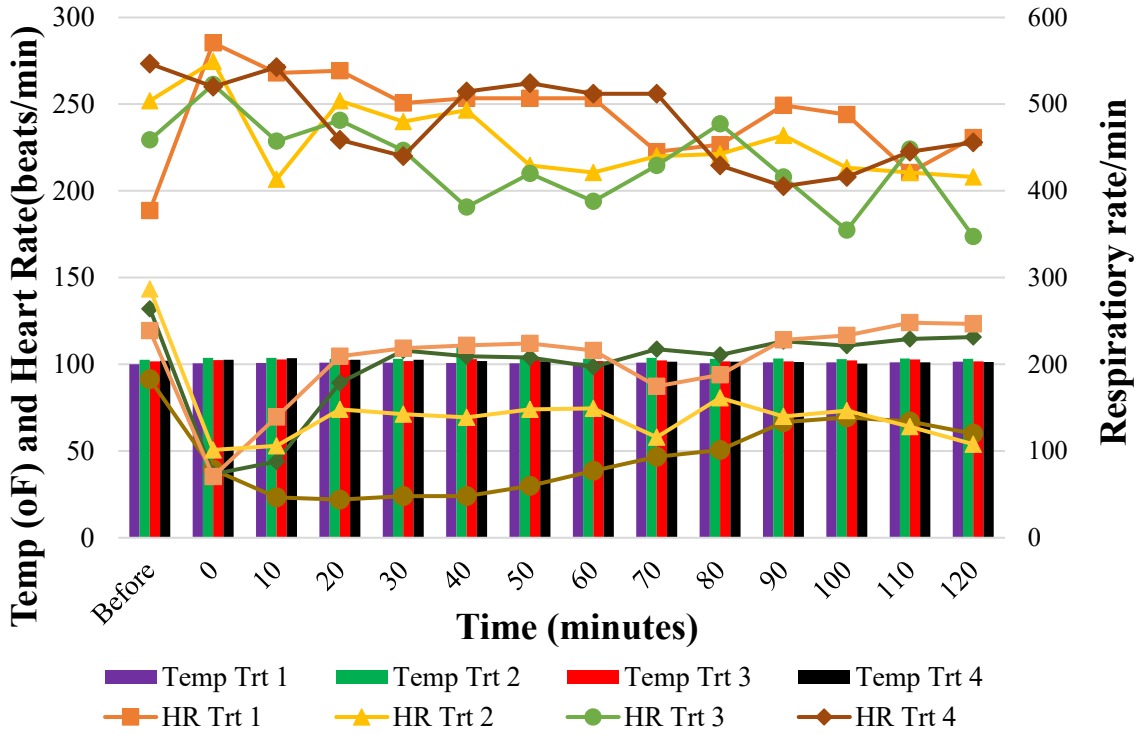

Figure 1: Graphical representation of Effect of different doses and combination of anesthetics on Heart rate (beats/min), respiratory rate (per min) and temperature (°F) of laboratory rabbit

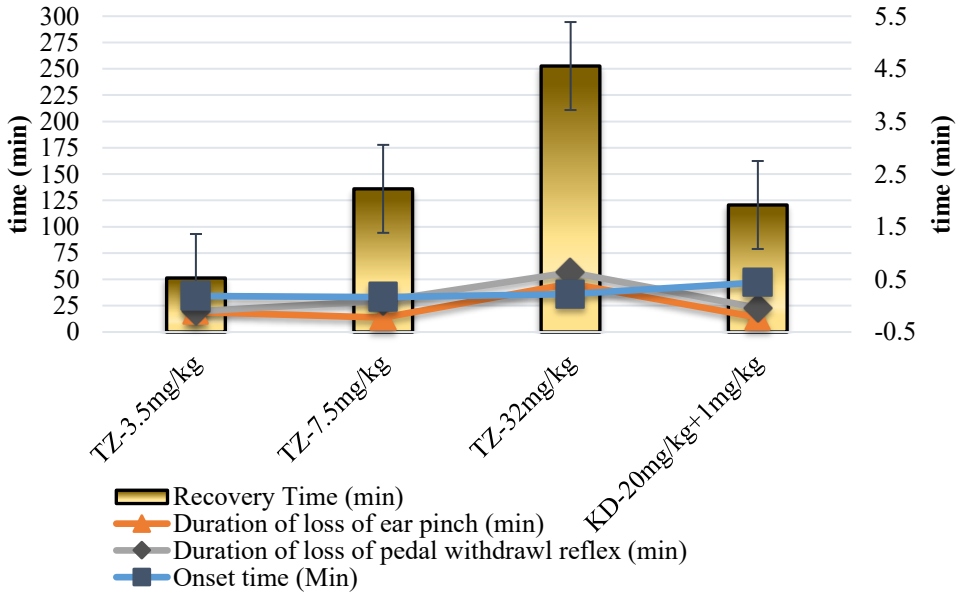

Figure 2: Graphical representation of Analgesic responses of different combination of anesthetics on laboratory rabbit

Histopathological Findings

Gross abnormalities were not seen in heart from rabbits of group A, B, C, and D. The most prominent histologic change was inflammatory cell infiltrates associate with focal cardiomyocytes necrosis and interstitial edema in group 1 of 3 group A and 1 of group B rabbits. Also, moderate congestion and hemorrhage with interstitial edema was also seen in 1 of group A rabbits whereas, mild congestion and hemorrhage was seen in myocardium of 1 of group D rabbits. There was a marked multifocal disintegration of myocardiocyte with mild interstitial edema and inflammatory cells in 1 of 3 group A rabbit's Moderate fatty degenerative change was seen in 1 of 3 group A and 1 of 3 group B rabbit. Mild fatty degenerative change in myocardium was observed in 1 of group C rabbit. Whereas, very mild degenerative change was seen in 2 of group C Rabbit. In mild cases, degenerative change and hemorrhage in myocardium was seen in 1 of group D and mild congestion in myocardium also seen in 1 of group D rabbit.

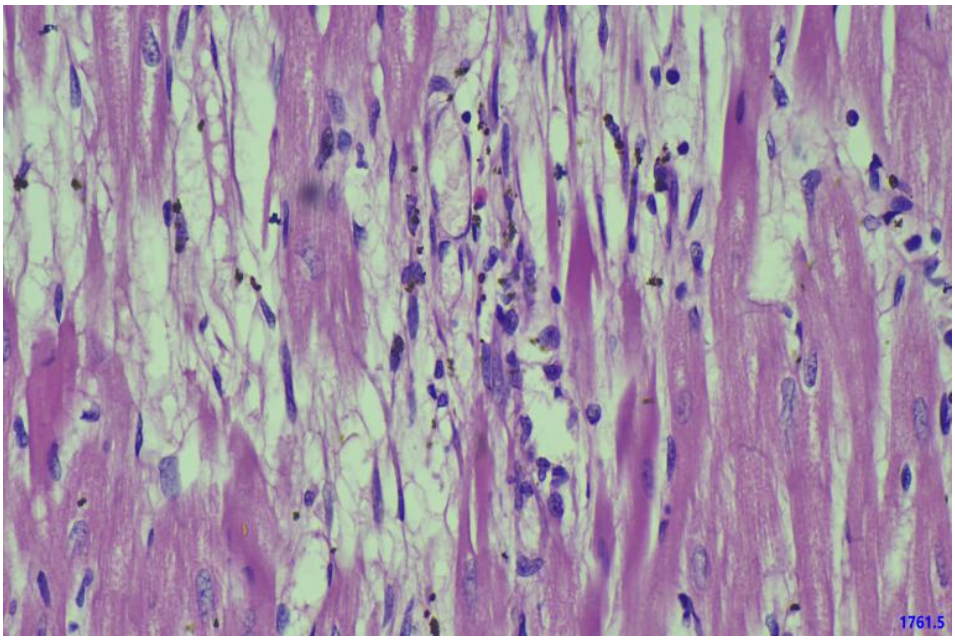

Figure 3: Inflammatory cell infiltrates associate with focal cardiomyocytes necrosis and interstitial (40x)

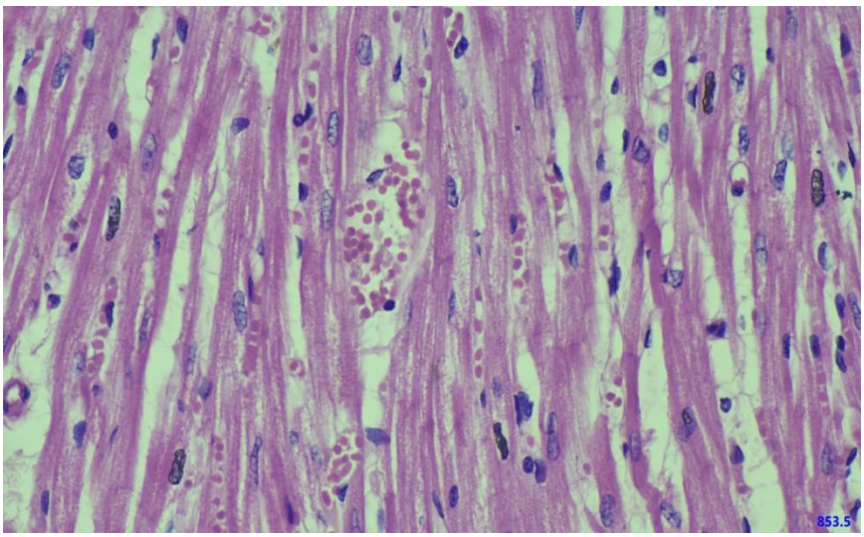

Figure 4: Moderate congestion and hemorrhage with interstitial edema (40x)

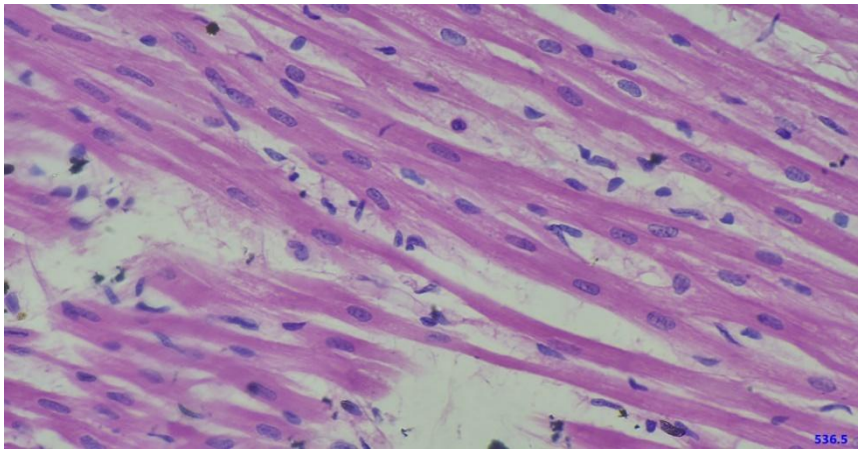

Figure 5: Multifocal disintegration of myocardiocyte with mild interstitial edema and inflammatory cells (40x)

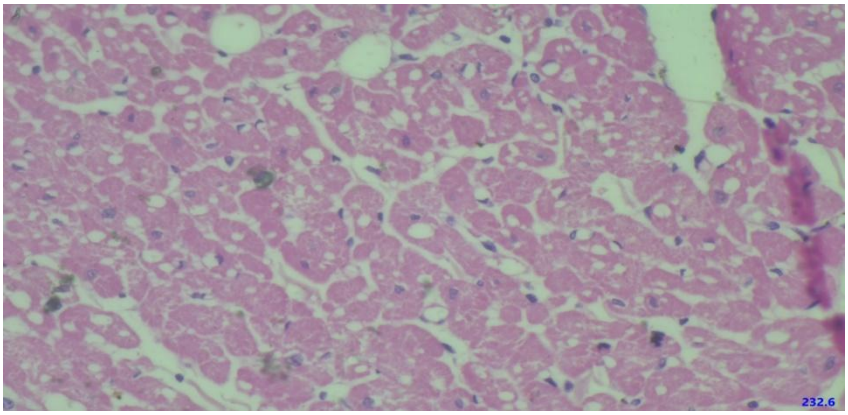

Figure 6: Moderate fatty degenerative changes in Myocardium (100x)

IV. DISCUSSION

Anesthetics can alter physiological parameters and affect the structure and function of organs, and these effects have been widely studied. However, information regarding infusion anesthetics in rabbits remains limited. In the present study, anesthetic depth was evaluated through reflex examinations without any surgical intervention. Previous studies reported induction times of 2.5–4.6 minutes following the administration of XK, TZ, and XTZ combinations at different doses (Oguntoye & Oke, 2015). Reported anesthesia durations include 67.7 minutes for TZ, 61.4–109.5 minutes for XK, and 104.6–125.5 minutes for XTZ (Dupras et al., n.d.).

In this study, induction was fastest in the TZ-7.5 mg/kg and TZ-3.5 mg/kg groups, followed by TZ-32 mg/kg and KD. The longest recovery time occurred in the TZ-32 mg/kg group (252.7 ± 20.4 min), followed by TZ-7.5 mg/kg (136.0 ± 15.6 min), KD-20 + 1 mg/kg (120.67 ± 2.33 min), and TZ-3.5 mg/kg (51.3 ± 10.3 min). Ogun Toye & Oke (2015) similarly reported longer recumbency in rabbits receiving KD (60 mg/kg) and AK (75 mg/kg) when compared to XK (32 mg/kg).

Mean heart rates across all TZ and KD groups remained within the normal physiological range for resting rabbits (130–325 beats/min; Harkness & Wagner, 1995), indicating that these anesthetic regimens are clinically safe. Previous reports observed myocardial necrosis and fibrosis in rabbits administered detomidine alone or combined with ketamine or diazepam (Hurley et al.), and age-related differences in drug metabolism may contribute to cardiac changes (Herman et al., 1996). The XTZ combination (5 + 15 mg/kg) has been shown to mildly reduce respiratory rate without significantly affecting heart rate (Kaya et al., 1996). Increased heart rate under tiletamine–zolazepam is attributed to sympathetic stimulation and reduced vagal tone, and both direct and indirect drug actions help maintain cardiovascular function (Hellyer et al., 1989). Telazol generally produces less profound cardiovascular depression than anesthetics such as pentobarbital and ketamine in rats and dogs (Ward et al., 1974), and offers rapid, smooth induction in ostriches (Lin et al., 1997).

All groups in the present study exhibited significant decreases in respiratory rate, with the most pronounced reduction in the TZ-32 mg/kg and KD-20 mg/kg groups. Previous studies have similarly demonstrated decreased respiratory rate with XK anesthesia (Lester et al., 2023; Mercatello, 1990). In contrast, lower-dose groups in this study experienced only slight reductions during the first 10–20 minutes, likely due to reduced

anesthetic dosage. The mean heart rates in all dose groups remained within the normal resting range (Martinic, 1995), further supporting the safety of these protocols.

Multiple studies have reported no significant changes in body temperature in rabbits anesthetized with XK (González Gil et al.), XTZ (Kaya et al., 2002), or KD (Topal et al., 2023), consistent with the present findings. Reports on the effects of TZ on heart and respiratory rates vary: some found significant alterations (Tannus et al., 2013), whereas others reported no difference compared to KD (Topal et al., 2023). Studies using different XK dosages (3–10 mg/kg xylazine with 10–50 mg/kg ketamine) consistently documented respiratory depression, bradycardia, and hypotension (González Gil et al.; Kılıç, 2004; Yanmaz et al., 2016), though some found no significant change in heart rate (Kaya et al., 2002). Increased respiratory rate observed with XK was attributed to anesthetic excitement (Oguntoye & Oke, 2015). Xylazine–TZ has also been reported to reduce respiratory rate without significantly affecting heart rate (Kaya et al., 2002), while higher-dose XTZ combinations can lead to respiratory and cardiovascular depression (Popilskis, 2015).

Overall, the marked decline in respiratory rate in the TZ-32 mg/kg and KD-20 mg/kg groups in the present study aligns with most previous findings (Topal et al., 2023; Oguntoye & Oke, 2015).

V. CONCLUSION

Varying degree of histopathological changes were observed in heart at different dose combination of TZ abd KD as mention above .The finding reported here suggest that cardiovascular lession are induced when TZ and KD combinations is administered as described here .But comparison to other doses ,the very mild degenerative changes were seen at TZ-3.5mg/kg b.wt which resulted in less damage then other group doses .Also, it results to the shortest recovery interval time after anesthetic induction. However, the organ changes don't show severe fluctuation in physiogical parameter.

As a result of our study, we believe that in comparison to the drug dose administered during experiment ,TZ-3.5 mg/kg can be safely administered as an intravenous infusion in healthy rabbits according to heart rate examination and histopathological examination.

REFERENCES

[1]. Brodbelt, D. (2009). Perioperative mortality in small animal anaesthesia. In *Veterinary Journal* (Vol. 182, Issue 2, pp. 152–161). https://doi.org/10.1016/j.tvjl.2008.06.011

[2]. Dupras, J., Vachon, P., Cuvelliez, S., & Blais, D. (n.d.). *Anesthesie du lapin de Nouvelle-Zelande utilisant les combinaisons tiletamine-zolazepam et ketamine-midazolam avec ou sans xylazine*.

[3]. Ghaffari, M. S., & Moghaddassi, A. P. (2010). Effects of ketamine-diazepam and ketamine-acepromazine combinations on intraocular pressure in rabbits. *Veterinary Anaesthesia and Analgesia*, *37*(3), 269–272. https://doi.org/10.1111/j.1467-2995.2010.00531.x

[4]. Gonzá Lez Gil, A., Illera, J. C., Silvá, G., & Illera, & M. (n.d.). *Effects of the anaesthetic=tranquillizer treatments on selected plasma biochemical parameters in NZW rabbits*.

[5]. Green, C. J., Knight, J., Precious, S., & Simpkin, S. (1981). Ketamine alone and combined with diazepam or xylazine in laboratory animals: a 10 year experience. In *Laboratory Animals* (Vol. 15).

[6]. Grint, N. J., & Murison, P. J. (2008). A comparison of ketamine-midazolam and ketamine-medetomidine combinations for induction of anaesthesia in rabbits. *Veterinary Anaesthesia and Analgesia*, *35*(2), 113–121. https://doi.org/10.1111/j.1467-2995.2007.00362.x

[7]. Hellyer Peter, Hubbell JAE, & Sally J. (1989). *Cardiorespiratory Effects of the Intravenous Administration of Tiletamine-Zolazepam to Dogs*.

[8]. Herman, E. H., Zhang, J., Chadwick, D. P., & Ferransb, V. J. (1996). Age dependence of the cardiac lesions induced by minoxidil in the rat. In *Toxicology* (Vol. 110). ELSEVIER.

[9]. Karasu, A., Altug, N., Aslan, L., Bakir, B., & Yuksek, N. (2018). Evaluation of the anesthetic effects of xylazine-ketamine, xylazine-tiletamine-zolazepam and tiletamine-zolazepam using clinical and laboratory parameters in rabbits. *Medycyna Weterynaryjna*, *74*(10), 646–652. https://doi.org/10.21521/mw.6119

[10]. Kaya U., A. N. , K. A. , K. B. (2002). Comparision of cardiovascular and respiratorik effects xtlazine

[11]. tiletamine-zolazepam and xylazine-ketamine anesthesia in rabbits. Vet. Cer. Derg. 2002, 8, 63-68.

[12]. Kiliç, N. (2004). *A Comparison between Medetomidine-Ketamine and Xylazine-Ketamine Anaesthesia in Rabbits*. https://journals.tubitak.gov.tr/veterinary

[13]. Lester, P. A., Martin, T. L., & Myers, D. D. (2023). Anesthesia and analgesia in rabbits. In Anesthesia and Analgesia in Laboratory Animals (pp. 357–391). Elsevier. https://doi.org/10.1016/B978-0-12-822215-7.00021-4

[14]. Oguntoye, C., & Oke, B. (2015). A Comparison of xylazine/ketamine, diazepam/ketamine and acepromazine/ketamine anaesthesia in Rabbit. *Sokoto Journal of Veterinary Sciences*, *12*(3), 21. https://doi.org/10.4314/sokjvs.v12i3.4

[15]. Saha, D. C., Saha, A. C., Malik, G., Astiz, M. E., & Rackow, E. C. (2007). *Comparison of Cardiovascular Effects of Tiletamine-Zolazepam, Pentobarbital, and Ketamine-Xylazine in Male Rats*.

[16]. Stasiak, K. L., Maul, D., French, E., Hellyer, P. W., & Vandewoude, S. (2003). *Species-Specific Assessment of Pain in Laboratory Animals*.

[17]. Topal, A., Gul Satar, N. Y., Ates, O., Uckan, E. M., Yavas, O., & Cangul, I. T. (2023). Comparison of the Effects of Ketamine-Diazepam, Tiletamine-Zolazepam and Propofol Infusion Anesthesia in Rabbits. *Kafkas Universitesi Veteriner Fakultesi Dergisi*, *29*(2), 137–144. https://doi.org/10.9775/kvfd.2022.28744

[18]. Wilson, R. P., Zagon/, I. S., Larach, D. R., Lang, C. M., Wilson, R. P., Zagon, I. S., Larach, D. R., & Cardiovascular, C. M. L. (1993). Cardiovascular and Respiratory Effects of Tiletamine-Zolazepam. In *Pharmacology Biochemistry and Behavior* (Vol. 44).

[19]. Yanmaz, L. E., Doğan, E., Okumuş, Z., Şenocak, M. G., Prastiwi, A., & Yildirim, F. (2016). Beyaz Yeni Zelanda Tavşanlarında vitamin C premedikasyonu sonrasında ksilazin-ketamin anestezisi. *Kafkas Universitesi Veteriner Fakultesi Dergisi*, *22*(1), 115–118. https://doi.org/10.9775/kvfd.2015.13998

[20]. Zhang, Z., Bai, H., Zhang, B., Shen, M., & Gao, L. (2022). Comparison of cardiorespiratory and anesthetic effects of ketamine-midazolam-xylazine-sufentanil and tiletamine-zolazepam-xylazine in miniature pigs. *PLoS ONE*, *17*(7 July). https://doi.org/10.1371/journal.pone.0271325