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Studies on electrocardiographic changes in xylazine-butorphanol and dexmedetomidine-butorphanol premedicated goats with tiletamine-zolazepam induction and total intravenous anaesthesia (TIVA) and partial intravenous anaesthesia (PIVA) protocol

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Abstract

The present study was conducted to evaluate electrocardiographic changes of xylazine, dexmedetomidine and their combination with butorphanol in tiletamine-zolazepam induced goats with isoflurane and tiletamine-zolazepam maintenance, which underwent various surgeries. The electrocardiograms were recorded in a standard base apex lead system. Twenty- four goats were studied using four distinct anaesthetic regimens, with six goats in each group. Anaesthetic protocols produced transient changes in the electrocardiographic indices. The electrocardiographic abnormalities in goats premedicated with xylazine and butorphanol after induction included first degree heart block in one animal and modest T-wave changes in a few animals. All of these changes were corrected when the animals recovered from anaesthesia. Goats premedicated with dexmedetomidine-butorphanol showed little electrocardiographic changes after being induced; only a few transitory T-wave abnormalities were seen, and no additional abnormalities could be determined. The P-wave, QRS, and T-wave changes in the electrocardiographic indices during the anaesthetic study, i.e., before premedication, post-induction, and post-recovery were transient and within normal physiological limits. Thus, premedication with dexmedetomidine-butorphanol or xylazine-butorphanol in lower doses in a multimodal balanced anaesthetic approach with tiletamine-zolazepam induction, followed by tiletamine-zolazepam maintenance with CRI or isoflurane maintenance in goats for various surgeries was safe.

Key words: *Electrocardiograph, premedicated goat, xylazine-butorphanol, dexmedetomidine-butorphanol*

Introduction

Electrocardiography is a diagnostic procedure that records the electrical activity of the heart over time. It also identifies irregularities in cardiac rhythm. Several researchers have employed the bipolar base apex lead using limb lead I in goats and it has been demonstrated to be a suitable lead since the ECGs they recorded had clear waves and complexes. Animal movement has a minimal impact on the recording (Rezakhani *et al*., 2004).

In the present study, goats were premedicated with xylazine, dexmedetomidine and butorphanol, while tiletamine-zolazepam and isoflurane were used as anaesthetic agents. Various researchers reported electrocardiographic changes/abnormalities when

xylazine and dexmedetomidine were administered in different species. Electrocardiographic changes like increased PR and QT intervals after xylazine administration (Kinjavdekar *et al.*, 1999), lengthened RR, QT, and QRS complexes after dexmedetomidine administration (Kumari *et al.*, 2017) and depression of the T-wave, biphasic T-wave and spike of the T-wave after tiletamine- zolazepam and xylazine anaesthesia (Rajankutty, 1995) were among them.

Abalos *et al.* (2016) reported ECG abnormalities such as atrial fibrillation, ventricular premature contraction, premature P waves, ventricular tachycardia, sinoatrial block, atrioventricular block, and left bundle branch block in tiletamine-zolazepam and xylazine treated goats. The authors also reported that lower doses of tiletamine and zolazepam caused lesser ECG abnormalities and arrhythmogenic effects.

However, there are few reports comparing the electrocardiographic changes in anaesthetised goats with multimodal protocols including PIVA and TIVA . Hence, this study was conducted to assess the electrocardiographic effects of various drug combinations, including dexmedetomidine-butorphanol-tiletamine-zolazepam-tiletamine- zolazepam (D-B-TZ-TZ), xylazine-butorphanol-tiletamine-zolazepam-tiletamine-zolazepam (X-B-TZ-TZ), dexmedetomidine-butorphanol-tiletamine-zolazepam-isoflurane (D-B-TZ-ISO) and xylazine-butorphanol-tiletamine-zolazepam-isoflurane (X-B-TZ-ISO) in goats undergoing various surgical procedures.

Materials and Methods

The study was conducted in 24 goats reported with various surgical affections like abdominal hernia, overgrown and pointing horns, fracture of long bones, gangrenous mastitis, etc. at Teaching Veterinary Clinical Complex, Mannuthy and University Veterinary Hospital, Kokkalai, Thrissur of Kerala Veterinary and Animal Sciences University, Kerala and selected for respective surgeries under general anaesthesia.

Experimental design

The animals were randomly divided into four groups that are *viz.*, Group-I (X-B-TZ-TZ), Group-II (D-B-TZ-TZ), Group-III (X-B-TZ-Iso) and Group-IV (D-B-TZ-Iso) based on the anaesthetic agents used, each group consisting of six animals. All the animals fasted for 18 hours, and water was withheld for eight hours before the anaesthesia. The clinical status of the animals was assessed by recording heart rate, respiration rate, rectal temperature, electrocardiographic study and by conducting haematological and biochemical examinations.

For the premedication, Group I and Group III animals received a combination of xylazine intravenously at the dose rate of 0.02 mg/kg body weight and butorphanol at the dose rate of 0.05 mg/kg body weight. Group II and Group IV received a combination of dexmedetomidine intravenously at the dose rate of 2.5 µg/kg body weight and butorphanol at the dose rate of 0.05 mg/kg body weight as premedication. In all the animals, induction was done with tiletamine-zolazepam at the dose rate of 2.5mg/kg body weight intravenously. In Group I and Group II, anaesthesia was maintained with tiletamine-zolazepam as a continuous rate of infusion (CRI) at the dose rate of 2.5mg/ kg/h. While in Group III and Group IV, animals were maintained with isoflurane in oxygen.

Electrocardiography (ECG) was recorded before premedication, 10 minutes after induction of general anaesthesia and immediately after recovery from anaesthesia using a Cardiart (6108T) ECG machine (BPL Medical Technologies). The ECG was recorded on a bipolar base apex lead using limb lead I. Animals were kept in a standing position while taking ECG before premedication and held in lateral recumbency while taking ECG after 10 minutes of induction and post-recovery. The alligator type electrodes were attached to the skin after applying ECG gel. The positive electrode of lead I (left arm) was attached to the skin at the point of the elbow. The negative electrode (right arm) was attached to the skin on the jugular furrow about the lower one-third on either side of the neck. The earthing electrode was attached away from these two electrodes. All the ECGs were obtained on a single channel ECG machine with a paper speed of 25mm/s and calibration of 10mm equal to 1 mV. A magnifying glass was used to measure the ECG traces (Varshney, 2020).

Results and Discussion

Due to the deep penetration of the Purkinje fibres in the myocardium of ruminants, the ECG in these species is primarily used to identify cardiac arrhythmias rather than cardiac chamber enlargement. Since a base apex lead possesses the characteristic electrocardiographic waves and complexes required for this task, it appears to be the best and most widely used lead for monitoring goats for cardiac arrhythmias (Rezakhani *et al.*, 2004).

In the study, the P wave was consistently positive in all ECG traces with no variation. The QRS complex was primarily negative. The T wave could have been positive, negative, or biphasic. The T wave was more variable in ruminants than in canines. Hence, it cannot be utilised as a marker for cardiac issues (Rezakhani *et al.*, 2004).

Analysis of morphologies of P, QRS, and T (Tables 1 and 2)

Table 1: ECG parameters showing P (mV). P (sec), QRS (mV), QRS (s) and T (mV)

Groups	Time points	P (mV)	P (s)	QRS (mV)	QRS (s)	T (mV)
Group I X-B-TZ-TZ	Before premedication	0.113 ± 0.009	0.043 ± 0.002	0.472 ± 0.03	0.052 ± 0.004	0.263 ± 0.043
	After induction	0.100 ± 0	0.046 ± 0.002	0.487 ± 0.046	0.058 ± 0.005	0.344 ± 0.081
	At recovery	0.105 ± 0.005	0.055 ± 0.006	0.515 ± 0.054	0.052 ± 0.004	0.385 ± 0.103
Group II D-B-TZ-TZ	Before premedication	0.097 ± 0.003	0.048 ± 0.007	0.567 ± 0.192	0.073 ± 0.018	0.233 ± 0.054
	After induction	0.100 ± 0	0.048 ± 0.007	0.658 ± 0.169	0.067 ± 0.007	0.258 ± 0.051
	At recovery	0.100 ± 0	0.048 ± 0.007	0.658 ± 0.171	0.062 ± 0.007	0.267 ± 0.054
Group III X-B-TZ-Iso	Before premedication	0.130 ± 0.016	0.052 ± 0.007	0.555 ± 0.044	0.06 ± 0.005	0.18 ± 0.031
	After induction	0.116 ± 0.017	0.046 ± 0.003	0.52 ± 0.08	0.06 ± 0.007	0.24 ± 0.042
	At recovery	0.132 ± 0.02	0.060 ± 0.005	0.59 ± 0.093	0.06 ± 0.005	0.21 ± 0.033
Group IV D-B-TZ-Iso	Before premedication	0.108 ± 0.008	0.048 ± 0.004	0.542 ± 0.125	0.075 ± 0.018	0.258 ± 0.071
	After induction	0.113 ± 0.018	0.053 ± 0.006	0.7 ± 0.167	0.063 ± 0.008	0.288 ± 0.048
	At recovery	0.1 ± 0	0.041 ± 0.001	0.667 ± 0.117	0.065 ± 0.007	0.258 ± 0.049
Normal Reference Range Varshney, (2020)		0.1-0.2	0.04-0.06	0.40-1.4	0.06-0.1	0.10-0.70

Table 2: ECG parameters showing T (s) PR (s), T(s), ST (s), QT (s) and HR (bpm)

Groups	Time points	T (s)	PR (s)	ST (s)	QT (s)	Heart rate
Group I X-B-TZ-TZ	Before premedication	0.072 ± 0.005	0.117 ± 0.003	0.173 ± 0.027[b]	0.391 ± 0.016[b]	107.31 ± 13.26
	After induction	0.075 ± 0.005	0.135 ± 0.008	0.228 ± 0.019[a]	0.472 ± 0.032[a]	78.89 ± 2.59
	At recovery	0.087 ± 0.011	0.125 ± 0.007	0.212 ± 0.014[ab]	0.484 ± 0.036[a]	90.27 ± 7.73
Group I D-B-TZ-TZ	Before premedication	0.122 ± 0.033	0.153 ± 0.019	0.153 ± 0.012	0.407 ± 0.036[b]	82.79 ± 7.55
	After induction	0.13 ± 0.037	0.167 ± 0.024	0.18 ± 0.027	0.480 ± 0.043[a]	74.5 ± 4.88
	At recovery	0.131 ± 0.043	0.173 ± 0.03	0.2 ± 0.031	0.487 ± 0.019[a]	76.72 ± 7.54
Group III X-B-TZ-Iso	Before premedication	0.06 ± 0.007	0.104 ± 0.008[b]	0.160 ± 0.018[b]	0.384 ± 0.030[b]	115.83 ± 12.66
	After induction	0.08 ± 0.01	0.128 ± 0.007[a]	0.208 ± 0.019[a]	0.472 ± 0.016[a]	81.92 ± 3.96
	At recovery	0.084 ± 0.013	0.112 ± 0.007[a]	0.192 ± 0.016[a]	0.424 ± 0.030[ab]	105.63 ± 8.38
Group IV D-B-TZ-Iso	Before premedication	0.077 ± 0.013	0.133 ± 0.013	0.193 ± 0.019[b]	0.407 ± 0.019[b]	87.01 ± 4.21
	After induction	0.09 ± 0.009	0.147 ± 0.008	0.220 ± 0.031[b]	0.493 ± 0.042[a]	80.21 ± 3.86
	At recovery	0.072 ± 0.009	0.153 ± 0.016	0.260 ± 0.031[a]	0.500 ± 0.027[a]	79.81 ± 6.51
Normal Reference Range Varshney, (2020)		0.07-0.16	0.07-0.16	0.16-0.4	0.22-0.56	60-130

The mean values of the P wave amplitude (mV) and P wave duration (s) did not differ significantly (P□0.05) within groups as well as between the groups at various time points, i.e., before premedication, post-induction, and post-recovery. They fluctuated within the normal physiological limits, 0.1-0.2 mV and 0.04-0.06 s, respectively (Varshney, 2020). The mean values of the QRS amplitude (mV) and duration (s) did not differ significantly within groups as well as between the groups at various time points, i.e., before premedication, post-induction, and post-recovery. The variations in QRS amplitude (mV) and duration (sec) observed in all the treatments were within the normal physiological limits (0.40- 1.4 mV and 0.06-0.10 s).

The mean values of the T amplitude (mV) and T duration (s) did not differ significantly within groups as well as between the groups at various time points. The variations in T amplitude (mV) and T duration observed in all the treatments were within the normal physiological limits (0.10-0.70mV and 0.07-0.16 s) (Varshney, 2020).

The P wave, QRS complex and T wave during the anaesthetic study did not change, indicating that xylazine, dexmedetomidine, butorphanol, tiletamine-zolazepam and isoflurane treatment in multimodal anaesthetic approach had no impact on atrial depolarisation, ventricular depolarisation or ventricular repolarisation. Similar findings were reported by Hamed *et al.* (2015),

who studied dexmedetomidine in goats and Sarchahi *et al.* (2009), who studied xylazine in dogs.

The mean values of the heart rate (HR) (beats / min) did not differ significantly within and between groups at various time points. A non-significant decreasing trend in heart rate after tiletamine-zolazepam induction was found in all groups. Half of the study animals were premedicated with xylazine- butorphanol and half were given dexmedetomidine-butorphanol. The reduction in heart rate in xylazine and dexmedetomidine premedicated goats could be attributed to increased vagal tone and decreased sympathetic outflow from the central nervous system (CNS). Similar findings were reported by Kinjavdekar *et al.* (1999) in goats, by Singh *et al.* (2005) in calves after administration of xylazine, and by Kumari *et al.* (2017) in goats after administration with dexmedetomidine, respectively. However, at the time of recovery, heart rate was showing an increasing trend as tiletamine-zolazepam indirectly inhibits the neuronal re-uptake of catecholamines, especially norepinephrine; thereby, increasing heart rate (Pugh and Baird, 2020). All the fluctuations in the heart rate at various observation points were within normal physiological limits (Varshney, 2020).

Mean values of the PR interval (mV) did not differ significantly between the groups at various time points. PR interval was non-significantly increased after 10 minutes of induction in Group I (X-B-TZ- TZ), II (D-B-TZ-TZ), and IV (D-B-TZ-Iso). In contrast, a significant increase was noticed in Group III (X-B-TZ-Iso) after induction. The values that fluctuated during the study were within normal physiological limits (Varshney, 2020). The study found that the heart rate was reduced after induction and simultaneously the PR interval increased as HR and PR intervals are inversely proportional. Similar findings were reported by Filippi (2011) in canines.

The mean values of S-T segment (sec) did not differ significantly between the groups at various time points. There was a significant increase in the value in Groups I, III, and IV, but a non-significant increase was noticed in Group II. The variations in S-T segment values observed in all the treatments were within the normal physiological limits. A similar finding of an increase in the S-T segment was reported by Peshin *et al.* (1979) in dogs following the administration of xylazine.

The mean values of the Q-T interval (sec) did not differ significantly between the groups at various time points. A significant increase in the Q-T interval after 10 min of induction was noticed in all the groups. There was no significant difference found in the Q-T interval noticed at 10 min after induction and recovery. Still, all the variations in the Q-T interval were within normal physiological limits (0.22-0.56 sec) as reported by Varshney (2020). Similar findings were reported by Hamed *et al.* (2015) after the administration of dexmedetomidine in goats.

Electrocardiographic alterations occurred in ECG traces during the study

After induction of anaesthesia, the following electrocardiographic alterations were observed in different groups and were as follows:

In Group I, sinus rhythm was found in all the animals. T wave alterations like tall T were noticed in three animals, biphasic T in one animal, and reverse T wave in one animal. The deviation and inconsistency of the T wave might be a result of transient changes in the acid-base balance due to carbon dioxide retention (Peshin and Kumar 1979).

Changes in the polarity of the T wave and an increase in the amplitude of the T wave and inverted T wave noticed might be due to the anesthetic induced myocardial hypoxia (Tilley,1985), similar findings were noticed by Rajankutty (1995) in dogs after the administration of xylazine-tiletamine-zolazepam.

In Group II, sinus rhythm was found in all the animals after induction. T wave alterations like tall T were noticed in two animals, biphasic T in two animals, notched T in one animal and reverse T wave in one animal. All the changes in the T wave are in accordance with the studies reported by (Tilley 1985) and Rajankutty (1995) and might be due to the anesthesia induced myocardial hypoxia. All the changes in the T wave became normal at the time of recovery. At the time of recovery, T wave changes like reverse T, notched T, and biphasic T were noticed in one animal each and such changes in T wave were recorded

by Rajankutty (1995) and found to be normalised after 24 hours of the observation period in dogs administered with tiletamine-zolazepam.

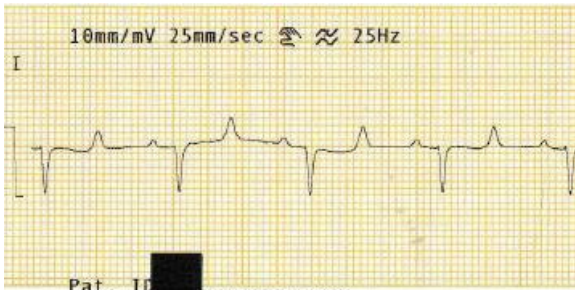
In Group III, sinus rhythm was found in all the animals after induction. Any other alterations were not noticed during induction and recovery except for the first-degree atrioventricular block in one animal, as the PR interval was found to be 0.24 seconds (more than 0.16 seconds) after induction, and the same was continued till recovery. Similar findings were recorded by Abalos *et al.* (2016) after the administration of tiletamine-zolazepam in goats. Similar findings of ECG alterations, first-degree heart block/atrioventricular block, was reported by Ramanakutty (2008) in dog after premedication with xylazine.

In Group IV, sinus rhythm was found in all the animals except for a few changes in the T wave after induction. ECG traces remained without any other alterations at all observations. T wave alterations like tall T were observed in two animals. In contrast, biphasic T was noticed in one animal, notched T was observed in one animal and reverse T wave was noticed in one animal. Carvalho *et al.* (2019) found similar T-wave changes after the administration of dexmedetomidine in cats, Rajankutty (1995) also reported similar changes after the administration of tiletamine zolazepam with xylazine in dogs. At the time of recovery, no changes were noticed in the ECG.

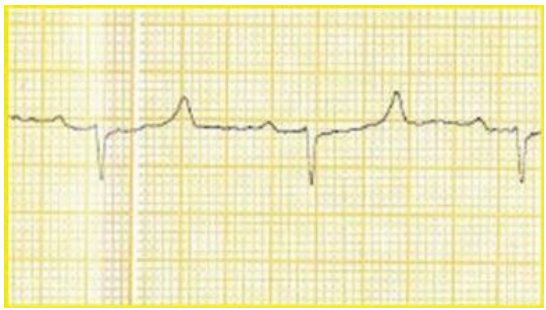
Conclusion

All anaesthetic combinations were safe in goats, producing only temporary and transient changes in the electrocardiographic indices. The recording of ECG before pre-medication and ECG changes after 10 minutes of induction and recovery helped to identify the exact nature of rhythm and heart rate under different anaesthetic protocols. Goats that had been premedicated with dexmedetomidine-butorphanol showed little electrocardiographic changes after being induced with tiletamine-zolazepam, only a few transitory T-wave abnormalities were seen, and no additional abnormalities could be determined. The results of the ECG recording indicated that life threatening myocardial abnormalities were absent with all four anaesthetic regimens under study.

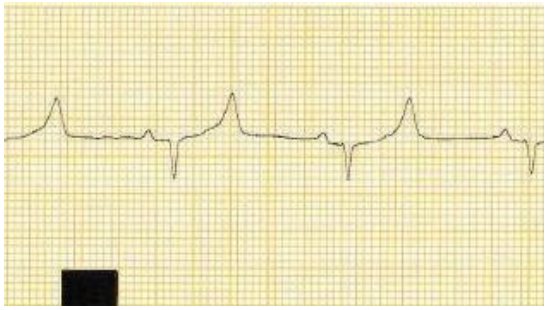
Plate 10. Electrocardiogram



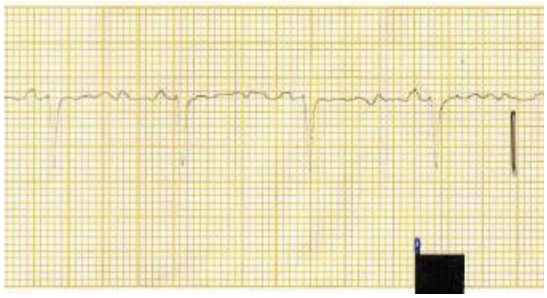
Normal electrocardiogram



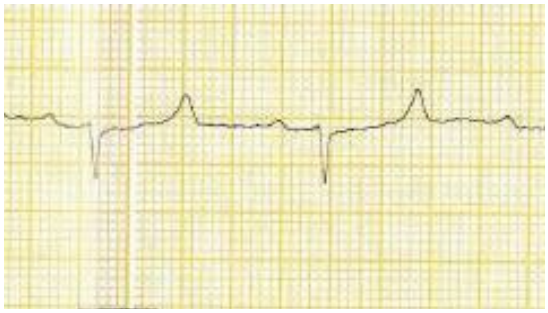
E: Increase in QT Interval (X-B-TZ-TZ)



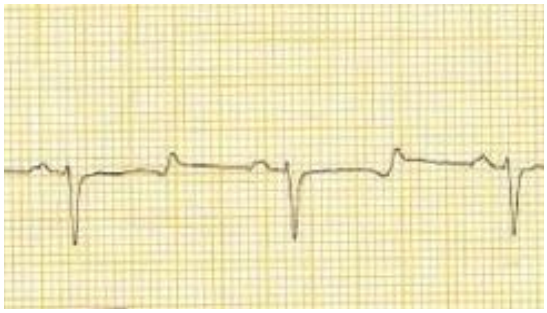
B: Tall T wave (X-B-TZ-TZ)



C: Reverse T wave (D-B-TZ-TZ)



F: 1st-degree heart block- (X-B-TZ-Iso)



G: Biphasic T wave (D-B-TZ-Iso)

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