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The Effects of Acepromazine, Xylazine and Butorphanol in Different Combinations on Electrocardiographic Measurements in Horses

A. Rajput, V. Malik, R.Vijay, H. Gangwar, R. P. Pandey

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Abstract Electrocardiogram is a good tool for monitoring the physiological status of animals and human during anesthesia. Objective of this study is to evaluate electrocardiographic effect of acepromazine, xylazine and butorphanol in different combinations during standing sedation in horses.

Keywords Acepromazine, Xylazine, Electrocardiogram, T-wave, ECG.

A. Rajput*
MVSc Student,
e-mail: abhishekvet08@gmail.com

V. Malik
Assistant Professor
e-mail: vickeyvet@gmail.com

R. Vijay
MVSc Student
e-mail: rohanvijay92@yahoo.com

H. Gangwar
MVSc Student
e-mail:drharigangwar009@gmail.com

R. P. Pandey
Professor and Head
e-mail:dr.rudrapandey@gmail.com

Department of Veterinary Surgery and Radiology, College of Veterinary Science and Animal Husbandry, DUVASU, Mathura 281001, UP, India
*Corresponding author

Introduction

The electrocardiogram (ECG) is a tool of great importance in equine practice. It informs diagnosis, provides information on prognosis and safety to ride and guides therapeutic interventions (Ruth Morgan 2012). Numerous studies have been carried out on electrocardiography in horses. The electrocardiogram is a recording of difference of electrical potential generated by the waves of the depolarization and repolarization traversing atrioventricular myocardium. These electrical potential projects to the point on the body surface. The normal electrocardiogram is composed of a P-wave, a QRS complex and T-wave, the QRS complex is composed of three separate waves the Q-wave, the R-wave, and the S-wave.

Electrocardiography is the ultimate diagnostic tool, relatively cheap and the know-how of a good quality recording is mandatory for a correct diagnosis (Verheyen et al. 2010). It is an important clinical diagnostic method to investigate the cardiac function of sports horses. Beside the standard peripheral leads, similar to those used for humans and dogs, some modified systems have been introduced in practice to measure cardiac biopotentials (apex/base lead). This lead is particularly suitable for tracking the heart rhythm of horses (Bonagura and Reef 2004).

Xylazine is used in veterinary medicine for sedation, anesthesia, and analgesia. At a single recommended dose rate, xylazine has variable and consid-

erable secondary effects on cardiovascular system especially cardiac arrhythmia in horses (Meyer and Maurer 2013). Acepromazine (ACP), a phenothiazine (PHE) commonly used in horses as a sedative agent in preanaesthetic protocols (McKelvey and Hollingsthead 2003), or in the treatment of laminitis has peripheral hemodynamic effects in horses : It induces an increase in the blood flow and has a concomitant vasodilatory effect (Peters et al. 2009). Undesirable effects of ACP are particularly prominent and may become life-threatening when horses suffer from hypotension, anemia, or dehydration (McKelvey and Hollingshead 2003). Accpromazine has also immunomodulatory, antioxidant and anti-inflammatory action (Sandersen et al. 2011). Butorphanol is commonly used in equine medicine and is considered an efficacious and safe visceral analgesic in adult horses which causes analgesia, respiratory modulation and cardiovascular depression (Boscan et al. 2006).

This experimental study was undertaken to determine the effect of intravenous (IV) administration of xylazine in combination with acepromazine and butorphanol on cardiac arrhythmia using EGG in horses.

Materials and Methods

Study was conducted on 24 adult horses of either sex weighing 200 to 400 kg presented for various surgical procedures. These animals were divided into four groups viz. A, B, Cand D comprising six animals in each group. The animals of group A received an intravenous bolus of mixture of acepromazine [Ilium acepril-10 injection (10mg/ml), Troy laboratories PTY. Limited, 35 Glendenning RD Glendenning new 2761 Australia (@ 0.04 mg/kg)] + butorphanol [Butrum (1 mg/ml), Astro Pharmaceutical Pvt Ltd. Mandideep dist. Raisen (MP) (@ 0.02 mg/kg)].Animals of group B received a mixture of xylazine [Xylazin (20 mg/ml), Indian immunologicals Limited, Stanex drugs and chemicals Pvt Ltd, Hyderabad @ 0.5 mg/kg)] + butorphanol (@ 0.02 mg/kg) as an intravenous bolus. Animals of group C received an intravenous bolus of a mixture of acepromazine (@ 0.04 mg/kg) + xylazine (@ 0.5 mg/kg). Animals of group D were administered with a cocktail of acepromazine (@ 0.03 mg/kg) + xylazine (@ 0.5 mg/kg) and butorphanol (@ 0.02 mg/kg), Intravenously. All these drugs weremixed in the same syringe and administered slowly through the intravenous catheter placed in jugular vein.

Horses were fasted for 8—12 h pre-operatively, but water was offered until pre-anaesthetic medication was given. The animals were weighed before administration of any drug using a large animal weighing machine. Rectal temperature, heart rate and respiratory rate were measured, heart and lungs were auscultated, and mucous membranes and skin turgor were evaluated before study. The skin at the site of intravenous injection i.e. left side of jugular veinwas shaved and aseptically prepared for injection before 20 min of the start of administration of drugs. Subsequently, an 18 gauge intravenous catheter was inserted percutaneously into the jugular vien and fixed with an adhesive. Administration of normal saline solution was started @ 20 drops per minute just to maintain the potency of catheter and the animal was left undisturbed for a period of 20 minutes. All the procedures were conducted in a separate and quite operation theater. The modified ambulatory standard base-apex lead for large animals was applied. Briefly, the clips of electrodes were fixed on the skin after shaving the hair and application of electrodes paste or acoustic gel. In the base-apex lead, the (black) electrode serves as a reference electrode for ECG and it was placed in the right side in front of the scapula, while the positive (green) electrode was placed on the left 5^{th} intercostal space over the apex beat area of the heart, caudal to left elbow, at the level of olecranon process while the negative (red) one was placed on the right side of thorax at 3^{th} intercostal space over the base of the heart behind the right elbow electrocardiograms were recorded by using non-invasive multiparameter monitor (Modelstar (55) L & T Pvt India Limited, Saki Vihar Road, Mumbai) at 1mV and 25 mm/sec paper speed.

The electrocardiograms were analyzed for the duration and amplitude of P-wave, QRS complex, T-wave and duration of PR and QT intervals and rhythm. The ECG and HR were recorded before (0 minutes) and at 15,30,45, 60 and 90 minutes after administration of each drug combination.

Results and Discussion

Electrocardiography in clinical practice is the recording at the body surface of electrical fields generated by heart. Specific wave forms represent stages of myocardial depolarization and repolarization.

P-wave

P-wave can be biphasic, bifid or simple positive and changes often with HR. At slower HR the P-wave is often bifid with the first peak representing the depolarization of the right atrium and the second peak originating from the left atrium (Verheyen et al. 2010).

When the HR changes, the P-wave morphology often changes as well, and even successive p-waves are not always identical in the normal horses. In the present study the values of amplitude and duration of P-wave remained within normal physiological limits and in most of the cases P-wave was of bifid configuration which represents slow heart rate. A non significant increase in P-wave with fluctuating trend around the baseline value was recorded among the different groups at different time intervals as well as in between different groups at different time intervals (Figs 1, 2). In contrary to this, a slight decrease in atrial depolarization area after medetomidine-butorphanol administration was reported in male buffaloes (Malik et al. 2011). Xylazine is known to cause major changes in hemodynamic and cardiac conduction system. In the present study no arrhythmogenic effects were noticed with the use of xylazine, acepromazine, and butorphanol.

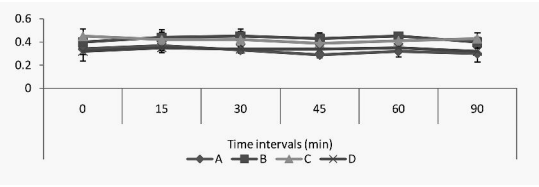

Fig. 1. Amplitude (mV) of P-wave recorded in different groups of animals at different time intervals.

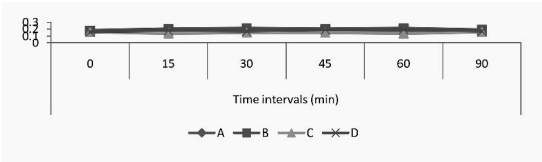

Fig. 2. Duration (sec) of P-wave recorded in different groups of animals at different time intervals.

QRS complex

The next detectable change is the depolarization of the ventricles which gives rise to the QRs complex that shall have duration of <0.14 seconds. The Q-wave is the first negative deflection, the R-wave is the first positive deflection and the S-wave is first negative deflection following the R-wave (Cunningham and Klein 2007), Verheyen et al. 2010). In the present study amplitude and duration of QRS complex remined within normal physiological limits and showed a fluctuating trend around the baseline values. However, slight increase in amplitude of QRs complex was reported in all the groups of animals at different time intervals (Figs. 3, 4).Similar finding has been reported after medetomidine administration in goats (Huger et al. 1998). In contrary to this slight decrease in amplitude of QRS complex was reported afteradministration of medetomidine-butorphanol in buffaloes (Malik et al. 2011).

PR interval

PR interval reflects the slow conduction through AV node and changes in interval are dependent on conduction velocity between the SA node and AV con-

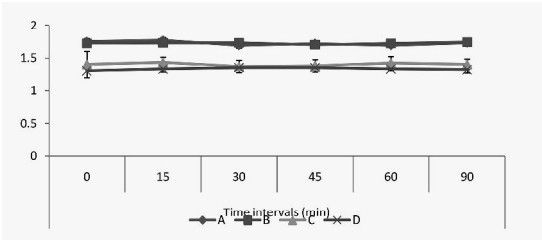

Fig. 3. Amplitude (mV) of QRS complex recorded in different groups of animals at different time intervals.

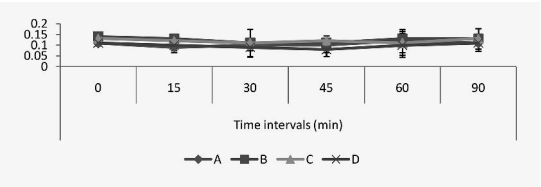

Fig. 4 Duration (sec) of QRS complex recorded in different groups of animals at different time intervals.

duction system and variation in PR interval may occur with alterations in vagal tone or secondary to presence of ectopic beats causing dissociation of atrial and ventricular activity (Tilley 1985). A fluctuating trend in PR interval was recorded in animals of all the groups at different time intervals. However, it remained within normal physiological limits (Fig. 5). The PR interval was closely associated with advanced left atrium remodeling due to atrial fibrillation (Park et al. 2014). In contrary to this statement, in the present study a decrease in PR interval was noticed during the observation period in comparison to baseline values.

QT interval

The QT interval, from beginning of the QRS complex to the end of the T-wave, is currently the only routinely used measurement of the ventricular repolarization (Haarmark et al. 2010). A fluctuating trend around baseline in QT interval was recorded in animals of all the groups at different time intervals except in B group, where a significant decrease in QT interval was noticed at middle of observation

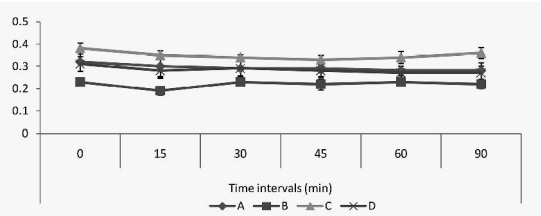

Fig. 5 Duration (sec) of PR interval recorded in different groups of animals at different time intervals.

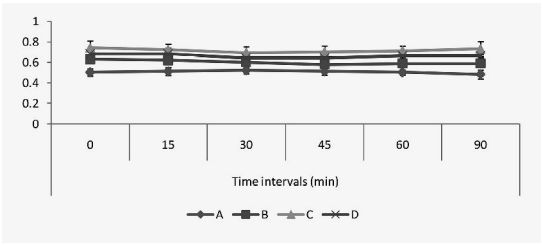

Fig. 6 Duration (sec) of QT interval recorded in different groups of animals at different time intervals.

period in comparison to baseline value, however, it remained within normal physiological limits. In the present study a non significant increase in QT interval was reported in a group at 15 min and remained so up to 45 min (Fig. 6). Similar finding has also been reported in buffaloes after medetomidine-butorphanol administration (Malik et al. 2011). The QT interval is negatively correlated with HR, leading to a decrease in the interval when the HR increases (Rajappan et al. 2003).

T-wave

The depolarization is followed by a repolarization of the ventricles and it is seen as the T-wave on the the ECG. The direction of the repolarization decides if the deflection is negative or positive. The morphology of the T-wave can be very different in horses and is particularly dependent on HR (Verheyen et al. 2010). A fluctuating trend around baseline in amplitude and duration of T-wave was recorded in all the groups of animals at different time intervals (Figs. 7, 8). However, it remained within normal physiological limits.

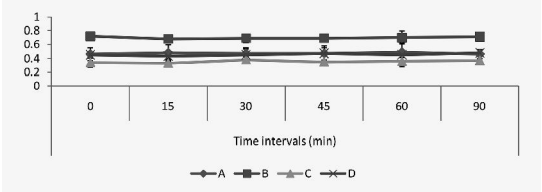

Fig. 7 Amplitude (mV) of T-wave recorded in different groups of animals at different time intervals.

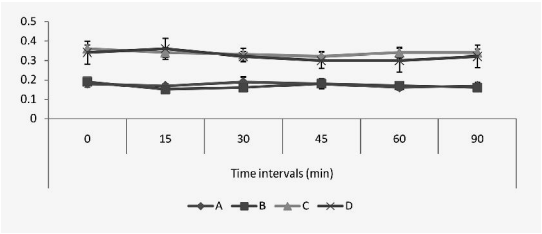

Fig. 8 Duration (sec) of T-wave recorded in different groups of animals at different time intervals.

Electrocardiogram findings in the study indicates that none of the sedative combination used in the present study produced any serious deleterious effect indicating their safety on various vital organ functions; hence all of these sedative drug regimens can safely be used in routine clinical cases of surgery of short duration under field conditions.

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