

Theses of doctoral (PhD) dissertation

Basic feasibility studies on interventional cardiology in horses

Szilvia Kovács, DVM

Supervisor: Zoltan Bakos *Ph.D., DipECEIM, MRCVS*



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Introduction and objectives

In horses, both physiological and pathological cardiac arrhythmias occur. Pathological cardiac arrhythmias can develop primarily as conductive disorders or secondarily as a result of changes in the structure of the heart, metabolic and endocrine disorders, systemic inflammation, low blood pressure, bleeding, anaemia, ischaemia, toxicosis, and various drug effects. The examination of arrhythmias is particularly important due to the haemodynamic changes that result from them (reduced blood pressure, decreased flow or perfusion) and the development of electrical instability (fibrillation, sudden cardiac death).

The cardiac rhythm of horses has been studied using electrocardiography (ECG) since the 1910s. The first electrocardiogram obtained from a horse was published in 1913. From the 1960s, with the aid of radiotelemetry devices, it became possible to record electrocardiograms from horses during exercise and by the 1980s, extensive knowledge was available regarding the physiological and pathological rhythm disorders in horses. Besides pharmacological and transvenous electrical cardioversion (TVEC), interventional methods have been developed in horses lately. There are a lot of technical issues that cause difficulties in the adaptation of human interventional methods in horses. The main differences are the larger size of the equine thorax and heart and the dissimilarities in the electrical properties of the conduction system in the heart.

Three topics are covered by this dissertation with the aims as follows.

Chapter I: in this chapter we discuss our own experiences with pharmacological cardioversion in two different arrhythmias, highlighting the importance of developing interventional cardiology methods in horses.

Chapter II: insertable cardiac monitors are often implanted to diagnose temporary arrhythmias, following catheter-based interventions to detect the possible recurrence of arrhythmias or to differentiate between neurological and cardiac disease in horses with syncope. In this feasibility study, we validated an implantable cardiac monitor in horses by concurrently using the internationally accepted Televet 100 telemetric and Holter ECG device (Jorgen Kruuse A/S, Langeskov). We investigated the development of short- and long-term complications as well as the diagnostic capabilities of the device in horses used in different disciplines.

Chapter III: as electrophysiological studies and catheter-based interventions in horses have been developing, an extensive comprehension of the histological properties of the equine heart has become necessary. This study aimed to investigate the conduction system of the pulmonary veins and their antrum with special attention to the myocardial sleeve using anatomical, histological and immunohistochemical methods. We aimed to identify adrenergic and non-adrenergic nerves, and we investigated cardiac gap junction proteins (connexins) in the equine heart as described previously in humans.

Chapter I

Treatment of atrial fibrillation in horses with orally administered quinidine sulphate.

Case reports

Atrial fibrillation is a relatively common and significant arrhythmia in horses, but the Hungarian literature lacks the information about its clinical presentation, diagnosis and therapy. The aim of our study was to present five cases of atrial fibrillation treated with orally administered quinidine sulphate. Five adult horses with suspected atrial fibrillation based on cardiac auscultation were referred for further investigation and therapy. Four of them showed exercise intolerance as well. Based on previous physical examinations, haematology and biochemistry, systemic diseases were excluded. On presentation, all horses were bright, alert and responsive, and they did not show signs of congestive heart failure. Atrial fibrillation was confirmed by resting electrocardiography using base-apex lead in all cases. Cardioversion with oral quinidine sulphate, administered via a nasogastric tube was attempted in four cases. This treatment was successful after two or three doses in two horses which remained in sinus rhythm until discharge from the hospital. Follow-up electrocardiography four to eight weeks later revealed sinus rhythm in both cases. Our findings highlight the importance of performing cardiac auscultation and ECG on horses with exercise intolerance.

Successful treatment of ventricular tachycardia with oral propranolol in three horses

Cardiac arrhythmias are relatively common in horses, but ventricular tachycardia is infrequent, therefore limited information is available about its therapy in the Hungarian literature. The aim of our study was to present three cases of ventricular tachycardia treated successfully with orally administered propranolol. Three horses with elevated heart rate and colic like signs were referred to our equine clinics for further investigation and therapy. After excluding gastrointestinal and systemic diseases, uniform ventricular tachycardia was confirmed by resting electrocardiography using base-apex lead. Cardioversion in all cases was started with lidocaine first administered in bolus, then as a continuous rate of infusion. This treatment did slow the rate temporarily but was unable to convert the rhythm. As soon as the continuous rate infusion was withdrawn, a quick and spontaneous return to a marked tachycardia occurred. Therefore, following human literature and reported dose rates in horses, propranolol was administered orally. This therapy subsequently led to conversion to sinus rhythm. All horses

received crystalloid fluids intravenously and other supportive treatment. Intravenous dexamethasone sodium phosphate was also given to two animals. After the conversion and successful recovery, horses were discharged, and the oral propranolol therapy was continued at home for different duration between eight days and one month. Follow-up cardiac examination four to eight weeks later revealed sinus rhythm in all cases. Our findings highlight the importance of performing ECG on horses with resting tachycardia exceeding 70-80/beats per minute.

Chapter II

Long-term use of an implantable loop recorder for ECG recording in horses

Potential arrhythmias recorded by cardiac monitors using the built-in human algorithm are as follows: number of total episodes, ventricular tachycardia, asystole, bradycardia, atrial tachycardia, atrial fibrillation, and the percentage of time spent in atrial tachycardia or atrial fibrillation. Long-term use of an insertable cardiac monitor (loop recorder) has been reported in horses earlier, however the accurate role as a diagnostic tool is still unclear. The aim of the present study was to investigate the long-term applicability of the Reveal XT cardiac monitor for recording cardiac arrhythmias in adult horses. In our study, the loop recorder was implanted in 12 horses under standing sedation. The median data recording duration for the population was 1169 days. The number of false positive detections of asystole and bradycardia was extremely high for all horses. Regarding atrial fibrillation, there were false positive detections in five horses and false negative detection in one horse. The present study showed that long-term use of the Reveal XT cardiac monitor is feasible, well-tolerated, and the devices worked reliably, without complications. The human algorithm could not be used for automatic detection of arrhythmic episodes in the study population. The device could detect atrial fibrillation in horses, but the recorded AF burden was inaccurate, and the stored ECGs had to be manually interpreted. Because the human analyser algorithm of this cardiac monitor fails to identify bradyarrhythmias in horses based on our results, this instrument is not capable for accurately determining the aetiology of episodic collapse in this species.

Chapter III

Morphological and histological investigation of the conduction system in the equine atrial muscle sleeve of pulmonary veins

Atrial fibrillation is the most common arrhythmia in horses causing poor performance. The role of pulmonary vein triggers in the pathogenesis has been identified in horses. Ablation methods have been investigated, but the available information on anatomical, histological and immunohistochemical assessment of the pulmonary vein ostia and the conduction system of the myocardial sleeve is still limited. The aim of the study was to describe the morphological properties of the myocardial sleeve in healthy horses. Eighty-three equine hearts were dissected. The number and diameters of pulmonary vein ostia were determined, and anatomical localisation was described. Fifty-eight tissue samples were collected for histology (haematoxylin and eosin stain) and twelve of these were used for immunohistochemistry (S100; tyrosine hydroxylase [TH], and connexin [Cx] 43, 45 antibodies). The mean number of pulmonary vein ostia was 4.5 (4 veins: 46 horses, 5 veins: 31 horses, 6 veins: 6 horses). Diameters (mean \pm SD) of the main ostia were as follows: vein I: 20.2 \pm 7.0 mm, vein II: 32.7 \pm 7.1 mm, vein III: 33.4 \pm 5.9 mm, vein IV: 18.1 \pm 4.5 mm. Diameters of supernumerary vein ostia varied between 3.0 and 28.0 mm (mean \pm SD: 11.5 \pm 5.5 mm). Early branching was found in 26 horses (31.3%) and 30 veins (vein I: 14, vein II: 9, vein III: 5, vein IV: 2). Histology confirmed the presence of a muscle sleeve composed of myocardial tissue in each pulmonary vein. S100 and TH positivity was detected in each vein, and it confirmed the presence of adrenergic and non-adrenergic nerve fibres within the myocardial sleeve. Cx43 and 45 positivity were also found in each vein indicating the presence of gap junctions. Future ablation techniques should consider that conductive tissue is present in the entire myocardial sleeve in all pulmonary vein ostia.

New scientific results

1. Long-term in vivo use of the Reveal XT loop recorder in horses is feasible, well-tolerated, and the devices worked reliably without complications.
2. The human algorithm could not be used for automatic detection of arrhythmic episodes in horses. The device could detect atrial fibrillation in horses, but the recorded AF burden was inaccurate, and the stored ECGs had to be manually interpreted.
3. Extensive numerical data on the pulmonary vein ostia is described in horses, including the exact diameters of the ostia and the changes in early branching.
4. Histological results confirmed the existence of myocardial sleeves in the antrum of all pulmonary veins of horses.
5. Based on our immunohistochemical findings, conductive tissue is present in the entire myocardial sleeve in all pulmonary vein ostia of horses.

Publications forming the basis of the doctoral thesis

1. Bakos, Z., Kovacs, S. (2019). Treatment of atrial fibrillation in horses with orally administered quinidine sulphate. *Magyar Állatorvosok Lapja*, 141(5) 259-269.
2. Kovacs, S., Dixon, J., Bakos, Z. (2019). Successful treatment of ventricular tachycardia with oral propranolol in three horses. *Magyar Állatorvosok Lapja*, 141(2) 67-77.
3. Kovacs, S., Bakos, Z. (2022). Methods of Interventional Cardiology in Horses. *Magyar Állatorvosok Lapja*, 144(12) 707-718.
4. Kovacs, S., Bodo, G., Zs. Toth, F., Neder, L., Bakos, Z. (2024) Long-term use of an implantable loop recorder in horses. *Acta Veterinaria Hungarica*,
5. Kovacs S, Racz B, Sotonyi P, Bakos Z. Morphological and histological investigation of the conduction system in the equine atrial muscle sleeve of pulmonary veins. *Equine Vet J.* 2023;1-9. doi: 10.1111/evj.13996. PMID: 37658818.