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Research Article
Pacemaker Implantation in Horse with Bradycardia-Tachycardia Syndrome

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Abstract

Background and Objective: An 18-years-old, Warm blood gelding presented with a history of exercise intolerance. Clinical evaluation revealed intermittent pauses with atrial fibrillation. The pauses occur repeatedly, particularly after exercise indicating sinus node disease. The objective of this study was to perform a permanent pacemaker implantation in sinus node dysfunction in horse and to evaluate heart function after the procedure. **Materials and Methods:** The horse underwent permanent single chamber pacemaker implantation. Regular rhythm was restored with threshold level of 2.1 Volts. Heart functions and other clinical evaluations were assessed at 30 and 90 days and 1 year after transplantation. Paired t-test was used to determine the difference between baseline and post-treatment. **Results:** Blood analysis revealed normal parameters, including cardiac troponin values. No side effects were observed, horse showed improvement in heart function and life quality after pacemaker implantation. **Conclusion:** Permanent single chamber pacemaker implantation can be considered as a treatment option for horses with bradycardia-tachycardia syndrome.

Key words: Arrhythmias, cardiac intervention, pacemaker, echocardiography, geriatrics, equine

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Sick sinus syndrome or bradycardia-tachycardia syndrome is defined as an abnormality in the typical cardiac rhythm of elderly adults. Atrial fibrillation can coexist with sinus node dysfunction[1]. It may cause symptoms such as in appetence, exercise intolerance and weakness. However, the link between these two conditions is poorly understood. A previous study has demonstrated that sinus node dysfunction may precede the onset of atrial fibrillation[2]. Horses with atrial fibrillation often progress to develop atrial remodeling and heart failure. Long-standing persistent atrial fibrillation is less likely to convert to sinus rhythm with medication such as quinidine sulfate and animals are more likely to suffer a recurrence[3,4]. Previous studies suggested that conversion of atrial fibrillation at the initial stage might be beneficial for success rate and early return to training[5]. Cardiac pacemaker implantation is the most common invasive cardiac electro physiological procedures. Transvenous cardiac pacing electrode insertion is simple, safe and widely used in human medicine[6,7]. In veterinary medicine, permanent pacemaker implantation has been increasingly considered in management of bradycardias caused by atrioventricular block and sinus node dysfunction. However, pacemaker implantation in horses has rarely been described for the treatment of cardiac arrhythmias. In this case, sinus node dysfunction was diagnosed in a horse. The purpose of this study was to evaluate the heart morphology and function after performing permanent pacemaker implantation in bradycardia-tachycardia syndrome in horse.

Case description: Sinus node dysfunction or bradycardia-tachycardia syndrome was diagnosed in an 18 years-old, 530 kg gelding Warmblood horse. The horse was used for jumping and for pleasure riding. Horse had less impulsion gait and exercise intolerance while being ridden at the canter. On physical examination, horse was found to be depressed. No lameness and neurological problems were found. However, pulse deficit and irregular rhythms were detected during examination. No murmur was heard in all valve regions on auscultation. The respiratory rate and lung sounds were normal. The complete blood count and blood chemistry were within reference limits and cardiac troponin T was within normal range (less than 0.014 ng mL^{-1})[8-9]. Blood profiles before, 30 and 90 days after pacemaker implantation are shown in Table 1. A full cardiac examination was performed, including electrocardiography, 2-Dimensional, M-Mode and color flow doppler echocardiography (Mindray, China) at baseline, 3, 30 and 90 days and 1 year after pacemaker implantation.

Table 1: Blood profiles before, 30 and 90 days after pacemaker implantation

		After	
	Before	30 days	90 days
WBC ($\times 10^3$ μL^{-1})	5.51	8.26	5.09
RBC ($\times 10^6$ μL^{-1})	6.68	6.43	6.59
HGB (g dL^{-1})	12.20	11.90	11.90
HCT (%)	31.00	32.40	31.00
BUN (mg)	9.60	12.60	15.90
Creatinine (mg)	1.63	1.62	1.96
Total protein (g)	6.00	5.50	5.50
AST (U L^{-1})	272.00	274.00	293.00
ALP (U L^{-1})	109.00	127.00	135.00
CK (U L^{-1})	133.00	190.00	117.00
Fibrinogen (mg)	200.00	200.00	200.00

WBC: White blood cell, RBC: Red blood cell, HGB: Hemoglobin, HCT: Hematocrit, BUN: Blood urea nitrogen, AST: Aspartate aminotransferase, ALP: Alkaline phosphatase and CK: Creatine kinase

MATERIALS AND METHODS

Electrocardiographic examination: A base apex lead electrocardiogram (ECG) recording (Kenz ECG 110, Single channel digital Electrocardiographs, Japan) was performed in standing position with a paper speed of 25 mm/sec and calibration of 10 mm for 1 mV. This study was carried out on March, 2016 at Kasetsart Veterinary Teaching Hospital, Kamphaeng Saen Campus. ECG revealed irregular heart rhythm with fibrillating waves. The heart rate calculated from the ECG recording was around 23 beats min^{-1} (bpm), which is lower than the normal heart rate of the horse. Therefore, the bradyarrhythmic rhythm from excessive vagal tone was investigated using the electrocardiographic recordings under light exercise conditions (10 min of walking). The ECGs are shown in Fig. 1a. After pacemaker implantation, ECG showed regular rhythm at pacing rate of 50 bpm (Fig. 1b) and 100 bpm (Fig. 1c).

Echocardiographic examination: The horse underwent a complete echocardiographic examination with continuous electrocardiogram monitoring to evaluate the underlying cardiac disease and to guide the lead positioning in the right ventricle (Fig. 2). Echocardiography was evaluated before and after pacemaker implantation by one skillful sonographer in order to evaluate the cardiac conditions and to monitor the progression of cardiac remodeling at baseline, 3, 30 and 90 days and 1 year after pacemaker implantation. The measurement was performed using 2.0 mHz cardiac transducer in parasternal long, short axis and apical four-chamber view in standing position with no sedation. Echocardiographic images were captured and stored for offline analysis. Left ventricular wall structure and function were calculated by measuring the images from two-

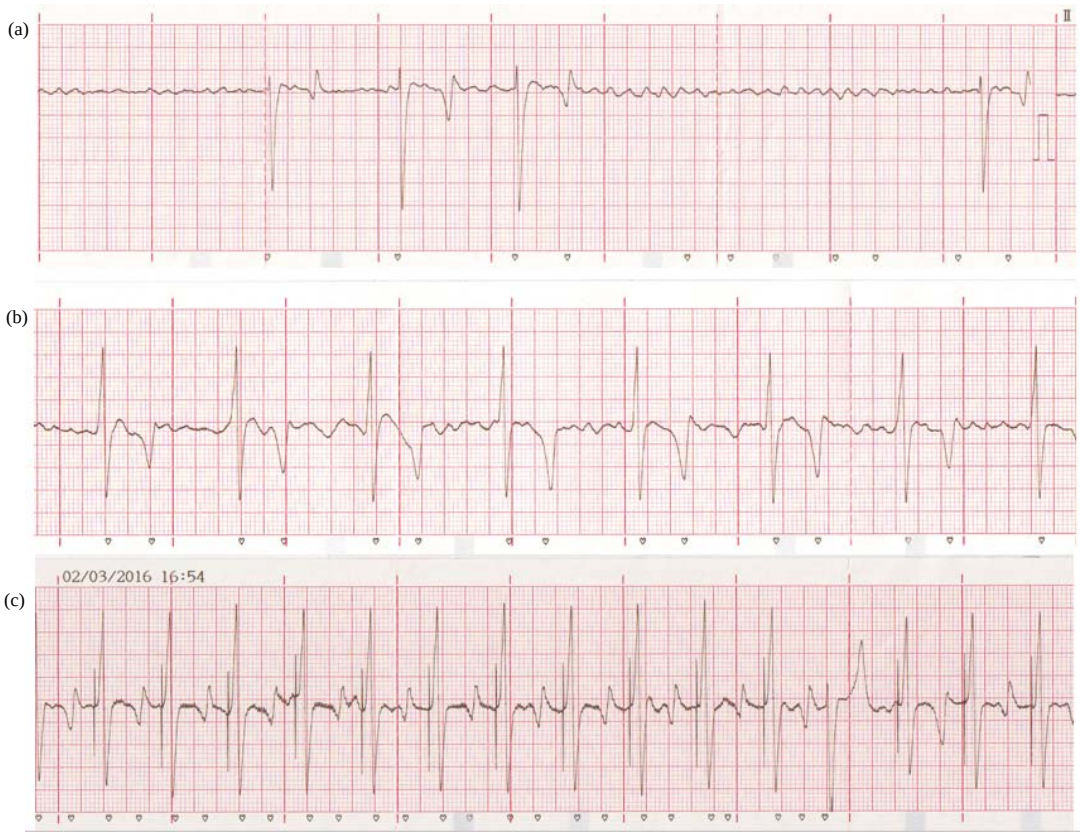

Fig. 1(a-c): Base apex electrocardiogram was recorded, (a) Recording of electrocardiogram after walking for 10 min, after implantation in (b) Regular rhythm of ventricular response and (c) At a pacing rate of 100 beat min^{-1} (25 mm sec^{-1}, 1 mV cm^{-1})

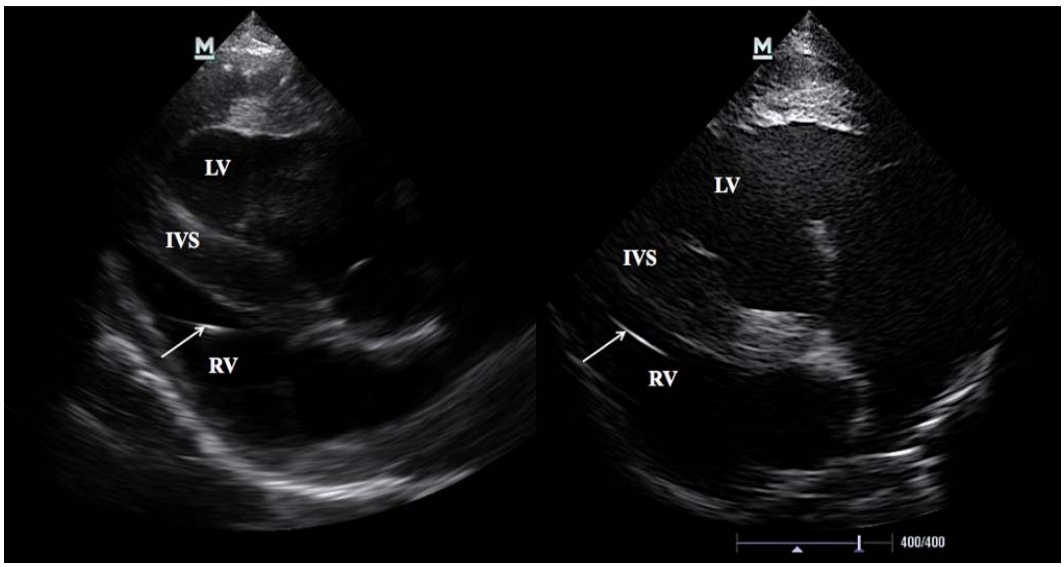

Fig. 2: Echocardiographic image showing the electrode lead was placed in the right ventricle septum (white arrow) during systolic (left panel) and diastolic (right panel) of cardiac cycle, LV: Left ventricle, RV: Right ventricle, IVS: Inter ventricular septum

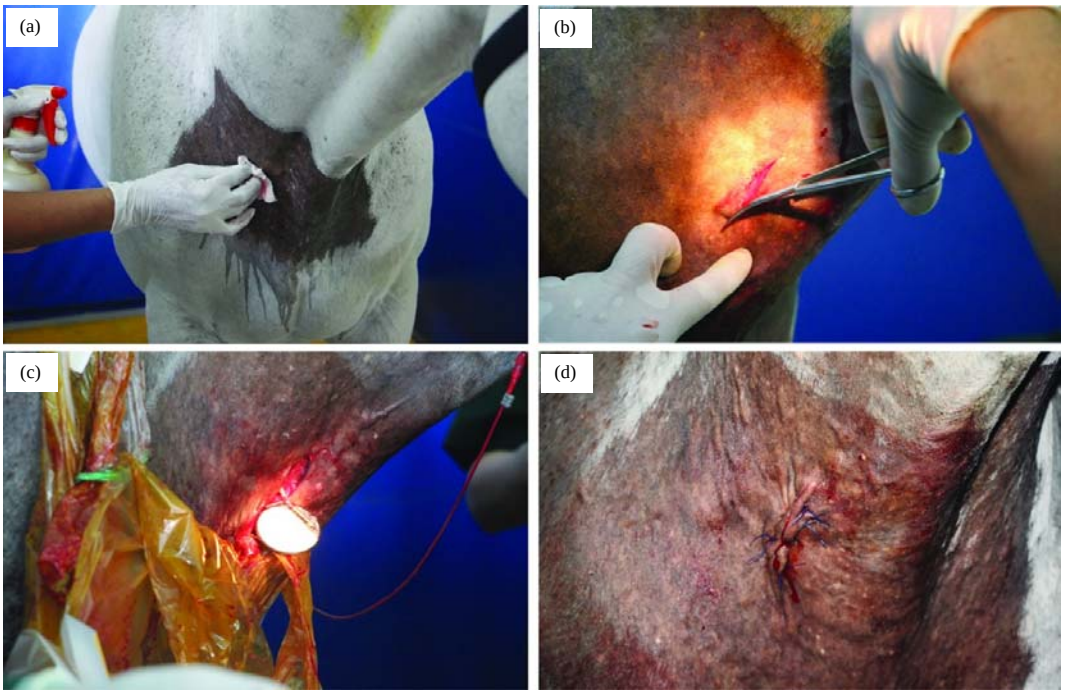

Fig. 3(a-d): Surgical technique sequence from (a-d) Perform transvenous single chamber pacemaker implantation in horse

Table 2: Echocardiographic database before, 30 and 90 days and 1 year after pacemaker implantation

Echocardiographic database	Before	After 30 days	After 90 days	After 1 year
IVSd (cm)	3.50	3.5	3.9	4.6
LVIDd (cm)	10.50	11.5	10.8	10.3
LVPWd (cm)	2.99	3.6	3.6	5.1
EDV (mL)	630.70	773.0	698.8	571.8
IVSs (cm)	3.27	3.6	4.2	4.9
LVIDs (cm)	7.16	7.5	7.3	5.3
LVPWs (cm)	3.27	3.5	5.5	5.7
ESV (mL)	269.90	393.7	280.2	151.5
EF (%)	57.20	49.1	61.8	73.5
FS (%)	31.90	35.1	33.9	48.4

IVSd: Interventricular septum diastolic diameter, LVIDd: Left ventricular end diastolic diameter, LVPWd: Left ventricular free wall diastolic diameter, EDV: End-diastolic volume, IVSs: Interventricular septum end systolic diameter, LVIDs: Left ventricular end systolic diameter, LVPWs: Left ventricular free wall end systolic diameter, ESV: End-systolic volume, EF: lEft ventricular ejection fraction and FS: Left ventricular fractional shortening

dimensional and M-mode planes. Ventricular wall thickness and dimensions were recorded during diastole and systole to obtain parameters such as diastolic inter ventricular septum thickness (IVSd), systolic interventricular septum thickness(IVSs), left ventricular end diastolic diameter (LVIDd), left ventricular end systolic diameter (LVIDs), left ventricular wall diastolic thickness (LVPWd) and left ventricular wall systolic thickness (LVPWs). The left ventricular ejection fraction (EF) was calculated as:

$$EF = \frac{EDV\text{-}ESV}{EDV} \times 100$$

Echocardiography results are shown in Table 2.

Pacemaker implantation: A 9F introducer sheath (Merit Medical, USA) was placed in the lower half of the jugular vein. The introducer has one single entrance port for insertion of pacing catheter (St. Jude, USA). Figure 3 displays the protocol of pacemaker implantation. Briefly, the horse was tranquilized with 0.02 mg kg^{-1} of acepromazine and then skin was shaved and sterilized with chlorhexidine solution. After 10 min of sedation with 0.8 mg kg^{-1} of xylazine hydrochloride, the catheter was inserted and positioned in the standing sedated horse under echocardiographic guidance from the left hemithorax. A base apex lead electrocardiography was used to determine the cardiac rhythm. The initial threshold of stimulation was adjusted at 2.1 V at a basal rate of 45 pulse min^{-1} (ppm), pulse amplitude of 4.5 V and pulse width of 0.37 msec. The pacemaker was connected to the electrode lead and positioned in a subcutaneous pocket at pectoral groove region. The skin was sutured and the pacing catheter was applied at a lower rate of 35 bpm (St. Jude, USA). The electrical characteristics of the pacemaker lead at the time of implantation, 30 and 90 days and 1 year after the implantation are shown in Table 3.

Clinical evaluations: Follow up visits and baseline results were documented before, 30 and 90 days and 1 year after the pacemaker implantation. The sequence of the study is shown in Table 4. Clinical outcomes were evaluated using a numerical rating scale based on a standardized questionnaire. The horse's owner was provided with a consent form and asked to complete a questionnaire with quality of life questions adapted from the Minnesota Living with heart failure questionnaire. The owner was asked to evaluate and score the questions regarding history, demeanor, exercise intolerance and appetite by means of the ordinal number, in which low scores indicate the worst quality of life (Table 5).

Statistical analysis: All results were expressed as mean±standard error of the mean (SEM). Statistical analysis was performed with Instat3 (GraphPad Software Inc., USA).

RESULTS

There was no significant difference in the left ventricular diameter between pre- and post-pacemaker implantation. Mildly decreased fractional shortening (FS) was observed before pacemaker implantation. However, post-implantation showed improvement in cardiac contractile function. Increase in the volume of blood pumped from the left ventricle was not detected until 30 days after implantation, as shown in Table 2 and Fig. 4. At 3 month follow up assessment, quality of life scores were significantly improved after pacemaker implantation (Fig. 5) and the horse was apparently healthy, in good body condition and weighing 550 kg.

This present study suggests that single chamber pacemaker could be used as a potential treatment for bradycardia-tachycardia syndrome in horse. It is a good alternative treatment for horses with arrhythmias that pharmacological treatment is ineffective. This study is also the first clinical application of successful pacemaker implantation in horse with sinus node dysfunction in Thailand.

DISCUSSION

Sinus node dysfunction is nota common rhythm disturbance in horse. However, intermittent pauses with atrial fibrillation were presented in this case. Cardiac intervention using pacemaker is a well proven therapeutic approach for the

Table 3: Pacemaker programming before, 30 and 90 days and 1 year after pacemaker implantation

		After		
	Before	30 days	90 days	1 year
Basal rate (ppm)	45.00	45.00	45.00	45.00
Pulse width (ms)	0.49	0.37	0.37	0.70
Pulse amplitude (v)	4.50	3.90	3.30	4.50
Pulse current (mA)	9.10	10.90	9.50	13.00
Lead impedance (W)	495.00	353.00	344.00	342.00
Percent of paced counts (%)	99.00	86.00	79.00	76.00

ppm: Pulse per minute, ms: Millisecond, v: Volt, mA: Milli-ampere and W: Ohm

Table 4: Clinical treatments and follow up visits on day 0, 3, 30 and 90 and 1 year after pacemaker implantation

Treatments	Day 0	Day 3	Day 30	Day 90	1 year
Physical examination	✓	✓	✓	✓	✓
Cardiac examination	✓	✓	✓	✓	✓
Blood sample	✓	-	✓	✓	-
Pacemaker battery monitoring	✓	-	✓	✓	✓
Follow up		✓	✓	✓	✓

Table 5: Domains and assessment items in questionnaire. Each domain contains related items that were scored on a scale of 1 to 5, where 1 is minimum level and 5 is maximum level

Variables	Score	Clinical sign
Demeanor	1	Unresponsive
	2	Minimally responsive
	3	Moderately depressed
	4	Mildly depressed
	5	Alert, responsive
Exercise intolerance	1	Inactive, only get up to eat and drink or urinate
	2	Less active than normal
	3	Able to move around a few times per day, avoided long walk
	4	Able to move around but the ability to run was reduced
	5	Able to move around and run but not able to fully exercise
Appetite	1	Markedly decreased
	2	Minimally decreased
	3	Decreased
	4	Normal
	5	Increased

management of sinus node disorders. Pacemaker implantation is a common procedure for the treatment of brady arrhythmias in dogs[10-17]. In this study, pacemaker implantation was also considered as a treatment option for horse with sinus node dysfunction or bradycardia-tachycardia syndrome. Previous studies demonstrated that long term right ventricular pacing at the apical area results in intraventricular conduction delay and cardiac remodeling. Alternative pacing sites, such as biventricular pacing and right ventricular septal pacing have been reported to relieve this adverse effect[18-19]. For this reason, the pacing site in this study was designed to place the pacemaker lead at the right ventricular septum.

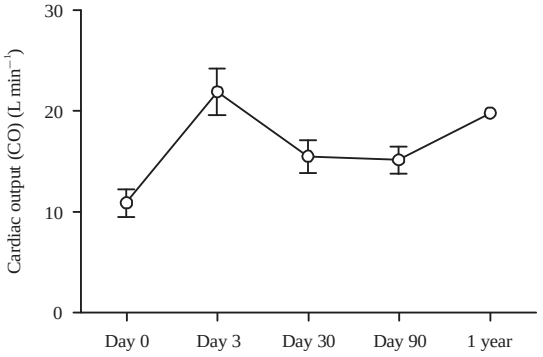

Fig. 4: Analysis of percentage (Mean±SEM) of cardiac output (CO) in horse at pre-(Day 0) and post-implantation (Day 3, 30, 90 and 1 year). After implantation showed improvement of cardiac output compared to the baseline

The left ventricular diameter and contractilefunction measurement at baseline and after pacemaker implantation were performed to monitor the heart structural and functional changes. There was a significant morphological change following pacemaker implantation in right ventricular septum position after 1 year follow up. These results are similar to previous reports that right ventricular pacing might result in cardiac remodeling[20]. Despite the thickening of the inter ventricular septum and left ventricular free wall, the horse remains stable and in good condition and heart function. This is similar to previous reports that pacemaker implantation might not reduce mortality but can decrease symptoms and improve the quality of life. However, further assessment of the horse's fitness level is required and an additional year of follow

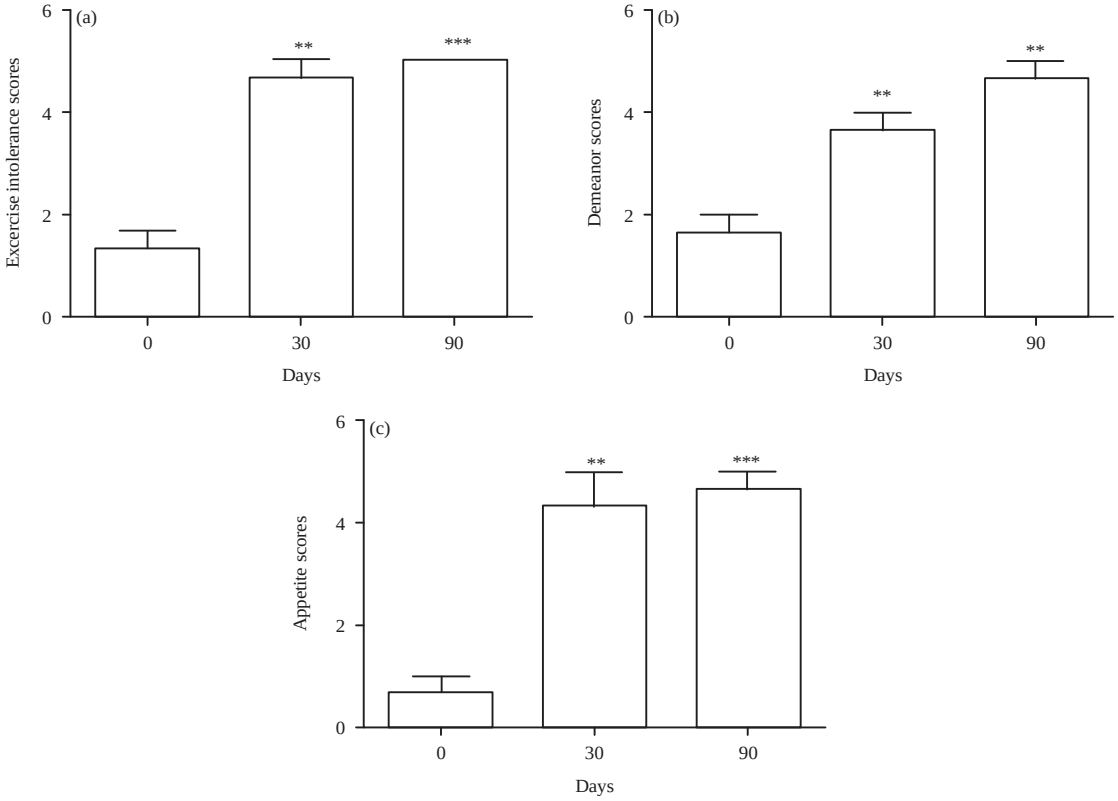

Fig. 5(a-c): Life quality scores in horse. Questionnaire included questions about exercise intolerance, demeanor and appetite status. Values are Mean±SEM, **p<0.01, ***p<0.001 compared with baseline

up may be necessary to investigate the ability to perform work in this case. There were 2 main limitations for performing pacemaker implantation in this case. One limitation was the lack of equipment facilities, including 24 h ECG monitoring, which is important during electrical cardioversion procedures and fluoroscopy, to confirm the position of an electrode lead. However, echocardiography images were used to guide the lead positioning instead of fluoroscopy. Another limitation of this study was the anesthetic consideration in a geriatric horse. Previous study reported that nearly 60% of patients suffered morbidity, specifically related to duration of anesthesia and age[21-22]. Under this circumstance, pacemaker implantation was performed under local anesthesia and sedation with horse in standing position.

CONCLUSION

The treatment procedure in this study provided the initial evidence in horse that single chamber pacemaker implantation is safe and has the potential to control the heart rate. However, it may be necessary to increase the duration of follow up after pacemaker implantation in order to investigate the heart remodeling response as well as exercise ability.

SIGNIFICANCE STATEMENT

This manuscript describes a treatment option for horse with bradycardia-tachycardia syndrome using intervention cardiology procedure. This study provided the initial evidences in horse that single chamber pacemaker implantation was safe and had a potential to control the heart rate.This study is the first clinical application on the success of pacemaker implantation in horse with bradycardia-tachycardia syndrome in Thailand.

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