

ATRIAL FIBRILLATION IN HORSES

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Abstract

Atrial fibrillation (AF) is a common arrhythmia in horses and often occurs in the absence of predisposing disease (lone AF). It does not cause any signs at rest is associated with reduced performance in athletic horses. Epistaxis, weakness, collapse or even sudden death may occur during exercise. Treatment of lone AF horses is rewarding as successfully converted horses do return to their previous level of exercise. Medical and electrical treatment can be used. Medical treatment is generally performed with repeated administration of quinidine orally until conversion or toxicity occurs. Toxic side effects during treatment are common. Intravenous administration of amiodarone has also been reported but had lower efficacy. Electrical treatment is performed transvenously, using cardioversion electrodes in the left pulmonary artery and the right atrium. Synchronised biphasic shocks are delivered and cardioversion is often obtained around 160-250 Joules. Transvenous electrical cardioversion has the highest success rate (> 90%) and has a lower risk for treatment. Overall recurrence rate is about 20-30%.

Keywords: arrhythmia, equine, quinidine, transvenous electrical cardioversion, defibrillation

Atrial fibrillation (AF) represents the most important cardiac rhythm disorder affecting performance in horses. The prevalence is about 0.5% with no clear gender or age predilection. Atrial fibrillation is an atrial tachyarrhythmia that is frequently found in the absence of other (detectable) cardiac pathology, especially in large breeds. In ponies, AF is only encountered as a result of severe cardiac disease.

Mechanisms and pathophysiology

Different theories have been described explaining initiation and perpetuation of AF in other species and they most likely apply to horses as well. The well-known multiple wavelet model assumes that during AF multiple electrical wavefronts move chaotically through the atrial myocardium. In order for AF to be self-sustained, a critical number of wavefronts must co-exist in the atria.

Atrial fibrillation occurs when both a trigger to start the arrhythmia and a substrate to maintain it, are present. The trigger can be one or more atrial premature beats, a rapidly firing focus or small reentry sites (spiral waves or rotors) that initiate reentry. These triggers occur because of increased myocardial excitability, myocardial damage or stretch, electrolyte disorders, or systemic disease. Whether or not the left atrium and the ostium of the pulmonary veins play an important role in horses remains unknown. Once initiated, the perpetuation of AF depends on the suitability of the substrate, the atrial myocardium. Factors in favour of AF are a large atrium, short refractory period, dispersion of refractoriness, slow conduction velocity and structural obstacles or lesions. Strenuous exercise with elevated left atrial pressures in horses (more than in other species), may lead to a higher burden of atrial stretch-related premature beats (triggers). High vagal tone, large atria and a short refractory period in relation to its size, makes the equine atria an almost perfect substrate for sustained, *lone* (primary) AF. Underlying cardiac disease further increases this risk (secondary AF).

Occasionally, AF is short-lived and terminates spontaneously, usually within the first 24-48 hours, which is called *paroxysmal* AF. This form of AF has been shown to be a cause of reduced performance in slowly finishing Thoroughbreds. Probably strenuous exercise triggers initiation of AF by stretching the atrial myocardium, leading to atrial premature beats and electrophysiological changes that are exacerbated by electrolyte disturbances, while the myocardium is not suited for maintenance of AF due to its size, structure or electrophysiological properties.

In most horses, however, once initiated, AF does not terminate spontaneously because of the size and properties of the atrial myocardium. In addition, experimental work has shown that immediately after AF occurrence, shortening in refractory period and loss of contractile function occur, both leading to further stabilisation of the arrhythmia. As a result, AF generally becomes *permanent* and will not terminate without treatment.

During AF, a continuous and chaotic, self-sustaining electrical activity is present in the atria at a 'rate' of about 300-500/min. Due to the high vagal tone in horses, the atrioventricular node blocks most of these electrical pulses and the final ventricular rate remains normal at rest. Within days to weeks after initiation of AF, atrial contractile function is almost completely lost, a process which appears

reversible after restoration of sinus rhythm. Although the atrial contraction contributes up to 20% to ventricular filling, loss of atrial contractility is not related to clinical signs at rest because passive filling is sufficient to maintain cardiac output. However, during exercise, when heart rate increases, the atrial contribution to filling becomes more important and may affect performance. In addition, exercise results in a predominantly sympathetic tone, whereby the atrioventricular node will suddenly conduct too many pulses to the ventricles, resulting in a disproportionate tachycardia during exercise. Heart rates well over 250-300/min are often encountered and instantaneous rates may exceed 400/min. Again, especially during vigorous exercise, this will affect exercise capacity, even if no underlying cardiac disease is present.

Some AF horses may present short runs of broad QRS tachycardia with an R-on-T-like phenomenon during sudden stress or exercise. This might be caused by aberrant conduction due to bundle branch block during rapidly conducted impulses over the atrioventricular node, although ventricular ectopy might be the cause as well. In most horses the R-on-T-like phenomenon is no longer found after successful conversion to sinus rhythm.

Clinical presentation

Clinical signs depend whether or not concurrent cardiac or non-cardiac disease is present. Horses with cardiac failure that suddenly develop AF will experience an increase in heart rate (usually around 60-70 bpm) with an aggravation of clinical signs.

Horses that have atrial fibrillation without underlying cardiac lesions usually present with a history of reduced performance at high level exercise (e.g. racehorses). Epistaxis may occur during exercise. Occasionally, a brief period of ataxia, distress or even collapse may be observed during fast work. Because of the influence on performance, diagnosis is often made in an early stage. In jumping horses, AF results in moderate reduction in performance, which makes that veterinary attention is sometimes sought in a later stage, delaying diagnosis of the arrhythmia. In non-competing horses, clinical signs may be absent and AF may be an incidental finding. Some owners do report subtle changes in the behaviour of their horse when AF occurs. The author has seen more narcolepsy symptoms in AF horses compared to the general clinic population but it is unclear if there is any relation between the two.

On auscultation of the heart, AF is characterised by an irregularly irregular rhythm with a loud first heart sound. Careful auscultation will easily distinguish between AF and 2nd degree atrioventricular block because during AF the rhythm is more irregular, the first heart sound is louder, an unexpected early beat will always be heard and an atrial sound is absent, also during a long pause. Additionally, after slight excitation, the arrhythmia remains. One should carefully interpret auscultation immediately after exercise because at high heart rates the irregularity in RR intervals is less pronounced due to the shortened diastolic time. In addition, post-exercise sinus arrhythmia commonly occurs in normal horses. Horses with secondary AF might present clinical signs related to the predisposing disease.

However, the horse with lone AF should not present signs of heart disease at rest. Arterial pulse quality is variable. Inspection of the jugular veins might show an intermittent filling of the veins during a long diastolic pause. This should be distinguished from any pathological pulsation of the veins as seen in case of right-sided heart failure.

Diagnosis of AF should be confirmed by ECG, which will show normal QRS morphology with irregularly irregular RR intervals, undulations of the isoelectric line ('f' waves) and absence of P waves. The f waves frequently shift from coarse to fine undulations. Due to aberrant conduction, a shortly coupled (normal) QRS complex might show a changed T wave morphology, whereby QRS and T polarity become opposite (Fig. 1). This should not be mistaken for a ventricular premature beat. Ventricular premature beats, however, are found in a number of AF horses either at rest or during exercise. In the absence of electrolyte disorders or systemic disease, they might indicate underlying, more widespread myocardial disease with (secondary) AF, rather than a consequence of AF. Whatever the cause, presence of ventricular premature beats warrants further investigation (ultrasound, troponin, post-cardioversion ECGs).

During an episode of broad QRS tachycardia with R-on-T, horses show an abnormal ventricular contraction pattern on ultrasound. These horses have been reported to show weakness, ataxia, collapse or even sudden death during exercise. This is the reason why such AF horses are not safe for ridden exercise.

Treatment

Atrial fibrillation *per se* is not a life threatening disease and horses at rest, broodmares, etc. have a normal life expectancy. Treatment of these animals is generally not required.

During the first 48-72 hours after initiation of AF, especially in race horses, no anti-arrhythmic treatment should be given as spontaneous conversion to sinus rhythm may occur. Electrolyte disorders must be corrected.

If AF lasts for more than 72 hours it will generally not convert spontaneously and thus become *permanent* AF. In these horses a full cardiac exam, including cardiac ultrasound, should be performed to search for a predisposing disorder, such as atrial dilatation, atrioventricular valve regurgitation or cardiac failure, before any attempt to treatment. If obvious predisposing disease is found, treatment of AF is generally not advised because of the higher risk of treatment, the lower success rate and the higher recurrence rate after successful cardioversion.

Most frequently, horses present with lone AF and a history of reduced performance. In these animals one should attempt to restore sinus rhythm as they generally return to their previous athletic ability after restoration of sinus rhythm. But even when horses in training do not show any symptoms, advice is given to treat AF because of a potential risk during exercise. In case the owner declines treatment but still wants to ride the horse, AF is considered a risk factor and ECG recordings during representative exercise tests should at least be free of R-on-T-like rhythms.

Cardioversion of AF can be achieved pharmacologically or electrically.

Pharmacological treatment

Quinidine sulphate

Quinidine sulphate (QS) administration through a nasogastric tube is the most widely used pharmacological treatment for AF in horses. However, in many countries the product has become expensive or is being taken off the market.

Quinidine is a class IA anti-arrhythmic drug that prolongs action potential duration by blocking sodium channels, which may lead to AF termination. QS induces hypotension by a negative inotropic effect and alpha-adrenergic blockade. Due to its vagolytic effects atrioventricular conduction increases, which results in an increased ventricular rate during treatment. For these reasons, treatment should be performed in a quiet environment, and the horse should remain in its stall during treatment. These side effects also explain why horses with AF and cardiac failure should not receive QS treatment. Permanent venous access must be available for administration of drugs. A continuous telemetric ECG facilitates immediate detection of unwanted cardiac effects of the drug.

A test dose of 10 mg/kg QS or the first full dose is used to check for idiosyncratic reactions, although these rarely occur. Treatment begins with administration of 22 mg/kg of QS via an indwelling nasogastric tube. The drug should not be given directly into the mouth because it is irritating to mucosa. The 22 mg/kg dosage is repeated every 2 hours to a maximum of 6 doses per day. Many horses do not tolerate 6 doses, however. The aim of the treatment is to titrate the drug to the therapeutic plasma concentration (2-5 µg/ml) but drug monitoring is generally not performed. When side effects start to occur, the dosing interval is often adjusted based on clinical signs, or is set to a 6-hour interval, which is the half life of quinidine. The longer plasma levels are kept in the therapeutic range, the more likely successful cardioversion will be achieved. Treatment should be terminated when sinus rhythm is restored or when the QRS duration prolongs by 25% or when severe side-effects occur.

Side-effects are encountered very frequently and one should distinguish between common, non-problematic signs such as depression, nasal oedema, and mild tachycardia, and more severe reactions that require termination of treatment including colic, diarrhoea, laminitis, ataxia, hypotension, collapse, or a ventricular rate exceeding 120/min. Emergency treatment includes fluid therapy and intravenous isotonic sodium bicarbonate (1 mEq/kg) to increase protein binding of free quinidine. When tachycardia occurs, one should distinguish between supraventricular tachycardia, which is the most common, and ventricular tachycardia. Because of the absence of P waves and because the quinidine treatment is associated with a mild widening of the QRS complex, differentiation might be challenging. Supraventricular tachycardia can be treated with digoxin (2.2 µg/kg IV), and, if unsuccessful, with propranolol (0.03 mg/kg IV). If no severe signs of hypotension are present,

administration of an α_2 -adrenergic agonist such as detomidine is often effective to slow down the supraventricular rate immediately. Ventricular tachycardia can be treated with magnesium sulphate (4 mg/kg every 2 minutes up to a total of 50 mg/kg). If ventricular tachycardia appears unstable lidocaine should be administered (0.25-0.5 mg/kg IV q 5-10 minutes to total dose of 2-4 mg/kg). Hypotension can be managed by IV administration of crystalloids and phenylephrine (0.1-0.2 μ g/kg/min up to 0.01 mg/kg).

It has been recommended that, if cardioversion is not achieved by the second day of treatment, the QS treatment should be combined with oral digoxin to slow down AV nodal conduction. However, one should be aware that both drugs are highly protein bound and that their concurrent use increases effective plasma levels of both agents, increasing the risk of adverse effects. In addition, from an electrophysiological point of view, digoxin would be expected to stabilize AF.

When sinus rhythm cannot be restored after a first attempt, a second QS treatment with a few days interval might be successful. Overall success rate of QS treatment in (race)horses with lone AF is around 85%.

Quinidine gluconate

Intravenous administration of quinidine gluconate has been reported for recent-onset AF (3-7 days duration). Slow IV administration of 1-1.5 mg/kg is repeated every 10 minutes until cardioversion, QRS widening of more than 25% over baseline, toxic side effects occur or a total dose of 12 mg/kg is administered. However, this treatment protocol, although more convenient, carries an increased risk of side effects.

Flecainide

Flecainide is a class IC anti-arrhythmic drug that depresses the upstroke of the action potential by blocking sodium channels. This drug is known to have pro-arrhythmic properties especially in the presence of structural heart disease.

In horses with chronic AF, IV administration of 0.2 mg/kg/min flecainide acetate during 10 minutes has a low efficacy and can induce potentially life-threatening ventricular arrhythmias. However, even in recent-onset, lone AF, this treatment protocol has led to fatal ventricular fibrillation. For these reasons, intravenous flecainide at the above mentioned dose should not be used in horses.

Amiodarone

Amiodarone is a class III anti-arrhythmic drug that prolongs repolarization predominantly by blocking potassium channels. In human medicine, the drug is used as an IV infusion for acute treatment or as an oral formulation for chronic administration.

In horses, bioavailability of oral amiodarone is low but intravenous amiodarone administration has been used to treat chronic AF. The described treatment protocol consisted of a loading dose (5

mg/kg/h) over one hour, followed by a continuous infusion (0.83 – 1.9 mg/kg/min) over 1 to 3 days, but resulted in only a moderate conversion rate (50%). Amiodarone administration over more than 36 hours was associated with an increased risk for side effects that included diarrhoea and hind limb weakness.

Propafenone

Intravenous treatment with propafenone, at 2 mg/kg over 15 minutes, followed by 7µg/kg/min over 2 hours, was reported not be effective in treating AF in horses. It has been suggested that 2 mg/kg propafenone orally TID, might convert AF in some horses, but no research data are available yet.

Non-pharmacological treatment: electrical cardioversion

In human medicine, electrical cardioversion using a direct current (DC) shock is a commonly used approach to convert atrial as well as ventricular fibrillation. Although the exact mechanisms are not fully understood, the DC shock probably causes complete depolarisation of the myocardium, bringing it into a refractory state, thereby blocking all fibrillation waves and creating the chance for normal sinus rhythm to restore. A critical amount of myocardium needs to be depolarized which can only be obtained by a sufficiently large current flow through the atria. The latter depends on the kind and location of the electrodes (electrode surface area, interelectrode distance and resistance, position of the electrodes in relation to the atria), and the applied energy. Besides the energy level (Joules), it is known from human medicine that the DC waveform morphology also plays an important role, whereby biphasic waves are more effective than monophasic waves. It is crucial not to deliver the DC shock on the T wave, as this can induce ventricular fibrillation. Shock delivery should therefore always be synchronized with the R wave. Because shock delivery might result in temporary bradycardia or asystole, ventricular backup pacing during electrical cardioversion in horses is recommended. As electrical cardioversion is painful, general anaesthesia is always required.

Transthoracic electrical cardioversion

Transthoracic electrical cardioversion of AF implies shock delivery between paddle electrodes placed on the skin at each side of the thorax. Because of the large size of the equine thorax with the atria covered by the insulating lungs, the final current flow through the atria, and thus efficacy, is very low, even when high energy levels are used.

Transvenous electrical cardioversion

Placement of the electrodes near or in the atria, results in a much higher amount of current flow through the myocardium. This approach is used during transvenous electrical cardioversion and has proven to be very efficacious in horses with AF. In the standing horse, 2 cardioversion catheters, with large surface area electrodes at the tip, are introduced via the jugular vein. Each catheter is then positioned using ultrasonography, radiography and/or pressure tracings from the catheter. To

encompass as much atrial myocardium between both electrodes as possible, one electrode is manoeuvred into the proximal left pulmonary artery while the other is placed in the right atrium. Subsequently, after induction of general anaesthesia and verification of catheter position, synchronized shocks are delivered. Starting at about 125 J, energy level is stepwise increased until a maximum of 360 J. Using biphasic waves, mean energy level to obtain cardioversion in horses with AF is reported to be around 160 J.

Aftercare

Successfully converted horses

After successful pharmacological or electrical cardioversion, depending on the duration of AF, the horse should be rested. Experimental work suggests that it takes about 4 to 6 weeks for the atrial refractoriness and contractile function to fully recover from chronic (6 months) AF, while it takes about 1 day for recent-onset (1 week) AF. Especially in high level race horses, long resting period are not always feasible. However, in these patients AF is often discovered quickly because of the marked drop in performance. Therefore, a resting period of a week, with gradual return to previous level over the next 2 to 4 weeks is usually advised. Owners should be advised to check cardiac rhythm regularly in order to discover recurrence of AF.

Twenty-four hour ECG monitoring one week after cardioversion may be useful to detect the burden of atrial premature beats, which are known to trigger AF recurrence. In horses with a high number of atrial premature beats, the resting period should be prolonged and anti-inflammatory treatment with corticosteroids may be considered.

Successfully converted horses without underlying cardiac disease have a good prognosis and usually return to their previous level of performance. Recurrence rate of lone AF after quinidine treatment has been reported to be around 20% in racehorses but appears slightly higher in Warmbloods (around 30%), and is expected to be unrelated to the cardioversion technique used.

Non-converted horses

If conversion cannot be obtained and the horse is not intended to perform, no further action is needed. Lone AF in non-performing horses does not usually cause clinical signs and does not progress to heart failure. High level performance should not be expected from AF-affected horses: these horses generally do not perform well and strenuous exercise might even be associated with epistaxis, ataxia or collapse. If only light or moderate work is demanded, a thorough exercise test with continuous ECG monitoring is necessary to identify any other exercise related arrhythmias or clinical signs. But even then AF is considered a potential risk factor.

Anti-arrhythmic treatment of horses with AF secondary to significant underlying cardiac disease is usually unrewarding. These horses usually need to be rested with supportive treatment. Anecdotal

evidence suggests that some of these horses might benefit from angiotensin converting enzyme inhibitor therapy.

Supplemental readings

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