Comments? Questions?
Email: compendium@medimedia.com
Web: VetLearn.com • Fax: 800-556-3288

CE **Article #5 (1.5 contact hours)**
Refereed Peer Review

Atrial Fibrillation in Horses: Treatment and Prognosis*

Oklahoma State University
Bradford G. Bentz, VMD, MS, DACVIM, DABVP (Equine)
Ronald S. Erkert, DVM
Margaret A. Blaik, DVM

KEY FACTS

- Treatment of atrial fibrillation often produces successful conversion to sinus rhythm when underlying cardiac abnormalities are not present.
- Pretherapeutic evaluation and close monitoring of the therapeutic course maximize the likelihood of successful cardioversion and minimize clinical signs of toxicity associated with medications.
- Successful conversion to sinus rhythm and rate of reversion to atrial fibrillation are inversely related to the duration of the arrhythmia and underlying heart disease.
- Most successfully converted horses with no underlying cardiac pathology may be expected to return to their previous level of competition.

ABSTRACT: Treating horses with atrial fibrillation is most successful when using quinidine sulfate delivered by nasogastric intubation at 2-hour intervals. The therapeutic window for quinidine is narrow. Monitoring plasma quinidine and digoxin levels is highly recommended but not always possible. Successful conversion is possible using 6-hour treatment intervals when 24 hours of steady-state quinidine levels have not resulted in cardioversion. A lack of underlying heart disease is associated with improved success of conversion and prognosis.

Atrial fibrillation is the most frequently reported cardiac arrhythmia in horses.[1–21] When maximal performance is affected by this arrhythmia, conversion to normal sinus rhythm carries a good prognosis if there is no significant underlying cardiac disease.[2,4,5,9,11,21–25] A return to performance at or above the previous level is common in such cases.

Treatment of atrial fibrillation, although frequently successful, requires thorough pretreatment evaluation and judicious use of therapeutic medications. Because the therapeutic window of commonly administered medications is narrow, careful patient monitoring is necessary.[1,26]

TREATMENT

Determining a treatment approach for a horse with atrial fibrillation should be based on the proposed activity of the horse. Horses with benign fibrillation that compete below maximal capacity or breeding animals may not require cardioversion. Some horses with acute onset of atrial fibrillation may spontaneously convert to sinus rhythm in 24 to 48 hours.[27] Horses with congestive heart failure (CHF) and atrial fibrillation should not receive quinidine sulfate but should be treated for CHF with positive inotropic agents, diuretics, and other medications necessary for stabilization.[1,27] It may be best to rest horses with suspected acute myocarditis for 1 to 2 months before treating an arrhythmia, and steroidal therapy for such horses may also be warranted.[28] Treatment toxicity and adverse reactions must be considered before treating any horse for atrial fibrillation. Sudden death is one such documented adverse reaction.[2] Therefore, owners should be fully apprised of the risks associated with treatment. However, the long-term prognosis appears to be better for horses that are converted to sinus rhythm.[8]

*A companion article entitled "Evaluation of Atrial Fibrillation in Horses" appeared in the September 2002 (Vol. 24, No. 9) issue of *Compendium*.

Quinidine

Only a few medications are commonly used to treat horses that have atrial fibrillation. The most commonly used drug for conversion to sinus rhythm is quinidine.[1,3,10,26,29–31]

Quinidine is a class I antiarrhythmic effective for treating atrial fibrillation by its vagolytic action and by increasing the fibrillation threshold of the atrial myocardium, concealed conduction through the atrioventricular (AV) node, and effective refractory period of the atrial myocardium. This α-adrenergic antagonist can significantly decrease vascular tone and mean arterial pressures. It has a negative inotropic effect on the myocardium and a positive chronotropic effect that can lead to supraventricular tachycardia.[1–3,8,10,26,29,31,32]

Quinidine sulfate is generally regarded as the most effective treatment for converting horses to sinus rhythm. Lower plasma peak concentrations and longer duration of effect may be factors in this observation.[1] Oral and IV forms of quinidine exhibit half-lives of approximately 6.5 hours and tissue and plasma equilibrium approximately 30 minutes after administration.

Plasma quinidine levels peak at approximately 131 minutes, with a range of 60 to 240 minutes after administering a single oral dose. The elimination half-life is approximately 6.65 hours, with a range of 3.3 to 12.55 hours. Quinidine is highly protein bound in plasma, and binding is pH dependent, with protein binding increasing as pH increases. The primary organ that eliminates quinidine is the liver. Biotransformation of quinidine occurs by hydroxylation. Approximately 17% of quinidine is eliminated unchanged in humans. Urine elimination is also pH dependent, and there is greater urinary elimination with higher urine pH.[1,3,10,26,32,33]

Acute supraventricular tachycardia (heart rates >200 bpm) requires emergency treatment. Sodium bicarbonate is administered IV at 1 mEq/kg to increase the percentage of quinidine bound to protein.[1,27,32] IV digoxin (0.0022 mg/kg) should also be administered for its negative chronotropic and positive inotropic effects. Digoxin decreases AV nodal conduction and ventricular response rate.[1,27,32] However, digoxin administration leads to higher plasma quinidine levels.

Persistent ventricular arrhythmias may be treated with IV lidocaine at 20 to 50 µg/kg/min. Activated charcoal may be administered to prevent continued absorption of orally administered quinidine. Hypokalemia and prolonged QT intervals may predispose patients to developing torsades de pointes,[1] which may be treated with IV magnesium sulfate at 1 to 2.5 g/450 kg/min without exceeding a total dose of 25 g.[1,27,32] If the horse's pulse becomes weak during treatment and severe hypotension occurs, phenylephrine at 0.1 to 0.2 µg/kg/min may be indicated. Some horses exhibiting quinidine toxicity have been successfully converted to sinus rhythm after the therapy was discontinued.[1]

Although quinidine sulfate is an oral preparation, it should be administered only by nasogastric intubation because oral administration may cause significant oral ulceration.[27] Treatment with quinidine sulfate is usually preceded by a test dose of 11 mg/kg to detect idiosyncratic adverse reactions, such as urticaria or other allergic responses, laminitis, and gastrointestinal upset.[1,3,10] Some hospitals use the first treatment of 22 mg/kg as a test dose.[29] After administering a test dose, quinidine sulfate should be given at a dose of 22 mg/kg by nasogastric tube every 2 hours until a total dose of 88 to 132 mg/kg is reached over a 24-hour period (a total of four to six doses).

Quinidine gluconate is an IV preparation. Its use is generally advocated for acute atrial fibrillation of less than 2 weeks' duration.[27] Quinidine gluconate has been used as a slow IV push at a dose of 6.2 mg/kg or as an IV bolus at a dose of 0.5 to 1.5 mg/kg administered every 10 to 15 minutes.[33] A total dose of quinidine gluconate beyond 10 to 12 mg/kg appears to cause significant decreases in mean arterial pressures.[3,26,32–36]

Plasma quinidine monitoring is advisable because of the narrow therapeutic range of quinidine. The therapeutic concentration of quinidine is approximately 2 to 3 µg/ml in humans[37] and apparently similar (approximately 2 to 5 µg/ml) in horses.[1] Conversion to sinus rhythm appears to be less likely with plasma levels greater than 5 µg/ml, and occurrence of quinidine toxicity becomes more common with plasma levels greater than 5 or 6 µg/ml.[1] If digoxin is used with quinidine, plasma levels are generally higher because of competitive protein binding by these two drugs.

Before initiating quinidine therapy, placement of an IV catheter is recommended in case rapid venous access is required for treating severe arrhythmia or hypotension associated with treatment. During treatment, continuous electrocardiographic (ECG) monitoring using a radiotelemetry unit is recommended. If such equipment is not readily available, ECGs should at least be obtained before each treatment and preferably at frequent intervals between treatments. Horses should remain in stall confinement during treatment; and emergency drugs for treating arrhythmias, hypotension, and toxicity should be readily available.[27] If blood levels of quinidine can be monitored and controlled, quinidine can be administered every 2 hours for 3 days. If plasma quinidine levels cannot be measured, treatment intervals should be decreased to every 6 hours (after using the 2-hour–interval protocol for the first 24 hours) to minimize the likelihood of quinidine toxicity.

Treatment should be discontinued if there are any signs of toxicity.

Complications of quinidine toxicity may include hypotension, cardiovascular collapse, depression, ataxia, weakness, colic, nasal mucosal congestion, convulsions, acute laminitis, dyspnea, sudden death, widening or increased amplitude of the QRS complex, increased ventricular rate, and T wave reversal.[1,3,10,26,29,32,34] Acute supraventricular tachycardia associated with toxicity may lead to heart rates of 220 to 300 bpm and acute death. Clinical signs of toxicity or high plasma levels of quinidine require consideration of the safety of continued treatment. If only mild signs of quinidine toxicity are present or plasma levels of quinidine are over 5 µg/ml, therapy may be successfully continued using 6-hour treatment intervals.[1] Quinidine therapy should be immediately discontinued if the heart rate exceeds 200 bpm or the horse has an acute collapse, hypotension, colic, severe diarrhea, or neurologic signs. Continuous radiotelemetry should be conducted or an ECG obtained before each oral dose of quinidine to evaluate for initial signs of quinidine toxicity, which is indicated by an increase in the QRS complex amplitude or widening of the QRS complex by approximately 25% of the pretreatment QRS duration.[1,29,32]

Treatment with quinidine is generally contraindicated if there is evidence of significant heart disease. A sustained heart rate faster than 60 bpm or fractional shortening of less than 25% may indicate underlying heart disease and require other specific therapy. The use of quinidine in horses with CHF is contraindicated.[8]

Digoxin

Digoxin has been successfully used to facilitate conversion to sinus rhythm. Indications for its use may include presenting findings of sustained tachycardia greater than 60 bpm and fractional shortening of less than 25%.

Digoxin is generally administered at 0.0022 mg/kg IV or 0.011 mg/kg PO bid. The therapeutic range for digoxin is 0.5 to 2 ng/ml. The half-life of digoxin is between 16 and 23 hours.[32]

Digoxin produces increased vagal tone and decreased AV nodal conduction and heart rate. It also increases the effective refractory period at the AV junction and is a positive inotrope.

The use of digoxin with quinidine appears to be beneficial in producing successful conversion of horses with atrial fibrillation when sustained steady-state plasma concentration of quinidine for 24 hours has not resulted in conversion. In one study, combined therapy of digoxin and quinidine sulfate was successful in converting 85% of horses treated on day 2 after 24 hours of unsuccessful therapy using quinidine sulfate alone.[1,3,32]

When significant underlying heart disease exists, digoxin and other medications are often required to support cardiac function. Quinidine should not be administered to these horses.

Digoxin toxicity may cause anorexia, nausea, salivation, diarrhea, colic, neurologic signs, rashes, and depression. Cardiac toxicity caused by digoxin includes premature beats, excessive slowing of AV conduction, AV block, AV dissociation, sinus bradycardia, sagging ST segments, PQ lengthening, and P wave widening.[32] Digoxin should not be administered for longer than 2 days without monitoring its blood levels.

Procainamide

Another medication suggested for cardioversion is procainamide, which can be administered at 25 to 35 mg/kg PO tid. An IV form of procainamide is administered at 1 mg/kg up to a maximum of 20 mg/kg. Procainamide appears to be less effective because of reduced vagolytic activity relative to quinidine.[10,23]

Flecainide

Therapy using the class Ic antiarrhythmic agent flecainide has reportedly converted atrial fibrillation to sinus rhythm safely at a dose of 1 to 2 mg/kg infused at a rate of 0.2 mg/kg/min.[37] Toxic side effects of treatment were significantly reduced compared with those associated with quinidine administration. However, doses that reached 3 mg/kg were associated with ECG and behavioral changes suggestive of toxicity. The horses used for this investigation received atrial fibrillation induction by a cardiac stimulator. Such experimental induction is associated with paroxysmal atrial fibrillation of various durations, and it is unclear if flecainide would prove to be as efficacious in treating naturally occurring atrial fibrillation in horses.

Biphasic Electrical Cardioversion

Low-energy biphasic electrical cardioversion is associated with greater first-shock efficacy than monophasic shock treatment of ventricular fibrillation and atrial cardioversion in humans and swine. Biphasic technology adjusts for transthoracic impedance, providing the same delivery of current through the heart at lower energy levels. It is associated with less myocardial dysfunction, fewer abnormalities on the ECG, and reduced burning of skin.

A report outlined successful conversion using this method in one of two horses.[38] The horse that was successfully converted received IV quinidine to facilitate cardioversion. The plasma levels at the time of conver-

sion were below the therapeutic range reported for horses. Although the success of treatment in the second horse was interesting, both horses required general anesthesia for electrical cardioversion, quinidine appeared to be required to assist with conversion, and preanesthetic electrolyte supplementation was reportedly necessary. Based on this one successfully treated patient, biphasic electrical cardioversion has been suggested as an alternative to quinidine, but its use requires equipment not commonly available in most equine hospitals. These factors make biphasic electrical cardioversion somewhat impractical and unlikely to be significantly used in the immediate future, despite the apparently reduced risk of quinidine toxicity.

PROGNOSIS FOR CONVERSION TO SINUS RHYTHM

The prognosis for conversion to sinus rhythm appears to be influenced by the duration of the arrhythmia. Horses that are presented with a history of atrial fibrillation of less than 4 months generally have an excellent prognosis for conversion, a low rate of recurrence, and few side effects associated with treatment. Horses with a history of atrial fibrillation of more than 4 months have more side effects associated with treatment and a decreased likelihood of conversion.[8] Recurrence of atrial fibrillation may be suggestive of underlying cardiac disease. With underlying cardiac pathology, the rate of conversion decreases and the recurrence of atrial fibrillation after successful conversion appears to increase. Horses with cardiac murmurs of grade III/VI or worse have lower rates of conversion to sinus rhythm. A presenting heart rate of less than 60 bpm implies a better prognosis for conversion.[8]

PROGNOSIS FOR SURVIVAL AND RETURN TO PERFORMANCE

Horses with atrial fibrillation that are not converted may have an overall poorer prognosis. If conversion is not attempted or achieved, owners should be apprised of the potential for sudden collapse if their horses are used beyond their athletic capability.

Horses successfully converted to sinus rhythm may return to light exercise 3 days after conversion.[28] Full training is resumed 7 to 10 days after conversion.[28] Horses without underlying cardiac disease often return to the same level or an improved level of performance and require no additional treatment after conversion. Those found to have underlying cardiac abnormalities have a poorer prognosis for survival and returning to the same level of performance. Horses that do not have significant underlying cardiac disease but do perform in events that require submaximal exercise of short duration or that are breeding may be capable of performing successfully without conversion to sinus rhythm.[8]

REFERENCES

1. Reef VB, Reimer JM, Spencer PA: Treatment of atrial fibrillation in horses: New perspectives. *J Vet Intern Med* 9(2):57–67, 1995.
2. Deem DA, Fregin GF: Atrial fibrillation in horses: A review of 106 clinical cases, with consideration of prevalence, clinical signs and prognosis. *JAVMA* 180:261–265, 1982.
3. Bertone JJ, Wingfield WE: Atrial fibrillation in horses. *Compend Contin Educ Pract Vet* 9(7):763–771, 1987.
4. Morris DD, Fregin GF: Atrial fibrillation in horses: Factors associated with response to quinidine sulfate in 77 clinical cases. *Cornell Vet* 72:339–349, 1982.
5. Holmes JR, Darke PGG, Else RW: Atrial fibrillation in the horse. *Equine Vet J* 1:211–222, 1969.
6. Muir WW, Reed SM, McGuirk SM: Treatment of atrial fibrillation in horses by intravenous administration of quinidine. *JAVMA* 197:1607–1610, 1990.
7. Stewart GA, Fulton LJ, McKellar CD: Idiopathic atrial fibrillation in a champion standardbred racehorse. *Aust Vet J* 67: 188–191, 1990.
8. Reef VB, Levitan CW, Spencer PA: Factors affecting the prognosis and conversion in equine atrial fibrillation. *J Vet Intern Med* 2:1–6, 1988.
9. Amada A, Senta T, Kubo K, et al: Atrial fibrillation in the horse: Clinical and histopathological studies of two cases. *Exp Rep Equine Health Lab* 11:51–69, 1974.
10. Bertone JJ: Atrial fibrillation in the horse: Diagnosis, prognosis and treatment. *Equine Pract* 6:6–12, 1984.
11. Helwig RW: Cardiac arrhythmias in the horse. *JAVMA* 170: 153–163, 1977.
12. Roos J: Auricular fibrillation in domestic animals. *Heart* 11:1–7, 1924.
13. Buchanan JW: Spontaneous arrhythmias and conduction disturbances in domestic animals. *Ann NY Acad Sci* 127:224–238, 1965.
14. Broojmans AWM: Electrocardiography in horses and cattle. *Lab Vet Physiol* 69–98, 1957.
15. Glazier DB, Nicholson JA, Kelly WR: Atrial fibrillation in the horse. *Irish Vet J* 13:47–55, 1959.
16. McGuirk SM, Muir WW: Diagnosis and treatment of cardiac arrhythmias. *Vet Clin North Am Equine Pract* 1:353–370, 1985.
17. Detweiler DK: Auricular fibrillation in horses. *JAVMA* 126: 47–50, 1955.
18. Deegan E, Buntenkotter S: Behavior of the heart rate of horses with auricular fibrillation during exercise and after treatment. *Equine Vet J* 8:26–29, 1976.
19. Shaftoe S, McGuirk SM: Valvular insufficiency in a horse with atrial fibrillation. *Compend Contin Educ Pract Vet* 9:203–207, 1987.
20. Amada A, Kurita H: Five cases of paroxysmal atrial fibrillation in the racehorse. *Exp Rep Equine Health Lab* 12:89–100, 1975.
21. Rose RJ, Davis PE: Treatment of atrial fibrillation in racehorses. *Equine Vet J* 9:68–71, 1977.
22. Else RW, Holmes JR: Pathological change in atrial fibrillation in the horse. *Equine Vet J* 3:56–64, 1971.
23. Fregin GF: The cardiovascular system, in Mansmann RA,

McAllister ES, Pratt PW (eds): *Equine Medicine and Surgery*, ed 3. Santa Barbara, CA, American Veterinary Publications, 1982, pp 645–704.

24. Glendenning SA: The use of quinidine sulfate in the treatment of atrial fibrillation in twelve horses. *Vet Rec* 77:951–960, 1965.
25. McGuirk SM, Muir WW, Sams RA: Pharmacokinetic analysis of intravenously and orally administered quinidine in horses. *Am J Vet Res* 42(6):938–942, 1981.
26. Collatos C: Treating atrial fibrillation in horses. *Compend Contin Educ Pract Vet* 17(2):243–245, 1995.
27. Reef VB: Tachyarrhythmias: Atrial fibrillation, in Marr CM (ed): *Cardiology of the Horse*. Philadelphia, WB Saunders, 1999, pp 186–197.
28. Patterson M: Cardiac arrhythmias, in Patterson M (ed): *Equine Cardiology*. Oxford, Blackwell Science, 1996, pp 172–205.
29. Blissit KJ: Diagnosis and treatment of atrial fibrillation. *Equine Vet Educ* 11(1):11–19, 1999.
30. Amada A, Kurita H: Treatment of atrial fibrillation with quinidine sulfate in the racehorse. *Exp Rep Equine Health Lab* 15:47–61, 1978.
31. Keen P: The use of drugs in the treatment of cardiac disease in the horse. *Equine Vet Educ* 2(2):81–82, 1990.
32. Muir WW, McGuirk SM: Pharmacology and pharmacokinetics of drugs used to treat cardiac disease in horses. *Vet Clin North Am Equine Pract* 1(2):335–352, 1985.
33. McGuirk SM, Muir WW, Sams RA: Pharmacokinetic analysis of intravenously and orally administered quinidine in horses. *Am J Vet Res* 42(6):938–942, 1981.
34. Muir WW, McGuirk SM: Hemodynamics before and after conversion of atrial fibrillation to normal sinus rhythm in horses. *JAVMA* 184(8):965–970, 1984.
35. Lekeux P, Muylle E, Henroteaux M, Bienfet V: Comparison of different treatments of atrial fibrillation in the horse. *Zentralbl Veterinarmed* 28:475–480, 1981.
36. Gerber H, Chuit P, Schatzmann HJ: Treatment of atrial fibrillation in the horse with intravenous dihydroquinidine gluconate. *Equine Vet J* 3:110–113, 1971.
37. Ohmura H, Nukada T, Mizuno Y, et al: Safe and efficacious dosage of flecainide acetate for treating equine atrial fibrillation. *J Vet Med Sci* 62(7):711–715, 2000.
38. Frye MA, Selders CG, Khursheed RM, et al: Use of biphasic electrical cardioversion for the treatment of idiopathic atrial fibrillation in two horses. *JAVMA* 220(7):1039–1045, 2002.

ARTICLE #5 CE TEST

The article you have read qualifies for 1.5 contact hours of Continuing Education Credit from the Auburn University College of Veterinary Medicine. *Choose the best answer* to each of the following questions; then mark your answers on the postage-paid envelope inserted in *Compendium*.

1. Treatment of atrial fibrillation most commonly involves which protocol?
   a. premedicating all horses with digoxin before treating with procainamide at 1 mg/kg IV
   b. treatment with quinidine sulfate at 22 mg/kg by nasogastric intubation every 2 hours until a total dose of 88 to 132 mg/kg has been reached in a 24-hour period
   c. treatment with IV xylazine before every 2-hour intubation to administer 22 mg/kg of quinidine gluconate
   d. administering a quinidine gluconate bolus at 6.2 mg/kg rapidly with a 2-g bolus of magnesium sulfate
   e. treatment is not generally indicated because atrial fibrillation is typically nonresponsive to any therapy

2. Plasma quinidine monitoring is generally indicated for which reason?
   a. horses tend to convert at levels of 2 to 5 µg/ml
   b. horses tend to exhibit more toxic side effects of quinidine when plasma levels are greater than 5 µg/ml
   c. plasma levels of quinidine may be elevated when a horse is concurrently receiving digoxin
   d. all of the above
   e. none of the above

3. Treatment of acute ventricular tachycardia in horses receiving quinidine should include
   a. digoxin, sodium bicarbonate, and activated charcoal.
   b. immediate euthanasia.
   c. systemic antimicrobials.
   d. ketamine anesthesia and atropine.
   e. epinephrine.

4. Digoxin may be administered to horses with atrial fibrillation for which reason?
   a. sustained tachycardia of more than 100 bpm before treatment
   b. poor fractional shortening (less than 25%) before treatment
   c. signs of supraventricular tachycardia associated with quinidine treatment
   d. failure to convert in the first 24 hours of quinidine treatment using a 2-hour treatment interval protocol
   e. all of the above

5. Which ECG finding is an early indication of quinidine toxicity?
   a. bifid P waves
   b. reduced amplitude of the QRS complex
   c. widening of the QRS complex by 25%
   d. second-degree AV block
   e. ventricular premature complexes

6. Which treatment is most likely to be effective for pharmacologic cardioversion of atrial fibrillation to sinus rhythm?
   a. lidocaine hydrochloride
   b. magnesium sulfate
   c. sodium bicarbonate
   d. flecainide
   e. phenylephrine hydrochloride

7. Which of the following indicates a decreased likelihood of conversion to sinus rhythm?
   a. atrial fibrillation for more than 4 months
   b. presenting heart rate of fewer than 60 bpm
   c. cardiac murmur of grade II/IV
   d. lack of underlying cardiac disease
   e. none of the above

8. Which of the following is considered to be a specific indication for digoxin administration with quinidine for conversion of atrial fibrillation to sinus rhythm?
   a. ventricular premature complexes
   b. fractional shortening less than 25%
   c. a presenting heart rate of fewer than 60 bpm
   d. systemic hypotension
   e. widening of the QRS complex

9. Which of the following is not an effect of digoxin on the heart?
   a. increased vagal tone
   b. increased effective refractory period
   c. decreased AV nodal conduction
   d. positive inotropic effect
   e. supraventricular tachycardia

10. Which statement regarding the prognosis for return to performance is correct?
    a. Horses that are converted to sinus rhythm and have no underlying cardiac disease are more likely to return to the same level of performance.
    b. Horses that are successfully converted and have no underlying cardiac disease are likely to require retreatment.
    c. Horses with underlying cardiac disease most often return to the same level of performance.
    d. Horses without underlying cardiac disease have a poor prognosis for life despite their often successful conversion.
    e. Horses that have had atrial fibrillation have a shortened lifespan regardless of whether they are successfully converted.