Journal of Veterinary Cardiology (2008) **10**, 111—115

ELSEVIER

Journal of Veterinary Cardiology
ESVC

www.elsevier.com/locate/jvc

Chronic oral therapy with enalapril in normal ponies

Meg M. Sleeper, VMD [a,*], Sue M. McDonnell, PhD [b], John J. Ely, PhD [c], Virginia B. Reef, DVM [a]

[a] *New Bolton Center, Section of Sports Medicine, Department of Clinical Studies, University of Pennsylvania Veterinary School, 382 W. Street Rd., Kennett Square, PA 19348, USA*
[b] *Hoffman Center, New Bolton Center, University of Pennsylvania Veterinary School, 382 W. Street Rd., Kennett Square, PA 19348, USA*
[c] *Alamogordo Primate Facility, Holloman Airforce Base, NM 88330, USA*

Received 6 February 2008; received in revised form 10 August 2008; accepted 14 August 2008

KEYWORDS
ACE inhibitor;
Enalapril;
Equine;
Horse;
Cardiovascular disease

Abstract Enalapril is an angiotensin converting enzyme (ACE) inhibitor that is frequently used in human, feline and canine patients with cardiac disease. Its use has been associated with impotence in human patients. The purpose of this study was to evaluate if enalapril (0.5 mg/kg PO, q24h) is likely to alter behavior in stallions and to assess its effect on ACE activity at the standard dose used in dogs and cats. Twelve pony stallions were evaluated by physical examination and echocardiography followed by treatment with enalapril ($n = 6$) or placebo ($n = 6$) for 2 months. After one month, blood was drawn and stored to evaluate ACE activity in the 2 groups. At the end of the study, repeat physical examination and echocardiography were performed. Physical examination, echocardiographic indices, and reproductive performance were unchanged and there was no suppression of ACE activity. Results of this study suggest that enalapril (0.5 mg/kg PO, q24h) is either poorly absorbed in the horse or is inadequately converted to the active form of the drug, enalaprilat.
© 2008 Elsevier B.V. All rights reserved.

Introduction

Acquired valvular disease is common in horses, involving approximately 25% of hearts examined.[1] The aortic, mitral and tricuspid valves are frequently affected.[1] Degenerative valvular changes are seen most commonly in aged horses[1] similar to other species. The hemodynamic consequence of valvular insufficiency is volume overload. Once the neurohumoral system is activated, causing vasoconstriction and water

* Corresponding author.
E-mail address: sleeper@vet.upenn.edu (M.M. Sleeper).

1760-2734/$ - see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.jvc.2008.08.002

retention, myocardial failure with secondary congestive heart failure can occur. Balanced vasodilators such as the angiotensin converting enzyme inhibitors (ACEI) have become a major plank in the treatment of valvular insufficiency and dilated cardiomyopathy in humans, dogs, and cats. Compared to placebo, ACEI lower the heart rate, mean systemic arterial blood pressure, and mean pulmonary arterial blood pressure while increasing cardiac output and reducing morbidity and mortality in dogs.[2–4] Additionally, ACEI have been shown to alleviate symptoms and prolong useful life in humans and dogs.[2,5] Enalaprilat, the active metabolite of enalapril, inhibits angiotensin converting enzyme (ACE) activity by more than 75% in horses.[6]

Because of drug cost in horses, enalapril therapy may be avoided in many cases. Considering the expense, the most likely candidate for ACEI therapy would be the aged breeding stallion with valvular insufficiency, an individual that might gain additional breeding seasons with the benefit of ACEI therapy. In these cases the cost is most likely to be offset by possible income from the additional breedings. Enalapril is currently the only ACEI approved for use in veterinary species in the USA. However, erectile dysfunction is one reported side effect linked to enalapril therapy in men,[7] which could limit its use in breeding animals. The primary purpose of this study was to evaluate the effects of a 2-month course of oral enalapril treatment on erection and ejaculatory function in normal stallions. A secondary objective was to evaluate the effect of chronic, enalapril treatment (0.5 mg/kg PO, q24h) on ACE activity in the equine.

Animals, material and methods

Twelve clinically normal Shetland pony (size 120—300 kg) stallions, aged 3—19 years, with baseline sexual behavior and semen characteristics within the range of normal were used in this study. All stallions were normal on physical examination and complete echocardiographic examination. Echocardiograms were performed with a VingMed echocardiographic machine[d] from the right parasternal window using a 3.5 mHz probe to obtain routine measurements of heart size and systolic function as has been described elsewhere.[8] The same sonographer (MMS) performed all examinations and 3 sets of measurements were obtained and averaged for each variable. Matched pairs based on age, baseline semen and sexual behavior characteristics were assigned to the enalapril or control treatment groups. The 6 enalapril subjects were administered 0.5 mg/kg enalapril orally in molasses vehicle daily for 2 months. The 6 control subjects received vehicle only on the same schedule. The investigators remained blind to the group assignments. After one month of treatment, blood samples were collected at 0, 15, 30, 45 min, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, 18, 24, 36, and 48 h post-administration of enalapril to evaluate ACE activity. Blood samples were collected from control ponies at 15, 30, 45 min, 1, 1.5 and 4 h post-administration of vehicle. Blood was centrifuged, separated and serum was frozen at −80 °C until ACE activity was assessed (6 years later). Samples were analyzed by the Laboratory Corporation of America using a kinetic test.[e] During the final week of the study, the 12 ponies were re-evaluated by physical examination and echocardiography.

Sexual function and semen output were assessed in standard semen collection trials conducted twice daily for 5 consecutive days during the week preceding onset of treatment (baseline) and again beginning 8 weeks after the start of treatment (the last week ponies received treatment). Measures of erection and ejaculatory function included erection rigidity (graded as normal erection sufficient for insertion, decreased from normal, or increased tumescence), the number of organized thrusts to ejaculation on the ejaculatory mount, the number of urethral contractions palpable at the base of the penis during ejaculation, gel-free semen volume, gel volume, semen pH, and total number of sperm. Erection was also evaluated in 10-h videotaped samples of spontaneous erections obtained during the last week of treatment. Specific measures included the frequency, duration, and graded tumescence of spontaneous erections, which occur on an average of every 90 min in stallions.

The echocardiographic variables were compared for differences between groups, using the analysis of variance on the difference between pre- and post-treatment values within each horse. This is statistically equivalent to a paired *t*-test, with each individual horse serving as its own control. ACE activity data were evaluated using SYSTAT Version 11.0.[f] Repeated measures analysis of variance was used to assess changes within-subjects and differences between groups. A total of 6 time points had complete data in both experimental and control groups (15 min, 30 min, 45 min, 60 min, 90 min, 4 h). The Normality assumption was tested with the

[d] General Electric Healthcare, United Kingdom.

[e] Olympus AU400E; Center Valley, Pennsylvania.

[f] SYSTAT Software, Inc., Richmond, CA.

Download English Version:

https://daneshyari.com/en/article/2400300

Download Persian Version:

https://daneshyari.com/article/2400300

Daneshyari.com