Optimization of Timing of Furosemide Treatment: A Comparison of Pulmonary Vascular Pressures of Thoroughbred Horses During Strenuous Exertion 1, 2, 3, and 4 h Postadministration

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The attenuating effect of furosemide premedication on exercised-induced pulmonary capillary hypertension is similar when the drug is administered 2, 3, or 4 h before exercise. However, this effect is not observed when furosemide is administered 1 h pre-exertion. Authors’ address: Depts. of Veterinary Clinical Medicine (Magid and Goetz) and Veterinary Biosciences (Manohar), University of Illinois at Urbana-Champaign, 1008 W. Hazelwood Dr., Urbana IL 61802. © 1998 AAEP.

1. Introduction

Exercise-induced pulmonary hemorrhage (EIPH) is associated with strenuous exertion in the horse, and the incidence in racehorses is suggested to be very high. It has been observed in Quarter Horse, Thoroughbred, and Standardbred racehorses, roping horses, barrel racing horses, and other equine athletes.

Exercise-induced pulmonary hemorrhage is thought to be caused by the stress failure of pulmonary capillaries resulting from increased pulmonary capillary blood pressure during strenuous exercise. A disruption of the blood–gas barrier allows bleeding into the airways, resulting in EIPH. In more severe cases of EIPH, epistaxis and sudden death may even occur.

Furosemide is used as a treatment or prophylactic agent in racehorses experiencing EIPH. Its use is regulated in most racing jurisdictions. In Illinois, furosemide is not administered less than 4 h prior to race time, and the dose is limited to 250 mg/horse without provision for body weight. Previous studies have shown that the administration of furosemide (250 mg/horse) 4 h prior to work attenuates the exercise-induced rise in pulmonary capillary blood pressure, possibly reducing the severity of EIPH in racehorses.

The effect of furosemide on pulmonary vascular pressures may be mediated by means of a reduction in plasma volume. A study by Hinchcliff et al. reported that the furosemide-induced decrease in plasma volume peaks 15–30 min after administration and that plasma volume recovers during the next 3.5 h. From the results of this study, we hypothesized that furosemide might be more effective in attenuating the exercise-induced rise in pulmonary capillary blood pressure if given at shorter intervals before exercise.
2. Materials and Methods

Seven healthy, sound, exercise-trained Thoroughbred horses (one filly and six geldings, aged 3–6 years and weighing between 378 and 490 kg) were used in these experiments. The horses were housed in an air-conditioned building (temperature maintained between 18°C and 20°C) and were accustomed to being handled. They were fed a diet of alfalfa hay and oats, and free access to water was provided.

The horses were studied at rest and during exercise performed at their maximal heart rate in the control and furosemide experiments. In the control study, horses received no medications and had no restriction of food and water. Furosemide treatments included the drug administration (furosemide 250 mg IV) at intervals of 1, 2, 3, and 4 h before exercise. After furosemide administration, access to food and water was denied. The sequence of treatments was randomized, and 7 days were allowed between treatments.

Measurements of heart rate and of right atrial, pulmonary arterial, and pulmonary artery wedge pressures were made at rest and during exercise at 14.2 m/s on a 3.5% uphill grade by using standard techniques. This workload elicited the maximal heart rates of the horses. Mean pulmonary capillary blood pressure was calculated as 0.5 (mean pulmonary artery pressure + mean pulmonary artery wedge pressure).

An endoscopic examination of the nasopharynx, larynx, and trachea down to the carina was performed 30, 45, and 60 min after each experiment. If blood was observed in the airway, horses were considered to be EIPH positive for that experiment.

Experimental data were subjected to a split-plot design, repeated measures analysis of variance by using the SAS statistical software package. Treatments were compared by using the least-squares difference method, with a probability of \( p < 0.05 \) considered statistically significant. The data are presented as mean ± 1 SEM.

3. Results

In the control experiments, resting values of heart rate, mean right atrial pressure, mean pulmonary arterial pressure, mean pulmonary artery wedge pressure, and mean pulmonary capillary pressure were 35 ± 2 beats/min, 8.4 ± 1 Torr, 28 ± 1 Torr, 25 ± 1 Torr, and 21 ± 1 Torr, respectively. With exercise at 14.2 m/s on a 3.5% uphill grade, these variables increased to 217 ± 3 beats/min, 60 ± 3 Torr, 108 ± 5 Torr, 88 ± 3 Torr, and 67 ± 3 Torr, respectively.

Instanding horses, statistically significant reductions (\( p < 0.05 \)) occurred in the mean right atrial pressure only at 2 h after furosemide administration. None of the other resting parameters differed significantly from the control values.

The mean right atrial pressure in exercising horses at 1, 2, and 3 h after furosemide administration was similar and was significantly (\( p < 0.05 \)) less than that in the control study. During exercise performed 4 h after furosemide administration, the mean right atrial pressure was similar to that in the control experiments.

In exercising horses 2, 3, and 4 h after furosemide administration, mean pulmonary arterial, mean pulmonary artery wedge, and mean pulmonary capillary blood pressures were similar to each other and were significantly (\( p < 0.05 \)) less than those in the control experiments.

In the control experiments, five out of seven horses were EIPH positive during exercise. In the 1-h postfurosemide experiments, six out of seven horses were EIPH positive. In the 2-h, 3-h, and 4-h postfurosemide experiments, four out of seven, five out of seven, and four out of seven horses were EIPH positive, respectively.

4. Discussion

Our observations in the control and 4-h postfurosemide experiments confirmed previous research that showed that exercising horses develop significant right atrial, pulmonary arterial, pulmonary artery wedge, and pulmonary capillary hypertension and that furosemide is effective in significantly attenuating this exercise-induced pulmonary hypertension. New findings of this study are as follows. First, significant pulmonary hemodynamic effects in exercising horses are not observed when furosemide (250 mg IV) is administered 1 h prior to exercise. Second, furosemide (250 mg IV) is equally effective when administered at 2, 3, or 4 h prior to exercise in attenuating the exercise-induced pulmonary arterial, pulmonary artery wedge, and pulmonary capillary hypertension in Thoroughbred horses. Our observations do not support the hypothesis that the administration of furosemide at shorter intervals before exercise might be more effective in attenuating the exercise-induced rise in pulmonary capillary blood pressure.

5. Conclusions

In conclusion, it appears that the minimum interval for administering furosemide to racehorses experiencing EIPH is 2 h prior to exercise.

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References and Footnotes


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