Pulmonary Vascular Pressures of EIPH-Positive Thoroughbred Horses During Exercise Performed at Maximal Heart Rate After Administration of Various Doses of Furosemide

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A linear dose response to furosemide in terms of attenuation of the exercise-induced pulmonary capillary hypertension does not exist in Thoroughbred horses. Furosemide 2.0 mg/kg IV given 4 h before exercise further significantly \((p < 0.05)\) attenuates the exercise-induced pulmonary capillary hypertension compared with the 250-mg dose routinely used at Illinois racetracks. Authors’ address: 212 Large Animal Clinic, College of Veterinary Medicine, 1102 W. Hazelwood Dr., University of Illinois at Urbana-Champaign, Urbana, IL 61801. © 1997 AAEP.

1. Introduction
The incidence of exercise-induced pulmonary hemorrhage (EIPH) in racehorses is reported to exceed 75%.\(^1\,^2\) Strenuously exercising horses exhibit dramatic pulmonary arterial, capillary, and venous hypertension,\(^3\,^4\) and the blood-gas barrier (which has to be thin to provide for diffusion of respiratory gases) is thus exposed to high transmural (intracapillary minus perivascular/alveolar) pressure. Disruption of the blood-gas barrier because of high transmural force—a phenomenon known as stress failure of pulmonary capillaries—is now recognized as the probable cause of EIPH in racehorses.\(^3\,^5\)

It has been demonstrated in horses premedicated with furosemide (250 mg, 4 h before exercise) that there is a significant attenuation of the exercise-induced rise in pulmonary capillary blood pressure.\(^8\,^9\,^11\) This effect of furosemide is observed not only in incremental high-intensity exertion\(^8\,^9\,^11\) but also in rapid acceleration to supramaximal exercise.\(^10\) Despite the fact that furosemide has been used in racehorses experiencing EIPH for the past several years, to our knowledge there have been no studies examining the furosemide dose response in terms of attenuation of the exercise-induced pulmonary capillary hypertension. In this context, it is worth noting that there is a considerable variation in the dosage-administration regimens of furosemide in various U. S. racing jurisdictions.\(^9\) Thus, our primary objective in this study was to examine the furosemide dose response in terms of attenuation of the exercise-induced pulmonary arterial, capillary, and venous hypertension in Thoroughbred horses performing at maximal heart rate.

According to Illinois horse racing regulations, the furosemide dose permitted for use in horses experi-
ening EIPH is 250 mg regardless of body weight, and the drug is administered 4 h before racing. Thus, in the present study we compared the effects of furosemide administered intravenously at higher dosages (1.0, 1.5 and 2.0 mg/kg body weight; 4 h pre-exercise) against the 250-mg dose.

2. Materials and Methods
Experiments were carried out on seven healthy, sound, exercise-trained Thoroughbred horses by using a split plot, repeated measures experimental design. The sequence of control (no medication) and various furosemide dose (250 mg, 1.0 mg/kg, 1.5 mg/kg, and 2.0 mg/kg) experiments was randomized for every horse, and 7 days were allowed between experiments. In each experiment, hemodynamic measurements were made at rest and during treadmill exercise performed at 14.2 m/s on a 3.5% uphill grade. This workload elicited maximal heart rate (215 ± 3 beats/min) of the horses. In all furosemide experiments, the drug was administered intravenously 4 h before exercise. In the present study, the furosemide dose of 250 mg amounted to 0.56 ± 0.03 mg/kg body weight.

Right heart, pulmonary arterial, pulmonary capillary, and pulmonary artery wedge (venous) pressures were determined by using standard techniques and procedures.3–6,8–11 An endoscopic examination of the nasopharynx, larynx, and trachea (up to the carina) was performed 55–60 min postexercise, and the presence of fresh blood in the trachea was regarded as evidence for the occurrence of EIPH.

3. Results
Furosemide administration resulted in a significant (p < 0.05) decrease in mean pulmonary arterial, pulmonary capillary, and pulmonary artery wedge pressures of standing horses, but significant differences among the various furosemide doses were not observed at rest. Exercise at maximal heart rate in the control experiments was attended by a significant (p < 0.05) right atrial (49 ± 1 Torr) as well as pulmonary arterial (96 ± 2 Torr), capillary (78 ± 2 Torr), and venous (60 ± 3 Torr) hypertension, and all horses experienced EIPH. Compared with the control (no medication) study, following furosemide administration at each of the four doses, the exercise-induced rise in mean right atrial as well as pulmonary arterial, capillary, and venous pressures was significantly (p < 0.05) attenuated. However, statistically significant differences were not discerned between the furosemide doses of 250 mg, 1.0 mg/kg, and 1.5 mg/kg in the right heart or pulmonary vascular pressures of exercising horses. A further statistically significant (p < 0.05) reduction in the pulmonary vascular pressures of horses exercising at maximal heart rate was observed when the furosemide dose increased to 2.0 mg/kg. At 2.0 mg/kg of furosemide, although all horses still experienced EIPH, the quantity of fresh blood present in the trachea was markedly reduced.

4. Discussion
In agreement with previous observations,3–6 it was observed that exercising Thoroughbreds develop significant right atrial, as well as pulmonary arterial, capillary, and venous hypertension, and that intravenous furosemide administration at 250 mg (4 h pre-exercise) significantly (p < 0.05) attenuates the exercise-induced right atrial as well as pulmonary arterial, capillary, and venous hypertension.8–11

Statistical analyses of the right heart or pulmonary hemodynamic data obtained during strenuous exertion using the furosemide doses revealed the following: (a) A linear dose response to furosemide in terms of attenuation of the exercise-induced pulmonary arterial, capillary, and venous hypertension does not exist in Thoroughbred horses. (b) In comparison with the currently used furosemide dosage at Illinois racetracks (250 mg regardless of body weight), a significant advantage in terms of further attenuation of the exercise-induced pulmonary capillary hypertension is not gained by increasing the furosemide dose to 1.0 or 1.5 mg/kg. (c) At a furosemide dose of 2.0 mg/kg, a further significant (p < 0.05) attenuation of the mean pulmonary capillary blood pressure occurred in horses exercising at 14.2 m/s ± 3.5% uphill grade. In terms of stress failure of pulmonary capillaries, the greater attenuating effect of a 2.0 mg/kg dose of furosemide on the exercise-induced pulmonary capillary hypertension would be considered beneficial in that the transmural force exerted on the pulmonary capillaries is greatly reduced. Because of this further reduction in the force responsible for extravassation of blood from the pulmonary capillaries, the extent or severity of EIPH is likely to be diminished.

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References and Footnotes


