

MESSAGE FROM THE GRAYSON-JOCKEY CLUB RESEARCH FOUNDATION

EXERCISE INDUCED PULMONARY HEMORRHAGE

Results of a pair of research projects



Grayson-Jockey Club
Research Foundation

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TWO RESEARCH PROJECTS on Exercise Induced Pulmonary Hemorrhage solicited by The Grayson-Jockey Club Research Foundation and funded in cooperation with The Jockey Club, the AAEP Foundation, Keeneland Association, Oak Tree Racing Association, The Stronach Group, Churchill Downs, Kentucky Downs, New York Racing Association, The Del Mar Thoroughbred Club, Oaklawn Park, and The Thoroughbred Horseman's Association have now appeared in peer-reviewed journals.

Knych HK, Wilson WD, Vale A, et al. Effectiveness of furosemide in attenuating exercise-induced pulmonary haemorrhage in horses when administered 4- and 24-h prior to high speed training. Equine Vet J. 2017;50:350-355.

Bayly W, Lopez C, Sides R, et al. Effect of different protocols on the mitigation of exercise induced pulmonary hemorrhage in horses when administered 24 hours before strenuous exercise. J Vet Intern Med. 2019;

1-8. <https://doi.org/10.1111/jvim.15574>

In March of 2015, a special call for research on exercise induced pulmonary hemorrhage was issued by the Grayson-Jockey Club Research Foundation. Emphasis was placed on strategies to control EIPH without race-day medication. Two projects were selected. The premise of the research was to look at the post-treatment effect of furosemide (Salix, or Lasix) if it had been given 24 hours before exercise with water intake limited to maintenance

water levels (which are known).

One project submitted by the University of California at Davis under the direction of Dr. Heather Knych proposed to take 15 fit Thoroughbreds with no known history of bleeding and assess three treatments head-to-head against each other: saline placebo, furosemide four hours before exercise, and furosemide 24 hours before exercise with limited water access. The horses were paired in five-furlong simulated exercise sessions and assessed for bleeding via endoscopic examination using the conventional 0-4 scoring system and via broncho alveolar lavage (BAL) counting the number of red blood cells (RBC) found in the lung lavage post exercise. The horses trained conventionally at a racetrack, and the exercise sessions were separated by a two-week interval.

The results showed with 24-hour administration the pharmacologic level of furosemide is approximately 1/100th the level of circulating medication when compared to four-hour pre-exercise ad-

ministration. So, more than 99% of the medication has cleared by 24 hours.

In the horses with no known bleeding history, there was one bleeder. He bled with no treatment, and he bled through both treatments, though the four-hour furosemide treatment reduced his grade of bleeding. There were three endoscopic graders and blood in the trachea was seen in 11 of the 43 endoscopic exams; on four exams was the blood more than a grade 1 (trace) and three of those four observations were accounted for by the one horse that bled continuously.

On average there were low levels of RBC's present in the BAL in all horses after exercise, even with no blood visible endoscopically, but the levels were less than 200(105/ml), even with the bleeding horse included.

So the conclusion from the study was that, though blood was seen on the endoscopic exam of 11 of 43 endoscopic exams, the four-hour furosemide reduced the number of times blood was observed compared to the 24-hour treatment, and the BAL results suggest the 24-hour treatment is not as effective as the four-hour treatment in attenuating the increase in RBC's associated with exercise in these horses with no known history of bleeding.

The second project done at Washington State University under the direction of Dr. Warwick Bayly took seven fit

fects are secondary to a decreased inspiratory resistance, lowered inspiratory muscle work and altered intrapulmonary pressures."

In the years following the initial study, Kansas State University did several more trials testing nasal strips, and Kentucky Equine Research, University of Califor-

nia at Davis, and Michigan State University are also among those that have researched the usefulness of nasal strips. They all reached similar conclusions.

In 2001 the KER study "Effects of an external nasal strip and furosemide on pulmonary haemorrhage in Thoroughbreds following high-intensity exercise"

was published in the *Equine Veterinary Journal*. During the study, eight Thoroughbreds were asked to complete four sprint exercise tests on a treadmill.

The study aimed to see what effects an external nasal strip, furosemide, and a combination of the two had on Thoroughbreds by assessing the red blood cell

Thoroughbreds that were known to be clinical EIPH patients during racing and look at seven different treatment protocols.

The target was to assess the efficacy of furosemide at the maximum and minimum dosage administered 24 hours prior to exercise compared to the conventional four-hour treatment prior to exercise. This required seven different maximum exercise sessions from all seven of the horses separated by two weeks of routine training. The seven treatment protocols were designed to separate all the effects of furosemide and the timing of its administration to pinpoint the differences in effect of each treatment component.

The study was a two-phase project: The first segment was to look at the components of treatment with horses performing only on a treadmill, where exercise could be controlled and the horses taken beyond their aerobic capacity (115% of VO₂ Max) and exercised to fatigue where they could no longer maintain a constant speed of exercise. Each of the horses was examined with the conventional endoscopic examination and with BAL RBC assessment post-exercise. But since the horses were known “bleeders,” the BAL counts compared differences in BAL numbers two days before exercise and BAL numbers post-exercise in addition to absolute RBC numbers to pinpoint further the effect of the treatment protocols on the “bleeding” occurring in these horses. Then with the results of these trials the horses were returned to the racetrack, trained for

an additional month conventionally, and ran a simulated five-furlong race from the starting gate with all horses receiving the most promising treatment selected by the treadmill trial data and competing against each other in the races.

All seven horses underwent the seven components of the study in a double-blinded, randomized fashion: placebo (saline), conventional (low dose, 250mg, 5ml) furosemide four hours pre-exercise, controlled water access only with no medication (maintenance water access for 24 hours pre-exercise), low dose furosemide (250mg, 5ml) 24 hours pre-exercise with free access to water, high dose furosemide (500mg, 10ml) 24 hours pre-exercise with free access to water, low-dose furosemide with maintenance water access, and high-dose furosemide with maintenance water access.

In the study of horses that were known bleeders (Washington State), the findings were as follows:

No treatment produced a statistically significant difference in the endoscopic bleeding score on the treadmill because all horses bled, and the differences on the 0-4 bleeding scale were not enough to show significant changes.

However, in the BAL’s assessment, where the counting range was much larger and more sensitive, the low dose (250mg) furosemide with 24-hour maintenance water was the only treatment that statistically significantly reduced the increase in the number of RBC’s in the BAL fluid after exercise.

So, it was the treatment that was selected for validation in the simulated races of the six horses, one race with low-dose furosemide and one race with the saline control. The horses were fit after the treadmill exercise, but they were trained an additional month on the racetrack before the simulated race. The races were among six horses going 1,100 meters (5½ furlongs) from the starting gate and were separated by two weeks of training between.

The results after simulated racing produced some interesting changes in results. The difference between the BAL RBC’s in the control horses and the treated horses narrowed, dropping the confidence of a treatment effect to 90% from 95%. This is below the traditional 95% significance threshold reached on the treadmill study but is still 90% certainty the low-dose furosemide with controlled water access lowered the BAL RBC’s during the simulated races. But, the endoscopic EIPH scores on the racetrack actually changed in the opposite direction; i.e., the bleeding was worse, and the endoscopic bleeding scores became statistically significantly lower with the low-dose furosemide, water-restricted horses when compared to the control exercise values.

In conclusion, it looks like low-dose 24-hour furosemide with controlled water access shows great promise as a replacement treatment for our conventional four-hour pre-race treatment for EIPH in horses that are bleeding. It was less effective in horses that were not known bleeders. **BH**

count in BAL fluid. A control—meaning neither treatment—was also performed.

“We conclude that both the external nasal strip and furosemide attenuate pulmonary hemorrhage in Thoroughbred horses during high-speed sprint exercise,” the KER researchers summarized. “The external nasal strip appears

to lower the metabolic cost of supramaximal exertion in horses. Given the purported ergogenic effects of furosemide, the external nasal strip is a valuable alternative for the attenuation of EIPH.”

The same year, Kansas State University’s study titled “Efficacy of Nasal Strip and Furosemide in Mitigating EIPH in

Thoroughbred Horses” was published in the *Journal of Applied Physiology*.

Five Thoroughbreds were put on a treadmill and tested at maximum effort four times under the following circumstances: wearing a nasal strip (NS); medicated with furosemide (Fur); wearing a nasal strip and medicated with