Management of Exercise-Induced Pulmonary Hemorrhage in Nonracing Performance Horses

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Exercise-induced pulmonary hemorrhage (EIPH) is a major health concern for horses that are exercised intensely and is a cause of poor performance in equine athletes. EIPH occurs most notably in racing thoroughbreds and in other high performance nonracing equine athletes such as barrel and draft horses as well as those that participate in roping, polo, cross-country events, reining, cutting, hunting and jumping, and steeplechases. Significant progress has been made in recent years to understand the pathogenesis of EIPH in racing thoroughbreds.

Diagnosis
Exercise-induced pulmonary hemorrhage was recognized about 4 centuries ago. On the track, EIPH was first diagnosed by visible epistaxis, suggesting the incidence was very low (0.25% to 13%). In 1974, endoscopy was used to identify the lungs as the source of hemorrhage and subsequently demonstrated that the incidence of EIPH was much higher (13% to 40% in cross-country horses, 10% to 15% in polo ponies, 62% in quarter horses, 26% to 77% in standardbreds, 70% in steeplechase horses, and 44% to 75% in thoroughbreds). With repeated examination of individual horses, the incidence was documented to be 82% to 95%. Only a few studies have been conducted to determine the incidence of EIPH in nonracing performance horses. Bronchoalveolar lavage (BAL) has recently been used to quantify pulmonary hemorrhage and may be the method of choice. This technique is more sensitive for detecting blood in the airways and has the potential to identify EIPH in more horses with poor performance than might otherwise have been diagnosed.

Causes and Mechanisms
Numerous causes and pathophysiologic mechanisms have been proposed for EIPH, including small airway disease, upper airway obstruction, exercise-induced hyperviscosity, mechanical stresses of respiration and locomotion, redistribution of blood flow in the lung, alveolar pressure fluctuations, and pulmonary hypertension. Several factors may cause the pulmonary system to become heavily stressed to the point at which capillaries fail. Current evidence suggests that pulmonary vascular hyper-

ABSTRACT: Exercise-induced pulmonary hemorrhage (EIPH) is a major health concern not only for racehorses but also for all equine athletes, including nonracing performance horses. Diagnosis can be made by endoscopy; however, bronchoalveolar lavage may be the method of choice since it can more accurately quantify the amount of EIPH. Numerous factors contribute to EIPH, but pulmonary vascular hypertension combined with large negative intrapleural pressures is believed to constitute the primary factor leading to stress failure of the pulmonary capillaries. Horses with EIPH are frequently treated with furosemide, which reduces pulmonary vascular pressures; however, other treatments are being increasingly used.

KEY POINTS
- Furosemide reduces pulmonary vascular pressures during exercise, may be associated with a redistribution of blood flow in the lung, and can reduce the amount of exercise-induced pulmonary hemorrhage (EIPH) by approximately 90%.
- An equine nasal strip stabilizes the nasal passages during exercise, reduces upper airway resistance and the work of breathing, and can reduce the amount of EIPH by 40%.

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ment has been difficult due to controversy regarding the mechanisms that cause EIPH and failure of early investigations to quantify EIPH (prior to the use of BAL). There is a demand for effective prophylaxis and/or treatment to control the bleeding. Many pharmacologic agents have been tried, but few have proven efficacy in treating EIPH.

Different treatments may include pulmonary vasodilators, bronchodilators, drugs to decrease blood viscosity, surgical correction of laryngeal hemiplegia to decrease upper airway resistance, antiinflammatory drugs, drugs to inhibit platelet aggregation, hesperidin-citrus bioflavonoids to alter capillary fragility, aminocaproic acid and tranexamic acid to inhibit fibrinolysis, and estrogens, which have been used without a clear rationale.

Furosemide

Horses on the racetrack are frequently treated with furosemide, which attenuates the exercise-induced increases in right atrial, pulmonary arterial, pulmonary wedge, and pulmonary capillary pressures as well as the concentration of red blood cells in the BAL fluid. Furosemide may also be associated with a redistribution of pulmonary blood flow and a reduction in blood flow to the dorsal portion of the lung during exercise (the portion of the lung where EIPH is most predominant). Furosemide (1 mg/kg IV 4 hours prior to exercise) reduces EIPH by 90% in thoroughbred horses that run to 95% of their maximum aerobic capacity (Figure 1). The use of furosemide is controversial due to variable efficacy in treating the condition, variation in regulatory acceptance among certain associations and jurisdictions, its ability to mask other drugs, its performance-enhancing properties, and the necessity for intravenous administration since oral absorption is negligible in horses. Repeated intravenous administration by owners can cause horses to exhibit dangerous reactions, thus requiring a veterinarian to administer the product, especially in nonracing performance horses.

FLAIR™ Nasal Strip

In the equine athlete, 40% to 50% of total pulmonary resistance is located in the nasal passages. During inspiration, the extrathoracic airways account for more than 90% of the total resistance. Human athletes have increasingly adopted an external nasal dilator strip to reduce nasal resistance and to promote easier breathing during exercise. Since horses are obligate nasal breathers, nasal resistance is much more important in equine athletes than in human athletes. An equine nasal strip (FLAIR™; CNS, Inc., Minneapolis, MN) was recently introduced to stabilize the nasal passages, reduce upper airway resistance, reduce the work of breathing, and reduce intrapleural tension combined with large negative intrapleural pressures creates a high capillary transmural pressure, leading to hemorrhage. Decreased performance results from edema in the gas exchange region of the lung (interstitial edema) and blood in the airways (alveolar edema and hemorrhage). This culminates in irritation and inflammation of the airways, exacerbation of small airway disease, and perpetuation of the cycle. With repeated strenuous exercise (either in training or actual competition), the hemorrhage results in fibrosis/scarring, a weakened blood–gas barrier, and sustained inflammation. The blood within the alveoli may adversely affect lung health and exercise capacity by interfering with gas exchange. EIPH often worsens with repeated exercise and increased age.

Prevention and Treatment

The development of an ideal treatment has been difficult due to controversy regarding the mechanisms that cause EIPH and failure of early investigations to quantify EIPH (prior to the use of BAL). There is a demand for effective prophylaxis and/or treatment to control the bleeding. Many pharmacologic agents have been tried, but few have proven efficacy in treating EIPH. Different treatments may include pulmonary vasodilators, bronchodilators, drugs to decrease blood viscosity, surgical correction of laryngeal hemiplegia to decrease upper airway resistance, antiinflammatory drugs, drugs to inhibit platelet aggregation, hesperidin-citrus bioflavonoids to alter capillary fragility, aminocaproic acid and tranexamic acid to inhibit fibrinolysis, and estrogens, which have been used without a clear rationale.

Figure 1—Exercise-induced pulmonary hemorrhage (EIPH) was significantly reduced (*P <.05) in the nasal strip (NS), furosemide (FUR), and (NS + FUR) trials compared with the control (CON). FUR and NS + FUR further reduced (*P <.05) the EIPH response compared with NS. RBC = red blood cells; BAL = bronchoalveolar lavage. (From Kindig CA, McDonough P, Fenton G, et al: Efficacy of nasal strip and furosemide in mitigating EIPH in Thoroughbred horses. J Appl Physiol 91:1396–1400, 2001; with permission.)

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and alveolar pressure swings that may contribute to high pulmonary capillary transmural pressures and EIPH (Figure 2).11,15,16 Experimental studies have demonstrated that horses wearing the nasal strip have a 30% to 40% decrease in the number of red blood cells in BAL fluid (Figure 1). Whole body oxygen consumption is reduced by 5% to 6%, suggesting a reduced oxygen cost of ventilation (i.e., decreased work of breathing).

**Equine Concentrated Serum**

Seramune® (Sera, Inc., Shawnee Mission, KS) is a concentrated serum that contains equine IgG and other immunoglobulins. Field studies have demonstrated its efficacy and safety. Seramune® is used to treat horses with chronic bleeding at a dosage of 20 ml intratracheal and 10 ml IV for 5 days consecutively (with a booster dose weekly and 24 to 48 hours before heavy exercise or racing).

**Herbal Formulations**

A number of herbal formulations are used to treat horses with EIPH; however, no published scientific research has been conducted to determine the effectiveness of these remedies. The stated goals of herbal formulations are to clear heat and edema from the lung, cool and nourish the blood, and move stagnated blood from the airways.17–18

**Yunnan Paiyao** (Mayway Corporation, Oakland, CA), a patent Chinese herbal formula empirical for hemorrhage, has been shown to significantly shorten bleeding time in rats and significantly reduce the clotting time in rabbits and humans when compared with respective saline-treated controls.19 The dose for horses is 4 g of powder PO bid for 3 days before performance and on the morning of performance.

**Single Immortal™** (Du Sheng Tang; Jing-Tang Herbal Company, Reddick, FL) is an herbal formulation designed to stop bleeding in horses with EIPH.20 Results from an unpublished study indicated that five horses with EIPH responded well to the formula. The recommended dosage is 30 to 50 g of powder PO bid 3 to 7 days prior to racing/ training, during racing/ training, and 3 days after strenuous exercise.21 This formulation is reported to stop lung hemorrhage, shorten bleeding time, enhance agglutination of red blood cells, shorten thrombin time, lower blood pressure, and reduce capillary permeability.

**Red Lung™** (Jing-Tang Herbal Company) is an adaptation of an ancient herbal formulation (Qing-Fe-San) used to treat hemorrhage and epistaxis. Western uses for this formulation are prevention and treatment of EIPH. The dosage is 15 g bid PO drench for 30 days before racing. It can be used up to 45 days in consecutive duration, then alternating months of treatment with non-treatment. Some of the effects of Red Lung™, determined in clinical and pharmacologic research, include vasodilation/lowering blood pressure, bronchodilation, reduction of capillary permeability, diuresis, and increased endurance. It can be used in combination with Red Lung Plus™ and Single Immortal™.

**Red Lung Plus™** (Jing-Tang Herbal Company) is an herbal formulation specifically formulated to reduce EIPH. It is top dressed on the feed at a dose of 15 to 30 mg bid and is given 3 days prior to and 3 days after performance. In horses with severe bleeding, Red Lung Plus™ can be used in combination with Single Immortal™. During periods of heavy performance, the use of Red Lung Plus™ can be alternated with Single Immortal™. After 2 to 3 months of alternating 2 to 3 weeks with Single Immortal™ and 1 month of Red Lung Plus™, horses must be taken off of both herbal formulations.

As stated above, there is a lack of rigorous scientific evaluation of the efficacy of these (or any) herbal remedies to reduce EIPH. Thus there is a

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Figure 2—The FLAIR™ equine nasal strip (CNS, Inc., Minneapolis, MN) placed on a quarter horse.
clear and present need for such research to either refute or support widespread use of herbal remedies.

**Other Treatments**

Other palliative treatments include nitric oxide (however, recent research\(^2\) suggests that nitric oxide inhalation may exacerbate EIPH), hyperbaric oxygen, ipratropium bromide, homeopathy (phosphorus), magnesium sulfate, acupuncture, dimethyl sulfoxide with sodium iodide, nutrition supplements, essential fatty acids, antioxidants, and trace mineral supplements. Horses should be stabled with proper ventilation to minimize dust and airborne particles. Dust should also be minimized in feed, bedding, and the environment.

**References**