A Review of Exercise-induced Pulmonary Hemorrhage and New Concepts for Prevention

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Exercise-induced pulmonary hemorrhage (EIPH) is a major health concern and cause of poor performance in the equine athlete. Significant progress has been made in recent years in our understanding of the pathogenesis of EIPH. The purpose of this paper is to review the causes, mechanisms, prevention, and treatment of EIPH. Author’s address: College of Veterinary Medicine, Kansas State University, Manhattan, Kansas 66506-5602. © 2000 AAEP.

1. Introduction

Exercise-induced pulmonary hemorrhage (EIPH) occurs in Quarter Horses, Standardbreds, and Thoroughbreds worldwide during sprint racing. The problem was first documented at least four centuries ago.1 EIPH is of great concern to the racing industry because of the financial implications resulting from decreased performance, lost training days, necessity for prerace medication, and banning of horses from racing.2 It is an important cause of exercise intolerance and results from strenuous exercise and/or pathophysiological changes in the equine lung.3–5 EIPH is characterized by pulmonary hypertension, edema in the gas exchange region of the lung, rupture of the pulmonary capillaries, intra-alveolar hemorrhage, and the presence of blood in the airways.

2. Diagnosis

EIPH was diagnosed originally by visible epistaxis. It was originally believed to be a serious problem but not widespread because epistaxis occurred only in 0.25 to 13% of all sprinting horses.6–8 As knowledge concerning the pathology and etiology of EIPH advanced, so did the sensitivity of diagnosis. In 1974, Cook6 used a rigid endoscope to identify the lungs as the source of hemorrhage. When endoscopy was used as a diagnostic tool, the incidence of EIPH after racing increased to 26–77% in Standardbreds,9,10 to 62% in Quarter Horses,11 and to 44–75% in Thoroughbreds.7,12–15 The incidence was even higher (82–95%) with repeated endoscopic examination of each individual horse.10,13,14

Tracheal lavage has also been used to detect EIPH by determining the presence of hemosiderophages in the aspirated fluid. However, with this technique, estimating the time course of the hemorrhage is difficult and there is poor correlation between the tracheal wash cytology and histopathology of the lungs.16–18 Furthermore, the cell population in the tracheal fluid differs substantially from fluid obtained from the lower respiratory tract.17,18

To detect the presence of blood in alveoli and small airways, bronchoalveolar lavage (BAL) may be the technique of choice.19,20 This technique provides
an accurate reflection of the cytological population in the terminal airways and alveolar spaces. A good correlation has been found between BAL cytology and histopathology in horses with EIPH. \(^{19,21,22}\) The method provides a more sensitive and accurate assessment of the presence and extent of EIPH than endoscopy or tracheal lavage,\(^ {21,23}\) and has the advantage of possibly identifying more horses that bleed, with greater sensitivity.\(^ {24,25}\) BAL studies suggest that hemorrhage occurs in essentially all horses in racing or training.\(^ {25,26}\) BAL studies correlate well with pulmonary histopathology, clinical disease, and endoscopic evidence of EIPH.\(^ {25}\)

3. Causes and Mechanisms

Numerous causes and pathophysiologic mechanisms have been proposed for EIPH, including small airway disease, upper airway obstruction, exercise-induced hyperviscosity,\(^ {27-29}\) mechanical stresses of respiration and locomotion,\(^ {30,31}\) redistribution of blood flow in the lung,\(^ {32}\) alveolar pressure fluctuations, and pulmonary hypertension. Current evidence suggests that stress failure of the pulmonary capillaries results from pulmonary vascular hyper- tension combined with large negative intrapleural pressures or large changes in pressure which create a high capillary transmural pressure leading to hemorrhage.\(^ {33-36}\) The cause of hypertension may also be related to the enormous cardiac output demanded by the racehorse associated with maximal recruitment and distension of the pulmonary capillaries.\(^ {37}\) Other factors which may limit ventricular function and contribute to elevated left atrial pressure and pulmonary vascular pressures are:

1. The cross-sectional area of the atrioventricular valves may be too small to allow high flow without a large increase in driving pressure
2. The high ventricular pressure associated with exercise may result in regurgitation through the AV valves during ventricular systole
3. The rate of relaxation of the ventricular myocardium may be too slow to allow rapid filling at normal filling pressure when cardiac output and heart rate are high.\(^ {38}\)

4. Furosemide

Horses with EIPH frequently are treated with furosemide,\(^ {39-44}\) which attenuates the exercise-induced increases in right atrial, pulmonary arterial, pulmonary wedge, and pulmonary capillary pressures\(^ {45-50}\) as well as the concentration of red cells in the BAL fluid.\(^ {50}\) The reduction in pulmonary vascular pressures is compatible with a reduction in the stress failure of the pulmonary capillaries, reduced transcapillary filtration, reduced accumulation of lung water during exercise, and reduced EIPH. The hemodynamic effect of furosemide is mediated, in large part, by a reduction in plasma and blood volume.\(^ {51,52}\) The mechanisms responsible for the effects of furosemide and reduced vascular pressures during exercise may also be associated with a redistribution of pulmonary blood flow. In vitro studies have shown that equine pulmonary arteries in the dorsal portion of the lung dilate more in response to methacholine than do vessels located in the ventral portion of the lung.\(^ {53}\) The effect of furosemide on the spatial distribution of pulmonary blood flow has been determined with fluorescent-labeled microspheres in resting and exercising Thoroughbred horses.\(^ {54}\) The primary finding of this study was that pulmonary blood flow redistribution occurred from rest to exercise, both with and without furosemide. However, there was less blood flow to the dorsal portion of the lung during exercise postfurosemide compared with prefurosemide. Recent studies, however, suggest that furosemide is associated with enhanced athletic performance in Thoroughbred horses.\(^ {55,56}\) The association between enhanced athletic performance and furosemide treatment may be attributable to a reduction in body weight, but other mechanisms may play a role, such as the reduction in pulmonary vascular pressures and bronchodilation. Bayly et al.\(^ {57}\) suggested that a positive effect on race performance is at least partly attributable to an increase in mass-specific maximal oxygen consumption but not to improvements in breathing mechanics or gas exchange.

5. Nitric Oxide

Nitric oxide (NO) is a vascular smooth muscle relaxing factor that is produced by the action of NO synthase on L-arginine predominately within vascular endothelial cells. There is little information, however, about the role of NO during exercise in the horse. Inhaled nitric oxide reduces the pulmonary artery pressure in horses during strenuous exercise.\(^ {58,59}\) Nitroglycerin, either intravenous or oral, does not appear to protect the pulmonary vascular bed from exercise-induced hypertension.\(^ {58,60}\) L-arginine analogs, such as L-NAME, competitively inhibit NO formation from L-arginine and have been used to determine the role of NO in blood flow regulation. Mills et al.\(^ {61}\) demonstrated that L-NAME increases pulmonary artery pressure during submaximal exercise. On the other hand, Manohar and Goetz\(^ {62}\) reported that L-NAME infusion did not significantly alter exercising pulmonary vascular pressures in Thoroughbred horses across a range of exercise intensities. To further investigate the role of NO in cardiopulmonary function during exercise, we studied 5 horses on a treadmill at speeds that were equivalent to 50, 80, and 100% of peak pulmonary oxygen uptake.\(^ {64}\) Each horse underwent one control and one L-NAME trial in randomized order. L-NAME reduced exercise tolerance, as well as cardiac output, oxygen delivery, and both pulmo
nary and systemic vascular conductances at peak running speeds. Administration of L-NAME significantly increased EIPH in all 5 horses despite a reduced maximal pulmonary arterial pressure and cardiac output in 4 of the 5 horses. These data demonstrate that the NO synthase inhibitor, L-NAME, impairs hemodynamics during exercise in the horse, suggesting an important role for NO in mediating endothelial function during exercise.

6. The FLAIR® Equine Nasal Strip

During quiet breathing, as well as during exercise, 40–50% of the total pulmonary resistance may result from the nasal passages.65 During inspiration, the extrathoracic airways account for more than 90% of the total resistance. An external nasal dilator strip has been increasingly adopted by human athletes to reduce nasal resistance and to promote easier nasal breathing during exercise.66,67 Horses are obligate nasal breathers; thus nasal resistance is likely of much greater importance than in humans. During exercise, partial collapse of the unsupported nasal passages may occur during inspiration. The FLAIR® nasal strip was introduced recently for horses to prevent or reduce collapse of the nasal passages and to decrease upper airway resistance, particularly nasal resistance and to reduce intrapleural and alveolar pressure swings that may contribute to high pulmonary capillary transmural pressures and EIPH. We evaluated 7 horses on the treadmill under control conditions and wearing an intrapulmonary pressure swing attachments for exercise-induced pulmonary haemorrhage in Quebec Standardbred racehorses. Equine Vet J 1994;26:482–485.

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References


