The Use of Shock Wave Therapy in the Treatment of Exercise Induced Pulmonary Hemorrhage

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Study Objectives

- Evaluate the effect of ESWT of the caudodorsal lung on successive bleeding episodes of barrel racing horses with confirmed EIPH.
- Compare performance of barrel racing horses with EIPH that are treated with ESWT to barrel racing horses that are treated with furosemide.

Clinical Significance of Exercise Induced Pulmonary Hemorrhage

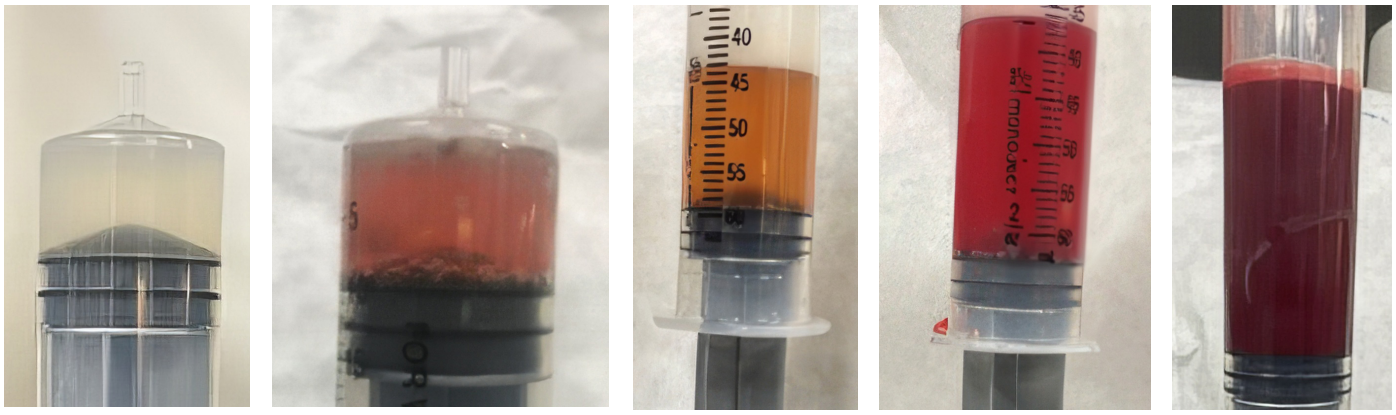
Exercise induced pulmonary hemorrhage (EIPH) is a condition caused by strenuous exercise that is commonly seen in speed event horses of all breeds. Hemorrhage from the pulmonary vasculature into the alveoli and lower airways occurs typically in the caudodorsal lung segments. Clinical signs of EIPH are variable, but can include epistaxis, dyspnea, coughing, and excessive swallowing.[1] The implication of grade 3 and 4 EIPH in causing impaired performance make its prevention and treatment a significant concern of horsemen and veterinarians.[2,3] Currently, the only available therapies shown to have efficacy for the reduction of EIPH are furosemide and nasal strips. Extracorporeal shock wave therapy (ESWT) has been used to treat EIPH in standardbred racehorses with anecdotal reports of success; however, there is no published data available.[4]

Study Design

The study was conducted on barrel racing horses in central Texas in 2022 and 2023. To be considered, the horse must have exhibited epistaxis, or the rider must have had a high suspicion of EIPH during a barrel race within 2 days prior to examination. Screening procedures consisted of physical exam, upper airway endoscopy, thoracic ultrasound, and bronchoalveolar lavage (BAL). Endoscopy was used to screen for gross pathology of the upper respiratory tract. Scores were also assigned for mucous, blood, and tracheal septum thickness. On thoracic ultrasound, the thickness of the pleura was evaluated and given a score of 0-3. BALs were performed using a blind technique. Collected egress fluid was given a 0 to 4 score based on visual grading of the red blood cell concentration. (**Figure 1**.) BAL fluid was also submitted for cytologic examination. To be enrolled in the study, horses must have been free of upper respiratory pathology and have an RBC score of 3 or 4.

ESWT of the caudodorsal lung field was performed bilaterally with the PulseVet electrohydraulic shock wave device. The target area was marked during ultrasound evaluation and the skin prepared with isopropyl alcohol and ultrasound gel. A dose of 750 pulses per side were delivered in a vertical intercostal pattern with the 80mm trode at an energy setting of E8 and a frequency of 480 Hertz. After treatment, horses were prescribed 1 week of light exercise before resuming normal workout routine. Horses then competed in a barrel race 2 – 4 weeks after ESWT treatment. No changes in pre-race medication were allowed, i.e. horses that had not been treated with furosemide prior to inclusion could not treat prior to the second race; horses that were treated with furosemide prior to inclusion must have been treated prior to the second race. Within 2 days after competing, horses were re-examined and BAL was performed.

Figure 1. RBC Scoring System for Bronchoalveolar Lavage Fluid



Grade 0 | Grade 1 | Grade 2 | Grade 3 | Grade 4

A visual scoring system was developed to quantify red blood cell (RBC) content of bronchoalveolar lavage (BAL) samples.

Results

A total of 42 horses were screened with 21 horses meeting the inclusion criteria and completing the study. Of those, 13 exhibited epistaxis in the initial race and 9 competed on furosemide before and during the study. Of the 21 horses enrolled, no animal showed an increased BAL RBC grade after ESWT treatment and on average the BAL score was reduced by 1.5 grades after ESWT treatment (paired t-test, $p < 0.0001$). 16 of 21 horses (76%) improved at least 1 grade on BAL RBC score. 10 of 21 horses (47%) improved at least 2 grades. (**Table 1**.) Horses with a history of epistaxis on prior runs were less likely to improve more than 2 grades, as they comprised 17% of the ≥2 grade improvements and 72% of the 1 or 0 grade improvements.

Table 1. Summary of BAL RBC Grade Changes

RBC Grade Improvement	# of Horses
4 Grades	1
3 Grades	4
2 Grades	5
1 Grade	6
No Improvement	5

Improvement in RBC grade on post-treatment BAL compared to pre-treatment BAL.

Notably, all horses in the study had concurrent equine asthma syndrome as defined by greater than 5% neutrophils, greater than 2% mast cells, or greater than 2% eosinophils on initial BAL cytology. All horses had a neutrophilia ranging from 7% to 38% with a mean of 20%. Four horses had concurrent mastocytosis and two had concurrent eosinophilia.

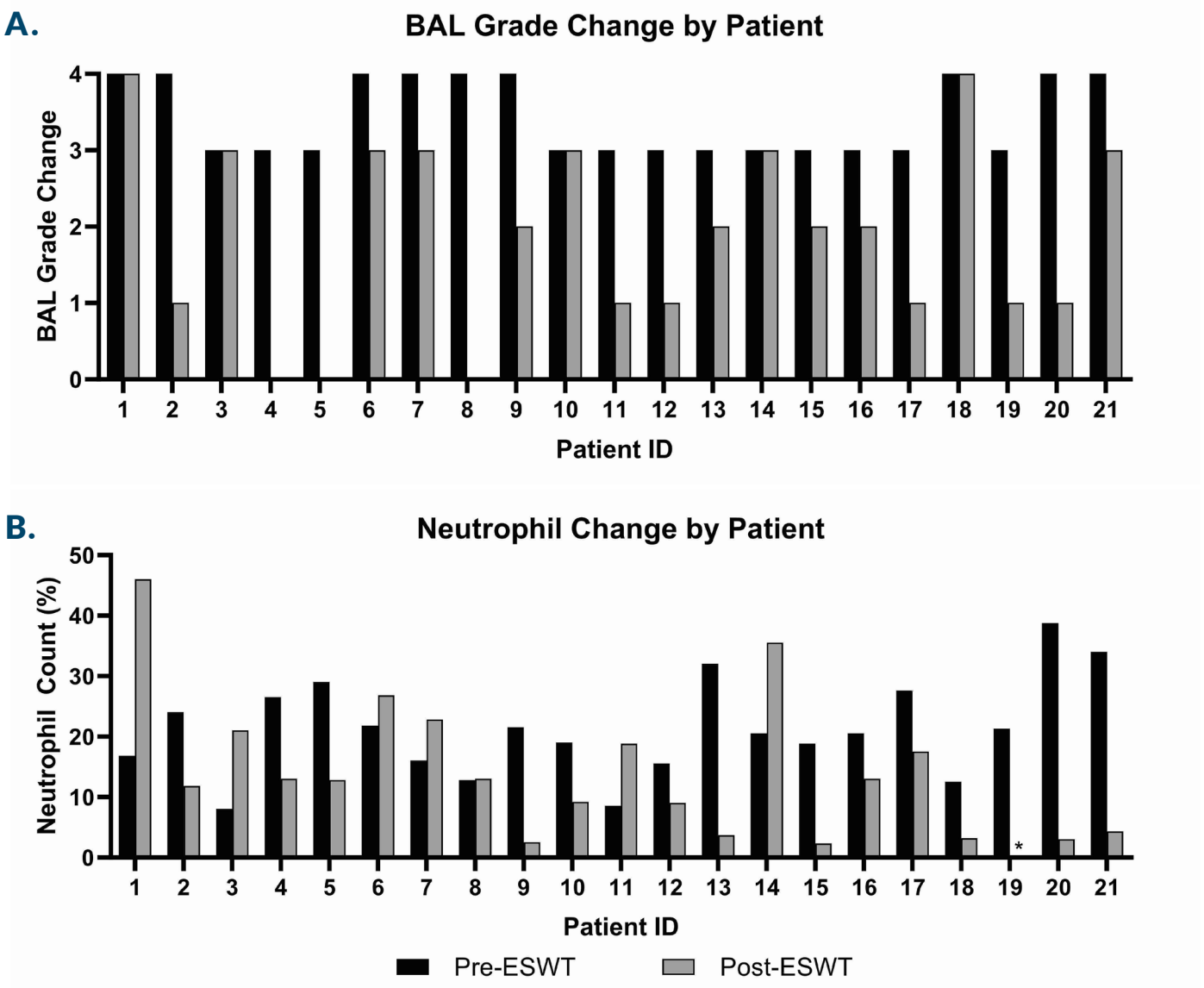
Thirteen of 20 horses (65%) improved at least 6% on neutrophil count (the post-treatment BAL on patient 19 was unreadable). All but 2 horses that improved at least 2 grades (80%) improved at least 6% on neutrophils and overall, there was a positive correlation between BAL grade change and neutrophil change ($r = 0.45$, $p < 0.05$). One of the two horses had identical pre- and post-treatment neutrophil counts, but improved 4 grades on the BAL blood score. Of the 11 horses that either did not improve or only improved one grade on the BAL blood score, 5 (45%) increased and 6 (55%) decreased in neutrophil percentage on BAL. (**Figure 2**.)

Discussion

Historically, ESWT of the lungs has been contraindicated due to concern about the effect of shock wave energy on lung tissue. An unpublished study conducted at the University of Cordoba examined the effects of pulmonary ESWT on two horses slated for euthanasia for unrelated reasons. ESWT was performed at two sites with a stationary trode, delivering 1,000 and 3,000 pulses per site at the highest energy setting with the 80mm trode. At necropsy, no gross lung lesions were noted in either animal. On histopathology, mild hyperemia of the pleural surface was noted and was judged by the pathologist to be clinically insignificant.[5] Additionally, there have been no adverse events associated with shock wave treatment of the lungs in over 80 treatments performed by the investigator.

In the present study, 76% of horses with EIPH improved at least 1 grade on BAL RBC score after pulmonary ESWT. 46% of horses improved at least 2 grades. Studies evaluating the efficacy of furosemide in treating or preventing EIPH have shown similar results. Two studies comparing furosemide-treated horses to saline-treated controls revealed a reduction in EIPH score of 64% and 67.5%.[6,7]

Figure 2. BAL Grade and Neutrophil Count Change by Patient



BAL grade (A) and neutrophil count (B) were measured within 2 days of competing for 21 patients before ESWT treatment and 2-4 weeks after ESWT treatment. *The post-ESWT neutrophil count for patient 19 was unreadable and therefore not reported.

The degree of equine asthma affection in this study population was an unexpected finding. Given the strong correlation between improvement in BAL RBC scores and a decrease in BAL neutrophil counts, it is possible that the improvement in EIPH is a result of decreasing airway inflammation.

The mechanism of action whereby ESWT exerts its effect on lung tissue is currently unknown. We postulate that ESWT of the lungs affects local gene expression of cytokines and chemokines that downregulate immune pathways contributing to equine asthma syndrome and recruitment of neutrophils to the airway. Three studies have demonstrated the role of shock wave therapy in upregulation and down regulation of proteins that are critical in the immune pathways that govern equine asthma syndrome:

- IL-1ß and IL-6 were significantly down-regulated while TNF-∂, IL-1RA and TLR2 were significantly up-regulated[8]
- Shock wave therapy can downregulate IL-17A and IL-1B[9]
- Shock wave therapy produced a significant increase in IL-10 and reduction in IL-1ß production[10]

IL-1 and IL-6 are two of the cytokines that upregulate the Th-17 immune pathway. Th-17 lymph nodes then upregulate IL-17, among others, to recruit neutrophils to the airway. All 3 of these cytokines have been shown to downregulate with shock wave therapy. IL1ra and IL-10 are anti-inflammatory cytokines that also downregulate IL-17.

Summary

Shock wave therapy is a safe and effective modality that can be used for treatment of EIPH in barrel horses as part of a comprehensive approach that may include furosemide and/or asthma therapies. The larger finding of this study is the correlation of shock wave therapy with improvement of asthma. This has much broader application than the treatment of EIPH, as all horses of all breeds and disciplines can suffer from equine asthma syndrome, while EIPH is limited to horses competing at high exertion and speed. There may be non-asthma associated mechanisms at play contributing to improvement in EIPH scores that were not elucidated in this study due to the cohort of horses and the region of the country. Similar studies in racehorses would need to be performed to make this determination.communication and patient treatment.

References

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