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NEW APPROACHES AND TRENDS ON IAD THERAPY NOUVEAUTÉS ET PERSPECTIVES POUR LE TRAITEMENT DE L'IAD

Laurent Couëtil, DVM, PhD, Dip. ACVIM(LA), Purdue University School of Veterinary Medicine, Department of Veterinary Clinical Sciences, West Lafayette, Indiana, 47907 USA.

Résumé:

Il y a de nombreuses similitudes entre l'asthme de l'homme et la pousse ainsi que la maladie inflammatoire des petites voies respiratoires du cheval. Puisque des suppléments alimentaires riches en acides gras omega-3 ont prouvé être bénéfiques chez les asthmatiques, il est possible que ces suppléments améliorent les signes cliniques chez les chevaux atteints de pousse ou de maladie inflammatoire des petites voies respiratoires. Les résultats préliminaires d'un essai clinique contrôlé sur la supplémentation en acides gras omega-3 montre un effet bénéfique sur les signes cliniques de chevaux souffrant de pousse ou de maladie inflammatoire des petites voies respiratoires.

Mots-clefs : acides gras omega-3 ; supplémentation ; inflammation chronique ; antioxydant

Summary:

Equine recurrent airway obstruction (RAO) and inflammatory airway disease (IAD) present many similarities with asthma in people. Based on experiences in human asthma, feed supplements containing omega – 3 fatty acids have been proposed to improve clinical signs in horses with chronic inflammatory airway disease such as RAO and IAD. Preliminary results from a controlled trial suggest that feed supplementation with omega – 3 fatty acids improves clinical signs of chronic inflammatory airway in horses.

Keywords: omega-3 fatty acids; supplementation; chronic airway inflammation; antioxidant

Chronic airway inflammation, mediated by the overexpression of a large number of inflammatory genes, pro-inflammatory cytokines, chemokines and adhesion factors, is the key feature of recurrent airway obstruction [1]. Reactive oxygen species (ROS) released by inflammatory cells have been shown to play a role in the pathogenesis of inflammatory airway diseases. The end products of this process, such as lipid hydroperoxides, phospholipids, aldehydes and isoprostanes promote lung inflammation. Markers of oxidative stress including glutathione (GSH), glutathione disulphide (GSSG) and 8-Epi-PGF_{2α} have been shown to be increased in the BALF of RAO-affected horses during an acute crisis. Studies have described the antioxidant status of RAO-affected horses in clinical remission when compared to healthy controls [1], and the role of antioxidant supplementation on pulmonary performance and systemic anti-oxidant status of RAO affected horses [2]. Based on this information, measurements of markers of oxidative stress along with levels of anti-oxidant substances (ascorbic acid and α tocopherol) in the peripheral blood can provide adequate assessment of the magnitude of lipid peroxidation associated with the ongoing inflammation in the lungs.

Omega-3 polyunsaturated fatty acids in the management of respiratory inflammatory conditions

Increased consumption of omega-3 polyunsaturated fatty acids (PUFAs), such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) results in greater integration of these fatty acids into the inflammatory cell phospholipids. The role of omega-3 PUFAs in inflammatory conditions is multifactorial. The incorporation of EPA and DHA occurs in a dose dependent fashion at the expense of arachidonic acid, and as a result, less substrate is available for the synthesis of eicosanoids during an inflammatory process. Another role of omega-3 PUFAs has been recently described, with the discovery of resolvins. These mediators are derived from EPA (E-series resolvins) and DHA (D-series resolvins), and have been shown to have direct anti-inflammatory properties. Additional roles of omega-3 PUFAs in inflammation include decreasing activation of NF κ B, and as a result, decreased generation of inflammatory cytokines (TNF- α , IL-1 β , IL-6, IL-8) and expression of adhesion molecules.

Multiple clinical studies have been undertaken to investigate the efficacy of omega-3 PUFAs in chronic pulmonary inflammatory conditions in people with variable results. Based on these current studies, it appears that the doses as well as the length of supplementation play an important role in the overall efficacy of omega-3 PUFAs in the management of chronic lower airway conditions in people.

There are only a limited number of trials published in the veterinary literature evaluating the effects of supplementation with omega-3 PUFAs in animals. Efficacy has been shown in the management of canine atopic dermatitis, where dogs were supplemented with different preparations of omega-3 PUFAs for 10 weeks, and then clinical scores were compared to the placebo group. An experimental trial assessing the effects of omega-3 PUFA administration for 4 weeks on airway hyperresponsiveness and inflammation in cats with experimentally-induced asthma revealed successful integration of polyunsaturated fatty acids in erythrocyte cell membranes and some beneficial effects on airway responsiveness through a leukotriene A₂ dependent pathway [4]. The most challenging aspect of omega-3 PUFA supplementation in horses is finding the effective dose that is yet financially feasible. In a recent study, evaluating immune function of healthy yearling horses after omega-3 PUFA supplementation, the investigators found a dose of 6g/100 kg to effectively alter the composition of plasma and red blood cell phospholipids after a 35-day supplementation period [5]. This study however did not evaluate lower doses. A randomized, cross-over trial was reported on horses diagnosed with RAO and supplemented with sunflower oil (rich in linolenic acid) or seal blubber oil (rich in omega-3 PUFAs) [3]. A 10-week supplementation period revealed successful integration of omega-3 PUFAs into leukocyte membranes and a decrease in overall leukocyte count in the BALF, but no effects on clinical score or pulmonary function. While this study used a high dose of daily supplementation (65g/day), some flaws in the experimental design make the pulmonary function results questionable [3].

Preliminary findings from a clinical trial:

Horses affected with chronic lower airway inflammatory diseases need long term (IAD) or even lifelong (RAO) management that can require significant commitment (both time and financial) from owners. Ideal strict environmental management achieves maintenance of clinical remission in the majority of horses. **Based on limited evidence in the human and veterinary literature, omega-3 fatty acid containing feed supplement may be beneficial in improving clinical signs in horses affected by chronic lower airway inflammatory diseases (RAO and IAD).**

The purpose of the study was to evaluate the clinical efficacy of an equine omega-3 fatty acid containing feed supplement in improving the clinical signs in horses affected by chronic lower airway disease. We hypothesized that daily administration of the supplement to horses with chronic lower airway disease along with low-dust diet for 8 weeks would result in greater improvement in clinical score, BALF variables and pulmonary function when compared to horses fed a placebo and low-dust diet.

The goal is to recruit 34 horses for the study. So far, 20 horses have qualified for the study and 11 have been tested at baseline and after an 8-week supplementation period (placebo, n=3; 1x dose, n=3; 2x dose, n=5). Initial data analysis indicate that clinical score of horses fed the omega-3 fatty acid containing supplement was significantly improved compared to placebo treated horses.

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